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# II Guidelines for Perioperative Evaluation of the Brazilian Society of Cardiology

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## **NORMATIVES AND GUIDELINES COORDINATOR**

Iran Castro

---

## **WRITING COMMITTEE**

Danielle Menosi Gualandro

Pai Ching Yu

Daniela Calderaro

Bruno Caramelli

---

## **TASK FORCE MEMBERS**

Alina Coutinho Rodrigues Feitosa, André Coelho Marques, Bruno Caramelli, Beatriz Ayub, Carisi A. Polanczyk, Carlos Jardim, Carolina L. Zilli Vieira, Claudio Pinho, Daniela Calderaro, Danielle Menosi Gualandro, Denise Iezzi, Dimas T. Ikeoka, Dirk Schreen, Elbio Antonio D'Amico, Elcio Pfeferman, Emerson Quintino de Lima, Emmanuel de A. Burdmann, Enrique Pachon, Fabio Santana Machado, Filomena Regina Barbosa Gomes Galas, Flávio Jota de Paula, Francine Corrêa de Carvalho, Gilson Soares Feitosa-Filho, Gustavo Faibischew Prado, Heno F. Lopes, José Jaime Galvão de Lima, Julio Flavio Meirelles Marchini, Luciana S. Fornari, Luciano F. Drager, Luciano Janussi Vacanti, Ludhmila Abrahão Hajjar, Luis Eduardo P. Rohde, Luís Henrique Gowdak, Luiz Francisco Cardoso, Marcelo Luiz Campos Vieira, Maristela C. Monachini, Milena Macatrão, Pai Ching Yu, Paula Ribeiro Villaça, Pedro Silvio Farsky, Renato Delascio Lopes, Renato Scotti Bagnatori, Roberto Henrique Heinisch, Sandra F. Menosi Gualandro, Tarso Augusto Duenhas Accorsi, Walkiria Samuel Ávila, Wilson Mathias Jr.

**This guideline should be cited as: Gualandro DM, Yu PC, Calderaro D, Marques AC, Pinho C, Caramelli B et al. II Guidelines for Perioperative Evaluation of the Brazilian Society of Cardiology. Arq Bras Cardiol 2011; 96(3 suppl.1): 1-68.**

**Mailing Address:**

Bruno Caramelli

Instituto do Coração do Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo

Av. Dr. Eneas de Carvalho Aguiar, 44 - andar AB - bloco 2 - setor C6

05403-000 - São Paulo - SP

E-mail: bcaramel@usp.br

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If, in the last 3 years, the Guideline author/collaborator:

Physicians name	Participated in clinical and/or experimental studies subsidized by the pharmaceutical or equipment industry related to the guideline in question	Was a lecturer in events or activities supported by the industry related to the guideline in question	Was (is) a member of the Board of Advisors of the pharmaceutical or equipment industry	Participated in Normative Committees of scientific studies sponsored by the industry	Received personal or institutional grants from the industry	Was the author of scientific texts in journals sponsored by the industry	Owens stock in the industry
In case of positive answer, the name of the company (ies) should be mentioned.							
Danielle M Gualandro	No	No	No	No	No	No	No
Pai Ching Yu	No	No	No	No	No	No	No
Daniela Calderaro	No	No	No	No	No	No	No
André C Marques	No	No	No	No	No	No	No
Claudio Pinho	No	No	No	No	No	No	No
Bruno Caramelli	No	Boehringer-Ingelheim	No	No	No	Boehringer-Ingelheim	No
Alina Coutinho Rodrigues Feitosa	No	No	No	No	No	No	No
Beatriz Ayub	No	No	No	No	No	No	No
Carisi A Polanczyk	No	No	No	No	No	No	No
Carlos Jardim	No	No	No	No	No	No	No
Carolina L Zilli Vieira	No	No	No	No	No	No	No
Denise Iezzi	No	No	No	No	No	No	No
Dimas T Ikeoka	No	No	No	No	No	No	No
Dirk Schreen	No	No	No	No	No	No	No
Elbio Antonio D'Amico	No	No	No	No	No	No	No
Emerson Quintino de Lima	No	No	No	No	No	No	No
Emmanuel de A Burdman	No	No	No	No	No	No	No
Enrique Pachon	No	No	No	No	No	No	No
Fabio Santana Machado	No	No	No	No	No	No	No
Filomena Regina Barbosa Gomes Galas	No	No	No	No	No	No	No
Flávio Jota de Paula	No	No	No	No	No	No	No
Francine Corrêa de Carvalho	No	No	No	No	No	No	No
Gilson Soares Feitosa-Filho	No	No	No	No	No	No	No
Gustavo Faibischew Prado	No	No	No	No	No	No	No
Heno F Lopes	No	No	No	No	No	No	No
José Jaime Galvão de Lima	No	No	No	No	No	No	No
Julio Flavio Meirelles Marchini	No	No	No	No	No	No	No
Luciana S Fornari	No	No	No	No	No	No	No
Luciano F Drager	No	No	No	No	No	No	No
Luciano Janussi Vacanti	No	No	No	No	No	No	No
Ludhmila Abrahão Hajjar	No	No	No	No	No	No	No
Luis Eduardo P Rohde	No	No	No	No	No	No	No
Luis Henrique Gowdak	Astra-Zeneca	Boehringer, Servier	No	No	Boehringer, Servier, Novartis	Boehringer	No
Marcelo Luiz Campos Vieira	No	No	No	No	No	No	No
Maristela C Monachini	No	No	No	No	No	No	No
Milena Macatrão	No	No	No	No	No	No	No
Paula Ribeiro Villaçã	No	No	No	No	No	No	No
Pedro Silvio Farsky	No	No	No	No	No	No	No
Renato Delascio Lopes	No	No	No	Bristol-Myers Squibb	Research Grant from Bristol-Myers Squibb	No	No
Renato Scotti Bagnatori	No	No	No	No	No	No	No
Roberto Henrique Heinisch	No	No	No	No	No	No	No
Sandra F Menosi Gualandro	No	No	No	No	No	No	No
Tarso Augusto Duenhas Accorsi	No	No	No	No	No	No	No
Walkiria Samuel Ávila	No	No	No	No	No	No	No
Wilson Mathias Jr	No	No	No	No	No	No	No



### 1. Definition of the Problem

#### 1.1. Purpose of these Guidelines

When the first version of these guidelines was finished at the end of 2007, the task force members had already thought on topics and issues that should be modified because of new evidence. They even discussed the validity of publishing an opinion based on evidence that might not be the most recent since new data had been presented at a recent conference. However, production of scientific knowledge in medicine is continuous, and, to develop guidelines, it is necessary to establish artificial pauses for a critical reflection on the available evidence. The choice of when to stop adding new evidence is arbitrary and can be criticized. The time required to propose a revision of the previous guidelines seems to be less controversial. The most appropriate decision is to wait until there is enough evidence to generate the motivation for the new guidelines. The identification of this moment is also subjective. For the task force members of the present guidelines the decision came from the stimulus of the population for which the guidelines are addressed: there was a rapid and progressive increase in the demand for interpretation and analysis of studies in the perioperative period during medical conferences. This is not surprising because perioperative medicine includes more than 240 million surgeries per year worldwide. This figure, which has already surpassed the number of births, is equivalent to 3.5% of the world population and has raised concern among health authorities because of the alarming increase in the costs related to surgical procedures and their complications. The recent publication by the World Health Organization of a sequence of mandatory controls (checklist) before starting the surgery proved to be effective in reducing the rate of complications. These measures, because of their administrative nature, are beyond the goals of the present Guidelines. On the other hand, considering the pathophysiology of complications, pharmacoprotection involving statins and beta-blockers, the growing population of surgical patients using potent antiplatelet agents, glycemic control, and endocarditis prevention are some of the concepts that have undergone significant changes in recent months.

Many of the basic goals of the 2007 Guidelines remain valid in the present document:

- Refine and unify the terminology used by the entire multidisciplinary team, including the patients and their family;
- Establish new routines, change indication for surgery according to the information obtained during the perioperative evaluation;
- Inform the patient and the team on the possible risks related to the intervention. Based on these data, personal experience, knowledge of the other side of the story, the underlying disease, its risks and the risk attributable to the surgery itself, the surgeon can decide with the patient and their family if the risk/benefit ratio suggests the intervention;
- Data or scientific evidence are not always available to allow all the different situations to be analyzed. As customary in medical practice, minute analysis of the patient and problem and the common sense of the team must prevail;

- The surgical intervention does not finish when the patient is bandaged or leaves the operating room. The concept of the word perioperative includes the need for a postoperative surveillance whose intensity is determined by the individual level of risk of the patient.

#### 1.2. Methodology and Evidence

There is currently a lively discussion in the literature about who should be the authors of a medical Guideline: methodologists and experienced clinicians, with clinical researchers being responsible for generating and building the evidence. A more complex definition is that of the first group ideally including individuals holding a graduate degree, having advanced training in clinical epidemiology and broad experience with interpretation and generation of new knowledge based on clinical research. Those who defend the methodologists do not exclude the participation of the other two groups, but emphasize the requirement that the degree of recommendation must be defined by them because they would be less exposed to conflicts of interest or biases. The arguments from the other side include the fact that the lack of experience may be a potential generator of meaningless recommendations or recommendations incompatible with the medical practice and appreciation of systematic revisions that grouped together very different clinical situations and, therefore, clinically (methodologically) inadequate<sup>1</sup>. The choice of one or another writing strategy also depends on the topic of the Guideline. The lack of evidence means that experienced clinicians are essential while methodologists are crucial for the organization, interpretation, and analysis of the guidelines. The middle ground and balanced distribution seemed the most appropriate to the present Guidelines. Thus the concept that guided the first version prevailed; and the participants of these guidelines were chosen among health sciences specialists with hands on and academic experience. The basics of perioperative evaluation and the current recommendations were established in order to decrease perioperative complications. The methodology and the evidence levels adopted were the following:

#### Degree/Class of Recommendation - reflecting the size of treatment effect

**Degree of Recommendation I** - Benefit >>> Risk; the treatment/procedure must be indicated/administered;

**Degree of Recommendation IIa** - Benefit >> Risk; the choice for the treatment/procedure may help the patient;

**Degree of Recommendation IIb** - Benefit > Risk; is not defined if the treatment/procedure can help the patient;

**Degree of Recommendation III** - Risk > Benefit; the treatment/procedure must not be performed since it does not help and may be harmful for the patient.

#### Levels of Evidence

**A.** Evidence in several populations from multiple randomized clinical trials or meta-analyses;

**B.** Evidence in a limited group of populations from single randomized clinical trial or non-randomized clinical studies;



C. Evidence in very limited group of populations from consensus and experts' opinions, case reports and series.

The final message of the presentation of the previous Guidelines remain totally compatible with this revision:

*"Unfortunately, we have not yet eliminated the stress caused by surgery or all its consequences, but the reader will notice that there is much that can be done for the surgery to run smoothly and have a successful outcome without hurting scientific truth."*

## 2. General Assessment

### 2.1. History

Collection of clinical history is the first step of perioperative evaluation. The interview conducted with the patient or family members can collect data on the clinical conditions that determine the estimated surgical risk. The algorithms for perioperative risk assessment use data obtained through history and physical examination. The study of medical records in medical charts and anesthetic records is useful to retrieve previous data.

Information obtained through the patient's history to guide the evaluation of surgical risk should include:

- Investigation of the underlying disease indicating the need of surgical procedure;
- Clinical, demographic, and cultural data, such as age, gender, blood type, hepatitis C virus positive serology, transfusion acceptance;
- Minute investigation of the past surgical or anesthetic history that can show potentially preventable complications and allergies or the existence of comorbidities;
- Investigation of the clinical condition of the patient and the need to compensate for coexisting diseases;
- Identification of severe heart diseases, such as advanced heart failure, coronary artery disease, and symptomatic arrhythmias and/or with hemodynamic consequences;
- Determination of functional capacity, asking about their daily activities;
- Investigation of risk factors for heart disease;
- Record the presence of pacemaker or implantable cardioverter defibrillator;
- Diagnosis of peripheral vascular disease, renal failure, cerebrovascular disease, diabetes mellitus, liver disease, bleeding disorders, thyroid diseases, and chronic lung disease.
- Use of medications, drugs, herbal drugs, alcohol, illicit drugs, and evaluation of potential impact on the surgery;
- The surgeon's opinion about the urgency, risk of the procedure, site of the procedure, availability of Intensive Care Unit, staff and equipment technical support, type of anesthesia, surgical time, need for transfusion, committee of hospital infection control;
- Doubts of the patient and their family regarding the procedure and its risks. Awareness and agreement regarding

the risk and benefits of procedures. Awareness that the surgical risk is not limited to intraoperative period and occasionally there will be need for late follow-up. Awareness that complications are not limited to the cardiovascular system;

- Data obtained in the clinical evaluation must be dated and recorded in appropriate documents. Day and time of receipt of visit request and delivery of written evaluation should be recorded. A system aimed at speeding up the response to requests for medical reports in the institution. Information should be available in a legible and explicit manner. Relevant information should be underlined. The medical report may not be completed in the first evaluation visit. Make sure that the medical report was submitted and, if necessary, make personal contact with or use any means of communication to talk to the surgeon or anesthesiologist.

### 2.2. Physical Examination

Physical examination is useful during the perioperative risk assessment process and it should not be limited to the cardiovascular system. The objectives are: to identify preexisting or potential heart disease (risk factors), define the severity and stability of the heart disease and identify comorbidities.

Patients with heart disease whose general condition is compromised by other conditions such as neurological diseases, renal failure, infections, liver abnormalities, malnourishment or pulmonary dysfunction are at higher risk of cardiac complications since these conditions exacerbate surgical stress<sup>2</sup>.

The incidence of ischemic heart disease in patients with peripheral arterial disease is high and it is a predictive factor for perioperative complications. Information obtained upon physical examination, such as changes in pulse rate or carotid bruit, should be investigated. On the other hand, jugular vein distension signaling high central venous pressure (CVP) indicates that the patient may develop pulmonary edema after surgery<sup>3,4</sup>. Finding the third heart sound (S3) during perioperative evaluation indicates a bad prognosis with increased risk of pulmonary edema, myocardial infarction, or cardiac death<sup>5</sup>. (Table 1)

**Table 1 - Physical examination and risk of perioperative complications**

Sign	Sensitivity (%)	Specificity (%)	LR+
S3 predictive of pulmonary edema	17	99	14.6
S3 predictive of AMI or cardiac death	11	99	8.0
High CVP predictive of pulmonary edema	19	98	11.3
High CVP predictive of AMI or cardiac death	17	98	9.4

Source: modified from McGee, 2001<sup>6</sup>. B3 - third heart sound; AMI - acute myocardial infarction; CVP - central venous pressure; LR+ - Likelihood ratio for a positive result: the values indicate the extent to which a diagnostic test will increase the pre-test probability of a target condition, allowing one to estimate that the likelihood of something occurring is high (values greater than 10), moderate (values greater than 5 and lower than 10), low (values ranging from 2 to 5), and insignificant (values ranging from 1 to 2)<sup>6</sup>.

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The presence of bilateral lower limb edema must be analyzed together with the presence of jugular vein distension. If the amplitude of the pulse wave of the internal jugular vein reveals high CVP, then heart disease and pulmonary hypertension are at least partially responsible for the patient's edema. If CVP is not high, then the edema is probably caused by something else such as liver disease, nephrotic syndrome, chronic venous insufficiency, or some medication. The presence of edema and unknown CVP is not a definite sign of heart disease<sup>7</sup>. If heart murmurs are present, the physician should be able to distinguish organic from functional murmurs, determine if they are significant or not and determine their origin. The origin will indicate if endocarditis prophylaxis or assessment of valvular lesion severity is necessary.

### 2.3. Additional Tests

The request for laboratory tests, electrocardiogram (ECG) and radiography (X-ray) of the chest in the preoperative evaluation of patients scheduled for surgical procedures is a common and routine clinical practice. This practice has been adopted since the 1960s and was recommended for all surgical patients regardless of age, type of procedure, and surgical size, even in asymptomatic healthy patients. However, this practice is associated with a high economic cost for the health system. From the 1990s, after reviews conducted by various medical associations<sup>8-10</sup> on this issue, the rational use of diagnostic tests has been advocated to reduce costs, since there is no evidence that routine tests performed prior the surgery are related to reduction or are predictive of perioperative complications.

There are only two randomized clinical studies in the literature comparing the effect of performance or not of routine preoperative tests on the occurrence of events and postoperative complications<sup>11,12</sup>. In both studies, the population consisted mostly of patients at low clinical risk, with no severe diseases or uncontrolled clinical conditions, and who underwent minor surgery such as cataract corrections and outpatient procedures. Patients were randomized to the proposed surgery with or without preoperative tests (ECG, chest X-ray, blood count, urea, creatinine, electrolytes, and glucose). There was no difference in the perioperative morbidity and mortality rates between patients who underwent preoperative assessment with additional tests and those without additional tests. Therefore, for low-risk procedures in patients at low clinical risk, the surgery could be performed without preoperative tests.

For other types of surgical procedures and other patient risk profiles, there is no indication for routine preoperative tests in asymptomatic patients. Abnormal findings obtained in routine tests are relatively frequent, but hardly these results lead to modifications of surgical techniques or even surgery cancellation. In addition, abnormal results in preoperative tests are not predictors of perioperative complications.

The indication for preoperative tests should be individualized according to the patients' comorbidities and diseases, as well as the type and size of the proposed surgery.

#### 2.3.1. Electrocardiogram (ECG)

The ECG analysis may complement cardiac evaluation and allow the identification of patients at high cardiac risk during

surgery. The ECG can detect arrhythmias, conduction defects, myocardial ischemia or previous acute myocardial infarction (AMI), overloaded chambers, and problems caused by electrolyte disturbances or medication effects. It is also important to have a baseline ECG to assess changes that occur during the perioperative period in patients at high risk for cardiovascular events.

On the other hand, routinely using a test with a limited specificity may lead to false-positive results in asymptomatic patients, since electrocardiographic changes usually worry the surgical and anesthesia team and often may prompt the unnecessary cancellation of the surgery<sup>13</sup>. The abnormalities found on ECG tend to increase with age, and presence of comorbidities associated with these ECG changes usually have low predictive power of perioperative complications<sup>14,15</sup>. In a retrospective study including more than 23,000 patients, the presence of preoperative ECG changes was associated with higher incidence of deaths from cardiac causes within 30 days<sup>16</sup>. However, in the group of patients at low or moderate risk, preoperative ECG showed limited prognostic information.

Thus, the indication for preoperative ECG should be based on the patient's medical history and diseases<sup>8,10,17</sup>.

Recommendations for requesting an ECG:

#### Degree of Recommendation I, Level of Evidence C

- Patients with a history and/or abnormalities on physical examination suggestive of cardiovascular disease;
- Patients with a recent episode of ischemic chest pain or considered to be at high risk after algorithmic assessment or according to the assistant physician;
- Patients with diabetes mellitus.

#### Degree of Recommendation IIa, Level of Evidence C

- Obese patients;
- All patients older than 40 years.

#### Degree of Recommendation III, Level of Evidence C

- Routinely request an ECG for asymptomatic individuals who will be submitted to low-risk surgeries.

#### 2.3.2. Chest X-ray

The studies that evaluated the routine use of chest radiography (X-ray) in the preoperative evaluation showed that the test result rarely interferes with the management of the anesthetic technique and is not a predictor of perioperative complications. The abnormalities found on the X-ray are usually related to chronic diseases, including COPD and/or cardiomegalies and are more frequent in male patients, aged > 60 years, with higher cardiac risk, and more associated comorbidities<sup>18</sup>. The indication of preoperative chest x-ray should be based on careful baseline evaluation according to the patients' clinical history and physical examination. There is no indication for routine chest X-rays in asymptomatic patients as part of the preoperative evaluation<sup>8,10,17</sup>.

Recommendations for requesting a chest X-ray:

#### Degree of Recommendation I, Level of Evidence C

- Patients with a history or diagnostic tests suggestive of cardiorespiratory diseases.

**Degree of Recommendation IIa, Level of Evidence C**

- Patients older than 40 years;
- Medium to major surgeries, mainly intra-thoracic and intra-abdominal surgeries.

**Degree of Recommendation III, Level of Evidence C**

- Routine in asymptomatic individuals.

**2.3.3. Recommendations for requesting laboratory tests<sup>8,10,17</sup>**

**A. Full blood count**

**Degree of Recommendation I, Level of Evidence C**

- History of anemia or other hematologic diseases or liver diseases;
- When anemia is suspected during physical examination or when chronic diseases associated with anemia are present;
- Moderate/high-risk surgeries if a need for transfusion is anticipated.

**Degree of Recommendation IIa, Level of Evidence C**

- All patients older than 40 years.

**Degree of Recommendation III, Level of Evidence C**

- Routine in asymptomatic individuals.

**B. Hemostasis/coagulation tests**

**Degree of Recommendation I, Level of Evidence C**

- Patients on anticoagulation therapy;
- Patients with liver failure;
- Patients with coagulation disorders (history of bleeding);
- Patients who will be submitted to intermediate or high-risk surgeries.

**Degree of Recommendation III, Level of Evidence C**

- Routine in asymptomatic individuals.

**C. Determination of serum creatinine**

**Degree of Recommendation I, Level of Evidence C**

- Patients with kidney disease, diabetes mellitus, hypertension, liver failure, heart failure and whose serum creatinine has not been determined in the last 12 months;
- Patients who will be submitted to intermediate or high-risk surgeries.

**Degree of Recommendation IIa, Level of Evidence C**

- All patients older than 40 years.

**Degree of Recommendation III, Level of Evidence C**

- Routine in asymptomatic individuals.

**2.4. Perioperative Evaluation Algorithms**

Algorithms are suggested to facilitate the process of perioperative evaluation. An algorithm is a set of well defined and ordered rules and guidelines aimed at solving a problem or a class of problems in a finite number of steps.

The suggested steps in the algorithm include the preoperative evaluation period. This period is called perioperative because it encompasses period of time related to the preoperative, intraoperative, and postoperative period

(up to 30 days). Risk assessment, strategies to reduce risks, and diagnosis and treatment of complications are included among the interests of the guideline. The sequence of steps related to the construction of the algorithm is shown next<sup>19</sup>:

**2.4.1. Steps of Perioperative Evaluation**

**Step I.** Check the patient's clinical condition.

The risk variables associated with cardiac complications, such as data obtained from the patient's history, physical examination, and diagnostic tests, are identified during this stage. Risk factors independently associated with cardiac events in the perioperative period may vary<sup>20,21</sup>.

**Step II.** Assess the functional capacity.

Based on the clinical history, it is possible to have information about the patient's functional capacity. Limitations in terms of fast walking, climbing stairs, performing household chores, practicing regular exercises are investigated. The probability of poor postoperative outcome is higher in patients with low functional capacity<sup>21-23</sup>.

**Step III.** Establish the intrinsic risk associated with the type of surgery.

The non-cardiac procedures can be classified as high, intermediate or low risk according to the likelihood of developing cardiac events (death or nonfatal myocardial infarction) in the perioperative period<sup>21</sup>. (Table 2).

**Step IV.** Decide on the need for further evaluation tests.

**Step V.** Adjust treatment.

Evaluate the therapy being employed, correcting the dosage and the classes of cardiovascular drugs that being used, adding new medication and guiding the perioperative management of the medications used (which should be kept and which should be discontinued). Assess the need for invasive procedures, angioplasty, or cardiac surgery.

**Step VI.** Perform perioperative follow-up.

**Table 2 - Stratification of cardiac risk for noncardiac procedures**

<b>High (Cardiac risk ≥ 5%)</b>	Vascular surgeries (aortic and other major vascular surgery, peripheral vascular surgery) Urgent or emergency surgeries
<b>Intermediate (Cardiac risk ≥ 1,0% and &lt; 5,0%)</b>	Carotid endarterectomy and endovascular repair of abdominal aortic aneurysm Head and neck surgery Intraperitoneal and intrathoracic surgeries Orthopedic surgeries Prostatic surgeries
<b>Low (Cardiac risk &lt; 1,0%)</b>	Endoscopic procedures Superficial surgeries Cataract surgery Breast surgery Outpatient surgery

Source: Adapted from Fleisher et al., 2007<sup>21</sup>.

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The assessment is not limited to the preoperative period. Consider the need for electrocardiographic monitoring and laboratory measurements of myocardial injury markers, correction of electrolyte disturbances, identification and treatment of anemia, infection, or respiratory failure. Consider prophylaxis for deep venous thrombosis and pulmonary embolism.

### Step VII. Plan long-term therapy.

This is an opportunity to identify and educate patients on cardiovascular risk factors: smoking, hypercholesterolemia, diabetes mellitus, hypertension, sedentary lifestyle. The cardiovascular diagnoses established will be treated and followed up: arrhythmia, hypertension, coronary artery disease, valvular heart disease.

### 2.4.2. Considerations on the Preoperative Cardiac Evaluation Algorithms

Several algorithms have been proposed for estimating the risk of perioperative complications, such as the algorithm of the American College of Physicians (ACP)<sup>24,25</sup>, the American College of Cardiology/American Heart Association (ACC/AHA)<sup>21</sup>, the EMAPO<sup>26</sup> and the Revised Cardiac Risk Index (RCRI)<sup>27</sup>. These algorithms are not perfect<sup>28</sup>, but all of them are better than chance in predicting perioperative complications and should be used during the evaluation. All of them have advantages and disadvantages that should be considered during their use. The algorithm complements the personal opinion of the evaluator and, in cases where the physician who performed the evaluation believes that the algorithm is underestimating the real risk, this observation should be mentioned in the assessment report.

The II Guidelines for Perioperative Evaluation of the Brazilian Society of Cardiology has proposed a flowchart for perioperative evaluation using the existing algorithms (Flowchart 1).

## 3. Additional Perioperative Evaluation

### 3.1. Assessment of Left Ventricular Function

Left ventricular function can be accurately assessed by several additional tests such as transthoracic and transesophageal echocardiography, contrast ventriculography, magnetic resonance, and multi-detector cardiac CT. Usually, two-dimensional echocardiography is the test of choice because of its broad availability and since it also allows the assessment of the structure and dynamics of the valves or the presence of ventricular hypertrophy<sup>27,29-32</sup>. Routine preoperative assessment of left ventricular function is not recommended. A meta-analysis has demonstrated that LV ejection fraction < 35% had 50% sensitivity and 91% specificity for predicting nonfatal events, concluding that the evaluation of the left ventricular function is highly specific for predicting risk of major cardiovascular events during the perioperative period of vascular surgeries, in spite of its relatively limited positive predictive value<sup>33</sup>. In particular, patients presenting with signs suggestive of cardiac failure or clinically significant valvular heart diseases

Flowchart 1 - Flowchart for perioperative evaluation

Step I - Exclude acute cardiac conditions		
In case of unstable angina, acute myocardial infarction, cardiogenic shock, acute pulmonary edema, severe bradyarrhythmia or tachyarrhythmia, the patient has very high spontaneous risk, the noncardiac surgery should, whenever possible, be canceled and reconsidered only after cardiac stabilization		
Step II - Stratify the risk according to preferred algorithms: RCRI, ACP, EMAPO ( <a href="http://www.consultorioidigital.com.br">http://www.consultorioidigital.com.br</a> )		
A. Evaluation according to RCRI		
Intraperitoneal, intrathoracic or suprainguinal vascular surgery	<b>Risk classes</b> I (no variable, risk 0.4%); II (one variable, risk 0.9%); III (two variables, risk 7%); IV ( $\geq 3$ variables, risk 11%)	
Coronary artery disease (Q waves, ischemic symptoms, test+, use of nitrate)		
Congestive heart failure (clinical, chest X-ray with congestion)		
Cerebrovascular disease		
Diabetes treated with insulin		
Preoperative creatinine > 2.0 mg/dL		
B. Evaluation using the algorithm of the American College of Physicians (ACP)		
AMI < 6m (10 points)	Non-sinus rhythm or SR plus premature atrial beats in ECG (5 points)	
AMI > 6m (5 points)	> 5 premature ventricular contractions in ECG (5 points)	
Class III angina (10 points)		
Class IV angina (20 points)	PO2 < 60, pCO2 > 50, K < 3, BUN > 50, Cr > 3.0 or bedridden (5 points)	
APE in the last week (10 points)	Age > 70 years (5 points)	
Previous history of APE (5 points)	Emergency surgery (10 points)	
Suspected critical aortic stenosis (20 points)		
Risk classes: if $\geq 20$ points: High risk, higher than 15%. If 0 to 15 points, evaluate the number of variables of Eagle and Vanzetto to discriminate low and intermediate risk.		
Age > 70 years	History of heart failure	If at most 1 variable: low risk: < 3%
History of angina	History of myocardial infarction	
DM	Ischemic ST changes on ECG	If $\geq 2$ variables: intermediate risk: between 3 and 15%.
Q waves on ECG	Hypertension with severe LVH	
Step III - Management		
<b>Low risk</b> RCRI: Class I and II / ACP low risk/EMAPO: up to 5 pts.  Immediate surgery	<b>Intermediate risk</b> RCRI: Class III and IV (+ heart failure or angina, at most FC II) / ACP: intermediate risk/EMAPO: 6 to 10 pts.  Functional test of ischemia, if changing management in the following situations: Vascular surgery (IIa, ev. level B); Intermediate risk surgery (IIb, ev. level C).	<b>High risk</b> RCRI: Class III and IV (+ heart failure or angina, FC III or IV) / ACP: high risk/EMAPO: $\geq 11$ pts.  Whenever possible, postpone the surgery to stabilize the cardiac condition. If the nature of the risk is ischemic: catheterization.

Patients should always undergo surgery using optimized clinical therapy. For cases of intermediate and high risk, surveillance is indicated for early detection of events: ECG and myocardial necrosis markers up to the 3<sup>rd</sup> postoperative day. For cases of high risk, there should be perioperative surveillance. ACP - American College of Physicians; EMAPO - Estudo multicêntrico de Avaliação Perioperatória; AMI - acute myocardial infarction; APE - acute pulmonary edema, SR - sinus rhythm; Cr - creatinine; BUN - blood urea; DM - diabetes mellitus; LVH - left ventricle hypertrophy; ECG - electrocardiogram; RCRI - revised cardiac risk index; FC - functional class; pts - points; ev. level - evidence level.



will benefit most from further evaluation. From a practical standpoint, although the prognostic value of the assessment of the ventricular function to predict perioperative events has been documented, little is known about the impact of this information to define perioperative management with clinical consequences. Individuals with higher risk for complications and clinical findings with higher probability of abnormal tests or those with outstanding cardiovascular symptoms may be considered for evaluation.

Recommendations for preoperative transthoracic echocardiography:

**Degree of Recommendation I, Level of Evidence B**

- Suspected valvular heart diseases with important clinical manifestations;
- Preoperative evaluation of liver transplantation.

**Degree of Recommendation IIa, Level of Evidence C**

- Heart failure patients without prior assessment of ventricular function.

**Degree of Recommendation IIb**

- Patients who will undergo high-risk surgeries; Level of Evidence B;
- Preoperative evaluation of bariatric surgery, Level of Evidence C;
- Grade 3 obesity, Level of Evidence C.

**Degree of Recommendation III, Level of Evidence C**

- Routine for all patients.

### 3.2. Noninvasive Stress Testing for Detection of Myocardial Ischemia

Noninvasive tests are aimed at identifying those patients most at risk of presenting adverse cardiac events in the perioperative period and, thus, reducing the perioperative risk, morbidity, and mortality.

The tests used for stratification should present good accuracy and high positive and negative predictive values. The test should also provide additional information besides the known clinical variables, thus, allowing for changes in the management. Therefore, the test should be recommended for those patients eligible for myocardial revascularization or those who will no longer be candidates for noncardiac surgery because of results indicating high cardiac risk. And finally, the stratification must show a favorable cost-benefit ratio.

The evaluation of myocardial ischemia in the perioperative period generally takes place through a functional test with physical or pharmacological stress associated with an imaging method. Myocardial perfusion scintigraphy with dipyridamole, dobutamine or physical stress (when there is no physical limitation for its implementation) and dobutamine stress echocardiography have excellent rates of accuracy, with high negative predictive value and are comparable<sup>34</sup>. Unfortunately, such functional tests are not widely available at all health care facilities, while usually two extremely different tests are offered: exercise electrocardiography and coronary cineangiography.

Exercise electrocardiography is not as accurate as imaging tests and has limitations in patients with resting electrocardiographic changes, such as bundle branch blocks, ventricular hypertrophy, and ventricular repolarization changes that may interfere with the result analysis. However, in a select group of patients who manage to reach 85% of the expected heart rate, the test has a high negative predictive value and allows the functional capacity to be objectively assessed<sup>35</sup>.

No risk factor alone is enough for a recommendation of noninvasive stress testing. According to the current guidelines of the ACC/AHA<sup>21</sup> and ESC<sup>36</sup>, the indication for further stratification is based on the association of variables including the patients' functional capacity, presence of risk factors and size of the surgeries. Thus, functional tests are not indicated for low-risk patients since there would be no additional benefits, nor are they indicated for high-risk patients since these usually require an invasive stratification.

Patients who have been submitted to some sort of functional test in the previous two years and whose symptoms have not changed do not need to repeat the test. The same applies to patients who have been submitted to complete myocardial revascularization (surgical or percutaneous) carried out more than 6 months and less than five years ago and remain clinically stable<sup>21</sup>.

#### 3.2.1. Exercise Stress Testing

An important limitation of this test in perioperative evaluation for noncardiac surgeries is the fact that 30% to 50% of the patients referred to the cardiologist for preoperative evaluation for major or vascular surgeries cannot achieve sufficient load during exercise to assess cardiac reserve<sup>37-39</sup>.

The gradient of severity in the test is also highly correlated with perioperative outcome: the onset of the ischemic response at low load is associated with significantly increased perioperative and long-term cardiac events, while myocardial ischemia with high loads is associated with lower risk. A recent review of the Mayo Clinic confirmed this finding. Patients who were able to tolerate exercise up to a load of 4-5 METS had a good perioperative and long-term prognosis, since this load is equivalent to the physiological stress of most noncardiac surgeries requiring general anesthesia<sup>41</sup>.

Perioperative exercise electrocardiography is an inexpensive, easy to perform and highly reproducible test, and although it is inferior to imaging tests, it is adequate for the reality of many towns in Brazil<sup>42</sup>.

#### 3.2.2. Radionuclide Myocardial Perfusion Imaging Methods

Even though exercise electrocardiography has a good cost-benefit-risk ratio in the perioperative stratification, it also has some limitations that prevent its implementation or analysis: the patient's physical limitations and (primary or secondary) ST changes on baseline ECG, respectively. For these patients, a method of imaging with pharmacological stress (adenosine, dipyridamole or dobutamine) should be used. In this context, myocardial perfusion scintigraphy (MPS), associated with exercise or pharmacological stress, has good accuracy and good prognostic value. In a meta-analysis

involving 1,179 patients who underwent vascular surgery, MPS with dipyridamole was able to predict a larger number of perioperative cardiovascular events the greater the presence and extent of perfusion defects. In this study, patients with reversible ischemia in up to 20% extension of the left ventricle did not have more events than those without ischemia. However, when the affected area was 20%-29%, 30%-49%, and above 50%, the probability of events was significantly higher: 1.6, 2.9, and 11 times greater, respectively<sup>(43)</sup>. Another meta-analysis using the same method and similar profile of patients showed that patients without perfusion defect, with a fixed defect and reversible defect, had the following mortality and nonfatal infarction rates: 1%, 7% and 9%, respectively. It also showed that patients with two or more perfusion defects had a high incidence of cardiac events<sup>(44)</sup>. More recently, MPS associated with gated SPECT, which allows both the assessment of myocardial perfusion and cardiac function, has proved to be a useful tool in risk stratification for vascular surgeries. Patients with normal perfusion but with impaired contractility had significantly more cardiac events than those with normal contractility and perfusion: 16% vs. 2% ( $p < 0.0001$ ), respectively. The abnormal end-systolic volume (above twice the standard deviation) was the only independent variable for predicting cardiac events<sup>(45)</sup>.

In conclusion, in the context of perioperative evaluation, the indications for MPS associated with gated SPECT would be similar to those for exercise electrocardiogram, which is disregarded in favor of the CPM due to physical limitation or impossibility of interpretation because of baseline change in the ST. And also in those situations aimed at diagnosis clarification, in which the result of the exercise electrocardiogram was interpreted as false positive.

### 3.2.3. Dobutamine Stress Echocardiography

Stress echocardiography is accurate and safe in identifying patients with coronary artery disease, and it plays an important role in predicting cardiac events<sup>(46,47)</sup>.

Dobutamine and exercise stress echocardiographies present similar diagnostic accuracies and are more accurate than dipyridamole stress echo<sup>(48)</sup>. If dobutamine stress echo does not reveal the presence of residual ischemia in a patient with a history of myocardial infarction, the prognosis is good and the likelihood of another myocardial infarction is low in the perioperative period of a noncardiac surgery<sup>(33)</sup>.

The use of dobutamine stress echocardiography to assess perioperative risk is already well documented in the literature, with a positive predictive value ranging from 25% to 55% and a negative predictive value ranging from 93% to 100% for cardiac events in patients submitted to noncardiac surgery<sup>(33,49,50)</sup>. The results were usually used to influence the preoperative clinical management, mainly the decision of performing the coronary cineangiography or myocardial revascularization before or after the elective surgery.

A meta-analysis of 15 studies comparing dipyridamole thallium-201 and dobutamine stress echocardiography in vascular risk stratification before surgery demonstrated that the prognostic value of abnormalities in both imaging modalities for perioperative ischemic events is similar<sup>(44)</sup>.

### 3.2.4. Recommendations for Stress Myocardial Perfusion Scintigraphy or Echocardiography during the Preoperative Period

#### Degree of Recommendation IIa, Level of Evidence B

- Patient with intermediate risk for complications and vascular surgery scheduled.

#### Degree of Recommendation IIb, Level of Evidence C

- Patients with intermediate risk for complications and intermediate-risk surgery scheduled;
- Patients with low functional capacity with intermediate- and high-risk surgeries scheduled.

### 3.2.5. Health Care Facilities that do not offer Imaging Tests for Detection of Myocardial Ischemia

Coronary cineangiography and coronary angiotomography are not substitutes for scintigraphy or stress echocardiography and should not be performed routinely in the evaluation of patients with intermediate risk;

Exercise electrocardiography can be used, provided that the patient reaches the recommended heart rate with the following recommendations:

#### Degree of Recommendation IIa, Level of Evidence C

- Patient with intermediate risk for complications and vascular surgery scheduled.

#### Degree of Recommendation IIb, Level of Evidence C

- Patients with intermediate risk for complications and intermediate-risk surgery scheduled.

### 3.3. Holter Monitor

Continuous electrocardiographic monitoring with Holter is a method that assesses the presence and complexity of atrial and ventricular arrhythmias, in addition to identifying dynamic changes in ST consistent with myocardial ischemia. In preoperative evaluation, its use is rarely useful, since patients with suspected ischemic heart disease will be preferentially evaluated by other methods and those suspected of severe and/or symptomatic arrhythmias possibly would have done it previously. The main application of Holter in the perioperative context relates to the monitoring of possible ischemic events that occur both in the perioperative and, mainly, in the postoperative period; it should be used in intermediate- or high-risk patients for ischemic events<sup>(51,52)</sup>.

### 3.4. Coronary Angiography

Coronary angiography is a well-established invasive diagnostic procedure, allowing the visualization of coronary anatomy and ventricular function, but is rarely indicated for risk assessment in noncardiac surgeries. There is a lack of information from randomized clinical trials proving its usefulness in patients scheduled for noncardiac surgery. In patients with myocardial ischemia, the indications for preoperative cardiac catheterization and revascularization are similar to the indications for angiography in other situations<sup>(53-56)</sup>. Adequate control and treatment of ischemia before the surgery, both clinically and by means of intervention, is recommended whenever the noncardiac surgery can be postponed.

Cardiac catheterization should be performed when the patient has acute coronary syndromes, stable angina not controlled with medication, and stable angina with left ventricular dysfunction. When coronary disease is suspected based on noninvasive tests, such as exercise electrocardiography, myocardial scintigraphy or dobutamine stress echocardiography, catheterization should be indicated when moderate to large areas of induced ischemia and/or high-risk characteristics are demonstrated<sup>57</sup>. When the noninvasive tests are inconclusive and there is high likelihood of coronary disease, catheterization may be indicated before high-risk surgeries.

Patients referred for vascular surgery and a high likelihood of coronary artery disease may occasionally have catheterization recommended even in the absence of noninvasive tests. Monaco<sup>58</sup> conducted a randomized study in patients referred for vascular surgery and Revised Cardiac Risk Index > 2. Patients were randomized to immediate catheterization or according to the presence of ischemia on noninvasive testing, and there was improved survival rate ( $p = 0.01$ ) and cardiac event-free survival in three years ( $p = 0.003$ ) for the group of immediate catheterization. This group presented a higher rate of immediate revascularizations (58.1% vs. 40.1%,  $p = 0.01$ ) compared to the group of catheterization according to the presence of ischemia.

Recommendations for requesting preoperative coronary angiography:

#### Degree of Recommendation I

- Patients with high-risk acute coronary syndrome; Level of Evidence A;
- Patients with noninvasive test indicative of high risk. Level of Evidence C.

#### Degree of Recommendation IIa

- Patients with indication for test based on current guidelines for coronary artery disease, regardless of the surgical procedure in elective surgeries. Level of Evidence C.

### 3.5. BNP

In recent years, several studies<sup>59-63</sup> in the literature have shown that the measurement of BNP or NT-proBNP levels in the preoperative period may help identify patients at risk for cardiovascular complications and postoperative cardiovascular events. Observational studies have suggested that high BNP or NT-proBNP levels in the preoperative period are independent predictors of perioperative cardiovascular complications in noncardiac surgeries. However, we must emphasize that the available data were obtained from observational studies, with different inclusion criteria, usually with small numbers of patients, and limitations and methodological flaws for the definition and identification of postoperative events.

In the meta-analysis<sup>64</sup> conducted with 15 prospective observational studies and 4,856 patients, the authors found that higher preoperative BNP or NT-proBNP levels were associated with an increased risk of major cardiovascular events, cardiac mortality and mortality from all causes during the perioperative period (< 43 days after surgery). In the outpatient setting, the increase in the BNP or NT-proBNP

levels in the preoperative period was associated with risk of major cardiovascular events and mortality from all causes up to six months after the surgery. Thus, data from the studies are consistent regarding the fact that high BNP levels are predictors of perioperative cardiovascular events and mortality after noncardiac surgery. BNP or NT-proBNP can potentially be used for surgical risk stratification.

However, the studies conducted so far have not been able to determine the optimal cutoff point of BNP or NT-proBNP to better predict cardiovascular events, because of the wide variation of values adopted among the studies presented. We do not know whether the measurement of these markers in the preoperative period brings some additional information regarding the existing stratification strategies and which population would most benefit from its indication. Larger studies with adequate statistical power are necessary to determine the real benefit of this method, its optimal cutoff point and its additional indication for well-established stratification strategies.

Recommendation for measurement of BNP in the preoperative period:

#### Degree of Recommendation IIa, Level of Evidence B

- The measurement of BNP or NT-proBNP in the preoperative period can be used as a predictor of perioperative cardiovascular risk and mortality of noncardiac surgeries.

## 4. Disease-specific Approaches

### 4.1. Coronary Artery Disease (CAD)

It is essential to clearly distinguish the surgical risk of each specific CAD condition in order to prevent and reduce the morbidity associated with perioperative events. Around four decades ago, perioperative risk assessment of coronary disease patients consisted exclusively of determining the time elapsed between an ischemic cardiovascular event and surgery date. However, today we weigh not only the time elapsed but also all the factors that are known to be relevant in the prognosis of patients with CAD, regardless of perioperative context, such as symptoms of angina or heart failure, electrocardiographic signs of ischemia, degree of ischemia, ischemic threshold and coronary anatomy in pertinent cases. There are no proven benefits of routinely and indiscriminately requesting additional tests, especially functional tests and coronary cineangiography for patients with diagnosed CAD. A careful investigation of the medical history of a patient associated with diagnostic tests that focus on the circulatory system and basic additional tests, such as resting electrocardiogram and chest x-ray, is often enough to determine the surgical risk of CAD patients.

### 4.2. Hypertension

The previous diagnosis of hypertension is the most common medical condition for the postponement of a surgery<sup>65</sup>. It is well established that during a surgical procedure, major hemodynamic changes may occur, especially in patients with hypertension. Increasing knowledge on the pathophysiology and therapeutics of hypertension and the development of new anesthetics and muscle relaxants with minimal



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hemodynamic effects, as well as protocols of pain control in the postoperative period, have contributed to minimize the occurrence of complications during the perioperative period of hypertensive patients.

One of the mechanisms involved is the sympathetic activation observed during anesthesia induction and in the postoperative period. The increase in the sympathetic activity can cause significant higher blood pressure rates, especially in patients with uncontrolled hypertension. Supporting the importance of sympathetic overactivity, evidence suggests that clonidine, when used in the perioperative period of hypertensive patients, showed significant reduction in the variation of blood pressure and heart rate and reduce the need for anesthetic (isoflurane) and supplemental narcotics in these patients<sup>66</sup>.

In general, stage 2 hypertension (systolic blood pressure > 180 mmHg and diastolic blood pressure > 110 mmHg) must be controlled before surgery. However, when there is mild or moderate hypertension without associated metabolic or cardiovascular, there is no evidence of benefit in postponing the surgery<sup>67</sup>.

Patients with some degree of autonomic disorder, including hypertension, are more susceptible to hypotension during surgery than patients with normal blood pressure. This is particularly true for patients who take angiotensin-converting enzyme (ACE) inhibitors before surgery. In most of the patients, this may be associated with reduced intravascular volume. Thus, it is crucial to avoid hypovolemia in the perioperative period. However, abrupt cessation of these drugs should not be done because both uncontrolled blood pressure and decompensation of heart failure may increase the risk of cardiovascular complications.

Patients with suspected secondary hypertension should be investigated before surgery, except in emergency cases. Although there is no conclusive evidence on increased perioperative risk in patients with secondary hypertension, patients with undiagnosed pheochromocytoma have operative mortality of around 80%<sup>68</sup>.

During surgery, monitoring heart rate and blood pressure of hypertensive patients is crucial to detect changes in blood pressure and signs of ischemia as soon as possible. Hypertension is not only a risk factor for CAD but it is also associated with ventricular hypertrophy, systolic dysfunction, renal failure and cerebrovascular events during the perioperative period. This aspect must be taken into account when doing the perioperative management of the blood volume of hypertensive patients with changes in ventricular geometry and artery elasticity, especially elderly patients<sup>69</sup>.

Recommendations:

### Degree of Recommendation I

- If blood pressure is high and there is enough time before surgery to reduce it with proper medications, do so; Level of Evidence C;
- The antihypertensive medication (including ACE inhibitors) must be continued during the perioperative period, including on the day of the procedure. Level of Evidence C;
- If blood pressure is high and there is not enough time before surgery to reduce it with proper medications,

administer a beta-1 receptor blocker with rapid onset (esmolol) to keep the blood pressure from rising during intubation. Oral clonidine can be used when esmolol is contraindicated; Level of Evidence C;

- Hypokalemia, if present, must be corrected before surgery; Level of Evidence C;
- The reintroduction of antihypertensive medication, preferably the one that the patient was using before surgery, should be done as soon as possible; Level of Evidence C;
- Volume management should be done during the perioperative period; Level of Evidence C.

### 4.3. Congestive Heart Failure

The presence of heart failure in the perioperative period is considered a major risk factor for cardiovascular complications<sup>3,70,71</sup>. It is important to highlight that the functional status, based on severity of signs and symptoms of each patient during surgery, and not just the detection of (systolic or diastolic) ventricular dysfunction by imaging studies, is crucial in determining a higher risk. Patients with signs and symptoms of decompensated heart failure must be treated in the preoperative period in order to optimize their hemodynamic balance and ensure a safer surgery. The use of pharmacological and dietary resources to improve the clinical status of the patient is very valuable but so far there is not a single intervention that has demonstrated reduction of mortality or morbidity in patients with heart failure in the perioperative period. Fluid administration must be done with caution during and after surgery with the purpose of avoiding consequences of both hypervolemia and low cardiac output. Regarding anesthetic agents, prefer those that cause less myocardial depression.

When clearly symptomatic patients (NYHA functional classes III and IV) are submitted to urgent surgeries, they must be monitored closely during the postoperative period, preferably in the ICU. The use of flow-directed pulmonary artery catheter is indicated for this group to monitor hemodynamic parameters during and after surgery, mainly for large surgeries with the purpose of more adequate management of fluids and vasoactive drugs<sup>72</sup>. However, there is no definite evidence that this practice improves survival rate or reduces complications<sup>72</sup>.

The recommendations for perioperative evaluation are based on the pathophysiology of the cardiomyopathy process. Every effort must be made before surgery to determine the cause of cardiomyopathy. For example, infiltrative diseases such as amyloidosis can lead to both systolic and diastolic dysfunction. The identification and quantification of these changes may change the management of intraoperative and postoperative volume.

In patients with a history and signs of heart failure, evaluation of left ventricular function is recommended in order to quantify the severity of systolic and diastolic dysfunction, which can be done by means of an echocardiography.

Hypertrophic cardiomyopathy leads to perioperative special problems. Reduction of blood volume, decreased systemic vascular resistance and increased venous capacitance

may cause decreased left ventricular volume (LV) potentiating the effects of obstruction of the LV outflow present in these patients. In addition, a reduction of filling pressures may result in a significant decrease in the systolic volume because of decreased compliance of the hypertrophic ventricle. Volume infusion in these patients should be very careful. Catecholamines should be avoided because they may increase the degree of dynamic obstruction and decrease diastolic filling. They can also trigger the onset of severe ventricular and supraventricular arrhythmias<sup>73,74</sup>.

Recommendations:

#### **Degree of Recommendation I, Level of Evidence C**

- Assessment of patients with CHF symptoms must focus on determining its etiology and functional consequences of myocardial dysfunction;
- Treatment must be optimized before surgery and patient must continue to take medications during the entire perioperative period (including the day of surgery);
- Anesthetic agents that depress myocardial contractility must be avoided in patients with CHF;
- Volume management must be rigorous. Invasive monitoring can be useful during the intraoperative and early postoperative periods of patients with severely depressed cardiac function;
- The use of beta-adrenergic agonists must be avoided in patients with hypertrophic cardiomyopathy;
- Patients in NYHA functional class III/IV should have elective surgery postponed until the optimization of medication and symptom improvement, if possible.

#### **4.4. Valvular Heart Diseases**

Patients with heart murmur should be carefully evaluated for confirmation of organic valvular lesion and, if present, anatomic severity, degree of ventricular remodeling and ventricular function should be quantified<sup>75</sup>. When valvular heart disease is suspected after clinical history and physical examination, the complementary method of choice is Doppler echocardiography<sup>76</sup>. In case of persistent diagnostic uncertainty, other methods are possible, such as contrast ventriculography, MRI, and catheterization<sup>77</sup>. Anatomically important valvular heart disease is an independent risk factor for perioperative cardiac complications, which can be: pulmonary congestion/acute pulmonary edema, cardiogenic shock, acute myocardial infarction, tachyarrhythmia, embolic events, bleeding, and infective endocarditis<sup>3,78,79</sup>. In addition to being more prevalent, left ventricle valve diseases have consequences in the perioperative period. The worse the extent of the valvular heart disease, the worse the degree of associated systolic ventricular dysfunction and the more the patient is symptomatic, the greater the risk of complications<sup>3,80</sup>. In general, critical stenosis have more management complications and difficulties in relation to important regurgitant lesions<sup>21</sup>.

Symptomatic patients with anatomically important valvular heart disease have a high mortality and morbidity rates in the natural history of valvular heart disease and are recommended to undergo interventional treatment of valvular disease<sup>77</sup>.

This group of patients is at high risk for perioperative cardiac complications when undergoing noncardiac surgery<sup>21</sup>. Therefore, valvular heart disease should be treated first, so that the patients can undergo noncardiac surgery later. Patients with mitral valve disease may be candidates for mitral balloon valvuloplasty, or open heart surgery with or without valve replacement; this decision should be based on echocardiographic criteria and intraoperative findings. Patients with aortic valve disease are generally treated with prosthetic valve implantation. It is important to emphasize that routine aortic balloon valvuloplasty in the preoperative period is not recommended for patients with aortic stenosis given the bad results obtained with this technique<sup>81</sup>. Currently it is possible to perform implantation of percutaneous aortic bioprosthesis; this procedure is performed only in patients at high risk of death during the heart valve surgery<sup>82</sup>. If, based on the opinion of the medical team discussed with the patient and his/her family, the patient undergoes noncardiac surgery without prior valve repair, the surgery should be done with the best possible compensation of heart failure using medication and behavioral measures. Regurgitant lesions are compensated with vasodilators and diuretics. Mitral stenosis benefits from beta-blockade and diuretics. Aortic stenosis is difficult to manage using medication. Diuretics may be used, but vasodilators should be prescribed with caution because of the risk of low output and syncope<sup>75,77</sup>.

The presence of asymptomatic valve disease is also an important risk factor for perioperative complications, especially when there is aortic stenosis<sup>83,84</sup>. Besides hemodynamic complications, severe aortic stenosis also brings risk of excessive bleeding because of the change in the von Willebrand factor<sup>85</sup>. Initially, indication for surgical valve according to current recommendations should be assessed. Priority valve surgery is acceptable when the estimated risk of cardiac surgery is low and the patient requires major noncardiac surgery with great benefit expected. Patients with aortic stenosis undergoing noncardiac surgery should be carefully monitored to maintain their sinus rhythm and avoid variations in blood volume (hypo- and hypervolemia), i.e., they require careful monitoring of anesthesia during surgery. Spinal anesthesia should also be avoided in patients with important aortic stenosis because of the consequent vasodilation<sup>86</sup>. Patients with major regurgitant lesions tend to have fewer complications and benefit from perioperative invasive blood pressure being carefully monitored to avoid increased peripheral resistance<sup>87</sup>.

Patients with anatomically mild to moderate valvular heart disease are at low risk for complications, since there is little or no hemodynamic consequence. Again there is emphasis on aortic stenosis, which even when anatomically moderate brings higher risk of complications than the other valve diseases.

There are no studies evaluating the use of beta-blockers during surgery in patients with valvular heart diseases, thus they should not be routinely prescribed<sup>88</sup>. There may be harmful effect (exacerbation of heart failure) due to the use of beta-blockers in patients with anatomically important aortic stenosis, aortic insufficiency, and mitral regurgitation. However, beta-blockers may be part of the drug treatment

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in patients with mitral stenosis and they should not be contraindicated in this situation.

There are no studies evaluating the use of statins during surgery in patients with valvular heart diseases, thus they should not be routinely prescribed<sup>89</sup>.

There are no studies evaluating the use of nitroglycerin and other vasodilators during surgery in patients with valvular heart diseases, thus they should not be routinely prescribed<sup>90</sup>.

Patients with heart valve prostheses need to receive special interventions. If there is dysfunction of the prosthesis, the case should be conducted as if the patient had an equivalent native valvular heart disease. It is noteworthy that the presence of prosthesis is a risk factor for infective endocarditis (IE), which requires specific assessment to indicate possible IE prophylaxis. Patients with mechanic prostheses are at high risk of cardioembolic events; therefore, permanent chronic oral anticoagulation therapy is recommended. In case of noncardiac surgery, specific assessment should be performed before discontinuation of oral anticoagulation therapy with heparin in the perioperative period<sup>91</sup>.

Cardiac monitoring with continuous electrocardiography is recommended, ideally with multiple derivations, whose changes can be predictive of cardiac events<sup>92,93</sup>.

Use of routine pulmonary artery catheter in patients with valvular heart disease is not recommended, primarily due to lack of studies involving this group of patients, little benefit demonstrated in other groups of patients, and also because of frequent coexistence of pulmonary hypertension and tricuspid insufficiency that make it difficult to interpret data<sup>94,95</sup>. Patients at high risk of complications should be treated as follows: postoperative period at ICU, maintenance of electrocardiographic monitoring for 72 hours, and serial plasma markers of myocardial necrosis in an attempt to diagnose ischemia/myocardial infarction<sup>93</sup>.

Patients who had postoperative instability should initially be treated with medications – vasodilators, diuretics, inotropic drugs – and evaluated for the need for emergency heart surgery.

Recommendations:

### Degree of Recommendation I

- Patients with valvular heart disease, mainly if anatomically important, should be referred to a cardiologist before noncardiac surgery; Level of Evidence C;

- Patients with valvular heart disease with indication for valve intervention treatment should primarily receive cardiac treatment and then undergo the noncardiac treatment proposed, Level of Evidence B;

- Symptomatic patients with valvular heart disease undergoing noncardiac surgery should receive optimal drug and behavioral treatment, including on the day surgery, Level of Evidence C;

- Control of blood volume and electrolytic disorders must be given special attention in patients with important valvular heart disease; Level of Evidence C;

- Monitoring with invasive blood pressure can be used in patients with important valvular heart disease; Level of Evidence C;

- There is no indication of beta-blockers, statins or routine nitroglycerin in patients with valvular heart disease; Level of Evidence C;

- All patients with valvular heart disease should be assessed regarding the need for prophylaxis of infective endocarditis; Level of Evidence B;

- All patients with heart valve disease or prosthetic valve on continuous oral anticoagulation therapy should be assessed regarding the need for adjustments and anticoagulation with heparin in the perioperative period; Level of Evidence B.

### Degree of Recommendation IIa

- Patients with severe asymptomatic aortic stenosis with intermediate and high-risk noncardiac surgery scheduled should be submitted to the interventional treatment of heart valve disease before noncardiac surgery. Level of Evidence C.

## 4.5. Cardiac Arrhythmias

The prevalence of heart rhythm disturbances increases with age, as well as acquired structural heart diseases such as ischemic heart disease and cardiomyopathies. Likewise, older individuals undergo surgical interventions more often.

In the perioperative period, the occurrence of atrial or ventricular arrhythmias may be prior to surgery in question or may be a recent and temporary event triggered by physical and emotional stress, increased sympathetic nerve activity, or due to metabolic and electrolyte disturbances (hypokalemia, hypomagnesemia, hypoxemia) related to the intervention, and the toxicity of certain drugs used to control perioperative complications.

During the preoperative evaluation of individuals who have a history of cardiac arrhythmias, physicians should primarily define the presence or absence of symptoms and association with structural heart disease and functional impairment, especially coronary disease and several forms of heart failure. Occasionally, arrhythmias are found on routine electrocardiogram during preoperative evaluation. The presence of ventricular extrasystole, even the repetitive and frequent forms, in asymptomatic individuals and those without structural heart disease does not imply higher risk<sup>96</sup>.

The history of cardiac arrhythmias in the preoperative period was not identified as a risk predictor for postoperative myocardial ischemia in patients undergoing noncardiac surgery<sup>51</sup>. In addition, the frequency of ventricular arrhythmias in the intra and postoperative period of patients with structural heart disease and repetitive forms of ventricular extrasystole (diagnosed in the preoperative evaluation) undergoing noncardiac surgery was not associated with adverse cardiovascular events<sup>97</sup>.

These findings demonstrate that cardiac arrhythmia alone is not associated with an increased cardiovascular risk in the perioperative period. However, in symptomatic patients and/or patients with associated heart diseases (myocardial ischemia, ventricular dysfunction), a more detailed preoperative evaluation is needed with the purpose of achieving a better stratification and recognition of the extent of involvement of the concomitant structural heart disease. The reason is that in such individuals the occurrence of atrial or ventricular arrhythmias may be harmful,

bringing the risk of triggering myocardial ischemia – because of the increase in oxygen consumption related to elevated heart rate (HR) – or causing symptoms of low cardiac output, especially in individuals with moderate to severe ventricular dysfunction.

In patients with permanent atrial fibrillation, control of resting HR to less than 90 bpm is recommended because the perioperative stress carries a risk of increased heart rate and consequent related symptoms.

The use of beta-blockers such as metoprolol (100 mg/day) in the perioperative period of surgeries related to a high incidence of atrial fibrillation, such as thoracic surgery, was associated with a lower frequency of this arrhythmia without bringing significant side effects<sup>98</sup>.

Situations in which cardiologist assessment should be strongly considered before surgery because of the presence of cardiac arrhythmias:

#### **Degree of Recommendation I, Level of Evidence C**

- Symptoms related to low output or syncope, in the presence of structural heart disease associated with compromised left ventricular systolic function and/or myocardial ischemia;
- Symptoms related with tachyarrhythmias in patients with ventricular preexcitation syndrome with well-defined sudden onset and termination, associated or not with low output, without clinical findings or adequate treatment.

#### **Degree of Recommendation IIa, Level of Evidence C**

- Symptoms related to tachyarrhythmias, regardless of structural heart disease, in patients with well-defined, frequent and recent symptoms of tachycardia episodes of sudden onset and termination;
- Symptoms related to low output or syncope in elderly patients with a baseline heart rate below 50 bpm;
- Asymptomatic patients with permanent atrial fibrillation to assess control of heart rhythm;
- Asymptomatic patients with very frequent isolated ventricular arrhythmias or repetitive ventricular arrhythmias associated with structural heart disease.

### **4.6. Conduction Disorders**

Atrioventricular and intraventricular conduction disorders are less common than cardiac arrhythmias secondary to the origin of the impulse. When asymptomatic, these disorders often represent benign conditions and do not result in additional risk, even in the perioperative period. Among these conditions are: first-degree AV block, Mobitz type I second-degree AV block, and bundle branch or bifascicular AV block<sup>96</sup>.

Other atrioventricular and intraventricular conduction disorders may represent more severe situations, especially if individuals report symptoms of presyncope, syncope, weakness, dyspnea. These findings could be related to cases of second-degree AV block type II, advanced AV block, and complete AV block. In these situations, more complex diagnostic tests are necessary for an adequate evaluation of perioperative risk and the definition of appropriate therapy, including the implantation of cardiac pacemakers.

Situations in which cardiologist assessment should be strongly considered before surgery:

#### **Degree of Recommendation I, Level of Evidence C**

- High degree AV block: Type II second-degree AV block, 2:1 AV block, paroxysmal third-degree AV block, permanent third-degree AV block or AV dissociation.

#### **Degree of Recommendation IIa, Level of Evidence C**

- Low-risk AV block on resting ECG but with symptoms that suggest low output or syncope;
- Trifascicular block;
- Bifascicular AV block on resting ECG but with symptoms that suggest low output or syncope.

### **4.7. Implanted Pacemakers and Implantable Cardioverter Defibrillators**

Artificial cardiac stimulation has advanced significantly in recent years with the development of an array of new implantable devices that are capable of responding to abnormal heart rhythms. Moreover, an increasing number of patients are submitted each year to the implantation of these prostheses. People often wonder if electrocautery and other equipment will cause electromagnetic interference with pacemaker function.

#### **4.7.1. Individuals with Conventional Single-, Dual- or Multi-chamber Pacemakers**

##### **4.7.1.1. Pacemakers Implanted in the Last 60 Days**

Most leads found in current pacemakers have an active fixation element, that is, a device that allows them to be actively fixed in the endocardium. These leads are rarely displaced, which is a possible complication during this period. The location where the generator was implanted is recovering from surgery, therefore, inflammatory phenomena, hematoma, edema, rejection and even subclinical infection may occur during this phase. The pacemaker and the leads are susceptible to infection from other foci of the body and even surgical manipulations of any kind. To minimize the risk of complications, it is recommended, if possible, to wait until the end of the 2<sup>nd</sup> month after implantation to perform the elective surgery.

##### **4.7.1.2. Almost Dead Pacemaker Batteries**

Pacemakers whose batteries are almost dead should be replaced by new and modern units before elective surgeries. The reason for that is that such devices may behave strangely when submitted to certain events that may happen during elective surgery.

##### **4.7.1.3. Safe Cardiac Stimulation**

These patients need to see their pacemaker physicians before being submitted to elective surgeries for a complete assessment of the stimulation system. The physician will determine if the pacemaker settings need to be changed, issue a document with warnings for the surgeon and anesthesiologist and describe the behaviors that the pacemaker may display during surgery. Usually, the biggest concern involves those patients who will be submitted to major surgeries with the use of electrocautery. In these cases, a safety procedure should



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be done always in a pacemaker check-up clinic and by a certified pacemaker physician. If electrocautery<sup>99-101</sup> cannot be substituted by ultrasonic scalpel, the document must contain at least the recommendations listed in below:

- Continuous cardiac monitoring with ECG monitor and pulse oximetry (heart rhythm monitoring is possible even during electrocautery);
- Use bipolar electrocautery. If bipolar is not available, use monopolar electrocautery but place the grounding pad far from the pacemaker and prepare the skin and in the region, eliminate oils using alcohol-ether. If the dispersive lead is reusable, apply a thin and homogeneous layer of electrolyte paste on its surface;
- The dispersive lead should be placed far from the pacemaker, preferably near the surgical field, minimizing the electrical field. Thus, in an abdominal or pelvic surgery, the dispersive lead should be placed near the tailbone; in a surgery on the right hand, the dispersive lead should be placed in the right forearm, and in a head surgery, the dispersive lead should be placed on the neck. The pacemaker and its leads must always stay away from the electric field generated by the electrocautery;
- Ground the electrocautery device properly by connecting it to a good grounding wire;
- Limit the use of the electrocautery probe as much as possible and to very short periods and always monitor the ECG or heart rate. Generally, when the electrocautery probe is used, the ECG monitor is unreadable and monitoring can be done by plethysmography, which does not suffer interference from the electrocautery;
- If bradycardia or tachycardia occur during electrocautery (because of electromagnetic interference), place a magnet over the pacemaker every time the electrocautery probe is used. The magnetic response of each pacemaker can be different, and in some cases it may not exist (to be turned off by default). A good practice is to do some testing before surgery, but the patient must keep being monitored, allowing to observe the magnetic response of the device. Additionally, the magnetic behavior of the pacemaker of each patient must be informed by the patient's specialist doctor, as this depends on the set up of the device;
- Remind the patient to return to the pacemaker checkup clinic after the postoperative recovery period so that the original settings can be restored and the pacemaker reassessed;
- In individuals with multisite cardiac resynchronization device, the presence of more leads in the heart undeniably increase the likelihood of complications due to external interferences on the stimulation system. Most stimulation leads used in the venous system of the left ventricle are unipolar, thus more susceptible to external interferences, especially those caused by electrocautery; however, there is a current trend to use bipolar leads, but many unipolar leads have been implanted and will remain so for many years. The presence of more electrodes and unipolar electrodes requires doctors to carefully consider the items mentioned above, more accurately and giving greater attention to signs that there is interference on the multisite stimulation system. In addition, these patients are at higher risk because of their heart failure.

### 4.7.2. Patients with Implantable Cardioverter-Defibrillators (ICDs)

The behavior complexity and diversity of these devices, the risk of severe arrhythmias during surgery and the possibility of electrocautery causing electromagnetic interferences lead us to recommend the presence of the pacemaker physician and the necessary equipment to program the ICD in the surgery room so that it can be adjusted during surgery if necessary and according to the metabolic needs of the patient.

Antitachycardia function must be disabled and the patient properly monitored. As this function is disabled, the physician needs to be ready to respond to a high-risk arrhythmia with an external defibrillator and antiarrhythmic medications. It is not unusual for the pacemaker physician to have this type of patient stay in the ICU during the early postoperative period so that they can be closely monitored, specially while the antitachycardia function is not working.

### 4.7.3. Emergency Electrical Cardioversion or Defibrillation

During the perioperative period, patients with a pacemaker or implantable cardioverter-defibrillator may have complications that require an electrical cardioversion or defibrillation. Although the generators can theoretically withstand the shocks, in practice it is advisable to avoid them whenever possible. When indispensable, some cautions must be taken to preserve the pacemaker or defibrillator, the leads and the lead-heart interface, as described below.

- Internal cardioversion is preferred in patients with internal ICD since it uses less energy, biphasic pulse and internal safety resources of the device itself;
- For external shocks, prefer cardioverters that come with adhesive pads. Place them anteroposteriorly, according to the polarity informed by the manufacturer. Avoid the standard placement of the pads (between the base and apex of the heart – parallel to the leads) since the myocardium may be injured by the tip of the lead;
- Attach the pads as far as possible from the generator and leads;
- Use as little energy as possible. Modern cardioverters delivering biphasic shocks should be preferred;
- Place a magnet over the generator, except in ICDs that can disable the antitachycardia function if the magnet remains over them for longer than 30 seconds. Older pacemakers invariably shut down when a magnet is placed over them and become asynchronous. Conversely, modern rate-responsive devices are programmable and can have different behaviors. Thus, placing a magnet over the generator does not necessarily protect the device during a cardioversion;
- Verify the sensing and pacing thresholds after the procedure. Consider reassessing the device in 24 hours and monitor the patient during this time.

### 4.7.4. Lithotripsy

When lithotripsy is required in patients with pacemaker and/ or defibrillator, direct the focus away from the area of the device and leads. Turn off atrial stimulation when using ECG-triggered

lithotripsy to avoid that the device synchronize according to the atrium. Setting up the atrial channel with less energy and in the bipolar mode can solve the problem, keeping the dual-chamber stimulation more physiological. A test may be performed before the effective application, observing the behavior and interaction of devices. Do not immerse the body part that contains the pacemaker or ICD when performing immersion lithotripsy.

#### 4.7.5. MRI

Patients with pacemakers or defibrillators should not be undergo MRI tests. There is a risk of dysfunction of the prosthesis and leads, and they can be displaced because of the magnetic field generated. Although there are pacemakers prepared to support the field of resonance, they depend on specific leads and specific set up during the procedure, requiring the presence of an expert along with the programmer of the generator during the test. Even these prostheses were designed to withstand limited magnetic fields (0.5 Tesla).

#### 4.7.6. Radiotherapy

Radiotherapy can be used provided that the focus of radiation is not directed to the pacemaker/ICD. If the devices are close to the focus of radiation, the area should be covered using a lead shield. If the irradiated site is exactly in the region of the implant or very close to it and the patient needs many radiotherapy sessions, the possibility of reimplanting the pacemaker or ICD in another site far from the point of irradiation should be considered. Radiotherapy on the pacemaker can cause temporary or permanent dysfunction and premature wear of the battery. Radiotherapy on the leads may cause fibrosis and loss of command because of increase in the stimulation threshold.

#### 4.7.7. Recommendations

The operative period was divided into preoperative evaluation, preoperative preparation, intraoperative care, and postoperative care. The recommendations were grouped in these periods to facilitate the monitoring of patients with pacemakers or ICDs. The suggested sequence should be followed for each patient<sup>102</sup>:

##### A. Preoperative Period

###### Degree of Recommendation I

- Determine if the patient uses a single or dual-chamber pacemaker, resynchronizer, defibrillator or multiple prostheses based on the clinical history, physical examination, scar evaluation, electrocardiographic record, and chest or abdomen X-ray; Level of Evidence C;

- Use the identification card, radiological identification number or hospital records to determine what type of device the patient is using; Level of Evidence C;

- Determine if the patient depends on the pacemaker by reviewing clinical history (syncope and/or dizziness before the implant; successful nodal ablation), data from previous assessments or decreasing the timing of the device to the lowest rate and observing if an escape focus occurs and its stability; Level of Evidence C;

- Assess whether there is a risk of electromagnetic interference during the surgical procedure planned; Level of Evidence B;

- Evaluate the possibility of interaction between the anesthetic technique, anesthesia equipment and drugs to be used during the procedure and the patient with pacemaker or defibrillator; Level of Evidence C.

###### Degree of Recommendation IIa, Level of Evidence C

- Determine the function of the pacemaker with an assessment by an expert to adjust the set up; if an expert is not available, at least check if there is effective pacemaker pacing artifact (that generates pacing) in the ECG and contact the manufacturer of the prosthesis about additional recommendations;

- Advise the surgical team to use the bipolar or ultrasonic electrocautery when possible;

- Discontinue the antitachycardia therapies according to the possibility in each case.

###### Degree of Recommendation IIb, Level of Evidence C

- Assess whether reprogramming the pacemaker to asynchronous mode and disabling the sensor frequency is advantageous to the procedure.

##### B. Intraoperative Period

###### Degree of Recommendation I, Level of Evidence C

- Equipment for temporary artificial cardiac stimulation and defibrillation must be available in the surgery room for immediate use;

- All patients must be monitored by continuous ECG and plethysmography (or auscultation, pulse palpation or ultrasound) regardless of the type of anesthesia;

- Electrocautery: follow the recommendations listed in item I.3;

- Radio frequency ablation: place the grounding pads far from the generator and leads and do not allow the ablation catheter to touch the pacemaker's leads;

- Cardioversion or defibrillation: follow the recommendations listed in item III;

- Radiotherapy – follow the guidelines outlined in item VI.

###### Degree of Recommendation IIa, Level of Evidence C

- Lithotripsy – follow the guidelines outlined in item VI;

- MRI - follow the recommendations listed in item V.

##### C. Postoperative Period<sup>103,104</sup>

###### Degree of Recommendation I, Level of Evidence C

- Heart rate and rhythm must be continuously monitored during the postoperative period;

- Cardioversion/defibrillation equipment and resources for cardiac stimulation must be available;

- If the functions of the pacemaker were changed for surgery, reprogram it back to its usual settings as soon as possible;

- The antiarrhythmic medications that were being used before surgery should be resumed as soon as possible.

### 4.8. Transplants

#### 4.8.1. Liver

Since its introduction in clinical practice, liver transplantation has become the surgery of choice for terminal liver diseases. In recent decades, both the surgical technique and clinical management of these patients' immunosuppression have progressed much. Morbidity due to immunosuppressive regimens has also been drastically reduced, allowing for increasing survival rates and better quality of life.

However, after the introduction of the MELD score as a criterion for prioritization in the transplant waiting list, more severe patients and those with more comorbidities were prioritized for indication and performance of surgery<sup>105,106</sup>. Also, the indication for transplantation in patients older than 50 years has been increasingly frequent<sup>107-109</sup>, and with increasing life expectancy, these patients tend to develop or complicate coronary artery disease more often than the population the same age and sex<sup>108,110,111</sup>.

Prior to transplantation, the presence of risk factors such as diabetes, smoking, peripheral vascular disease, age, obesity, and etiology of the liver disease, can not only lead to increased prevalence of coronary disease, but also compromise the ventricular function regardless of coronary disease, for example, the coexistence of cardiomyopathy due to chronic alcoholism or hemochromatosis<sup>112-114</sup>.

The major hemodynamic changes caused by hepatectomy, graft reperfusion phenomena, bleeding and, metabolic, electrolyte and acid-base abnormalities may trigger previously asymptomatic myocardial ischemia<sup>115,116</sup>. Before surgery, some patients undergo passage of transjugular intrahepatic portosystemic shunt (TIPS), resulting in increased venous flow and ventricular hypertrophy, which may cause pulmonary edema and decompensation during the perioperative period<sup>106</sup>.

In general, candidates for liver transplantation should be carefully evaluated, similarly to what happens to other patients undergoing major surgery. However, there is great difficulty in standardizing the preoperative evaluation of these patients, mainly because of the heterogeneity of this group. Usually electrocardiogram and chest X-ray are included in the preoperative routine of these patients. In almost 50% of the patients, the QT interval is extended, it tends to improve with the use of beta-blockers, but no specific therapy has proven beneficial<sup>106,117</sup>.

The echocardiogram is also part of the routine of most groups, not only in order to assess ventricular function and possible structural defects, but also to detect pulmonary hypertension, which has higher prevalence in the cirrhotic patients and can be a contraindication to transplantation<sup>118-121</sup>. However, in spite of the fact that echocardiography has a high sensitivity for detection of pulmonary hypertension in cirrhotic patients, its specificity is reduced in such cases. Therefore, in patients whose echocardiography suggests high pressure in the pulmonary artery (SPAP > 40 mmHg or 50), it is indispensable to perform right heart catheterization with pressure measurements directly from the pulmonary artery<sup>120,121</sup>.

Ischemia tests (myocardial scintigraphy and dobutamine echocardiography) have proven to be useful in several studies to assess the candidate for liver transplantation<sup>117,122-124</sup>. When associated with physical exercise protocols, both tests have similar sensitivity and specificity. When associated with pharmacological stimulation with dobutamine, the scintigraphy is more sensitive and less specific compared to the echocardiography; both tests show better performance to induce ischemia when performed with dobutamine in comparison with dipyridamole or adenosine. The most valuable information provided by these tests, however, is because of their high negative predictive value<sup>117</sup>. The recommendations of these tests in the preoperative period of liver transplantation follow the usual recommendations.

The presence of severe coronary disease, advanced valvular disease, moderate to severe ventricular dysfunction, or any other heart disease that causes a high risk of myocardial infarction, severe arrhythmias, sudden death or heart failure in the perioperative period continues to be contraindications for liver transplantation<sup>115,116,125</sup>.

Recommendations for additional tests in the preoperative period of liver transplantation:

#### Degree of Recommendation I

- Request ECG and chest X-ray routinely for all patients; Level of Evidence C;
- Request transthoracic echocardiography for all patients; for patients with SPAP higher than 40 mmHg, further evaluation with hemodynamic measurements. Level of Evidence B.

#### 4.8.2. Kidney

Patients with chronic kidney disease compose one of the groups with the highest cardiovascular risk, with mortality rates for cardiovascular disease 10 to 50 times higher than those found in the general population<sup>126</sup>. Cardiovascular disease is the leading cause of death after renal transplantation, especially due to coronary artery disease<sup>127</sup>. In the first 30 days after successful renal transplantation, approximately half of the deaths occur due to cardiovascular disease secondary to acute myocardial infarction<sup>128</sup>. On the other hand, in the late follow-up, chronic ischemic heart disease<sup>127</sup> is responsible for more than one third of the deaths in patients with functioning grafts. Thus, during the preoperative evaluation of renal transplant candidates, the identification of the presence and extent of coronary artery disease is crucial because it enables the medical team to establish more precisely the risk/benefit of transplantation, potential need for coronary intervention in the preoperative period, use of cardioprotective measures in the perioperative period, and control of risk factors in the postoperative period.

The identification of significant coronary artery disease, in turn, is a huge challenge in renal transplant candidates who are asymptomatic or mildly symptomatic. The purpose of this section is to provide cardiologists with the most appropriate means to determine the cardiovascular risk in a very special population of patients usually excluded from studies establishing operative risk. The main role is to specifically



identify among renal transplant candidates those most likely to have a diagnosis of coronary artery disease. Thus, it is directed to asymptomatic patients or patients with symptoms about which there are doubts about the fact that they are related to coronary artery disease; for those individuals with clinical evidence and/or findings from diagnostic testing suggestive of coronary disease, further investigation and treatment should follow the rules proposed for the general population.

The application of noninvasive methods such as exercise electrocardiography, myocardial perfusion scintigraphy, and pharmacological stress echocardiography, all routinely used in the general population, shows lower sensitivity and specificity rates than in subjects with normal renal function, providing a large number of false-negative results<sup>129,130</sup>. On the other hand, the indiscriminate use of invasive investigation by means of coronary angiography is not justified because it is a high cost, non-invasive method with risk of complications; in addition, the prevalence of significant coronary artery disease in patients indiscriminately evaluated by invasive methods is less 50%<sup>131,132</sup>. Therefore, it is necessary to determine a strategy that allows tracking those patients with a higher chance of having significant CAD and who should thus be referred for angiography; by doing so we would be able to reduce the number of patients improperly classified as having low cardiovascular risk because of failure in the preoperative risk stratification and hence being exposed to greater risk of cardiovascular events.

#### Risk Stratification for the Presence of Coronary Artery Disease

The clinical parameters most strongly associated with post-transplant ischemic disease are age > 50 years, diabetes mellitus and prior evidence of cardiovascular disease (history and/or findings from tests)<sup>133</sup>. The prevalence of significant CAD (stenosis  $\geq$  70%) increases with the number of risk factors present<sup>134</sup>. These three risk factors have been the basis to formulate investigation algorithms of coronary heart disease in patients with chronic kidney disease for several Medical Societies<sup>133,135</sup> and based also on a national study<sup>134</sup>.

Based on the results of existing studies<sup>134-138</sup>, we propose the following risk stratification of asymptomatic patients with chronic renal failure from a cardiovascular standpoint being evaluated for kidney transplantation according to the presence or absence of three risk factors mentioned above:

##### Degree of Recommendation I

- Patients with no risk factors are considered at low cardiovascular risk, with no indication for further investigation. Level of Evidence C.

##### Degree of Recommendation IIa

- Patients who have only one of the risk factors are considered to be at intermediate cardiovascular risk and should undergo noninvasive stratification. In case of a positive result, perform further research on invasive coronary angiography, and in case of a negative, do the transplant. Level of Evidence C;

- Patients who have at least two risk factors are considered to be at high cardiovascular risk and should undergo invasive test before transplantation. Level of Evidence C.

## 4.9. Heart Disease and Pregnancy

Non-obstetric surgical procedures should be avoided during pregnancy because they are associated with higher maternal morbidity and obstetric and fetal risks. It is estimated that rates of non-obstetric surgeries do not to exceed 0.75% of pregnancies and the indication is due to acute complications or worsening of a disease refractory to clinical treatment.

During pregnancy, the physiological changes<sup>139</sup> shown below take place and they should be investigated in the preoperative period of pregnant women with heart disease because they cause higher maternal risk and promote differentiation of surgical and anesthetic strategies to be taken in the perioperative period.

- Progressive increase in cardiac output of 50% starting at the first quarter peaking at 32 weeks of gestation and an increase of 30% during labor and postpartum;
- Physiologic anemia of pregnancy starting at the second quarter due to hemodilution;
- Increased glomerular filtration rate;
- Activation of coagulation factors (II, VII, IX, X) which result in hypercoagulable state;
- Reduction of venous return by 30% due to compression of the inferior vena cava by the gravid uterus starting at 20 weeks of gestation;
- Anatomic variations of the airways and hyperventilation due to compression of the diaphragm and chest compressed by the gravid uterus;
- Gastroesophageal sphincter incompetence, delayed gastric and bile ducts emptying.

The most frequent indications for non-obstetric surgery are: acute appendicitis (1/1500 births), cholelithiasis (0.5/1,000 pregnancies), diseases of the ovaries (1/1300 pregnancies), trauma, breast disease, cervical intraepithelial neoplasia and bowel obstruction (1/1500-3500 births)<sup>140</sup>.

### 4.9.1. Maternal Risks

Depending on the mother's type of heart disease and clinical condition. Emergency surgeries are always associated with increased maternal-fetal mortality. In Brazil, rheumatic valve disease predominates in 55% of pregnant women followed by congenital heart defects in 22% of the cases<sup>141</sup>. The clinical markers of maternal perioperative prognosis are pulmonary congestion, ventricular dysfunction, pulmonary hypertension, and cyanosis. Hypercoagulable state, venous stasis of the uterine plexus and lower limbs associated with heart disease increase the risk of postoperative thromboembolism. Subcutaneous or intravenous heparin is the elective anticoagulant in pregnancy to prevent thromboembolism because it does not penetrate the placenta<sup>142</sup>.

### 4.9.2. Obstetric Risks

Spontaneous abortion, hemorrhage, infection, labor and preterm delivery. These complications can be minimized if surgery is elective and performed during the second quarter of pregnancy. The cesarean section is performed for obstetric

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indications. In abdominal surgery, the recent incision does not prevent the second stage of labor.

### 4.9.3. Fetal Risks

Depend on the gestational age and the mother's clinical condition. Preterm birth rates are higher when the surgery is performed in the third quarter of pregnancy reaching 9% of the cases. The rates of newborns small for gestational age because of preterm birth or restriction of intrauterine growth are higher than the population of pregnant women who do not undergo surgery; therefore, the use of steroids when the procedure is performed between 24 and 34 weeks is recommended to reduce perinatal morbidity and mortality resulting from prematurity.

Classically, heart rate and variability of the fetal heartbeat suffer a significant reduction during induction of general anesthesia; however, adequate oxygenation and maintenance of maternal uterine perfusion promote good fetal tolerance to surgery and anesthesia.

### 4.9.4. Considerations Regarding Anesthesia

The regional technique is preferred during pregnancy; general anesthesia has been indicated for patients with ventricular dysfunction, pulmonary hypertension, cyanosis, and severe valvular or intracavitary obstructive lesions, considering that the more modern inhalation agents are not teratogenic. Pregnant women are more sensitive to hypoxia because they have increased baseline metabolism and reduced functional residual capacity. The association with heart disease aggravates this hypoxia that develops more sharply during the anesthesia induction of apnea. Another area of concern is the control of hypotension resulting from regional anesthesia characterized by peripheral sequestration of blood that can be aggravated by the supine position leading to low cardiac output and placental hypoperfusion. One of the strategies used by anesthesiologists is hydration during surgery; however, this approach is risky in pregnant women with heart disease because of the risk of pulmonary congestion after surgery. Potent inhalation agents like halothane, isoflurane, and enflurane reduce uterine flow and inhibit labor. When there is bradycardia, tachycardia or repeated accelerations of fetal heartbeat, the anesthesiologist should optimize uteroplacental oxygenation and make sure that there is no compression of the inferior vena cava, maintaining maternal normocarbica, correcting hypovolemia and increasing the concentration of inhaled oxygen.

### Laparoscopic Surgery<sup>143</sup>

It has been avoided during pregnancy because of the following risks: 1) fetal hypoxia caused by reduction in the uteroplacental blood flow resulting from increased intra-abdominal pressure; 2) fetal acidosis caused by absorption of carbon dioxide; and 3) mechanical trauma of the fetus that can be harmed either directly or indirectly due to uterine perforation by trocar catheter or Veres needle. Therefore, laparoscopic surgery has been limited to selected cases and should be performed on during the first and second quarters of pregnancy.

### 4.9.5. Safety for Additional Tests in the Preoperative Period of Pregnant Patient with Heart Disease<sup>144</sup>

#### Degree of Recommendation I, Level of Evidence C

- Resting or dynamic ECG and Doppler echocardiography do not pose any risk for mother or fetus;
- Chest X-ray can be used;
- Myocardial scintigraphy is not advised (exposure to radiation); Gallium-97 scintigraphy is contraindicated;
- Coronary cineangiography can be performed using abdominal protection;
- Nuclear magnetic resonance is not contraindicated during pregnancy.

### 4.9.6. General Recommendations for Non-obstetric and Non-cardiac Surgery in Pregnant Women with Heart Disease

#### Degree of Recommendation I, Level of Evidence C

- Surgery should preferably be done between 13 and 24 weeks of gestation according to the following recommendations:
  - Intra- and postoperative continuous fetal monitoring using cardiotocography or Doppler ultrasound in pregnancy with viable fetuses (> 24 weeks);
  - Intraoperative maneuver for the deviation of the uterus to the left with the aid of a pad under the right flank in pregnancies after 20 weeks;
  - Prophylactic therapy with corticosteroids in the preoperative period for pregnant women between 24 and 34 weeks;
  - Presence of the team of obstetricians and neonatologists for possible emergency cesarean section (> 24 weeks);
  - Reduced manipulation of the uterus to prevent uterine contraction;
  - Tocolytic prophylaxis in the intra- and postoperative period with use of progesterone (250 mg/day/vaginal) should be decided by the obstetric team;
  - Prophylaxis with metoclopramide and H2 antagonists for gastric protection; Opioids and antiemetic drugs; Prevention of adynamic ileus;
  - Effective analgesia and sedation for pain relief and anxiety;
  - Preoxygenation at 100% using oxygen mask during 3-5 minutes before induction for effective oxygenation;
  - Extreme hyper- and hypoventilation cause reduction in the placental flow and maternal-fetal hypoxia;
  - Solid food fasting for at least 8 hours before surgery;
  - Crystalloid solution during surgery can cause acute pulmonary edema in the postoperative period;
  - Solutions containing glucose should be avoided when delivery is imminent to reduce the risk of neonatal hypoglycemia;
  - Foley catheter to prevent build up of urine in the bladder;
  - Maintenance of routine cardiovascular medication and antibiotics;
  - Early ambulation can cause preterm birth;

- Subcutaneous or intravenous heparin should be the anticoagulant of choice in conventional doses;
- Non-steroid anti-inflammatory drugs should be avoided because they may cause premature closure of the ductus arteriosus (> 32 weeks);
- Converting enzyme inhibitors and angiotensin I blockers are contraindicated.

#### 4.10. Dental Procedures

The preparation of dental procedures in cardiac patients is not solely based on the use of antibiotic prophylaxis, vasoconstrictors and/or control bleeding after surgery. The presence of foci of infection in the oral cavity may represent a factor of postoperative complication. The incidence odontogenic bacteremia increases significantly in the presence of infective foci such as periodontal disease and endodontic lesions.

Although the occurrence of bacteremias is commonly reported during the performance of dental procedures, they can be caused even by simple actions, such as toothbrushing and chewing<sup>145</sup>. Therefore, dental assessment with elimination of infective foci and intensive control of oral hygiene of in-patients is advisable whenever possible before surgical procedures in patients with or without heart disease in order to reduce perioperative complications (Degree of Recommendation IIa; Level of Evidence A).

##### 4.10.1. Use of Local Anesthetics: to use or not to use Local Vasoconstrictors

There is controversy regarding the use of local anesthetics with vasoconstrictors in heart disease patients. Local anesthetics with vasoconstrictors increase the quality and duration of analgesia and reduce bleeding<sup>146</sup>. Local anesthetics without vasoconstrictors last very little, are rapidly absorbed (high toxic potential), do not kill pain adequately, which may lead to hemodynamic changes and even cardiac arrhythmias, and promote slight vasodilation, which, in turn, increases bleeding.

Lidocaine with epinephrine is the most common local anesthetic used worldwide<sup>146</sup>. Although the interaction of epinephrine and beta blockers, tricyclic antidepressants, diuretics and cocaine is reported in the literature, the use of 2 to 3 tubes of 2% lidocaine with 1:100,000 epinephrine (36-54 mg of epinephrine) seems to be well tolerated in most patients, including in individuals with hypertension or other cardiovascular diseases, and the use of epinephrine appears to have more benefits than risks<sup>146</sup>.

##### Degree of Recommendation I, Level of Evidence C

- In cardiac patients, the use of small amounts of local anesthetics with vasoconstrictor for dental procedures is safe and should be used preferentially.

##### 4.10.2. Dental Procedures in Patients Using Antithrombotic Drugs (Aspirin, Clopidogrel, Heparin, Oral Anticoagulants)

During antithrombotic therapy, dental procedures may be performed by following a few precautions<sup>147</sup>:

##### Degree of Recommendation I

- INR control at least 24 hours before the dental procedure. Level of Evidence C;
- Patients with INR < 3.0 do not have to discontinue oral anticoagulation therapy before simple surgeries (extraction of ≤ 3 teeth, gingival surgery, periodontal scaling). When the INR ≥ 3.0 and the planned procedures are more extensive, discuss with the physician in charge. Level of Evidence C;
- Do not discontinue use of aspirin for dental procedures. Level of Evidence B.

##### 4.10.3. Specific Considerations for Dentists

Some precautions and measures can be adopted to reduce bleeding in patients on antithrombotic drugs:

##### Degree of Recommendation I, Level of Evidence C.

###### Preoperative Care

- Assess the patient's complete medical history;
- Measure the INR 24 hours before the dental procedure. In patients with stable INR control, evaluation 72 hours before the procedure is acceptable.

###### Intraoperative Care

- Minimize surgical trauma;
- Schedule larger number of visits when there is extraction of more than three teeth;
- Reduce areas of periodontal surgery and scaling and root planning (per quadrant);
- Plan the surgeries earlier in the day and in the beginning of the week.

###### Control of Postoperative Bleeding

- Removal of nonabsorbable suture after 4-7 days;
- Compression with gauze for 15-30 minutes after the surgical procedure;

Use of coagulating agents: gelatin sponge, oxidized regenerated cellulose, synthetic collagen, tranexamic acid mouthwash in 4.8% aqueous solution during and 7 days after the surgery, using 10 ml, 4 times a day for 2 minutes or mouthwash with ε-aminocaproic acid (when possible);

- Appropriate sutures to close wounds.

##### 4.10.4. Associated Use of Antibiotics and Anticoagulants

The antibiotics commonly used for prophylaxis of infective endocarditis (amoxicillin, erythromycin) in dental procedures may interfere with the metabolism of oral anticoagulants. Patients using anticoagulants should be advised about the possibility of increased bleeding and should control the INR, if necessary. There is no need to change the anticoagulation regimen when a single dose of prophylactic antibiotic is used.

##### 4.10.5. General Recommendations

##### Degree of Recommendation I, Level of Evidence C

- Cardiac patients on optimal medication can safely undergo dental procedure safely with usual routine precautions;

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- Individuals using pacemakers and automatic implantable cardiac defibrillators are not affected by high or low rotation speed drills, amalgam mixer, electrical pulp testing, laser, electric toothbrushes, endodontic ultrasound, periodontal ultrasound, and radiography. The use of electrocautery has specific guidelines (see item 4G).

### 4.11. Aortic Surgery

Patients with abdominal aortic aneurysm (AAA) have a high prevalence of coronary artery disease and other comorbidities that contribute to a high-risk surgery, and acute myocardial infarction is the leading cause of postoperative mortality, responsible for up to 40% of deaths<sup>148</sup>.

Endovascular surgeries have started to be performed in the 1990s<sup>149</sup> and were initially developed for high-risk patients with unfavorable prognosis for open surgery. Because of the technical evolution of stents and surgery, currently its use is much widespread. It is considered a minimally invasive procedure, with less blood loss, less hemodynamic instability and cardiac stress, leading to reduced length of stay in ICU and shorter hospital stay<sup>150</sup>. It is also associated with lower incidence of perioperative cardiac complications such as arrhythmias, troponin elevation, myocardial ischemia, acute myocardial infarction, and overall mortality<sup>151-153</sup>. Thus, in the most recent guidelines on Perioperative Evaluation of the AHA/ACC, endovascular repair of aortic aneurysm was considered a moderate-risk surgical procedure, whereas the aortic open surgery is considered a high-risk procedure<sup>21</sup>.

Two important randomized studies have compared the two surgical techniques for treatment of abdominal aortic aneurysm: endovascular x open surgery in patients with adequate clinical conditions for the two proposed surgical procedures. The two studies, EVAR trial 1<sup>154</sup> and DREAM trial<sup>154,155</sup>, showed similar results: the 30-day mortality rate was lower in the endovascular group. The EVAR 1 trial showed a 30-day mortality of 1.7% for endovascular repair compared with 4.7% for open surgery<sup>154</sup>, and the DREAM trial showed a mortality rate of 1.2% for endovascular repair and 4.6% for open surgery<sup>155</sup>. Based on these two studies, it is possible to conclude that endovascular repair of abdominal aortic aneurysm may be preferable to conventional surgery because it presents a low perioperative mortality.

However, in the patients' medium-term follow-up, there was no difference in the mortality rate between the two groups. The perioperative survival advantage of endovascular repair was not maintained during the follow-up period and it is associated with increased need for reinterventions and related to higher cost<sup>156,157</sup>. In the EVAR trial 1, there was only a significant reduction in the mortality rate related to aneurysm in the endovascular group (4% vs. 7%,  $p = 0.04$ )<sup>156</sup>.

In patients at high surgical risk and with unfavorable prognosis for open surgical approach, endovascular repair may be a good alternative for the treatment of AAA. Two studies have tried to assess the results of percutaneous treatment in patients with this clinical profile. In the EVAR 2 trial<sup>158</sup>, high-risk patients (age > 60 years, aneurysm with diameter > 5.5 cm, and at least one comorbidity – cardiac, pulmonary or renal) were randomized to endovascular

treatment or conservative medical treatment. The 30-day mortality rate of patients undergoing endovascular procedure was 9%, similar to that of the group patients receiving clinical treatment. The main criticism of this study is that the high mortality rate in the intervention arm can be attributed to the long time between randomization and intervention, 52% of deaths in this group occur in the preoperative period. In another study, a retrospective analysis of data compiled from studies evaluating the efficacy of endovascular stenting versus conventional surgery for repair of aortic aneurysm<sup>159</sup>, high-risk patients undergoing repair of aortic aneurysm showed 30-day mortality rate of 2.9% for the endovascular group and 5.1% for the open surgery; these rates are much lower compared with the results of the EVAR 2 trial.

Recently, long-term clinical follow-up studies of the EVAR 1 and 2 trials have been published<sup>160,161</sup>. In the long-term follow-up of the EVAR 1 trial<sup>160</sup>, with median of follow-up of 6 years (minimum 5 and maximum 10 years), the benefit of lower perioperative mortality in the endovascular group was not sustained, as already observed in the results of analysis of medium-term studies<sup>156</sup>. There was no difference in mortality between the two groups at the end of the follow-up period (hazard ratio 1.03, 95%CI 0.86~1.23,  $p = 0.72$ ). However, the endovascular group had higher rates of complications and needed re-intervention related to the stent, which substantially increased hospital costs<sup>160</sup>.

In the follow-up of the EVAR 2 trial<sup>161</sup>, with median of follow-up of 3.1 years (minimum 5 and maximum 10 years), the 30-day mortality rate in the endovascular group was 7.3% and the aneurysm rupture rate in the group without intervention was 12.4/100 people per year. At the end of the follow-up study, aneurysm-related mortality was lower in the group treated with endovascular stent (hazard ratio 0.53, 95%CI 0.32 to 0.89,  $p = 0.02$ ), but there was no difference in the overall mortality rates between the two groups. About 48% of the patients treated with endovascular stent had stent-related complications and the costs were much higher in the endovascular group compared with the conservative group<sup>161</sup>.

The results of these two studies corroborate the findings of the observational cohort study matched by propensity score using U.S. Medicare data<sup>153</sup>. In the comparative analysis of 45,660 patients undergoing AAA repair via open surgery or endovascular surgery, 22,830 in each group, endovascular repair showed better results in the perioperative period compared with the open surgery group. The authors found lower perioperative mortality (1.2% vs. 4.8%,  $p < 0.001$ ), less acute myocardial infarction (7.0% vs. 9.4%,  $p < 0.001$ ), and shorter hospital stay ( $3.4 \pm 4.7$  x  $9.3 \pm 8.1$ ,  $p < 0.001$ ) in the endovascular group. However, these advantages of the endovascular technique remained for three years of follow-up after surgery and, after this period, survival was similar in both groups. Starting at the fourth year of follow-up, the stent rupture rate was 3 times higher in the endovascular group (1.8% vs. 0.5%,  $p < 0.001$ ), as well as the need for re-intervention (9% endovascular vs. 1.7% open surgery,  $p < 0.001$ )<sup>153</sup>.

In conclusion, evidence from existing studies suggests that the technique of endovascular repair of AAA can be a good alternative to conventional open approach surgery for



high-risk patients because of the lower perioperative mortality. However, endovascular repair is associated with higher rates of stent-related complications in the long-term, with greater need for re-interventions, while the conventional open surgery is associated with higher rate of laparotomies and abdominal surgery, with no difference in the mortality rate between the two surgical techniques in the late follow-up. It is also important to bear in mind that often the anatomy and/or location of an aneurysm does not allow percutaneous repair. Thus, the choice of the surgical technique must be defined by the surgical team, taking into account the anatomical variables of the aneurysm, the patient's clinical and surgical risk variables and the patient's choice.

Recommendation:

#### **Degree of Recommendation IIa, Level of Evidence A**

- In patients considered to be at high surgical risk and with anatomy conducive to percutaneous treatment, endovascular repair of aortic aneurysm is preferable to open surgery because of lower perioperative mortality.

## 5. Considerations for High-risk Patients

### 5.1. When the Cardiovascular Risk is Very High – to Operate or not to Operate?

Contraindication for noncardiac surgical intervention was not part of the list of duties of the physician performing the perioperative evaluation. However, a further reflection on this issue along with the referral of more severe patients for surgical interventions made it necessary to include this topic in the current Guidelines<sup>162</sup>. Sometimes the perioperative evaluation concludes that the risk of complications is high and most often related to cardiovascular complications such as myocardial infarction and stroke. These situations are abrupt, and the short-term impact on patients' survival is generally independent of the prognosis of the underlying disease that caused the indication for surgery. Thus it is important to know the prognosis of the underlying disease particularly for patients at high risk of cardiovascular complications in the perioperative environment. This information should be requested from the surgeon who requested the evaluation (Degree of Recommendation I, Level of Evidence C). A careful analysis of the high risk of cardiovascular complications compared with the prognosis of the underlying disease may represent a contraindication to perform the surgery.

Recommendations for contraindication of noncardiac surgery:

#### **Degree of Recommendation IIa, Level of Evidence C**

- Situations where there are objective information that the risk of serious cardiovascular complications such as cardiac death, nonfatal myocardial infarction, and stroke is higher than the risk of death from the underlying disease.

### 5.2. Choosing the Hospital

In special situations, the perioperative evaluation should include a reflection on the health facility where the surgery will be performed. Whereas the perioperative analysis involves

not only the patient's condition and the surgery performed, but also the hospital care to be offered, it is important to include some considerations about it in these Guidelines. According to this point of view, based on the wide variation in the death rate among U.S. hospitals, Chaferi et al. assessed the complication and mortality rates in patients after major perioperative complications<sup>163</sup>. Data were obtained from the records of the National Surgical Quality Improvement Program. This database has 186 participating centers and more than 130 surgical variables involved. The study included 84,730 patients undergoing general and vascular surgery with expected mortality rate higher than 1%. The primary objectives were to assess the complication and mortality rates among patients with major complications. Major complications were: deep infections, renal failure requiring dialysis, postoperative bleeding requiring transfusion, myocardial infarction, pneumonia, pulmonary embolism, stroke, unplanned intubation, dehiscence, prolonged mechanical ventilation, septic shock, and loss of vascular grafts. Hospitals were categorized into five strata according to the previously known rate of perioperative mortality. Hospitals with very low mortality rate (3.5%) were allocated to the first quintile, and those with very high rate (6.9%) were in the lowest quintile. The types of procedures performed by hospitals were similar. Although the complication rate did not differ among the hospitals, the mortality rate after major complications was much higher in hospitals initially categorized as having very high mortality rate. In these hospitals, the probability of death after a major complication was almost twice that in hospitals with a very low mortality rate.

Based on these results, it is possible to conclude that the mortality rate in this population was not correlated with the frequency of complications, since their occurrence was similar among the hospitals studied. The authors suggest that failure to promptly recognize and treat the complication may be related to the increased mortality rate. That is, considering two types of hospitals, the delay in recognizing pneumonia, evolution to septic shock and late introduction of antibiotics and hemodynamic support could explain the higher mortality rate, although in both types of hospitals the rate of pneumonia was the same. The authors argue that the efficiency in recognizing and treating depends on a team with an effective communication system.

Other studies have already shown lower perioperative mortality in hospitals with more nurses per bed and in ICUs with daily visits of expert intensivists, which reflect effective systems of communication and probably higher probability of prompt recognition of complications<sup>164-166</sup>. Thus, these studies demonstrate the possibility that a hospital with a cohesive multidisciplinary team focused on early diagnosis and treatment of complications has a positive influence on postoperative results<sup>164-166</sup>. Additionally, there is evidence that hospitals with higher volume of procedures have lower perioperative mortality than hospitals with lower volume of surgeries, even after adjusting for other variables<sup>167</sup>. However, the relative importance of the volume of surgeries varies according to type of procedure, and procedures that require longer hospital stays and more postoperative care possibly suffer greater influence from the volume of surgeries<sup>168</sup>.

In conclusion, in the evaluation of surgical risk, it is also imperative consider the variables related to the health institution where the procedure will be performed with the purpose of providing broader guidance to our patients. It is quite possible that many, albeit empirically, already have some degree of knowledge on key local institutions. However, we are not sure on how accurate this assessment is. It is therefore important to conduct a survey to prepare a national registry of surgical procedures including variables such as complication rates, length of stay, comorbidities, and mortality.

## 6. Steps to Reduce Surgical Risk

### 6.1. Perioperative Medical Therapy

#### 6.1.1. Beta-blockers

Although beta-blockers are an important tool in clinical management and reduction of perioperative cardiac risk, currently they are focus of great controversy because of recent and seemingly conflicting evidence. Pioneering prospective and randomized studies conducted in the 1990s have suggested that perioperative use of beta-blockers could reduce cardiovascular mortality and morbidity in a wide spectrum of patients: from those with only risk factors for cardiovascular disease, even if low perioperative risk<sup>169</sup>, to those at high risk of events because they show evidence of myocardial ischemia on functional test and are candidates for vascular surgeries<sup>170</sup>. In 2001, the same group that demonstrated the benefits of beta-blockade in high risk patients with vascular diseases, also showed benefit for intermediate-risk patients in the perioperative period of vascular surgery<sup>171</sup>. However, between 2005 and 2006, three randomized trials have not confirmed the protective effect of perioperative beta-blockade in vascular patients with low or intermediate risk, highlighting potential harm because of the association with increased incidence of bradycardia and hypotension<sup>172-174</sup>. The benefit of beta-blockers was then also questioned in meta-analyses<sup>175,176</sup>. Currently, the largest retrospective study on perioperative beta-blockers, which analyzed more than 780,000 patients undergoing noncardiac surgery, showed that the impact of beta-blockers depended on the estimation of cardiac risk; i.e., in patients at high risk beta-blockers were associated with lower mortality, on the other hand, in low-risk patients there was no benefit and even a harmful effect. For intermediate-risk patients, there was a trend to benefit<sup>177</sup>. Finally, in 2008, the POISE study, which randomized 8,351 patients, mostly at intermediate risk, to receive placebo or metoprolol succinate, beginning 2-4hs before noncardiac surgery at doses up to 400 mg within the first 24 hours, found less incidence of myocardial infarction, reversed cardiac arrest and cardiac mortality in the beta-blocked group (5.8% vs. 6.9%,  $p = 0.03$ ), but at the expense of doubled incidence of stroke and increased overall mortality in this group (3.1% vs. 2.3%,  $p = 0.03$ ). The high incidence of hypotension (15%) and bradycardia (6.6%) was strongly associated with higher mortality and stroke<sup>178</sup>.

On the other hand, recently, another prospective randomized study designed to assess the impact of bisoprolol and fluvastatin in the perioperative period of nonvascular surgery in intermediate-risk patients, has shown great benefit

of beta-blockade, with a lower incidence of perioperative myocardial infarction and cardiac death in 533 patients who received bisoprolol: 2.1% vs. 6.0%,  $p = 0.002$ <sup>179</sup>.

A careful analysis of these data shows great heterogeneity among the studies, especially with regard to the dosage of beta-blocker use: dosages and timing. There are studies that initiated the beta-blocker few hours before the surgery, without enough time to titration to reach doses that could provide adequate control of heart rate<sup>172-174</sup> and in which some patients continued to receive beta-blockers despite showing bradycardia and/or hypotension, and, especially, with no time for hemodynamic adaptation and thus reduction of side effects<sup>178</sup>. On the other hand, there are studies that initiated the beta-blockers earlier, at least one week before surgery, with the purpose of performing titration until reaching adequate dosage<sup>170,171,179</sup>; these studies showed benefit.

In 2008, before the publication of the POISE study, an interesting study reviewed data from two major meta-analyses previously cited<sup>175,176</sup> based on the control of heart rate achieved in each study included in the meta-analyses. When the authors divided the data into two groups: the group that achieved strict control of heart rate and the group that did not reach it, the authors found that beta-blockers provided protection in the first group and did not change the outcome in the second group. It is worth mentioning that this study also demonstrated that beta-blockers in the perioperative period are associated with higher incidence of bradycardia<sup>180</sup>.

Thus, after evaluating the specific indications, the use of perioperative beta-blockade should always respect two principles:

**Safety:** The time of beginning medication should be as early as possible so that there is enough time to evaluate the hemodynamic response of each patient, avoiding bradycardia and hypotension. Low doses should be prescribed with gradual titration up to obtain heart rate (HR) between 55 to 65 bpm without hypotension (systolic blood pressure > 100mmHg). Medication must be administered for 30 days after surgery. Throughout the perioperative period there should be frequent monitoring of HR and blood pressure (BP). If HR < 50bpm or systolic BP < 100mmHg, beta-blockers should be temporarily discontinued until reaching hemodynamic and chronotropic balance.

**Effectiveness:** The benefit of beta-blockers is associated with heart rate control, thus the target should be HR 55-65 bpm in the preoperative and postoperative periods.

Finally, it is important to keep in mind that beta-blockers should not be discontinued in the perioperative period in patients who use them chronically for different indications. The acute discontinuation of beta-blockers is associated with significant increase in postoperative mortality<sup>181</sup>.

Recommendations for perioperative beta-blocker use:

#### Degree of Recommendation I

- Candidates for arterial vascular surgeries with symptomatic myocardial ischemia or myocardial ischemia on functional test; Level of Evidence B;

- Candidates for nonvascular surgeries with symptomatic myocardial ischemia or myocardial ischemia on functional test; Level of Evidence C;

- Patients already receiving beta-blockers chronically should keep using them throughout the perioperative period; Level of Evidence B.

#### Degree of Recommendation IIa

- Candidates for vascular surgeries with intermediate cardiac risk; Level of Evidence B.

#### Degree of Recommendation IIb

- Candidates for nonvascular surgeries with intermediate cardiac risk; Level of Evidence B.

#### Degree of Recommendation III

- Patients with contraindication to beta-blockers; Level of Evidence B.

### 6.1.2. Statins

The use of statins for prevention of cardiovascular events after vascular operations is well established, being based on prospective, randomized, placebo-controlled studies. In 2004, the first randomized study including 100 patients was published. The authors demonstrated that the use of 20 mg of atorvastatin was associated with significant decrease in major cardiovascular events (death, acute myocardial infarction, stroke, unstable angina) in the perioperative period and after 6 months of follow-up. This effect was independent of baseline cholesterol levels and was complementary to the benefit resulting from the use of beta-blockers (similar in both groups)<sup>182</sup>.

Recently, it has been shown that the use of 80 mg of slow-release fluvastatin in 250 patients undergoing vascular surgeries reduced the occurrence of postoperative myocardial ischemia and the combined outcome of myocardial infarction and cardiac death within 30 days, compared with the placebo group (247 patients)<sup>183</sup>. The introduction of atorvastatin 20 mg (40 mg or simvastatin) in patients undergoing vascular surgeries should be done preferably two weeks before the procedure and continued for 30 days. After this time, the dose should be adjusted to the LDL goal of each individual patient.

Discontinuation of perioperative statin in patients with chronic use of this medication is an independent predictor of cardiovascular events after vascular surgeries<sup>184</sup>. Therefore, statin should be maintained throughout the perioperative period. The use of statins in the perioperative period is safe. Although patients using statins have a higher baseline CPK level, the occurrence of elevation greater than five times its reference value or rhabdomyolysis is rare<sup>185</sup>.

On the other hand, evidence on the use of statins to prevent cardiovascular complications in nonvascular surgeries are weak. A study on the perioperative period of nonvascular surgeries has been recently published. This study involved 1,066 patients with intermediate cardiac risk who were randomized into four intervention groups: A: slow-release fluvastatin 80 mg; B: bisoprolol; C: both medications; or D: double placebo. The authors found no significant difference in the incidence of myocardial infarction or cardiac death within 30 days after surgery between patients receiving and not receiving statin, only bisoprolol showed cardiac protection in this study. Although this is the largest prospective study on statins in nonvascular surgeries and the outcome is disappointing, it is important to highlight that the power of this

study is too small for definitive conclusions, since the authors included only 1,066 of 6,000 patients initially planned for logistical reasons<sup>179</sup>.

The evidence favorable to pharmacoprotection by statins in the perioperative period of nonvascular surgeries is from a retrospective analysis. Lindenauer et al.<sup>89</sup> evaluated 780,591 patients undergoing noncardiac surgery (92% nonvascular surgeries) in a retrospective cohort study. Of these patients, 77,082 (9.9%) received statins. Patients who received statins had lower in-hospital mortality. In another case control retrospective study, which included not only vascular surgeries, with 989 cases of patients who died within 30 days after surgery and 1,879 controls, statin use was also associated with reduced mortality (OR = 0.4; CI 0.24-0.68)<sup>186</sup>.

Recommendations for perioperative use of statins:

#### Degree of Recommendation I

- Patients who will undergo vascular surgeries; Level of Evidence A;

- Patients diagnosed with coronary artery disease; Level of Evidence C;

Patients who already use statins; Level of Evidence B.

#### Degree of Recommendation IIb

- High-risk patients (ACP classes II and III); Level of Evidence C.

### 6.1.3. Alpha-agonists

Alpha2-agonists modulate the response to catecholamines to surgery and anesthesia, decreasing the release of noradrenaline, reducing blood pressure and heart rate. The first randomized trials using clonidine to prevent cardiovascular complications after noncardiac surgeries demonstrated a reduction in myocardial ischemia, but no reduction in clinical events or mortality<sup>187,188</sup>. On the other hand, a meta-analysis has demonstrated that alpha2-agonists reduced mortality and acute myocardial infarction in patients undergoing vascular surgeries, but not in those undergoing nonvascular surgeries<sup>189</sup>.

The European Mivazerol Trial (EMIT) assessed the use of mivazerol in 1,897 patients with coronary artery disease undergoing noncardiac surgery, and the authors found a reduction in overall mortality and myocardial infarction or cardiac death only in the subgroup of patients undergoing vascular surgeries<sup>190</sup>. Only a randomized, placebo-controlled study with 190 patients showed a reduction in mortality with the use of prophylactic clonidine in the perioperative period. Wallace et al. showed that the use of clonidine in patients who have coronary disease or with more than two risk factors for coronary artery disease (hypertension, age > 60 years, smoking, total cholesterol > 140mg/dl, diabetes mellitus) in the perioperative period of noncardiac surgeries reduced the incidence of postoperative cardiac ischemia and mortality within 30 days and in a 2-year follow-up<sup>191</sup>.

Recommendations for perioperative use of clonidine:

#### Degree of Recommendation IIa, Level of Evidence A

- Cardiac patients who will undergo vascular surgeries and have contraindications to beta-blockers.



## Guidelines

### 6.1.4. Calcium Channel Blockers

Evidence for the use of calcium channel blockers with the goal of reducing cardiovascular risk in postoperative noncardiac surgery is scarce. In a meta-analysis of 11 studies involving 1,007 patients, there was no reduction in mortality or acute myocardial infarction with the use of verapamil, diltiazem, or dihydropyridine<sup>192</sup>. Therefore, the use of calcium channel blockers to prevent perioperative cardiovascular events in noncardiac surgery is not recommended.

### 6.1.5. Antiplatelet Agents

The importance of continuous antiplatelet therapy in patients with coronary disease, as well as the risk related to acute discontinuation of this therapy is well-known: up to 10.2% of acute cardiovascular events are preceded by recent discontinuation of AAS<sup>193</sup>. On the other hand, there is concern about increased bleeding complications in surgeries performed in patients who take anti-platelet agents. Current evidence suggests that in fact there is an increase of up to 50% in the rate of perioperative bleeding in patients taking AAS, but no increase in the rate of severe bleeding, except in neurosurgery and transurethral resection of the prostate (example of procedure without primary hemostasis).

The first randomized study on maintenance or discontinuation of antiplatelet therapy after surgery<sup>194</sup> has been recently published. The study supports the concept that for the vast majority of situations, the assessment of the risk X benefit relation of antiplatelet therapy for patients with coronary disease who will undergo noncardiac surgery is favorable to the maintenance of AAS at a reduced dose of 75 to 100 mg/day.

When comparing patients with coronary disease, specifically those who underwent angioplasty with stent placement, the discussion is more complex. It has been established that after coronary stent implantation there is a transient increase in the risk of intra-stent thrombosis, an event of high mortality. 64.4% of infarction or death<sup>195</sup>. This period of increased risk lasts for 30 days after conventional stent implantation, and for at least 1 year after drug-eluting stents, and combined antiplatelet therapy should be used during this period: AAS 200 mg/day and a thienopyridinic derivative such as clopidogrel 75 mg/day. Thienopyridinic derivatives should ideally be discontinued 5 days before surgical procedures, but because they represent a significant increase in perioperative risk<sup>196</sup>.

When the patient is still in its period of greatest risk of stent thrombosis and requires noncardiac surgery in this period, we are dealing with an individual at high risk for cardiac complications, even if he/she is asymptomatic and without residual coronary lesions. The strategy that seems more reasonable in this situation is using AAS throughout the perioperative period, with thienopyridine discontinuation 5 days before surgery and reintroduction as early as possible, ideally before the patient completes 10 days without this medication<sup>197</sup> (Degree of Recommendation I, Level of Evidence C). In cases with low estimated bleeding risk inherent to the surgical procedure, it is possible to consider perform this surgery in the presence of dual antiplatelet

therapy<sup>198</sup> Degree of Recommendation IIa, Level of Evidence C)<sup>198</sup>. However, this strategy does not provide the same protection when compared to the ideal length of time and, therefore, surveillance for ischemic events should be maintained.

Attention should be given to the situation of patients receiving antiplatelet therapy with only thienopyridine for several reasons. There is evidence suggesting higher rates of perioperative bleeding attributed to thienopyridines based mainly on studies in which these agents were used in combination with AAS; thus the recommendation of these Guidelines is to consider bleeding risk as being inherent to the procedure. When the risk is moderate or high, thienopyridine should be discontinued 5 days before (Degree of Recommendation I, Level of Evidence C) and when bleeding risk is low, the antiplatelet agent should be used in the perioperative period (Degree of Recommendation IIa, Level of Evidence C).

Finally, specifically in relation to spinal anesthesia (spinal or epidural), there is concern regarding increased bleeding complications in patients who use antiplatelet agents. Spinal hematoma is a complication of this anesthetic technique; although rare, it can have catastrophic consequences if not promptly diagnosed and treated. Several studies have shown that the risk of developing this complication does not seem to be increased with the use of aspirin alone. A consensus of the American Society of Regional Anesthesia and Pain Medicine has been recently published and it does not recommend the discontinuation of aspirin when performing spinal anesthesia. Regarding the use of thienopyridines, there is shortage of information in the literature about the risk of spinal hematoma, which is the reason why discontinuation of thienopyridine is recommended before the procedure<sup>199</sup>.

Recommendations for antiplatelet agents before noncardiac surgeries:

#### Degree of Recommendation I

- Patients with coronary artery disease and noncardiac surgery scheduled should maintain the use of AAS at a low dose of 75 to 100 mg/day, except in neurosurgeries and transurethral resection of the prostate; Level of Evidence B;
- Patients using dual antiplatelet therapy by means of recent angioplasty with stent should keep receiving AAS throughout the perioperative period, with discontinuation of thienopyridine 5 days before surgery and reintroduction as early as possible, ideally before the patient completes 10 days of discontinuation; Level of Evidence C;
- Patients receiving antiplatelet therapy only with thienopyridine and surgery scheduled with moderate to high-risk of bleeding should discontinue medication 5 days before; Level of Evidence C.

#### Degree of Recommendation IIa

- Keep dual antiplatelet therapy in procedures with low risk for bleeding; Level of Evidence C;
- Patients receiving antiplatelet therapy only with thienopyridine and surgery scheduled with low risk of bleeding should continue medication in the perioperative period; Level of Evidence C.

## 6.2. Preoperative Coronary Revascularization

In some special cases, myocardial revascularization can be indicated before noncardiac surgery to reduce perioperative cardiovascular risk<sup>200,201</sup>. However, evidence is unfavorable to the routine use of this strategy<sup>202</sup>. In the context of optimized perioperative pharmacoprotection, potential situations of benefit of the prophylactic myocardial revascularization are increasingly restricted<sup>202,203</sup>, so most patients have this indication regardless of the perioperative context, being the only clear indication for this strategy. It is worth mentioning that revascularization should be considered only when there is evidence of ischemia related to the artery and not just based on anatomical findings.

The interval between myocardial revascularization and noncardiac surgery is an important factor, especially in cases of angioplasty<sup>204-207</sup>. On one hand, there is a risk of intracoronary thrombosis or restenosis when this interval is too short or too long, respectively. On the other hand, there is a risk of hemorrhagic complications associated with the use of potent antiplatelet agents such as clopidogrel. Finally, bear in mind that patients who received a drug-eluting stent should take clopidogrel for 1 year, so that in cases of angioplasty in patients with noncardiac surgery scheduled for next year, drug-eluting stent should not be used<sup>208</sup>. In these situations, depending on the urgency of the surgery, percutaneous treatment options are: use of conventional stent or angioplasty without stent<sup>208,209</sup>.

Recommendations for (surgical or percutaneous) myocardial revascularization before noncardiac surgeries:

### Degree of Recommendation I

- Patients with indication of myocardial revascularization, regardless of perioperative context who are scheduled to undergo elective noncardiac surgeries; Level of Evidence C;
- Patients with evidence during perioperative evaluation of extensive ischemic areas, low ischemic threshold, and high-risk coronary anatomy: lesion of left main coronary artery or triple-vessel disease with ventricular dysfunction; Level of Evidence C.

### Degree of Recommendation IIa

- Patients without high-risk functional or anatomical markers for perioperative cardiac complications but with indication of myocardial revascularization before intermediate or high risk noncardiac surgeries (e.g.: patients with single-vessel disease in right coronary artery, stable angina CSS II and without ventricular dysfunction with scheduled vascular, intraperitoneal and intrathoracic surgery); Level of Evidence C.

### Degree of Recommendation IIb

- Patients without high-risk functional or anatomical markers for perioperative cardiac complications but with indication of myocardial revascularization before low-risk noncardiac surgeries; Level of Evidence C.

### Degree of Recommendation III

- Patients in need of emergency, noncardiac surgery regardless of symptom severity or degree of coronary artery obstruction; Level of Evidence C;

- Patients with bad prognoses because of severe noncardiac illness who may be submitted to palliative surgeries such as gastrostomy, gastric/intestinal bypass, tracheotomy, etc. Level of Evidence C.

Recommendations regarding safe intervals between myocardial revascularization and noncardiac surgery:

### Degree of Recommendation I

- After surgical myocardial revascularization:
  - Ideal interval: 30 days; Level of Evidence C;
  - Minimum interval: depends on the clinical condition of the patient; Level of Evidence C.
- After balloon angioplasty without stenting:
  - Ideal interval: 14 days; Level of Evidence B;
  - Minimum interval: 7 days; Level of Evidence C.
- After angioplasty with conventional stenting:
  - Ideal interval: over 6 weeks; Level of Evidence B;
  - Minimum interval: 14 days; Level of Evidence C.
- After angioplasty with drug-eluting stent:
  - Ideal interval: undefined; Level of Evidence C;
  - Minimum interval: 365 days; Level of Evidence B.

**Table 3 - Recommended intervals between myocardial revascularization and noncardiac surgery. Note: For stenting surgeries, this interval includes the period of discontinuation of clopidogrel (5 days)**

Type of revascularization	Minimum interval	Ideal interval
Surgery	Variable: patient's condition	30 days
Angioplasty without stenting	7 days	14 days
Conventional stenting	14 days	> 6 weeks
Drug-eluting stent	One year	Indefinite

## 6.3. Venous Thromboembolism Prophylaxis

Adequate prophylaxis of venous thromboembolism in the spectrum of perioperative assessment involves detailed knowledge of risk factors for each patient and the risks of surgery.

It is important to consider that most hospitalized patients have one or more risk factors for venous thromboembolism<sup>210,211</sup> and that these factors have a cumulative character (Table 4). The incidence of venous thromboembolism in hospitalized patients without adequate thromboprophylaxis can vary from 10-40% for general surgery and 40-60% in major orthopedic surgery (Table 5).

There is strong evidence in the literature that the appropriate thromboprophylaxis in surgical patients is cost-effective with a great cost-benefit relation<sup>211</sup>, however, despite the evidence available with more than 20 guidelines recommending its use since 1986, its proper implementation has been underused, compromising patients' safety<sup>212</sup>.

**Table 4 - Risk factors for venous thromboembolism**

Surgery
Trauma (major traumas or lower limbs)
Immobilization, paralysis of lower limbs
Neoplasia
Cancer therapy (hormonal, chemotherapy, angiogenesis inhibitor or radiotherapy)
Previous venous thromboembolism
Venous compression (tumor, hematoma, arterial abnormality)
Old age
Pregnancy and postpartum
Contraceptives with estrogen or hormone replacement therapy
Selective estrogen receptor modulators
Erythropoiesis-stimulating agents
Acute clinical disease
Cardiac or respiratory failure
Inflammatory bowel disease
Nephrotic syndrome
Myeloproliferative disorders
Paroxysmal nocturnal hemoglobinuria
Obesity
Smoking
Central venous catheterization
Inherited or acquired thrombophilia

**Table 5 - Estimate risk DVT in hospitalized patients\***

Type of patient	Prevalence of DVT %
Clinical patient	10-20
General surgery	15-40
Major gynecological surgeries	15-40
Major urological surgeries	15-40
Neurosurgery	15-40
Stroke	20-50
Knee or hip arthroplasty	40-60
Hip fracture surgery	40-60
Major traumas	40-80
Spinal cord injury	60-80
Patients admitted to ICU	10-80

\* Scores based on objective diagnostic tests in patients with asymptomatic DVT without the use of thromboprophylaxis; DVT - deep vein thrombosis.

The most often accepted strategy of recommendation of thromboprophylaxis for venous thromboembolism today involves the prescription based on the risk groups which each patient belongs to<sup>213</sup> (Table 6).

The currently most accepted recommendations<sup>213</sup> are summarized below.

### 6.3.1. General Recommendations

#### Degree of Recommendation I

- Do not use aspirin alone in any group of patients as thromboprophylaxis for venous thromboembolism (VTE), Level of Evidence A;

- Use mechanical methods of thromboprophylaxis primarily in patients at high risk of bleeding; Level of Evidence A;

- With respect to each antithrombotic agent, follow the doses recommended in the guidelines of each manufacturer (Level of Evidence C). Generally, consider the use of prophylactic unfractionated heparin (UFH) at a dose of 5000 IU SC 12/12h or 8/8h; prophylactic low molecular weight heparin (LMWH) (dalteparin 5000 IU SC once a day, tinzaparin 4500 IU SC once a day or enoxaparin 40 mg SC once a day) and fondaparinux at doses of 2.5 mg SC once a day (in subjects > 50 kg);

- Assess renal function when considering the use and the dose of LMWH, fondaparinux, or other antithrombotic agent excreted by the kidneys especially in elderly and diabetic individuals, or those at high risk of bleeding (Level of Evidence A). In these circumstances, avoid the use of antithrombotic drugs with renal metabolism. Use lower doses of the drug, or monitor the serum level of the drug and its anticoagulant effect (Level of Evidence B).

#### Degree of Recommendation IIa

- Use mechanical methods of thromboprophylaxis in patients at high risk of bleeding with an adjuvant to anticoagulant thromboprophylaxis (Level of Evidence A).

### 6.3.2. General Surgeries

- For patients undergoing low-risk general surgery procedures such as minor surgeries that do not have other additional risk factors for VTE the only recommendation is early and frequent ambulation.

#### Degree of Recommendation I

- For patients undergoing moderate-risk general surgery such as a major procedure for a benign disease, use thromboprophylaxis with LMWH, prophylactic UFH, or fondaparinux; Level of Evidence A;

- For patients undergoing higher-risk general surgery such as a major procedure for neoplasia, use thromboprophylaxis with LMWH, prophylactic UFH 8/8h, or fondaparinux; Level of Evidence A;

- For patients undergoing general surgery with multiple risk factors for VTE who may be at a higher risk category, use a pharmacological method (LMWH, prophylactic UFH 8/8h,

**Table 6 - Recommended thromboprophylaxis according to the levels of thromboembolic risk in hospitalized patients\***

Risk classes	Approximate risk of DVT in the absence of thromboprophylaxis <sup>a</sup>	Options of thromboprophylaxis
<b>Low risk</b> Minor surgery in patients who can walk Clinical patients who can walk	< 10.0%	No specific thromboprophylaxis Early and intensive ambulation
<b>Moderate risk</b> Most general, gynecological and open urological surgeries Clinical patients confined to bed or seriously ill Moderate risk of VTE + high risk of bleeding	10-40.0%	LMWH (at recommended doses), low dose of UFH or 12/12h or 8/8h, fondaparinux  Mechanical thromboprophylaxis <sup>b</sup>
<b>High risk</b> Hip or knee arthroplasty, hip fracture surgery Major traumas, spinal cord injury High risk of VTE + high risk of bleeding	40-80.0%	LMWH (at recommended doses), fondaparinux, or warfarin (INR 2.0-3.0) Mechanical thromboprophylaxis <sup>b</sup>

\* The descriptive terms were purposely left undefined to allow for individual clinical interpretation; <sup>a</sup> Scores based on objective diagnostic tests in patients with asymptomatic DVT without the use of thromboprophylaxis; <sup>b</sup> Mechanic thromboprophylaxis includes intermittent pneumatic compression and/or elastic compression stockings. Consider returning to anticoagulant thromboprophylaxis after decreasing the risk of bleeding; VTE - venous thromboembolism, LMWH - low molecular weight heparin, UFH - unfractionated heparin; DVT - deep vein thrombosis; INR - international normalized ratio.

or fondaparinux) in combination with a mechanical method (elastic stockings and/or intermittent pneumatic compression-IPC); Level of Evidence C;

- For patients undergoing general surgery with a high risk of bleeding, use a mechanical method of thromboprophylaxis (elastic stockings and/or IPC); Level of Evidence A. Once there is a decreased risk of bleeding, replace it or add pharmacological thromboprophylaxis; Level of Evidence C.

- Regarding the duration of thromboprophylaxis, in major general surgery, keep it until hospital discharge; Level of evidence A.

#### Degree of Recommendation IIa

- Regarding the duration of thromboprophylaxis, in major general surgeries for selected patients at the highest risk, including those undergoing major surgery for cancer or with previous VTE, consider the use of thromboprophylaxis after hospital discharge with LMWH for up to 28 days. Level of Evidence A.

### 6.3.3. Vascular Surgeries

#### Degree of Recommendation I

- For patients undergoing major vascular surgeries with risk factors for VTE, use thromboprophylaxis with LMWH, prophylactic UFH, or fondaparinux; Level of Evidence C.

#### Degree of Recommendation IIa

- For patients undergoing vascular surgeries without other risk factors for VTE, use only early and frequent ambulation; Level of Evidence C.

### 6.3.4. Gynecological Surgeries

#### Degree of Recommendation I

- For patients undergoing minor, low-risk gynecological surgery without risk factors for VTE, use early and frequent ambulation; Level of Evidence A;

- Similarly, for gynecological patients undergoing laparoscopic surgeries, use only early and frequent ambulation; Level of Evidence B;

- For gynecological patients undergoing laparoscopic surgeries with additional risk factors for VTE, use thromboprophylaxis with LMWH, prophylactic UFH and/or elastic stockings and IPC; Level of Evidence C;

- For patients undergoing major gynecological surgery for benign disease without additional risk factors for VTE, use LMWH, prophylactic UFH (Level of Evidence A) or IPC immediately before surgery until the patient can walk (Level of Evidence B);

- For patients undergoing major gynecological surgery for neoplasia and for patients with multiple risk factors for VTE, use routine prophylaxis with LMWH, prophylactic UFH 8/8h (Level of Evidence A) or IPC immediately before surgery until the patient can walk (Level of Evidence A). Alternatively we can consider the combination of LMWH or prophylactic UFH associated with mechanical thromboprophylaxis with elastic stockings or IPC, or fondaparinux (Level of Evidence C);

- For patients undergoing major gynecological surgeries, keep thromboprophylaxis until hospital discharge; Level of Evidence A.



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### Degree of Recommendation IIa

- For patients at the highest risk, including those undergoing major surgeries for cancer, as well as those with a history of previous VTE, consider the use of thromboprophylaxis with LMWH for up to 28 days after discharge; Level of Evidence C.

### 6.3.5. Major Urological Surgeries

#### Degree of Recommendation I

- For patients undergoing transurethral surgeries, as well as other low-risk urological surgeries, use only early and frequent ambulation; Level of Evidence A;

- For patients undergoing major urological open surgeries, use routine thromboprophylaxis with prophylactic UFH 12/12h or 8/8h (Level of Evidence B), elastic compression stockings and/or IPC immediately before surgery until the patient can walk (Level of Evidence B), LMWH, fondaparinux or the combination of pharmacological and mechanical thromboprophylaxis (elastic compression stockings and/or IPC), Level of Evidence C;

- For urologic patients who have active bleeding or at high risk of bleeding, use mechanical methods of thromboprophylaxis adequately (elastic compression stockings and/or IPC) until the bleeding risk decreases; Level of Evidence A. Once there is decreased risk of bleeding, replace mechanical methods or add pharmacological thromboprophylaxis to the mechanical method; Level of Evidence C.

### 6.3.6. Laparoscopic Surgeries

#### Degree of Recommendation I

- For patients undergoing laparoscopic surgeries without risk factors for VTE, use only early and frequent ambulation; Level of Evidence A;

- For patients undergoing laparoscopic surgery with additional risk factors for VTE, use LMWH, prophylactic UFH, fondaparinux and/or elastic stockings or IPC; Level of Evidence C.

### 6.3.7. Bariatric Surgeries

#### Degree of Recommendation I

- For patients undergoing bariatric surgery, routinely use thromboprophylaxis with LMWH, prophylactic UFH 8/8h, fondaparinux or the combination of a pharmacological method with IPC; Level of Evidence C.

#### Degree of Recommendation IIa

- These patients should receive higher doses of LMWH (enoxaparin 40 mg SC 12/12h) or UFH (7500 UI SC 8/8h) than those commonly used in the prophylaxis of non-obese patients; Level of Evidence C.

### 6.3.8. Thoracic Surgeries

#### Degree of Recommendation I

- For patients undergoing major thoracic surgeries, routinely use thromboprophylaxis with LMWH, prophylactic UFH, or fondaparinux; Level of Evidence C;

- For patients at high risk of bleeding, properly use mechanical methods of thromboprophylaxis (elastic compression stockings and/or IPC); Level of Evidence C.

### 6.3.9. Orthopedic Surgeries

#### 6.3.9.1. Elective Hip Prosthesis Surgery

##### Degree of Recommendation I

- For patients undergoing elective hip prosthesis surgery (HPS), routinely use one of the following thromboprophylaxis regimens: A) LMWH (started 12 h before surgery or 12 to 24 h after surgery, or 4-6 h after surgery at half the usual dose, increasing to the usual dose the next day); B) fondaparinux (2.5 mg started 6 to 24 h after surgery); or C) warfarin started in the preoperative period or in the evening before surgery, keeping the INR between 2.0 and 3.0; Level of Evidence A. (up to INR above 2.0, also administer another prophylaxis method);

- Do not use the following methods as single thromboprophylaxis: aspirin, dextran or elastic compression stockings; Level of Evidence A;

- For patients with a high risk of bleeding, use IPC adequately; Level of Evidence A. Once there is a decreased risk of bleeding, replace the mechanical method or add pharmacological thromboprophylaxis; Level of Evidence C.

##### Degree of Recommendation IIa

When LMWH cannot be used for safety or availability reasons, use unfractionated heparin 5000 U 8/8h; Level of Evidence C.

#### 6.3.9.2. Elective Knee Prosthesis Surgery

##### Degree of Recommendation I

- For patients undergoing elective knee prosthesis surgery, routinely use thromboprophylaxis with LMWH, fondaparinux or warfarin (INR 2.0-3.0); Level of Evidence A;

- Proper use of the IPC in this group of patients can be done instead of pharmacological thromboprophylaxis; Level of Evidence B;

- Do not use aspirin as a single thromboprophylaxis method; Level of Evidence A;

- For patients with a high risk of bleeding, use IPC adequately; Level of Evidence A. Once there is a decreased risk of bleeding, replace the mechanical method or add pharmacological thromboprophylaxis; Level of Evidence C.

##### Degree of Recommendation IIa

- When LMWH cannot be used for safety or availability reasons, use unfractionated heparin 5000 U 8/8h; Level of Evidence C.

#### 6.3.9.3. New Drugs to Prevent Venous Thromboembolism in Elective Hip and Knee Prosthesis Surgeries

Dabigatran (Pradaxa) is a new drug that acts on the direct inhibition of the enzyme thrombin, which is responsible for converting fibrinogen into fibrin in the coagulation cascade.

Its use was approved by the European Medicines Agency in 2008 and recently Anvisa has approved it in Brazil, but not the FDA has not approved it yet. Its advantage is the fact that it is an oral drug that can be used in single daily dose, without the need to monitor its effect. However, as opposed to low molecular weight heparin and warfarin, dabigatran has no antidotes available.

Its use is approved as an alternative to the low molecular weight heparin in preventing venous thromboembolism in adults undergoing elective hip and knee prosthesis surgery. Its use was authorized based primarily on results of two randomized, double-blind trials of non-inferiority to enoxaparin (RE-NOVATE<sup>214</sup>, which evaluated 3,494 patients undergoing elective hip prosthesis surgery comparing the use of dabigatran 150 mg or 220 mg/day with enoxaparin 40 mg/day, both for 28-35 days; and RE-MODEL<sup>215</sup>, which evaluated 2,101 patients undergoing elective knee prosthesis surgery comparing the use of dabigatran 150 mg or 220 mg/day with enoxaparin 40 mg/day, both for 6-10 days). A third study, RE-MOBILIZE<sup>216</sup>, also a randomized, double-blind, controlled trial of non-inferiority to dabigatran involving 2,615 patients undergoing elective knee prosthesis surgery, compared dabigatran 150 mg and 220 mg/day with enoxaparin 30 mg twice a day. In this study, however, dabigatran was inferior to enoxaparin.

European guidelines<sup>217</sup> recommend dabigatran as an alternative to enoxaparin in elective knee and hip prosthesis surgeries, and its use should be initiated 1 to 4 hours after surgery at half the dose (110 mg). Then continue with the standard dose of 220 mg once daily for 28 to 35 days in hip prosthesis surgeries and for 10 days in knee prosthesis surgeries. In patients with moderate renal impairment, over 75 years old and those receiving amiodarone, the standard dose should be reduced to 150 mg/day (initial dose of 75 mg, followed by standard dose of 150 mg once daily).

#### 6.3.9.4. Knee Arthroscopy

##### Degree of Recommendation I

- For patients undergoing knee arthroscopy with risk factors for VTE or a complicated surgical procedure, use LMWH; Level of Evidence B.

##### Degree of Recommendation IIa

- For patients undergoing knee arthroscopy without additional risk factors for VTE, use only early ambulation; Level of Evidence B.

#### 6.3.9.5. Hip Fracture Surgery

##### Degree of Recommendation I

- For patients undergoing hip fracture surgery routinely use thromboprophylaxis with fondaparinux (Level of Evidence A), LMWH or warfarin, keeping INR between 2.0 to 3.0 (Level of Evidence B);

- Do not use aspirin as a single thromboprophylaxis method; Level of Evidence A;

- In patients for whom a delay in surgical correction is expected, use thromboprophylaxis with LMWH or

prophylactic UFH in the period between hospital admission and surgery; Level of Evidence C;

- For patients with a high risk of bleeding, use IPC adequately; Level of Evidence A. Once there is a decreased risk of bleeding, replace the mechanical method or add pharmacological thromboprophylaxis; Level of Evidence C.

##### Degree of Recommendation IIa

- When LMWH cannot be used for safety or availability reasons, use unfractionated heparin 5000 U 8/8h; Level of Evidence C.

#### 6.3.9.6. Beginning of Thromboprophylaxis in Major Orthopedic Surgeries

##### Degree of Recommendation I

- For patients receiving LMWH in major orthopedic surgeries, the beginning of its administration can be both preoperatively and immediately postoperatively; Level of Evidence A;

- For patients receiving fondaparinux as thromboprophylaxis, begin medication 6-8 h after surgery or the next day; Level of Evidence A.

#### 6.3.9.7. Prehospital Discharge Screening for DVT

##### Degree of Recommendation I

- For asymptomatic patients undergoing major orthopedic surgeries, routine use of venous Doppler ultrasound of lower limbs as screening method for DVT before hospital discharge is not recommended. Level of Evidence A.

#### 6.3.9.8. Thromboprophylaxis Duration

##### Degree of Recommendation I

- For patients undergoing hip and knee prosthesis surgeries or hip fracture repair, use thromboprophylaxis for at least 10 days after surgery; Level of Evidence A;

- For patients undergoing hip prosthesis surgery or hip fracture repair, prolong thromboprophylaxis from 10 to 35 days after surgery (Level of Evidence A) using LMWH (Level of Evidence A), warfarin (Level of Evidence B), or fondaparinux (Level of Evidence C).

##### Degree of Recommendation IIa

- For patients undergoing knee prosthesis surgery, prolong thromboprophylaxis from 10 to 35 days after surgery, using LMWH, warfarin, or fondaparinux. Level of Evidence B.

#### 6.3.9.9. Elective Spinal Cord Surgery

##### Degree of Recommendation I

- For patients who have additional risk factors for VTE such as neoplasia, neurological impairment, advanced age, previous VTE or previous surgery, use prophylactic UFH, LMWH, or IPC in the postoperative period; Level of Evidence B.

##### Degree of Recommendation IIa

- For patients undergoing spinal cord surgery without additional risk factors for VTE, use only early and frequent ambulation; Level of Evidence C;

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- For patients who have additional risk factors for VTE such as neoplasia, neurological impairment, advanced age, previous VTE or previous surgery, there is the possibility of considering the use of elastic compression stockings; Level of Evidence B;

- For patients with multiple risk factors, associate a pharmacological method of thromboprophylaxis (prophylactic UFH or LMWH) with a mechanical method (IPC and/or elastic compression stockings); Level of Evidence C.

### 6.3.10. Neurosurgery

#### Degree of Recommendation I

- For patients undergoing major neurosurgeries, use routine mechanical thromboprophylaxis by means of IPC; Level of Evidence A.

#### Degree of Recommendation IIa

- For patients undergoing major neurosurgeries, the use of postoperative LMWH (Level of Evidence A) and prophylactic UFH (Level of Evidence B) are acceptable alternatives;

- For patients with a higher risk of VTE, use a combination of a mechanical method (IPC and/or elastic compression stockings) and a pharmacological method (LMWH or prophylactic UFH postoperatively); Level of Evidence B.

### 6.3.11. Trauma

#### Degree of Recommendation I

- Whenever possible, use thromboprophylaxis in all patients suffering from major trauma, if possible; Level of Evidence A;

- In patients suffering from major trauma and without significant contraindications, use LMWH as early as possible considering safety issues; Level of Evidence A. A possible alternative is the combination of LMWH and a mechanical method of thromboprophylaxis; Level of Evidence B;

- In patients with contraindications to the use of LMWH because of active bleeding or high risk of bleeding, use a mechanical method of thromboprophylaxis such as IPC or possibly elastic compression stockings alone; Level of Evidence B. Once there is a decreased risk of bleeding, replace it or add pharmacological thromboprophylaxis; Level of Evidence C;

- Do not use inferior vena cava filter as a thromboprophylaxis method in patients suffering from trauma; Level of Evidence C;

- Keep thromboprophylaxis until hospital discharge; Level of Evidence C.

### 6.3.12. Acute Spinal Cord Injury

#### Degree of Recommendation I

- Use thromboprophylaxis for all patients with acute spinal cord injury (Level of Evidence A) by means of LMWH initiated once bleeding is confirmed (Level of Evidence B). Alternatively, the combination of IPC and/or prophylactic UFH (Level of Evidence C) or LMWH (Level of Evidence C);

- For patients at high risk of bleeding, use elastic compression stockings and/or IPC (Level of Evidence A). Once there is

decreased risk of bleeding, replace mechanical methods or add pharmacological thromboprophylaxis (Level of Evidence C);

- For patients with incomplete spinal cord injury associated with local hematoma evidenced on CT or MRI, use mechanical thromboprophylaxis during the first days after injury, Level of Evidence C;

- In this group of patients, do not use vena cava filter as a thromboprophylaxis method; Level of Evidence C;

- For patients receiving rehabilitation treatment after injury, keep LMWH or start warfarin (INR 2.0-3.0); Level of Evidence C.

### 6.3.13. Oncological Surgeries

VTE events are common in patients undergoing oncological surgeries. It has been reported that 40% to 80% of these patients can develop blood clots in the veins of the calf and 10% to 20% may have proximal thrombosis. However, in most cases these are asymptomatic VTE events. In the absence of thromboprophylactic measures, there is symptomatic pulmonary embolism in 4% to 10% of these patients, and 1% to 5% die<sup>218</sup>.

Patients undergoing oncological surgery remain at high risk for VTE for a long period, and recent studies have suggested that antithrombotic prophylaxis lasts for four weeks, which proved to be effective and safe. Different Cancer Societies have different criteria for the use of prophylaxis during four weeks, so that the U.S. societies recommend this period for patients at higher risk, while the European societies recommend it for all patients undergoing abdominal and pelvic oncological surgeries<sup>219</sup>.

#### Degree of Recommendation I

- Patients undergoing laparotomy, laparoscopy, or thoracotomy lasting longer than thirty minutes should receive prophylaxis with heparin, except if there are contraindications; Level of Evidence A;

- Thromboprophylactic mechanical methods can be associated with pharmacological methods, but not as a single therapy, unless there are contraindications to pharmacological methods; Level of Evidence A;

- Combined prophylaxis (mechanical and pharmacological) may be used, in order to increase efficiency, especially in patients at high risk. Level of Evidence A.

## 6.4. Perioperative Anticoagulation Management

The management of patients under anticoagulation therapy in the perioperative period depends on their individual risk of having thromboembolic events if therapy is discontinued and of bleeding if therapy is maintained. Perioperative anticoagulation is associated with a 3% increase in severe bleeding. There is consensus that INR < 1.5 is not associated with perioperative bleeding. Thus, it is important to adjust anticoagulation therapy properly in order to minimize thrombotic and hemorrhagic events<sup>220</sup>.

### 6.4.1. Risk of Thromboembolism<sup>221</sup>

#### 6.4.1.1. High-risk Patients

- Mechanical prostheses: any mechanical prosthesis in the mitral position, old aortic mechanical prosthesis or with stroke or TIA within the last 6 months;



- Atrial fibrillation (AF) with CHADS<sub>2</sub>\* greater than 5, associated with valvular heart disease or stroke or TIA within the last 3 months;

- Venous thromboembolism (VTE): recent (past 3 months) or associated with severe thrombophilia (deficiency of protein C, S, antithrombin or presence of antiphospholipid antibody).

#### 6.4.1.2. Intermediate-risk Patients

- Aortic mechanical prostheses with old AF, stroke, or TIA, older than 75 years, heart failure, hypertension, or diabetes;

- AF with CHADS<sub>2</sub>\* of 3 or 4;

- VTE in the last 3-12 months, mild thrombophilia (heterozygous mutations of factor V or factor II Leiden), recurrent VTE, active cancer.

#### 6.4.1.3. Low-risk Patients

- Aortic mechanical prostheses with no risk factors for stroke;

- AF with CHADS<sub>2</sub>\* from 0 to 2, without previous stroke or TIA;

- VTE longer than 12 months ago without other risk factors;

- \* CHADS<sub>2</sub>: heart failure = 1 point, hypertension = 1 point, age > 75 years = 1 point, diabetes = 1 point, stroke or TIA = 2 points<sup>222</sup>.

#### 6.4.2. Procedures with Low Risk of Bleeding

- Cataract surgery;

- Minor dermatological procedures;

- Dental procedures - hygiene, simple extraction, restoration, endodontic and prosthetic procedures.

#### 6.4.3. Recommendations

##### 6.4.3.1. Patients at High Risk of Thromboembolism

###### Degree of Recommendation IIa, Level of Evidence C

- Discontinue warfarin 5 days before surgery and wait for INR < 1.5 to perform the procedure;

- Unfractionated heparin (UFH) or prophylactic low birth weight (LMWH) can be used in the preoperative period if indicated;

- Postoperatively, use UFH or prophylactic LMWH if indicated by the type of procedure and resume warfarin 12 to 14 hours after surgery.

##### 6.4.3.2 Patients at Low Risk of Thromboembolism

###### Degree of Recommendation I, Level of Evidence C.

- Discontinue warfarin 5 days before surgery and wait for INR < 1.5;

- Start full-dose UFH or LMWH when INR < 2.0;

- Discontinue intravenous UFH 4 hours before surgery and subcutaneous LMWH 24 hours before surgery;

- Postoperatively, restart full-dose UFH or LMWH and warfarin and 12 to 24 hours after the procedure and discontinue heparin only when the INR is within therapeutic range.

##### 6.4.3.3. Patients at Intermediate Risk of Thromboembolism

###### Degree of Recommendation IIa, Level of Evidence C

- Depending on the individual assessment of each patient, the guidelines can be followed either for the high or low risk to the discretion of the physician in charge.

##### 6.4.3.4. Procedures with Low Risk of Bleeding

###### Degree of Recommendation I, Level of Evidence C

- Perform the procedure with an INR within the therapeutic range – it is not necessary to discontinue the anticoagulant;

- If INR > 3, discontinue anticoagulation therapy one or two days before surgery and reintroduce it the night after surgery.

##### 6.4.3.5. Urgent Procedures<sup>220</sup>

Discontinuation of anticoagulant, intravenous administration of vitamin K and replacement of deficient factors with prothrombin complex concentrate or fresh frozen plasma, according to the availability of these products.

#### 6.4.4. Reversal of Anticoagulant Therapy for Surgical Procedures

The therapeutic measures to be employed for the reversal of oral anticoagulation therapy will depend on how quickly the normalization of prothrombin time has to be reached - international normalized ratio (INR). For elective surgeries that can wait 18-24 hours to be performed, discontinuation of anti-vitamin K associated with the use of vitamin K1 at a dose of 2.5 to 5 mg intravenously usually produces normalization of INR when it was within the therapeutic range<sup>221</sup>.

When the normalization of the INR must be fast, replacement of deficient factors should be done. For this, two options are available: fresh frozen plasma (FFP) and prothrombin complex concentrate, emphasizing that the resolution - RDC No. 10, January 23, 2004 of the Agency for Sanitary Surveillance (ANVISA) provides that for "correction of hemorrhages using coumarin anticoagulants or rapid reversal of the effects of coumarin (...) the product of choice is the prothrombin complex. Because the availability of this type of concentrate is not yet sufficiently widespread in Brazilian hospitals, the use of FFP is an acceptable alternative<sup>223</sup>."

In the case of use of fresh frozen plasma, the recommended dose is 15 mL per kilogram of body weight, considering the possibility of fluid overload<sup>224</sup>. There is no standardization of the dose to be used for the prothrombin complex concentrate. Table 7 shows the doses used in some health care facilities in the UK. However, regardless of what is used to replace the vitamin K-dependent factors, the combined use of vitamin K1 (2.5-5 mg by slow intravenous or oral route) to maintain normal values of prothrombin time during the postoperative period is necessary<sup>221</sup>.

**Table 7 - Dose of prothrombin complex concentrate to be administered for reversal of oral anticoagulation according to the value of the PT-INR**

INR	Dose of prothrombin complex concentrate (U / kg, taking factor IX as basis)
2.0-3.9	25 U / kg
4.0-5.9	35 U / kg
≥ 6.0	50 U / kg

INR - international normalized ratio.

### 6.5. Endocarditis Prophylaxis

The key aspects of the diagnosis of infective endocarditis (IE) is to identify microorganisms commonly related to this disease in blood cultures and to view vegetation on the echocardiography. The treatment is long with high morbidity and mortality rates and almost always requires hospitalization<sup>225-227</sup>.

Because of all these characteristics, studies have always tried to identify not only the risk population, but also the conditions predisposing to IE in order to suggest preventive measures.

Endothelial damage (mainly due to a jet lesion in valvular heart diseases and congenital heart diseases) may lead to deposition of platelets and fibrin at the site, leading to formation of nonbacterial thrombotic endocarditis. With the occurrence of bacteremia, adherence of microorganisms to the compost of platelets and fibrin may take place, forming infective vegetation that triggers the whole pathophysiological process of the disease<sup>226</sup>.

Several studies have demonstrated the occurrence of bacteremia after medical procedures. Bloody interventions in the oral cavity, such as tooth extraction, periodontal surgery, and tonsillectomy have high average frequency of bacteremia, respectively, 60%, 88%, 35%. Esophageal dilatation and urinary tract dilatation have frequency of bacteremia of 45% and 28%, respectively, and bronchoscopy using a rigid bronchoscope has about 15% of bacteremia. Potentially contaminated surgeries also have high probability of bacteremia. Other conditions such as tracheal intubation, passage of catheters, and endoscopic procedures have a lower percentage of positive blood cultures<sup>227,228</sup>.

The existing prophylaxis models are based on observational studies and animal studies because of the great difficulty in conducting randomized, placebo-controlled trials due to the need for a large number of patients and ethical limitations due to the possibility of patient exposure to extremely serious disease.

Since 1955, there are recommendations from the American Heart Association for prevention of IE before dental procedures, and in the digestive tracts and genitourinary system. Initially, much emphasis was given to procedures that usually have bacteremia, particularly if performed in patients with valvular heart disease or congenital diseases. The analysis of subsequent studies has allowed some findings that have changed the recommendations for prophylaxis over the years<sup>77,225-232</sup>.

Some of the most important observations are:

- There is prophylactic efficacy by administering lower doses of antibiotics;

- Most patients with IE did not undergo dental medical procedures – surgical procedures;

- There is no clear correlation between the percentage of bacteremia after the procedure and the occurrence of IE;

- The risk of IE is higher in recurrent bacteremia (e.g. caused by poor oral health, active infections, long-term vascular catheters) compared to isolated events, such as specific dental postsurgical events, gastrointestinal or genitourinary procedure;

- The maintenance of good oral health is probably an IE prophylaxis more effective than antibiotics before a dental procedure;

- Antisepsis and asepsis before the procedures, treatment of active infections and reduction of vascular interventions are more effective measures than antibiotic prophylaxis;

- Few cases should be caused by procedures in the gastrointestinal and genitourinary systems;

- Antibiotic prophylaxis before procedures should avoid a minimum number of IE cases;

- Patients with serious risk of IE benefit most from prophylaxis;

- It is likely that the adverse effects of prophylactic antibiotic therapy administered in a liberal way exceeds the benefit;

- Most recommendations are still empirical and controversial.

The guidelines for valvular heart disease of the ACC/AHA in 2006 recommends as Class I that patients with prosthetic heart valves, previous to IE, complex cyanotic congenital heart disease, systemic-pulmonary surgically built shunts, acquired or congenital valve diseases, previous valvuloplasty, hypertrophic obstructive cardiomyopathy, and mitral valve prolapse with associated mitral regurgitation are at risk of experiencing IE, and therefore are candidates for prophylaxis prior to procedures with a high probability of significant bacteremia<sup>77</sup>.

However, an updated version of these guidelines published in 2007, in light of the above observations, does not put any patients in class I indication for prophylaxis, considering indication class IIa (probably helpful) only for patients at risk for severe IE undergoing dental procedures with high probability of significant bacteremia and class III (no benefit) prophylaxis for nondental procedures (especially those that do not penetrate the mucosa – bronchoscopy, transesophageal echocardiography, high digestive endoscopy, colonoscopy), except in the presence of active infection<sup>230</sup>. According to this publication, as opposed to the previous guidelines of the ACC/AHA, there is no recommendation for antibiotic prophylaxis for procedures involving the gastrointestinal or genitourinary system due to unclear evidence of correlation between these procedures and IE<sup>232</sup>.

However, the national experience of centers with a high prevalence of IE (which are usually referral centers for the treatment of patients with valvular heart disease and prosthetic heart valves) shows the common occurrence of cases of IE in patients with rheumatic valvular damage (even with high prevalence in Brazil) and degenerative valve disease. Likewise, there are records of several cases

of IE after gastrointestinal and genitourinary surgeries. There is also the perception of severe cases of IE, even in patients who do not fit the high risk group described by the ACC/AHA. Although it had been cited in the international literature, adverse effect of prophylactic antibiotic strategies is extremely rare. It is also important to highlight the high prevalence of poor oral health in our country. Therefore, it is probably more appropriate to expand the indication for antibiotic prophylaxis of IE in Brazil:

- All patients with anatomically significant valvular heart diseases, instead of using this strategy only for those with high risk of complications if they suffer from IE;
- Potentially contaminated procedures or with manipulation of the mucosa in the gastrointestinal and genitourinary systems.

### 6.5.1. Dental Procedures and Prevention of Infective Endocarditis

Thus, two aspects are crucial for the indication of prophylaxis for IE: the identification of patients at high risk for IE and who have a greater chance of progressing to severe IE (Table 8) and the identification of high-risk dental procedures for significant bacteremia (Table 9).

In this situation we must define the two approaches: the first is that the patient has a predisposition for infective endocarditis and the second is the potential of the procedure

**Table 8 - Patients at risk of acquiring severe infective endocarditis**

Patient with prosthetic heart valve
Valvular heart disease corrected with prosthetic material
History of infective endocarditis
Acquired valvular heart disease in patient who underwent heart transplant
Uncorrected cyanotic congenital heart disease
Corrected cyanotic congenital heart disease that evolves with residual lesion
Congenital heart disease corrected with prosthetic material

**Table 9 - Dental procedures and indication of infective endocarditis prophylaxis**

Indicated	Not recommended – any patients who will undergo the procedures below
For patients at risk for severe IE and who will undergo procedures involving manipulation of gingival tissue, periodontal region, or perforation of oral mucosa	Local anesthesia in non-infected tissue
	Dental X-ray
	Placement or removal of braces
	Adjustment of braces
	Placement of parts in braces
	Natural loss of milk tooth
	Bleeding originated from the trauma of the oral mucosa or lips

to generate bacteremia through an agent capable of causing infective endocarditis.

Dental procedures with higher risk for bacteremia are: subgingival placement of antibiotic fibers or strips, dental extractions, dental implants or reimplants, endodontic and periodontal procedures, placement of orthodontic bands and procedures with significant bleeding. Whenever high-risk patients undergo these procedures should receive antibiotic prophylaxis (Degree of Recommendation I, Level of Evidence C). It is likely that low-income populations with little access to health care, with heart diseases other than those cited in Table 8, also benefit from IE prophylaxis before dental procedures (Degree of Recommendation IIa, Level of Evidence C).

### 6.5.2. Surgical Procedures and Prevention of Infective Endocarditis

Although the indication of antibiotic prophylaxis for IE before procedures involving the gastrointestinal or genitourinary systems has been eliminated from the recommendations of the American Heart Association, as explained before, there is indication of maintenance of prophylaxis for these procedures in Brazil. All guidelines should be interpreted with caution; but they should be useful as a second opinion and as a guide<sup>(231)</sup>. In spite of scarce evidence, it is likely that high-risk patients for IE because of their underlying heart diseases would probably benefit from IE prophylaxis before genitourinary and gastrointestinal procedures (Degree of Recommendation IIa, Level of Evidence C). Non-high-risk patients with valvular heart diseases would also benefit of prophylaxis before these procedures. (Degree of Recommendation IIb, Level of Evidence C). The recommended regimen for this group is shown in Table 11.

In the case of procedures involving the respiratory tract, the major benefit of prophylaxis is also for patients at high risk for IE with mucosal incision or tonsillectomy with or bronchoscopy using rigid device. (Degree of Recommendation IIa, Level of Evidence C). Patients not at high risk possibly benefit from this conduct. (Degree of Recommendation IIb, Level of Evidence C). The recommended regimen is the same for dental procedures and for patients who will undergo procedures in the esophagus - Table 10.

### 6.5.3. Indications for Endocarditis Prophylaxis

#### Degree of Recommendation I

- Prophylaxis for patients at high risk for severe IE (Table 8) and who will be subjected to dental procedures with a high probability of significant bacteremia (Table 9). Antibiotic regimen in Table 10. Level of Evidence C.

#### Degree of Recommendation IIa

- Prophylaxis for patients with valvular heart disease or congenital heart disease that do not meet the criteria on Table 8 and who will undergo dental procedures with a high probability of significant bacteremia (Table 9). Antibiotic regimen in Table 10. Level of Evidence C;

- Prophylaxis for patients at high risk for severe IE (Table 8) and who will undergo genitourinary or gastrointestinal procedures associated with mucosal lesion. Antibiotic regimen in Table 11. Level of Evidence C;

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**Table 10 - Drug regimens for infective endocarditis prophylaxis before dental procedures**

Route of administration	Drug	Single dose 30 to 60 minutes before surgery	
		Child	Adult
Oral	Amoxicillin	50 mg/Kg	2 g
	Clindamycin	20 mg/Kg	600 mg
	Cafalexine	50 mg/Kg	2 g
Oral – penicillin allergy	Azithromycin or clarithromycin	15 mg/Kg	500 mg
	Ampicillin	50 mg/Kg	2 g
Parenteral (IV or IM)	Cefazolin or ceftriaxone	50 mg/Kg	1 g
	Clindamycin or Cefazolin or ceftriaxone	20 mg/Kg 50 mg/Kg	600 mg 1 g
Parenteral (IV or IM) - penicillin allergy			

IV - intravenous; IM - intramuscular.

**Table 11 - Prophylactic drug regimens for infective endocarditis before genitourinary and gastrointestinal procedures**

Route of administration	Drug	Single dose 30 minutes before surgery	
		Child	Adult
Parenteral (IV)	Ampicillin* + gentamicin	50 mg/Kg	2 g
		1.5 mg/Kg	
Parenteral (IV) - penicillin allergy	Vancomycin + gentamicin	20 mg/Kg	1 g
		1.5 mg/Kg	

\*Note: Make reinforcement with 1g 6 hours after the procedure.  
IV - intravenous; IM - intramuscular.

- Prophylaxis for patients at high risk for severe IE (Table 8) and who will undergo esophageal or respiratory tract procedures associated with mucosal lesion. Antibiotic regimen in Table 10. Level of Evidence C.

### Degree of Recommendation IIb

- Prophylaxis for patients with valvular heart disease or congenital heart disease that do not meet the criteria on Table 8 and who will undergo dental procedures that do not meet the criteria on Table 9. Antibiotic regimen in Table 10. Level of Evidence C;

- Prophylaxis for patients with valvular heart disease or congenital heart disease that do not meet the criteria on Table 8 and who will undergo genitourinary or gastrointestinal procedures associated with mucosal lesion. Antibiotic regimen in Table 11. Level of Evidence C;

- Prophylaxis for patients with valvular heart disease or congenital heart disease that do not meet the criteria on Table 8 and who will undergo esophageal or respiratory tract procedures associated with mucosal lesion. Antibiotic regimen in Table 10. Level of Evidence C.

### Degree of Recommendation III

- There is no indication for IE prophylaxis in patients with interatrial communication (IAC) alone; interventricular communication (IVC) or corrected patent ductus arteriosus and without residual flow; myocardial revascularization surgery; mitral valve prolapse without regurgitation after placement of stents; innocent heart murmurs; patients with pacemakers or

ICDs; history of Kawasaki disease or rheumatic fever without valve dysfunction who will undergo dental, esophageal, respiratory tract, genitourinary or gastrointestinal procedures;

- There is no indication for procedures that do not involve risk of bacteremia.

## 6.6. Glycemic Control

### 6.6.1. Preoperative

Patients with diabetes mellitus are more likely to undergo surgery and hospitalization than non-diabetic individuals. Brazilian epidemiological data are scarce and limited, but the data available show that diabetes mellitus is present in 7.8% of the population between 30 and 69 years and that diabetes is the fifth leading cause of hospitalization. Chronic complications of diabetes, particularly vascular complications, are the main causes of death and surgeries. About 30% of patients undergoing myocardial revascularization are diabetic.

Among the various aspects to be considered in the perioperative assessment of diabetic patients, blood glucose control is one of the most important. There is substantial observational evidence linking hyperglycemia to adverse surgical outcomes such as infection, longer hospitalization, disability after discharge, and mortality. A recent Brazilian study showed that 90% and 73% of patients with diabetes mellitus type 1 and 2, respectively, are not reached by the targets recommended for glycemic control (glycated hemoglobin less than 7%). Therefore, it is expected that most individuals in the preoperative evaluation require specific guidance in relation to glycemic control.

Although there are no randomized controlled trials (RCTs) evaluating the impact of glycemic control in the preoperative period of diabetic patients, preoperative evaluation becomes an additional opportunity to adjust doses of medication, education of the individual, and improvement of metabolic control. In the absence of level of evidence A to establish specific guidelines for glycemic targets in patients with diabetes in the preoperative period and out of intensive care environment, most recommendations are based on experience and clinical opinion. Using staggered scheme (insulin to correct capillary



glycemia) as sole therapy for prolonged periods should be avoided at all costs. This scheme is not effective for most patients. In addition, it contributes to glucose variability, thus trying to correct the “problem” (hyperglycemia) after it has already happened may even be harmful, predisposing to diabetic ketoacidosis in type 1 diabetics.

### Specific Glossary

*Prandial insulin* - dose of rapid-acting insulin (regular) or ultra-rapid acting insulin (lispro, aspart, glulisine) used to control postprandial glucose, used before meals.

*Basal insulin* - dose of intermediate-acting insulin (NPH) or slow-acting insulin (detemir or glargine) to control fasting glucose and interprandial period. Used in several regimens: fasting, before sleeping, and before meals, divided into 1-2 doses a day (detemir and glargine) and 1 to 4 doses a day (NPH).

*Correction or supplemental insulin* - dose of rapid-acting insulin (regular) or ultra-rapid acting insulin (lispro, aspart, glulisine) used to treat hyperglycemia taking place before or between meals or when the patient is fasting.

*Staggered scheme* - known as “insulin on demand,” “insulin-dextrose therapy.” Dose regimen of rapid insulin (regular) or ultra-rapid (lispro, aspart, glulisine) according to capillary glycemia to treat hyperglycemia.

*Basal scheme* - use of intermediate or slow-acting insulin alone.

*Basal-bolus or basal-prandial regimen* - use of basal and prandial insulin combined.

In summary, the main recommendations based on studies in the literature for the management of glycemic control in diabetic patients before surgery are<sup>233-239</sup>:

#### 6.6.1.1. Preoperative Glycemic Control in the Outpatient Degree of Recommendation I

- Request fasting glucose and glycated hemoglobin for all diabetic patients. Level of Evidence C;
- Request fasting glucose for patients with no history of DM. Level of Evidence C;
- Keep fasting glucose between 90 and 130 mg/dL, postprandial glycemia (2h) up to 180 mg/dL and glycated hemoglobin < 7%. Level of Evidence A;
- The individualization of goals should be considered for elderly patients, patients with CHF, children, and pregnant women. Level of Evidence C;
- There is insufficient evidence to support the postponement of elective surgery based on the value of fasting glucose and glycated hemoglobin, however HbA1c > 9% represents mean glycemia of > 212 mg/dL, being reasonable to adjust the control before surgery. Level of Evidence C.

#### 6.6.1.2. Ideal time to discontinue medications

##### Degree of Recommendation I, Level of Evidence C

- Biguanides (metformin): 24 to 48 hours before;

- Sulfonylureas:

- 1<sup>st</sup> generation (chlorpropamide) - 48 to 72 hours before;
- 2<sup>nd</sup> and 3<sup>rd</sup> generation (gliclazide, glibenclamide, glipizide, glimepiride) - on the day of surgery.

- Thiazolidinediones (rosiglitazone, pioglitazone): on the day of surgery;

- Acarbose: 24 hours before;

- Glinides (repaglinide, nateglinide): on the day of surgery;

- NPH insulin, glargine and detemir: evening dose can be maintained; in the morning of the surgery day, administer:

- 2/3 of the NPH insulin dose or slow-acting insulin when the surgery is performed early in the morning;

- 1/2 of the NPH insulin dose or slow-acting insulin when the surgery is performed in the morning;

- 1/3 of the NPH insulin dose or slow-acting insulin when the surgery is performed in the afternoon.

- Fast-acting or ultra-fast acting insulin – discontinue fixed prandial doses and keep staggered scheme while fasting;

- The adjustment of drug doses aimed at better glycemic control may require the aid of experts especially in insulin therapy users.

#### 6.6.1.3. Preoperative Glycemic Control in In-hospital Patient

If the diabetic patient with hyperglycemia and related metabolic stress is hospitalized and is undergoing surgery, glycemic control should be introduced briefly, minimizing the risk of hypoglycemia (below 70 mg/dL).

Hyperglycemia is related to several poor surgical outcomes in hospitalized diabetic patients. However, recently the role of glycemic variability (frequent peaks and valleys) as a predictor of death in patients hospitalized in intensive care units has been acknowledged and this is an additional aspect to be avoided during hospitalization.

##### Degree of Recommendation I

- Monitoring of capillary glycemia in diabetic patients; Level of Evidence A;

- To evaluate the HbA1c of these diabetic patients performed in an outpatient setting, if available;

- Control goals for patients with hyperglycemia (Level of Evidence C):

- Pre-prandial glycemia from 100 to 140 mg/dL;

- Random glycemia up to 180 mg/dL;

- Avoid hypoglycemia: below 70 mg/dL;

- Avoid variability (peaks and valleys).

- The goals may be different in specific subgroups such as pregnant women, elderly, patients with severe comorbidities or heart failure;

- Monitor fasting and random capillary glycemia in patients who are users of oral medications with HbA1c < 9%; Level of Evidence C;

- In patients taking oral medications with HbA1c ≥ 9%, consider delaying surgery or briefly controlling with insulin, evaluation with a specialist for brief control with insulin,

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capillary glycemia before meals and at bedtime; Level of Evidence C;

- In patients using insulin, measure capillary glycemia before meals and at bedtime;
- The adjustment or addition of oral medications are not indicated for rapid glycemic control in inpatients. Oral medications are slow acting and have limitations for some patients, such as patients with heart failure and/or renal failure. The best way to do it is through insulinization using several regimens (basal-prandial insulin with glucose correction). Level of Evidence C; If necessary request the assistance of a specialist.

### 6.6.1.4. Glycemic Control on the Day of Surgery (Fasting) for Patients with Hyperglycemia

#### Degree of Recommendation I

- Patients with diabetes should preferably be operated in the first hours of the day, especially those using insulin; Level of Evidence C;
- Hypoglycemia and glycemic variability should be avoided;
- Monitor capillary glycemia every 6 hours in patients who are users of oral hypoglycemic agents and every 4 hours in patients using insulin; Level of Evidence C;
- Keep glycemia between 100 and 180 mg/dL; Level of Evidence C;
- Suggestion staggered scheme while fasting:  
141 to 180 mg/dL = 01UI; 181 to 200 mg/dL = 02UI; 201 to 250 mg/dL = 03UI; 251 to 300 mg/dL = 04UI; 301 to 350 mg/dL = 06UI; 351 to 400 mg/dL = 08UI; above 401 mg/dL = consider using intravenous insulin pump or postponing elective surgery until better control;
- If glycemia levels below 100mg/dl = install intake of glucose in 5 to 10 g/hour. (e.g.: 100 mL/h of 5% SG);
- If glycemia below 70 mg/dL = 60 ml bolus of intravenous 25% hypertonic glucose, install glucose intake in 5 to 10 g/hour (prefer 10 g/hour), repeat blood glucose test repeat every 15 minutes until above 80 mg/dL.

### 6.6.1.5. Patients with Diabetes Mellitus Type 1

- Pre-hospitalization evaluation and intra-hospital follow-up with a specialist are recommended, if available;
- Monitor capillary glycemia: pre-meal and at 10 pm while keeping usual diet, every 4 hours during fasting, and every hour or two hours while using continuous intravenous insulinization;
- Never replace basal-bolus insulin in the preoperative period with staggered scheme alone – risk of diabetic ketoacidosis;
- Surgery preferably early in the morning;
- In medium to major surgeries or those lasting for over one hour, ideally use continuous intravenous insulin pump as soon as starting fasting or in the morning of surgery, keeping the therapy during the surgery and in the early postoperative period while fasting;

• Based on the limitations for the use of continuous intravenous insulinization out of intensive care environment, alternatively, you can use:

- Keep the insulin the night before surgery;
- On the day of surgery in the morning, reduce basal insulin according to item I.B;
- Remove prandial insulins, keeping basal insulin, capillary glycemia every 3 or 4 hours, and adding staggered scheme (prefer ultra-fast insulin);
- Install intake of glucose in the morning of surgery (before the usual time of breakfast in the morning) – keep intake from 5 to 10 g/hour. The choice of the amount of grams per hour depends on the glycemic control.

### 6.6.1.6. Emergency Surgery in Diabetic Patients

- Measure glycemia before surgery;
- Correct hypoglycemia and keep supply of glucose from 5 to 10 g/hour. Preferably control hyperglycemia with intravenous insulinization and keep glycemia levels between 80 and 140 mg/dL;
- Attention to potassium correction.

### 6.6.2. Intraoperative Period

Hyperglycemia and insulin resistance are common findings in patients undergoing surgical stress due to increased secretion of hyperglycemic counter-regulatory substances and decreased insulin secretion by the pancreatic beta cell.

Intravenous infusion of insulin during surgery offers advantages over its subcutaneous administration because it has more predictable absorption and possibility of faster adjustment for safer and more effective glycemic control. Another solution containing dextrose with electrolytes may be administered concomitantly with the aim of preventing hypoglycemia and hypokalemia.

#### Degree of Recommendation IIa

- Capillary glycemia should be measured at anesthesia induction if surgery is prolonged (surgery longer than 1 hour) or if high-risk patient; Level of Evidence C;
- Intravenous administration of insulin to all type 1 diabetics (regardless of surgical size) and type 2 diabetic patients undergoing surgery with planned duration exceeding 1 hour or when glycemia is too uncontrolled is recommended, Level of Evidence C;
- The goal should be a glycemic control between 100 and 180 mg/dL during surgery, when this control is necessary.

### 6.6.3. Postoperative Period

Evidence regarding glycemic control in the postoperative period of patients without diabetes is mainly based on studies of patients admitted to the intensive care unit<sup>240</sup>. However, the therapeutic goal, the moment of initiation of intravenous insulin therapy and how strict should be the glycemic control, are still controversial. Currently, it has been demonstrated that the

benefit of glycemic control relates to the improvement of clinical outcomes and not the use of insulin.

In 2001, one of the most important studies in this field, first demonstrated a clinical benefit of strict control of glycemia (90-100 mg/dL) in surgical patients compared with a more permissive control, where the patients had hyperglycemia during the postoperative period (150-160 mg/dL)<sup>241</sup>. This was a prospective, randomized and large study involving more than 1,500 patients and it demonstrated better results with the strict control of glycemia in the postoperative period: lower rates of in-hospital mortality, polyneuropathy, infection, acute renal failure, and shorter duration of mechanical ventilation and stay in intensive care units. Best long-term clinical outcomes were demonstrated only in patients undergoing cardiac surgery. Similar results to this study were subsequently demonstrated in non-surgical patients hospitalized in intensive care units<sup>242</sup>. Regarding the patient diagnosed with diabetes, the clinical benefit associated with strict glycemic control was also present, however, there was no impact on mortality reduction. Based on these studies, the recommendation was for a strict control in the postoperative period for patients undergoing noncardiac surgery.

Recently, the benefits of strict glycemic control, which were well accepted and implemented in guidelines<sup>36,139</sup> and in the clinical practice, were questioned by the important study called NICE-SUGAR<sup>243</sup>. This is a randomized, multicenter trial involving over 6,000 patients, with approximately 1/3 of surgical patients and 2/3 of clinical patients, which compared strict glycemic control (81-108 mg/dL) with conventional glycemic control (144-180 mg/dL). Patients were randomized to receive intravenous insulin within the first 24 hours of stay in intensive care units. Surprisingly, the group of patients randomized to receive strict control had higher mortality rates in 90 days (27.5%) compared with the conventional group (24.9%). There were no differences in other minor outcomes regarding the two groups. There are still doubts about the explanation for these results. The group where the glycemic control was stricter had higher rates of hypoglycemia (< 40 mg/dL) compared with the control group.

#### Degree of Recommendation I

- Until more studies are conducted and more evidence is available to better understand what is the most appropriate treatment goal for glycemic control in the postoperative period of patients undergoing noncardiac surgery, it is recommended that patients be individually assessed and that generally a value around 140 mg/dL is a reasonable goal for patients who have the profile and clinical scenario similar to those described in the NICE-SUGAR study; Level of Evidence A;

- The indication, however, to initiate therapy with intravenous insulin is valid only for patients admitted to intensive care units and whose glycemic levels are above 180 mg/dL. Level of Evidence A.

#### Degree of Recommendation IIa

- For patients undergoing elective surgery with no complications, and postoperative period in non-intensive care units, usually there is no need for glycemic control with intravenous insulin and the same hypoglycemic regimen used before the surgery should be used; Evidence Level C;

### 6.7. Anesthetic and Intraoperative Considerations

The anesthetic-surgical planning should include the implementation of perioperative measures that can reduce the patient's risk, taking into account the elements of preoperative evaluation. The recommendations for perioperative monitoring and implementation of measures to reduce major complications are described below.

#### 6.7.1. Supply and Consumption of Tissue Oxygen

Patients at high surgical risk who not receive adequate supply of tissue oxygen (DO<sub>2</sub>) during the perioperative period develop more postoperative complications, often fatal complications. The imbalance between supply and consumption of tissue oxygen occurs particularly in the intraoperative period and the first hours after surgery. The reduction of oxygen supply in this context is associated with lower overall oxygenation, tissue hypoperfusion, and a higher rate of postoperative complications. Aiming to adjust the supply of tissue oxygen in the perioperative period, some recommendations should be followed<sup>244-250</sup>:

##### Degree of Recommendation I

- During the perioperative period, the supply of tissue oxygen should be optimized with the purpose of adjusting tissue perfusion to avoid the occurrence of organ dysfunction; Level of Evidence A;

- The strategy for super-supply of oxygen (supra-maximum DO<sub>2</sub>) should be avoided because it results in prevention of organ dysfunction; Level of Evidence A;

- Volume replacement in the perioperative period should be careful and based on continually evaluated goals, preferably by means of dynamic parameters, such as PP delta (PP delta should be below 13%), systolic volume variation, increase in cardiac index (pulmonary artery catheter or echocardiography), and improvement in parameters of tissue perfusion such as SVO<sub>2</sub>, lactate and base excess; Level of Evidence A.

##### Degree of Recommendation IIa

- The optimization of oxygen supply should be accomplished through proper assessment of the patient's volume status, challenging the cardiovascular system by means of volume tests with continuous reassessments; Level of Evidence B;

- The use of inotropes such as dobutamine and dopexamine perioperatively in high-risk patients is indicated in cases of imbalance of oxygen supply and supply-consumption ratio when blood volume is adjusted. This should be initiated at low doses and the patient should be monitored for adverse effects such as ischemia and tachycardia; Level of Evidence B;

- Red blood cell transfusion should be performed in high-risk patients when there is tissue hypoxia or imbalance between oxygen supply and consumption; Level of Evidence A

- Replacement of fluid can be done using crystalloid or colloid, with no significant differences between them. Crystalloids is the recommend option, especially when the volume to be replaced does not exceed 50 mL/kg because of its lower cost and fewer harmful effects; Level of Evidence B;

- In situations of massive fluid replacement (volumes above 60 mL/kg, we recommend the use of lower molecular

## Guidelines

weight starches (tetrastarch) and/or albumin in association with crystalloid, provided that there are no contraindications; Level of Evidence B;

- A liberal strategy for fluid replacement in the perioperative period should be avoided, since this is associated with worse mortality rate. Level of Evidence B.

### 6.7.2. Hemodynamic Monitoring Guided by Goals

Therapy guided by hemodynamic goals refers to a protocol of perioperative care using cardiac output or tissue perfusion measures such as central venous oxygen saturation (SVO<sub>2</sub>) as goals of treatment with fluids and inotropes. Recent randomized studies have demonstrated reduced mortality and morbidity in high-risk patients undergoing perioperative care protocol based on goals such as optimization of cardiac output and/or SVO<sub>2</sub>. Some recommendations must be followed<sup>251,252</sup>:

#### Degree of Recommendation I

- High risk patients should have cardiac hemodynamics monitored in order to optimize parameters such as cardiac output and/or venous oxygen saturation; Level of Evidence A;
- Central venous oxygen saturation around 70% should be a target of the perioperative management of patients at high surgical risk; Level of Evidence B.

#### Degree of Recommendation IIa

- Patients at high surgical risk should have central venous oxygen saturation monitored using a central venous catheter. Level of Evidence B.

### 6.7.3. Perioperative Monitoring of Cardiac Output

The measurement of cardiac output in the perioperative period is a useful tool that allows for a more careful assessment of patients' volume status and measuring the response to therapy when there is organic infusion of fluids, vasoactive drugs, and transfusion of blood products. However, although widely used, the pulmonary artery catheter or Swan-Ganz, which measures cardiac output through the thermodilution technique, had its role as a monitoring tool questioned. This is caused by the risk of the procedure and the scarcity of studies without bias or sample analysis showing reduction of cardiovascular morbidity and mortality. The pulmonary artery catheter is useful when combined with good clinical sense, especially perioperative management of high risk patients, allowing accurate hemodynamic assessment and early detection of adverse effects caused by the therapy, such as elevation of filling pressures and decreased cardiac index.

A minimally invasive method to measure cardiac output can be performed using the following systems: FloTrac Vigileo, LiDCOplus or PiCCO. These technologies allow the measurement of cardiac output and other hemodynamic parameters without the need for a pulmonary artery catheter. Although advantageous because they are less invasive, these techniques have some limitations such as calibration errors and limitations in the measures in situations of major changes in vascular resistance. Currently, minimally invasive monitoring of cardiac output has become a useful tool in optimizing hemodynamics of patients at high surgical risk.

Recommendations for the perioperative use of pulmonary artery catheter<sup>253,254</sup>:

#### Degree of Recommendation IIa

- Surgery for repair of abdominal aortic aneurysm; Level of Evidence C;
- Patients with decompensated heart disease or cardiac dysfunction undergoing a major or high-risk surgical procedure; Level of Evidence B;
- Patients undergoing surgery who develop shock; Level of Evidence B;
- Patients with pulmonary hypertension undergoing a major or high-risk surgical procedure; Level of Evidence C;
- Patients undergoing surgery who develop severe sepsis or septic shock; Level of Evidence B.

Recommendation of other methods to measure cardiac output<sup>255,256</sup>:

#### Degree of Recommendation IIa

- Noninvasive measurement of cardiac output in the perioperative period can be performed using FloTrac Vigileo, LiDCOplus or PiCCO; Level of Evidence B.

#### Degree of Recommendation IIb

- Optimization of cardiac output in the perioperative period of high-risk patients can be made noninvasively using FloTrac Vigileo, LiDCOplus or PiCCO; Level of Evidence C.

### 6.7.4. Choosing the Anesthetic Technique

Technological advances with the development of improved monitoring techniques and new anesthetic drugs allows for safer anesthesia, resulting in improved patient recovery. The use of regional anesthesia requires greater hemodynamic stability and is associated with excellent analgesia intra- and postoperatively. It also results in lower incidence of thromboembolic events, respiratory complications and, some studies have shown that it reduces tumor recurrence and mortality. Contraindications to neuraxial blockade, such as coagulopathy, thrombocytopenia, and hemodynamic instability, should always be considered. The use of combined anesthesia can result in the use of lower doses of intravenous anesthesia, shorter anesthesia time, and better analgesia.

#### Degree of Recommendation I

- Regional anesthesia is contraindicated in patients with coagulopathy, thrombocytopenia, or hemodynamic instability. Level of Evidence A.

#### Degree of Recommendation IIa

- Anesthetic monitoring should be done carefully to allow continued assessment of anesthetic depth using the lowest possible doses of drugs. Level of Evidence A.

### 6.7.5. Choice of Anesthetic Agent

It is recommended that induction is always performed in a slow and safe manner, avoiding hemodynamic instability, myocardial ischemia, and stroke. The replacement of midazolam with propofol or etomidate, the replacement of fentanyl with low doses of remifentanyl or sufentanil and



non-use of muscle relaxants of renal elimination in patients with impaired renal function allow a faster recovery from anesthesia. In patients with hemodynamic instability or with reduced cardiovascular reserve, ketamine and etomidate should be the agents of choice for induction of anesthesia for minor hemodynamic interference, even though the use of etomidate can be associated with the occurrence of adrenal insufficiency. It is important to emphasize that propofol is contraindicated in these patients because it is associated with intraoperative hypotension, shock, and metabolic acidosis.

#### Degree of Recommendation I

- Fast-acting drugs of short duration and low residual effect should be preferably used in all anesthetic procedures. Level of Evidence B.

#### Degree of Recommendation IIa

- Propofol should be avoided in hemodynamically unstable patients or patients with cardiac dysfunction. Level of Evidence B;
- Ketamine and etomidate are drugs of choice for anesthesia of unstable patients or patients with ventricular dysfunction. Level of Evidence B.

#### 6.7.6. Maintenance of Body Temperature

The occurrence of intraoperative hypothermia is associated with increased response to stress, hypertension, and myocardial ischemic events, resulting in increased surgical morbidity and mortality.

#### Degree of Recommendation I

- Normothermia should be preserved for perioperative prevention of cardiovascular events. Level of Evidence A.

#### 6.7.7. Perioperative Use of Nitroglycerin

Nitroglycerin is a vasodilator drug with predominantly venous and coronary dilating properties. However, there is no evidence of reduced myocardial ischemia related to its use in the perioperative period<sup>257</sup>.

#### Degree of Recommendation I

- Intraoperative nitroglycerin should be used only for blood pressure control in CAD patients, with no intention to prevent perioperative ischemia. Level of Evidence C.

#### 6.7.8. Perioperative Ventilatory Support

Pulmonary gas exchange is systematically undermined during general anesthesia with mechanical ventilation (MV), resulting in reduced arterial oxygenation. The main cause is the collapse of the lung tissue (atelectasis), present in almost 90% of patients under anesthesia. A good correlation between the amount of atelectasis and pulmonary shunt has been demonstrated. Thus, anesthesiologists are concerned with knowing more about it and using procedures aimed at the prevention of atelectasis and/or reopening of collapsed lung areas.

Next, we present key recommendations for management of mechanical ventilation in the perioperative period<sup>258,259</sup>:

#### 6.7.8.1. Controlled Pressure versus Controlled Volume

- The comparison of different liquid ventilation intraoperatively demonstrated no benefit of one technique over another. A ventilatory method is not recommended over the other in order to prevent pulmonary complications;

#### 6.7.8.2. Tidal Volume

The use of variable tidal volume is not a practice widely used during mechanical ventilation in anesthetized patients. During this period, there are several changes in lung mechanics mainly related to the type of surgery, presence of retractors, extrinsic compression, and neuromuscular blockers. However, the use of high tidal volumes may be associated with the occurrence of high pressures, alveolar overdistention, and pulmonary inflammatory mediators that determine important changes in the lung function. Despite the scarcity of studies comparing anesthesia in the strategy of low tidal volume vs. high tidal volume, perioperative outcomes from the studies on acute lung injury (ALI)/Acute Respiratory Distress Syndrome (ARDS) serve as the basis for the clinical practice, recommending not to use high tidal volumes to avoid alveolar overdistention.

#### Degree of Recommendation IIa

- We recommend the use of tidal volume 80-10 mL/kg in volume control or peak/plateau inspiratory pressure sufficient to maintain the same volume in controlled pressure. Level of Evidence C.

#### 6.7.8.3. Positive End-expiratory Pressure (PEEP)

Recent studies show that the minimum PEEP of 5 cmH<sub>2</sub>O during surgery results in improvement of oxygenation parameters intra- and postoperatively, with a reduction in atelectasis. Current studies recommend the use PEEP in all patients undergoing general anesthesia, especially in patients at higher risk of pulmonary complications.

#### Degree of Recommendation IIa

- Use of PEEP during general anesthesia is recommended because it is associated with improvement of oxygenation and prevention of atelectasis. Level of Evidence B.

#### 6.7.8.4. Alveolar Recruitment Maneuver

Immediately after the administration of general anesthesia, atelectasis occurs in dependent areas, which are responsible for changes in oxygenation in the perioperative period. The use of recruitment maneuvers associated with PEEP in this period is crucial to open up collapsed alveoli and maintain its patency, resulting in improved oxygenation. Recent studies have shown benefits of recruitment maneuvers intraoperatively to prevent postoperative hypoxemia without causing hemodynamic impairment.

Another technique that has been used for alveolar recruitment is CPAP (continuous positive airway pressure) 20, 30 or 40 cmH<sub>2</sub>O for 20 to 30s. Although there are studies showing good results in terms of safety and reversal of hypoxia with this method in the intensive care environment, there are few specific studies conducted in the operating room.

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### Degree of Recommendation IIa

- The use of recruitment maneuvers is a recommended intraoperatively practice in order to avoid alveolar collapse. Level of Evidence B.

#### 6.7.8.5. Fraction of Inspired Oxygen

The use of low inspired oxygen concentrations (below 0.4) is not recommended during induction because it reduces the margin of safety if there is difficulty in handling the air. Limiting the use of high oxygen concentrations only during the induction of anesthesia may prevent the occurrence of atelectasis during the subsequent maintenance phase of anesthesia. Thus, ventilation during maintenance of anesthesia should be done with a moderate fraction of inspired oxygen (FIO<sub>2</sub> around 0.3 to 0.4), which should be increased only in the event of impairment of arterial oxygenation.

### Degree of Recommendation I

- During induction of anesthesia, the use the fraction of inspired oxygen of 1 is recommended to ensure adequate oxygen to perform the intubation. During maintenance of anesthesia, fraction of inspired oxygen sufficient to maintain oxygen saturation above 98% should be used. Level of Evidence C.

#### 6.7.8.6. Weaning from Mechanical Ventilation (MV)

Weaning from mechanical ventilation in the postoperative period is characterized by an increase in cardiovascular and metabolic stress. Therefore, we must advance weaning when the patient is hemodynamically stable, with good balance in terms of electrolyte, adequate analgesia, and level of consciousness sufficient for ventilatory control. Extubation can be performed in the operating room, postanesthesia recovery room or intensive care unit, provided that the above criteria are met.

### Degree of Recommendation IIa

- The removal of the VM can be performed using pressure support (PSV) or synchronized intermittent mandatory ventilation (SIMV). Level of Evidence C.

#### 6.7.8.7. Postoperative Analgesia and Postoperative Exercises to Increase Lung Volume

Effective postoperative analgesia is recommended as a method to reduce lung complications. There have been discussion about the best postoperative analgesia method for the prevention of these complications. There are studies demonstrating the superiority of epidural analgesia in the prevention of such complications, although the data are conflicting.

Among the methods used to increase lung volume after surgery, we highlight intermittent positive pressure ventilation, deep breathing exercises, incentive spirometry, and chest physical therapy.

### Degree of Recommendation IIa

- Obtaining adequate postoperative analgesia is associated with postoperative pulmonary function. Level of Evidence B;

- Postoperative maneuvers to increase mean lung volumes are demonstrably linked to the reduction of postoperative complications. Level of Evidence C.

### 6.8. Perioperative Surveillance

Early detection of cardiovascular events is key to reduce mortality after noncardiac surgery. Acute myocardial infarction (AMI) may occur in the absence of chest pain, thus it is necessary to carry out monitoring strategies for its diagnosis.

ST segment monitoring, 12-lead electrocardiogram (ECG), troponin dosage and intraoperative transesophageal echocardiography are methods that can be used to monitor for complications. There is little evidence on the usefulness of detecting changes in segmental contractility in intraoperative transesophageal echocardiography for diagnosis or as a predictor of events after noncardiac surgery<sup>260,261</sup>. Therefore, this method is not recommended for intraoperative monitoring of myocardial ischemia.

In a review of 14 studies involving 2,400 patients, Landesberg et al demonstrated that the use of the ST segment monitoring for detection of perioperative myocardial ischemia to predict perioperative events had a sensitivity between 55 and 100% and a specificity between 37 and 85%<sup>262</sup>. This wide range of sensitivity/specificity was due to the large methodological differences between the studies. The accuracy of ST segment monitoring depends on the type of lead (unipolar or bipolar), the number of leads used, the combination of leads used (V4 is the most sensitive for precordial derivation and the combination of DII, V4 and V5 have a sensitivity of 96%), the visual or computed analysis, the prevalence of CAD in the population studied, the definition of ischemia and events, and the time in which ischemia was detected<sup>263</sup>. ST segment monitoring should be done only with automated analysis, since the visual analysis performed by physicians only detects 20% of ischemic episodes<sup>264</sup>. The importance of finding intraoperative ischemia depends on the likelihood of patients having coronary artery disease. In a study of 170 healthy young women undergoing cesarean delivery, 26% of patients had intraoperative ischemia, but there were no cardiovascular events<sup>265</sup>. On the other hand, in 115 patients undergoing vascular operations, 21 patients had ischemia and 16 patients did not have cardiovascular events<sup>93</sup>. Besides the classic limitations of the interpretation of electrocardiograms (left ventricular hypertrophy, left bundle branch block, Wolff-Parkinson-White syndrome), there are limitations that affect the perioperative evaluation of ischemia such as hypothermia, electrolyte imbalance, artifacts (surgical field, electrocautery) or changes in ventilation. The incidence of postoperative ischemia has prognostic implication: Mangano et al. demonstrated that postoperative ischemia was an independent predictor of cardiovascular events in 454 patients undergoing general surgery in two years ( $p = 0.0001$ )<sup>266</sup> and Landesberg et al. showed that the occurrence of postoperative myocardial ischemia longer than 30 minutes was related to reduced survival after 5 years in 447 patients undergoing vascular operations ( $p = 0.008$ )<sup>267</sup>. Therefore, the use of ST segment monitoring is not routinely recommended for detection of myocardial ischemia, but may be useful in high-risk patients, always with automated analysis.

Most cardiovascular events occur within the third postoperative day. The use of 12-lead ECG during this period is a simple and effective method for detecting events. In a study of 3,564 patients aged over 50 years, signs of ischemia on ECG after surgery were independent predictors of cardiovascular events. However, ECG negative for ischemia did not decrease the risk of events<sup>268</sup>. In another study comparing series ECG with 3-lead Holter in 55 patients undergoing vascular surgeries, the ECG was as effective as the Holter to detect myocardial ischemia-related event<sup>269</sup>. Troponin measurement associated with the completion of the series ECG until the 3<sup>rd</sup> postoperative day is the best strategy for the diagnosis of acute myocardial infarction<sup>270</sup>.

The elevation of troponin without clinical evidence of myocardial ischemia or ECG changes detected by monitoring should not be regarded as a false positive result, but as a prognostic factor. Patients with troponin alone have a higher rate of cardiovascular events and lower survival in the long term, deserving an additional cardiac evaluation before hospital discharge<sup>271-273</sup>. However, if the patient has elevated troponin alone, alternative diagnoses that may present increased troponin and are common in the perioperative period, such as pulmonary embolism, acute pericarditis, congestive heart failure, myocarditis, sepsis, shock or renal failure<sup>274</sup> should be ruled out.

Recommendations:

#### Degree of Recommendation I

- Patients with an estimated perioperative cardiac risk of ischemic nature must remain in semi-intensive or intensive care units undergoing electrocardiogram (Level of Evidence B) and troponin (Level of Evidence A) daily until the 3<sup>rd</sup> postoperative day since most events occur in this period;
- If troponin measurement is not available, we recommend the replacement with CK-MB/CPK curve 8/8h. Level of Evidence B.

#### Degree of Recommendation IIb

- ST segment monitoring in the perioperative period of high-risk patients, Level of Evidence C.

## 7. Perioperative Acute Coronary Syndromes

AMI is the cardiac complication most feared in the perioperative period, occurring in about 1% to 1.8% of all operations<sup>3</sup>, varying with the type of operation and risk of the individual patient. It has shown high mortality (40%-50% in some series)<sup>275</sup>, probably related to the existence of comorbidities, diagnostic difficulty, and limitation to the use of anti-thrombotic and anti-platelet therapy classically used in acute coronary syndromes. The imbalance between supply and consumption of oxygen and the destabilization of coronary atherosclerotic plaques are the pathophysiological mechanisms involved in the origin of perioperative ischemia, which should be taken into consideration not only when defining strategies for prevention, but also in the treatment of patients suffering from perioperative AMI.

Although the clinical consequences of perioperative myocardial infarction are extremely severe, in most cases it is not clear and requires a high degree of clinical suspicion.

Most perioperative ischemia occurs within the first three days after surgery, and the classic clinical picture of chest pain is absent in more than half of patients<sup>3,275</sup>, which is partly explained by the residual effects of analgesics or sedatives used in that period. Furthermore, when present, chest pain is often attributed to other more obvious etiologies, such as incisional pain or patient position. Other manifestations such as dyspnea and nausea have alternative explanations in this period (atelectasis, effect of drugs), making perioperative myocardial infarction to be often undervalued by the medical team. Therefore, due to the difficulty in interpreting the clinical findings, the analysis of laboratory tests is crucial for the diagnosis of perioperative myocardial ischemia. The most important test are ECG, markers of myocardial necrosis, and transthoracic echocardiography.

On the analysis of the electrocardiogram, the vast majority of strokes are compatible alterations, but not pathognomonic of myocardial ischemia, which, however, are proven predictors of cardiac events for these patients<sup>268</sup>. In spite of being frequent, these findings lack specificity in the perioperative period, when it is common to have electrolyte disturbances, hypothermia and effects of drugs that can justify electrocardiographic findings mimicking myocardial ischemia. In addition, the pattern of evolution should also be taken into account during the analysis of the electrocardiogram. It is important to compare the changes obtained for subsequent strokes and prior to the event.

Among the markers of myocardial necrosis, troponin is undoubtedly the most often used because of its high sensitivity and specificity in diagnosing myocardial lesion. However, it is worth mentioning that this marker is higher in other situations of myocardial lesion besides the one caused by coronary artery disease. Other complications are commonly present in postoperative noncardiac surgeries, such as pulmonary embolism, heart failure, and sepsis also elevate markers and should be considered in the differential diagnosis. Furthermore, patients with renal failure often have elevated troponin, especially cardiac troponin T, showing, however, evolution of the plateau, without the pattern of rise and fall typical of AMI. CK-MB is less useful for diagnosis of perioperative AMI because of its lower sensitivity and specificity compared with troponin. This marker may increase after skeletal muscle injury during surgery and its relationship with CPK has low reliability in the identification of perioperative myocardial injury<sup>267</sup>.

Echocardiogram, which is increasingly available nowadays, is also an important tool for diagnosis. Despite normal findings, it does not rule out the diagnosis, the presence of a new change in segmental contractility in patients with suspected myocardial ischemia confirms the diagnosis. Moreover, it can also provide indirect data for alternative diagnoses, pulmonary embolism, and heart failure of nonischemic origin.

No data analyzed alone is able to confirm or exclude the diagnosis of perioperative myocardial ischemia. Although recent publications clearly define the criteria for the diagnosis of AMI, they do not include perioperative AMI, which remains without well-defined diagnostic criteria<sup>276</sup>. The diagnostic strategy proposed by these Guidelines for identifying patients with perioperative AMI is shown in Figure 1.

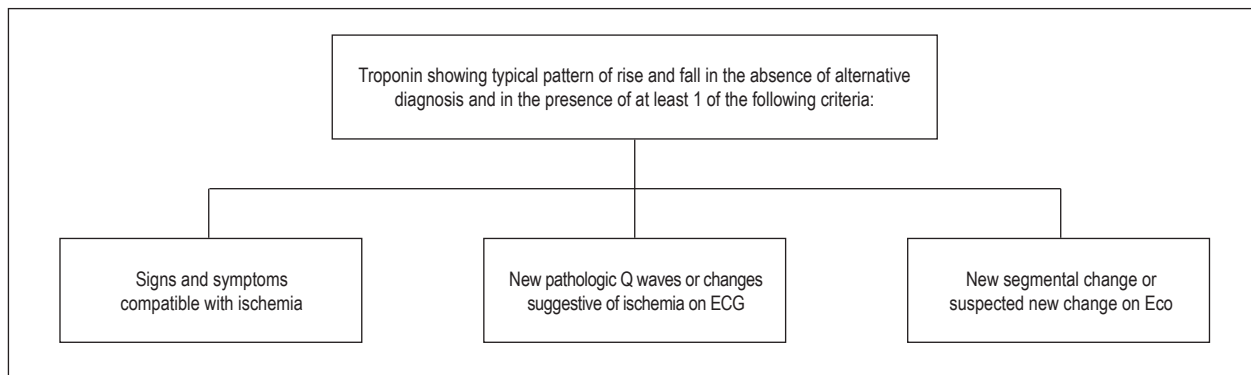


Figure 1 - Strategy for diagnosis of perioperative myocardial infarction provided by the present Guidelines.

Despite the frequency and prognostic significance, there are limited data in the literature regarding the treatment of perioperative myocardial ischemia. Most of the interventions used are extrapolations of what is already well established in acute coronary syndromes not related to surgical procedures. However, all therapeutic strategies require measures that lead to increased risk of postoperative bleeding, a fact that requires individual action and constant interaction with the surgical team.

The treatment of myocardial infarction without ST-segment elevation (most cases of perioperative AMI) initially requires correction of factors and triggers that may perpetuate the ischemic process. Therefore, correction of anemia, hypovolemia, and blood pressure fluctuations are the primary measures to be adopted in this situation. Additionally, and consistent with the pathophysiology of the event, coronary plaque stabilization should be considered an important measure in the treatment. Aspirin and anticoagulant therapy should be initiated if there is no contraindication. Although there is no study comparing the various methods of perioperative anticoagulation, it is prudent to give preference to the use of unfractionated heparin, since its half life is shorter and its effects can be quickly reversed if there is bleeding. Analogous to the treatment of ischemic event out of the perioperative context, analgesia with nitrates and/or morphine and the use of beta blockers, angiotensin-converting enzyme (ACE) inhibitors and statins are recommended. These patients should be treated aggressively, preferably with invasive risk stratification (cardiac catheterization), and early, before hospital discharge. This practice is essential to control the alarming morbidity and mortality in the short and long term.

Acute myocardial infarction with ST-segment elevation occurs in a minority of cases and assumes total occlusion of the coronary artery, requiring immediate intervention. Unlike AMI not related to surgical interventions, thrombolytic therapy is strongly contraindicated in the perioperative period because of high risk of bleeding. Thus, coronary angiography with primary angioplasty is the treatment of choice for these patients. This strategy is feasible and safe in patients without contraindications to therapy with heparin and antiplatelet agents, which are required during and after surgery, respectively<sup>277</sup>. In such cases, the benefits of revascularization must be considered in relation to the type

of surgery performed and the risk of bleeding, individualizing the decision in each case.

Increased troponin alone is a frequent event in the postoperative period, and this does not mean that there is acute coronary syndrome, however long-term prognostic implications are well-established<sup>267</sup>. Although there is no evidence available regarding the best strategy for the management of these cases, further investigation should be performed in all patients before hospital discharge, with the option of performing invasive and noninvasive cardiac stratification based on a cardiologist's assessment.

## 8. Emergency Surgery

When there is indication of urgent surgery, it is implicit that the urgency of the procedure surpasses the possible risks the surgery poses on the patient. However, even in such cases the preoperative evaluation should not be neglected, since the chances of cardiac complications are two to five times more frequent in this type of intervention<sup>278</sup>. High risk is caused both by lack of time and appropriate conditions to carry out a satisfactory assessment of the severity and comorbidities associated with the disease that motivated the surgery. Awareness about the patient's history of cardiovascular disease associated with minimal preliminary clinical data may allow for optimal use of resources and intra- and postoperative monitoring of the treatment. On the other hand, the vast majority of acute ischemic syndromes occur in the period between the surgery and the third postoperative day, which enables the medical team to set the time during which the patient must remain in intensive care unit.

## 9. Assessment of Comorbidities

### 9.1. Thyroid Disease

Thyroid disease is a very common clinical condition and in endemic areas the incidence of goiter is 15-30% of the adult population. It is therefore important to consider some peculiarities in the perioperative period of this population. Apart from technical difficulties in handling airways of patients with goiter, the hormonal imbalance can be a source of considerable morbidity and mortality<sup>279</sup>. Tetraiodothyronine



(T4) represents 80% of thyroid hormone production and 40% of it is peripherally converted into triiodothyronine (T3), which is five times more potent. Another 50% of T4 is converted into 3,5-triiodothyronine (T3r), which has no biological action. Only 0.2% of T3 and 0.3% of T4 are in the free and biologically active forms and the remainder is bound to plasma proteins (albumin, prealbumin, thyroglobulin). T3 and T3r are converted in the liver, kidneys, and central nervous system into inactive compounds. Systemic diseases, trauma, and drugs may block the peripheral conversion of T4 into T3 leading to euthyroid sick syndrome, which represents a physiological mechanism of energy saving in critical situations.

### 9.1.1. Hypothyroidism

The prevalence of hypothyroidism is estimated to be 5 of 1,000 patients and the prevalence of subclinical hypothyroidism is three times higher. Hypothyroidism is 10 times higher in females. The most common cause is iatrogenic (radioiodine therapy or surgical resection), and the second cause is autoimmune thyroiditis (Hashimoto). Besides the clinical picture (Table 12), levels of TSH, free T4 and free T3 are necessary for diagnosis.

Perioperative complications are rare when hypothyroidism is subclinical, mild or moderate.

Special attention should be given to severe cases whose chance of complications is higher<sup>279-284</sup>.

#### 9.1.1.1. General Recommendations

##### Degree of Recommendation I, Level of Evidence C

- Assess all risk factors of the patient;
- Do not worry about subclinical hypothyroidism when TSH value < 10 mU/dL;
- Elective surgery should only be performed when the patient is euthyroid;

**Table 12 - Clinical manifestations of hypothyroidism relevant perioperative**

Hypothermia
Myocardial depression
Decreased respiratory rate and difficulty in ventilatory weaning
Decreased heart rate
Abnormal response of baroreceptors
Hypotension or hypertension
Angina, myocardial infarction
Reduced blood volume
Anemia
Hypoglycemia
Hyponatremia (syndrome of inappropriate secretion of antidiuretic hormone)
Abdominal distension
Decreased hepatic metabolism of drugs

- Patients < 45 years old should receive full dose of L-thyroxine, which is usually 1.6 to 2.2 mcg/kg or 100 to 200 mcg a day. TSH levels normalize only after 4 to 6 weeks of appropriate dosage;
- Patients older than 45 years should start with 25-50 mcg/day, with the dose increasing every 2 weeks;
- Coronary patients should receive 15 mcg/day and this dose should be increased every week until a normal TSH;
- Do not postpone surgery in patients with hypothyroidism, but start oral hormone replacement;
- In surgical procedures with hypothyroidism, prophylaxis of hypothermia, cardiovascular monitoring and hydrocortisone 100 mg every 8 hours in 24 hours should be performed because of the chance to adrenal insufficiency;
- T4 has a half life of 7 days while T3 has a half life of 1.5 days. That is the reason why the user of T4 does not need to take it on the day of surgery, while the user of T3 should do it;
- To evaluate the possibility of difficult intubation due to goiter using radiography of the cervical region.

#### 9.1.1.2. Recommendations for Urgent Surgery in Patients with Severe Hypothyroidism or Myxedema Coma

##### Degree of Recommendation I, Level of Evidence C

- Administer 200-500 mcg of L-thyroxine or 40 mcg of intravenous T3 or 10-25 mcg of T3 every 8 hours before surgery, which corrects the hemodynamic and electrocardiographic changes. In the perioperative period, divide the dose by 50% T4 and 50% T3;
- The maintenance dose should be 40 to 100 mcg of T4 and 10 to 20 mcg of T3 intravenously every 24 hours;
- Administer 100 mg of hydrocortisone every 6 hours for a long time;
- As soon as possible, start hormone replacement by using the doses described above.

### 9.1.2. Hyperthyroidism

Thyrotoxicosis affects 2% of women and 0.2% of men. The prevalence of clinical and subclinical hyperthyroidism in the U.S. is, respectively, 0.2 and 1%. The most common causes are: Graves-Basedow disease, toxic nodular goiter, thyroiditis, and iatrogenic origin. Adrenergic effects pose a high risk for complications such as cardiac arrhythmias (10 to 15% of atrial fibrillation). These effects relate to the increased number and/or sensitivity of beta-adrenergic receptors. Mortality of hyperthyroidism is related to cardiovascular events<sup>279-284</sup>.

The diagnosis should be confirmed by laboratory tests in combination with clinical suspicion. TSH value should be low and free T4 should be normal (subclinical hyperthyroidism) or higher. Several situations may raise the total T4 by increasing the binding protein of T4, but it does not affect free T4 that has biological activity: pregnancy, cirrhosis, acromegaly, Cushing's syndrome, use of lithium, contraceptives, propranolol, amiodarone, and iodinated contrast media.

In cases of thyroidectomy, specific complications can occur: patients with large goiters can have complications

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during intubation and extubation (up to 35% of them have some degree of airway obstruction), recurrent laryngeal injury, tracheomalacia and laryngeal edema, and hypocalcemia can occur up to 36 hours after thyroidectomy in 20% of cases. Only 3% become permanently hypocalcemic and calcium must be intravenously replaced in this phase.

### 9.1.2.1. Clinical Manifestations in Hyperthyroidism with Effects on the Perioperative Period

- Cardiovascular: increased inotropy and chronotropism with decreased systemic vascular resistance, left ventricular hypertrophy, increased incidence of angina, heart failure, arrhythmias, and embolic events;
- Hematologic: anemia, thrombocytopenia, neutropenia, increased factor III, reduction of vitamin K-dependent factors, bleeding;
- Gastrointestinal: inadequate absorption of drugs;
- Metabolic/Renal: hypercalcemia, hypoalbuminemia, ketoacidosis, increased clearance of drugs;
- Lung: myopathy with respiratory failure;
- Endocrine: increased production and use of cortisol, glucose intolerance, weight loss, and protein catabolism.

### 9.1.2.2. General Information

#### Degree of Recommendation I, Level of Evidence C

- Parallel evaluation by an endocrinologist should be strongly considered in the perioperative period of patients with hyperthyroidism;
- Before the elective surgery, patients should be adequately treated with medication for hyperthyroidism;
- Thyroid medications - the most commonly used are propylthiouracil (PTU) and methimazole. These drugs inhibit the synthesis of thyroid hormones by preventing oxidation and organification of iodine. PTU has the additional benefit of inhibiting the peripheral conversion of T4 to T3 at higher doses, therefore, it is most commonly used in the perioperative period. The usual dose is 100 mg every 8 hours and the maximum dose is 400 mg every 8 hours. The doses of methimazole vary from 10 to 120 mg at a single dose. The dose should be reassessed every 4-6 weeks. Adverse effects are rarely severe: skin rash, fever, rash and arthralgia, transient elevation of liver enzymes, leukopenia. Agranulocytosis (0.5%), severe hepatitis, lupus-like syndrome and thrombocytopenia are more severe and less frequent adverse effects and require discontinuation of medication;
- Beta-blockers - the most used is propranolol at a dose of 10-80 mg every 6-8 hours (1 mg intravenous intraoperatively). Esmolol can be administered during surgery with a loading dose of 500 mcg/kg over 1 minute and maintenance of 25-300 mcg/kg/min.

### 9.1.2.3. Recommendations for Emergency Surgeries or Urgent Procedures

#### Degree of Recommendation I, Level of Evidence C

- Antithyroid drug - the drug of choice is PTU at high doses (1000 to 1200 mg divided into 3 doses);

- Beta-blockers - prefer intravenous administration;
- Iodine - can be used for a maximum of 10 days since the inhibition of organification is transient (Wolff-Chaikoff effect) and after that time there is escape and worsening of hyperthyroidism;
- Lugol's solution, which contains 5% iodine and 10% potassium iodide is the most used at a dose from 0.1 to 0.3 ml every 8 hours (3 to 5 drops);
- Iodinated contrast - ipodate sodium and iopanoic acid are used to compensate, with the advantage of giving less escape and inhibit the peripheral conversion of T4 to T3. The dose is 500 mg every 8 hours;
- Corticosteroid - must be administered when there is no compensation of hyperthyroidism in the intraoperative and postoperative periods due to higher peripheral degradation of cortisol. The dose is 100 mg at induction and 100 mg every 8 hours for 24 hours;
- Anesthesia - increased metabolism of anesthetic drugs and risk of difficult intubation because of goiter should receive special attention;
- Thyrotoxic storm - is associated with mortality rates of 20-30%. Based on the clinical abruptness, the treatment described in item C should be initiated promptly, even without laboratory confirmation.

### 9.1.2.4. Treatment of Thyrotoxic Storm

- Hydration;
- Cooling;
- Inotropes;
- PTU attack (1000 mg gastrointestinal tract);
- PTU maintenance 200 mg every 6 hours;
- Ventilatory support;
- Metabolic control through the digestive system;
- Hydrocortisone attack 300 mg intravenously;
- Maintenance of 100 mg hydrocortisone every 8 hours;
- Iodine in the form of Lugol through digestive tract or intravenous iodine at a dose of 1 g every 8 hours;
- If necessary, plasmapheresis, dialysis or cholestyramine to remove hormones from the circulation.

## 9.2. Adrenal Insufficiency

The increase in cortisol levels during acute stress is an important protective response. However, the metabolic stress caused by surgery can trigger acute adrenal insufficiency in patients with clinical and subclinical disorders that affect the hypothalamic-pituitary adrenal axis and the results can be catastrophic determining multiple complications and even the patient's death.

Physical stress increases adrenocorticotrophic hormone (ACTH) and cortisol secretion. Increased levels of cortisol, noradrenaline, and adrenaline characterize the hormonal changes induced by stress, surgical stress is minimal in small stress and progressively higher in moderate and severe stress, lasting no more than 24 hours in surgeries without complications.

The intraoperative period and mainly anesthesia recovery and extubation are the major determinants of axis activation with increased plasma cortisol levels returning to baseline within 24 to 48 hours<sup>285</sup>. With the increasing endogenous demand of steroids, patients with impaired function and compromised adrenal reserve may have acute adrenal insufficiency (AAI), thus it is essential to identify these individuals early for proper planning in order to avoid perioperative complications.

### 9.2.1. Clinical Picture of Adrenal Insufficiency

- Hypotension and hemodynamic shock (which may be resistant to vasopressors) with multiple organ dysfunction;
- Hypoglycemia;
- Tachycardia;
- Electrolyte disturbances: hyponatremia, hyperkalemia (primary AI), hypercalcemia, acidosis;
- Hypocontractility rate;
- Anemia, neutropenia, and eosinophilia;
- Nausea, vomiting, weakness, orthostatic hypotension, dehydration, abdominal pain or flank pain (acute adrenal hemorrhage), fatigue, weight loss;
- Vitiligo, abnormal skin pigmentation, hypogonadism, hypothyroidism.

One should suspect the diagnosis of AI if in the intra- or postoperative periods there is unexplained hypotension or shock or refractory to volume and drugs, discrepancy between disease severity and patient status, high fever without apparent cause (negative cultures) or if the patient does not respond to antibiotic therapy, unexplained mental changes, apathy, or specific psychiatric disorder. These cases should be treated as AI and confirmed later (Degree of Recommendation I, Level of Evidence C).

### 9.2.2. Identification of Patients at Risk of AI

- Patients with a diagnosis already established of AI<sup>286</sup>;
- Patients at risk for AI<sup>287</sup> and patients with relative hypoadrenalism (limited adrenocortical reserve):
  - Pituitary tumors (macroadenomas);
  - Radiotherapy in the pituitary region;
  - Previous pituitary surgery;
  - Postoperative period of Cushing's disease, bilateral adrenalectomy or unilateral adrenalectomy in case of other adrenal affected;
  - Chronic corticosteroid use (> 7.5 mg prednisone or equivalent for more than 30 days or > 20 mg for more than two weeks);
  - Patients with type 1 diabetes or autoimmune diseases (Hashimoto's disease, ovarian or primary testicular failure, hypoparathyroidism, vitiligo);
  - Individuals with suggestive symptoms (darkening of the skin, weakness, fatigue, nausea, vomiting, depression, hypotension, electrolyte disturbances, hypoglycemia, fever).

Recommendations:

#### Degree of Recommendation I

- Confirm the diagnosis by means of appropriate tests for patients at risk for AI and consider follow-up by an endocrinologist; Level of Evidence B;
- In cases of need for confirmation of AI by means of tests, use dexamethasone that does not interfere with the evidential test; Level of Evidence C;
- In cases of coexistence of hypothyroidism and untreated AI: first correct AI; Level of Evidence C;
- No need for mineralocorticoid supplementation because the doses of corticosteroid supplementation in surgical stress have mineralocorticoid activity; Level of Evidence C.

#### Degree of Recommendation IIa

- If unable to confirm the diagnosis before surgery, we recommend the corticosteroids supplementation as shown below; Level of Evidence C.

### 9.2.3. Supplemental Doses of Corticosteroids<sup>288-290</sup>

Recommendations:

#### Degree of Recommendation IIa

- No need for high doses of supplemental corticosteroids for prevention of AI; Level of Evidence B;
- High doses may increase the chance of complications such as hypertension and diabetes decompensation; Level of Evidence C.

#### 9.2.3.1. Mild Surgical Stress

##### Degree of Recommendation IIa

- Doubling or tripling the dose of corticosteroids in patients with established AI and chronic users, noting that adrenal suppression can occur rapidly with high doses or even after a long time without using corticosteroids (up to 48 months); Level of Evidence C;
- If the patient is fasting, supplement with 50 mg of intramuscular or intravenous hydrocortisone immediately before surgery and 25 mg of hydrocortisone twice a day or equivalent (dexamethasone 0.75 mg twice a day), reducing to the regular dose in 24 hours or once stress ceases; Level of Evidence C.

##### Degree of Recommendation IIb

- In patients without an established diagnosis and strongly suspected, treat for AI; Level of Evidence C.

#### 9.2.3.2. Moderate Surgical Stress

##### Degree of Recommendation IIa

- Additional 25 mg of hydrocortisone or equivalent, intramuscular or intravenous 8/8 hours, starting on the morning of surgery, with 50% reduction in dose per day until the usual dose; Level of Evidence C.

#### 9.2.3.3. High surgical stress

##### Degree of Recommendation IIa

- Supplemental hydrocortisone 50 mg/day or equivalent 6/6 hours with a 50% reduction in the dose per day until

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the usual dose once metabolic stress disappears (usually it lasts for 48 hours following surgeries for infections or other complications); Level of Evidence C.

### 9.2.3.4. Special Situation of Cushing's Syndrome

- It is advisable to ask for monitoring performed by an endocrinologist;
- Start the steroid upon arrival to the intensive care unit or the day after the surgery;
- In these cases, some groups of corticosteroids should be used only if there are symptoms, signs or laboratory results of AI;

## 9.3. Obesity and Bariatric Surgery

Obesity has reached pandemic proportions. In Brazil the rates of overweight are also increasing and it is estimated that about 40% of adults in the country are overweight (body mass index - BMI - above 25 kg/m<sup>2</sup>) and 8.9% of men and 13.1% of women are obese.

Obesity is related to comorbidities that influence the perioperative evaluation and management, such as atherosclerosis, heart failure, hypertension, pulmonary hypertension, deep vein thrombosis, and low functional capacity.

Severity of obesity may be characterized by different degrees:

- Obesity grade 1 BMI from 30 to 34.9 kg/m<sup>2</sup>;
- Obesity grade 2 BMI from 35 to 39.9 kg/m<sup>2</sup>;
- Obesity grade 3 BMI ≥ 40 kg/m<sup>2</sup>.

Classifications used in bariatric surgeries still categorize obesity in grade 4 and 5 when BMI is higher than 50 and 60 kg/m<sup>2</sup>, respectively.

### 9.3.1. Peculiarities in the Evaluation of Surgical Risk in Obese Individuals<sup>291,292</sup>

- Medical history limited by the difficulty in differentiating between dyspnea and cardiogenic pulmonary origins of obese patients' low functional capacity;
- Physical examination and detailing of the cardiopulmonary system are limited by obesity;
- Few risk scores used in perioperative evaluation include obesity and quantify the risk associated with this variable.

#### 9.3.1.1. Perioperative Risk Related to Obesity

- Higher prevalence of comorbid conditions that are risk factors for atherosclerosis and ischemia (hypertension, diabetes, and hyperlipidemia);
- Increased risk of thromboembolic events and surgical wound infection;
- Greater difficulty in measuring blood pressure and acquisition of intravenous access;
- Longer mechanical ventilation and longer hospital stay;
- Increased risk of renal failure;
- Increased sensitivity to opioids and sedatives;
- Increased risk of aspiration of gastric contents;

- Increased chance of hypoxemia due to hypoventilation, pulmonary restriction, postoperative atelectasis, increased occurrence of central apnea and obstructive sleep and hypercapnia;

- Increased mortality in intensive care in severely obese patients.

### 9.3.2. Specific Recommendations for the Preoperative Evaluation According to BMI and Surgical Size<sup>291,293,294</sup>

#### 9.3.2.1. Obesity of Any Degree and Minor Surgery

##### Degree of Recommendation IIa

- Assessment similar to nonobese individuals; Level of Evidence D.

#### 9.3.2.2. Obesity grade 1, 2 and 3 and intermediate and major surgery

##### Degree of Recommendation I

- History and physical examination;
- Clinical evaluation of obstructive sleep apnea using appropriate score; Level of Evidence B.

##### Degree of Recommendation IIa

- ECG if the patient is over 40 years or has a risk factor for heart disease; Level of Evidence B;
- Fasting glucose; Level of Evidence B;
- Polysomnography in patients with positive screening for scores apnea; Level of Evidence C.

##### Degree of Recommendation IIb

- Creatinine if patient is diabetic, has hypertension or a history of renal disease; Level of Evidence C;
- For obese grade 1 and 2, echocardiogram with assessment of diastolic function if signs or symptoms suggestive of CHF; Level of Evidence C;
- Echocardiogram with assessment of diastolic function for all obese grade 3; Level of Evidence C.

Specific recommendations for very obese patients:

##### Degree of Recommendation IIa

- Arterial gasometry if hypoventilation or pulmonary conditions are present; Level of Evidence C.

##### Degree of Recommendation IIb

- Chest radiography in a posterior-anterior and lateral position; Level of Evidence C;
- Noninvasive oximetry at rest and during sleep if signs of apnea; Level of Evidence C.

Notes:

- The additional testing and studies of coagulation tests are not mandatory and should not be routine in the preoperative evaluation of obese individuals. Additional tests are selected based on clinical history, Degree of Recommendation IIa, Level of Evidence B
- Bariatric procedures for resection of the stomach and gastric bypass surgeries are intermediate size surgeries;



**9.3.3. Recommendations for Risk Reduction**<sup>291,294-297</sup>**Degree of Recommendation I**

- Smoking cessation six weeks before surgery; Level of Evidence B.

**Degree of Recommendation IIa**

- Physical therapy; Level of Evidence C;
- If sleep apnea documented by polysomnography, consider installing CPAP preoperatively in patients who do not use CPAP and do not discontinue it in those who use it; Level of Evidence B.

**9.3.3.1. Intraoperative Care****Degree of Recommendation I**

- Blood pressure monitoring with a cuff appropriate for obese; Level B. Evidence;

**Degree of Recommendation IIa**

- Reverse Trendelenburg position during induction of anesthesia in severe obese individuals; Level of Evidence B;
- Pre-oxygenation (performed by providing 100% oxygen through a mask with the patient breathing spontaneously for a period of 3 minutes) or sitting with head elevated; Level of Evidence B;
- Rapid sequence induction with cricoid pressure during intubation; Level of Evidence B;
- Application of positive end-expiratory pressure (PEEP) improves oxygenation and prevents atelectasis; Level of Evidence B;
- Stretcher suitable for obese patients and avoid injuries caused by position on the surgical bed; Level of Evidence C;
- Noninvasive monitoring of oximetry in patients with hypoxemia in the preoperative period or in the presence of airway and pulmonary disease (sleep apnea, alveolar hypoventilation); Level Evidence B.

**Degree of Recommendation IIb**

- Consider individual invasive blood pressure monitoring; Level Evidence C.

**9.3.3.2. Postoperative Care****Degree of Recommendation I**

- CPAP in patients diagnosed with documented sleep apnea; Level of Evidence B.

**Degree of Recommendation IIa**

- Post-operative care in ICU of patients at high risk due to comorbidities, those who had failed on postoperative extubation, suffered complications during surgery or are super-obese (BMI > 70); Level of Evidence C;
- Maintaining blood volume; Level of Evidence C;
- Respiratory therapy to all those undergoing intermediate to major surgery; Level of Evidence C.

**Degree of Recommendation IIb**

- Perform continuous oximetry during recovery from anesthesia (Level of Evidence C), measurement after recovery

from anesthesia (if normal, not necessary to repeat) and measured continuously during sleep (in intermediate to major surgeries in patients with sleep apnea); Level of Evidence C.

**Prophylaxis for DVT in Obese Patients****Degree of Recommendation I**

- Drug prophylaxis with low molecular weight heparin or unfractionated heparin; Level of Evidence A.

**Degree of Recommendation IIb**

- Higher doses (40 or 60 mg of enoxaparin every 12 hours) results in fewer thromboembolic events and may be useful; Level Evidence C.

**9.3.4. Bariatric Surgery**

In addition to the general recommendations for obese patients described above, there are some additional considerations for bariatric surgery<sup>298</sup>. Two meta-analysis showed that mortality is less than 1% in 30 days, was lower for restrictive procedures (gastric banding with or without gastroplasty) against disabsorptive or ill-absorptive procedures (Roux-en-Y gastric bypass and bileo-pancreatic diversion)<sup>299-302</sup>. However, mortality increased, reaching 5% in 30 days in certain groups of patients and elderly males<sup>303,304</sup>. The volume of surgeries carried out in a center has been suspected as a possible risk factor, but a comparison of 253 U.S. hospitals did not support this hypothesis<sup>305</sup>. DeMaria evaluated 2,075 patients who underwent this surgery and found increased risk of death in the presence of certain factors<sup>306</sup>. The factors correlated with poor prognosis were: PTE or risk for PE, BMI > 50 kg/m<sup>2</sup>, male gender, hypertension and more than 45 years of age. The risk for PTE was defined as prior PTE, presence of a vena cava filter, right heart failure and/or pulmonary hypertension, chronic venous stasis and obstructive sleep apnea.

The largest prospective study to date, longitudinal assessment of bariatric surgery (LABS), whose results were published in July 2009 showed rates of minor complications, no corroborating the findings of DeMaria<sup>307</sup>. They found an overall mortality of 0.3% in thirty days and a composite outcome of death, DVT, PE, reintervention, and hospitalization longer than thirty days in 4.3% of patients. Some predictors of the composite outcome were similar, such as BMI, previous DVT or PE (8.8%) and apnea (5.0%). The authors also found a correlation between diabetes and the composite outcome (5.5%), type of surgery and the patient's ability to walk more than 61 meters without dyspnea (15.9%). The type of surgery with the best outcome was laparoscopic gastric banding (1.0%) compared to gastric bypass associated with laparoscopic Roux-en-Y (4.8%) and gastric bypass associated with Roux-en-Y by open surgery (7.8%). Other findings such as venous stasis and heart failure had a tendency to worse prognosis, but not statistically significant because the number of patients with these conditions was small.

BMI alone may be sufficient to identify high-risk patients: a group of 31 patients with BMI > 70 kg/m<sup>2</sup>, the mortality rate reached 7.35% in thirty days<sup>308</sup>.

Pulmonary thromboembolism occurs in 0.2% to 2.4% of the case postoperatively. However, there is no consensus

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about doses for prophylaxis. A Cochrane meta-analysis did not identify any benefit of different strategies, ranging from 40 mg to 60 mg per day of enoxaparin twice daily<sup>296</sup>. All patients receiving a dose of 60 mg twice daily had minimal levels of anti-Xa in the third dose, on the other hand, 25% had supratherapeutic levels<sup>309</sup>. The strategy of dividing the groups of patients according to BMI, and administering 40 mg twice daily to the group with BMI less than or equal to 50 kg/m<sup>2</sup> and 60 mg twice a day to the other group, 70% of patients achieved therapeutic levels of anti-Xa<sup>310</sup>.

Recommendations:

### Degree of Recommendation I

- For patients undergoing bariatric surgery routinely use thromboprophylaxis with LMWH, prophylactic UFH 8/8h, fondaparinux or a combination of a pharmacological method with the IPC; Level of Evidence C.

### Degree of Recommendation IIa

- For these patients, use higher doses of LMWH (enoxaparin 40 mg SC 12/12 h) or UFH (7500UI SC 8/8h) than those commonly used in the prophylaxis of nonobese patients; Level of Evidence C;

- Sleep apnea, previous DVT and PE, very high BMI and low functional capacity (factors related to worse prognosis) should be investigated. For patients with several of these factors, if possible, it should be considered to change the bariatric surgery for a type of surgery with better outcome (gastric banding only, preferably by laparoscopy) or to postpone the surgery. Level of Evidence B.

## 9.4. Blood Diseases

Blood disorders can increase morbidity and mortality in patients undergoing surgical procedures. Anemia is the most common blood problem found preoperatively. It is often a sign of underlying disease that may affect the surgical outcome. Anemia leads to overload of cardiovascular system, increasing cardiac output. Individuals with cardiovascular disease have a lower tolerance to anemia and its presence can increase a condition of myocardial ischemia and underlying heart failure. Guidelines regarding blood transfusion in the perioperative period are limited, however, the risks and benefits of this measure should always be questioned<sup>311</sup>.

A meta-analysis evaluated ten randomized clinical trials regarding transfusion triggering based on “restrictive” versus “liberal” strategy. Although it provided some important conclusions supporting the “restrictive” strategy, it found insufficient evidence for restrictive transfusion triggering in the context of cardiovascular and hematological disease and renal failure<sup>312,313</sup>.

The decision on a blood transfusion should be based not only on levels of hemoglobin, but also on suspicion of organic ischemia in the presence or risk of bleeding, intravascular volume status and susceptibility to complications from inadequate oxygenation<sup>314</sup>. Individuals with severe anemia should be transfused to a hemoglobin value that leads to improvement in their symptoms.

It should be borne in mind that one unit of packed red blood cells increases the hemoglobin level at approximately

1 g/dL and hematocrits by 3%. The optimal rate of administration of concentrated red cells should be guided by the clinical situation. Most patients can receive one unit of red blood cells every 1 hour to 2 hours. Patients at risk of volume overload should receive 1 mL/kg/hour. After each unit transfused patients should be reassessed and the hemoglobin level determined<sup>311</sup>.

Recommendations for red blood cell transfusion in the perioperative period:

### Degree of Recommendation I

- Patients with hemoglobin  $\leq$  7.0 g/dL, asymptomatic and, without ischemic heart disease should receive basic concentrated red cell; Level of Evidence A;

- In cases of acute coronary syndromes no evidence is available for limits of hemoglobin, it is recommended to maintain hemoglobin between 9.0 and 10.0 g/dL; Level of Evidence C.

Recommendations for perioperative management of patients with other blood conditions:

#### 9.4.1. Sickle Cell Disease (SS/SC/S $\beta$ tal)<sup>315-317</sup>

### Degree of Recommendation I

- Careful preoperative hydration, monitoring of oxygenation and meticulous postoperative management, including respiratory therapy are indicated for all patients undergoing general anesthesia. Level of Evidence C;

- Preoperative transfusion is not routinely indicated for patients undergoing minor surgical procedures not requiring general anesthesia. Level of Evidence C;

- For younger, non-complicated patients undergoing low/intermediate-risk procedures (including laparoscopic cholecystectomy) preoperative transfusion is recommended to increase hemoglobin levels to 10 g/dL. Level of Evidence C; For patients with Hb  $\geq$  9 g/dL, it is advisable to ask the opinion of a specialist;

- Partial transfusion to reduce the level of hemoglobin S to 30% or less should be considered for high-risk procedures and patients with history of pulmonary disease requiring prolonged anesthesia; Level of Evidence C; It is advisable to ask the opinion of a specialist.

#### 9.4.2. Thrombocytopenia

Patients with platelet count less than 50,000/mm<sup>3</sup> usually tolerate surgical procedures without excessive hemorrhagic symptoms, not requiring prophylactic transfusion of platelet concentrates, except in neurological and ophthalmic surgery, when there is need for platelet count equal or above 100,000/mm<sup>3</sup><sup>318</sup>.

Recommendations for platelet transfusion:

### Degree of Recommendation I, Level of Evidence B

- For any surgical procedure, when the platelet count below 50,000/mm<sup>3</sup>;

- For neurological and ophthalmological interventions, when platelet count less than 100,000 platelets/mm<sup>3</sup>;

### 9.4.3. Antiphospholipid Antibodies and Hereditary Thrombophilia

The higher prevalence of antiphospholipid antibodies in patients with stroke suggests an association between these antibodies and vaso-occlusive events. The increased risk of thrombosis in patients with higher titres of these antibodies further strengthens the evidence that this association is causal<sup>319</sup>. Patients with proved positive antiphospholipid antibodies (positive in two or more tests at intervals of twelve weeks between them), but no history of thromboembolic events, should receive thromboprophylactic treatment in the perioperative period<sup>320</sup>. Patients with antiphospholipid syndrome, thus on oral anticoagulant therapy, are considered at high thrombotic risk during surgical procedures<sup>221</sup>.

Hereditary thrombophilia does not present the same risk of thrombosis. It is larger in homozygous for the factor V Leiden mutation and G20210A prothrombin gene, the deficiencies of physiological coagulation inhibitors (antithrombin, protein C and protein S) and combinations of heritable thrombophilia. The presence of heterozygous factor V Leiden and G20210A prothrombin gene mutation occur with a lower risk of thrombosis<sup>221,321</sup>. Individuals with inherited thrombophilia when undergoing surgical procedures, trauma or immobilization, are at increased risk of venous thromboembolism, two to ten times higher compared to non-disabled individuals<sup>322-324</sup>. Thus, even asymptomatic carriers of inherited thrombophilia should be considered for thromboprophylaxis during short periods of increased thrombotic risk, such as surgical procedures<sup>323,325</sup>. For patients with hereditary thrombophilia on oral anticoagulant therapy in the preoperative period, it is recommended discontinuation of oral anticoagulant and temporary use of therapeutic doses of low molecular weight heparin subcutaneously or unfractionated heparin in continuous infusion; in patients with thrombophilia of lower risk of thrombosis, it is possible to use low doses of low molecular weight heparin<sup>221</sup>.

Recommendations for anticoagulant therapy in patients with hereditary thrombophilia or antiphospholipid antibodies:

#### Degree of Recommendation IIa

- For asymptomatic patients with inherited thrombophilia, we recommend the use of prophylactic doses of low molecular weight heparin or unfractionated heparin in the postoperative period. Level of Evidence C;
- For patients with hereditary thrombophilia on use of oral anticoagulation suspension, it is recommended the use of therapeutic doses of unfractionated heparin or continuous infusion of low molecular weight heparin in the preoperative period. When inherited thrombophilia has less thrombotic risk, low doses of low molecular weight heparin may be used. Level of Evidence C.

### 9.4.4. Hemophilia A (Factor VIII Deficiency) and B (Factor IX Deficiency)<sup>326</sup>

#### Degree of Recommendation I, Level of Evidence B

- Surgical procedures should be performed by a medical team experienced in the treatment of hemophilia;
- Before performing the procedure, ensure that there is sufficient availability of factor concentrate;

- Procedures should be performed in a center with laboratory support with adequate capacity to monitor the deficient factor;
- In preoperative laboratory evaluation, search for inhibitors of the deficient factor should always be included;
- The surgical procedure should be performed earlier in the week and earlier in the day to allow great support from laboratory and blood bank;
- For the intra-operative period, the plasma level of the deficient factor for hemostatically safe values should be corrected through the use of specific factor concentrate;
- Postoperatively, keep the plasma level of the factor deficient in adequate concentrations and time, according to the type and size of the surgery.

### 9.4.5. Von Willebrand Disease (VWF)<sup>327,328</sup>

Recommendations:

- Postoperatively, plasma levels of minimum FVIII:C and FVW:RCo will vary with the type and size of surgery.

#### Degree of Recommendation I

- Any surgical procedure must be based on laboratory measurements of the activity of factor VIII (FVIII:C) and ristocetin cofactor (VWF:RCo) after administration of DDAVP (desmopressin) and/or infusion of concentrate of von Willebrand factor; Level of Evidence B;
- During the intraoperative period, the concentrations of FVIII:C and VWF: RCo should be maintained at 100 IU/dL, through the infusion of VWF concentrate with or, in responding patients, administration of DDAVP; Level of Evidence B.

#### Degree of Recommendation IIa

- Whenever possible, surgical procedures should be performed in a hospital with a medical team, including a hematologist and a surgeon, experienced in the treatment of bleeding disorders and specialized laboratory support; Level of Evidence C;
- In the post-operative concentrations of FVIII:C should be equal to or less than 150-250 IU/mL and VWF:RCo below or equal to 200 IU/dL to reduce the risk of thrombosis; Level of Evidence C;
- Pharmacological antithrombotic prophylaxis should be done postoperatively; Level of Evidence C.

### 9.5. Renal Failure

Patients with renal failure are more prone to postoperative complications, longer hospital stay, greater costs of hospitalization, and have higher mortality than those without renal dysfunction<sup>27,329-332</sup>. Preoperative renal failure or dialysis has been consistently associated with postoperative complications and high mortality. Lee et al. built and validated a prognostic model for cardiovascular complications after noncardiac surgery<sup>27</sup>. The risk factors identified were (in increasing order of risk): history of congestive heart failure, coronary ischemia, high-risk surgery (abdominal aortic aneurysm, other vascular, thoracic, abdominal and orthopedic

surgeries), insulin-dependent diabetes mellitus, preoperative creatinine greater than 2.0 mg/dL and cerebrovascular disease. Even moderate chronic renal failure (creatinine 1.5 to 3.0 mg/dL or glomerular filtration rate between 30 and 60 mL/min) is a risk factor for cardiac and noncardiac complications postoperatively and is associated with mortality twice as high when compared with patients with normal renal function<sup>331,332</sup>. Surprisingly, the guidelines for perioperative evaluation of noncardiac surgery of the American College of Cardiology/American Heart Association consider renal failure only a moderate risk factor for postoperative cardiovascular complications<sup>57</sup>.

In the preoperative evaluation of patients with chronic renal failure on dialysis or kidney transplant, some aspects are relevant. Many of these patients have known risk factors for ischemic heart disease, such as advanced age, hypertension, or diabetes mellitus. Patients on renal replacement therapy program must undergo dialysis before surgery to avoid overload, correcting electrolyte disturbances and acid-base and reduce the risk of bleeding due to uremia. Immunosuppression in renal transplant recipients must be carefully adjusted by the nephrologist in the pre- and postoperative period due to the risk of acute rejection and nephrotoxicity.

Another serious postoperative complication is the development of acute renal failure (ARF). Depending on the type of surgery, it occurs in 1-30% of cases, with mortality around 50%<sup>333-335</sup>. It is important to highlight that currently it is considered acute kidney injury when the patient has acute worsening of renal function (48 hours) represented by an increase of at least 0.3 mg/dL in baseline serum creatinine and/or decreased urinary output values for less than 0.5 mL/kg/h in more than 6 hours<sup>336</sup>. There is evidence that small changes in serum creatinine are associated with increased morbidity and mortality in medical and surgical patients<sup>337-339</sup>.

The prevention of ARF in the postoperative period depends on the identification of risk factors for its development (especially preoperative renal failure), avoiding the use of nephrotoxic drugs, maintaining adequate hydration and preventing hypotension. Attempts to prevent ARF with drugs such as diuretics and vasoactive amines were ineffective<sup>340,341</sup>. Dopamine at "renal dose", which has been widely used in intensive care in the postoperative period, does not prevent renal dysfunction, does not reduce the need for dialysis and does not decrease the mortality of ARF<sup>342</sup>. Potentially nephrotoxic drugs should be avoided or used properly, with correction for the level of renal function. Aminoglycosides, amphotericin B, radiological contrast, angiotensin-converting enzyme inhibitors and nonsteroidal anti-inflammatory hormone-are examples of nephrotoxic drugs commonly used perioperatively. The effects of anti-inflammatory property of selective inhibition of cyclooxygenase II in renal function are not different from those promoted by selective nonsteroidal anti-inflammatory and its use should be avoided in patients at risk for nephrotoxicity inflammatory drugs (advanced age, previous renal failure, heart failure, dehydration, concomitant use of angiotensin-converting enzyme inhibitors and diuretics or other nephrotoxic agents)<sup>343,344</sup>.

The risk of postoperative complications are well defined in patients with renal insufficiency and in these cases,

evaluation by a nephrologist can be considered. You should always keep in mind that creatinine is an insensitive marker of renal function. Therefore, creatinine less than 1.5 mg/dL does not necessarily mean normal renal function, particularly in elderly patients or those with reduced muscle mass. The preoperative evaluation is an opportunity to connect with this patient and the clinical and surgical planning for prevention of deterioration of renal function and later delay the progression of chronic renal failure.

### 9.6. Asthma and Chronic Obstructive Pulmonary Disease

There is no evidence in the literature on the relationship between chronic obstructive pulmonary disease (COPD) or asthma and increased risk of cardiovascular complications. We know the high correlation between cardiovascular disease and COPD. Many of these patients are smokers, patients with coronary artery disease, hypertension, dyslipidemia etc. The absence of the relationship between COPD and asthma with an increased risk of cardiovascular complications could be associated with extra care of these patients, potentially more severe in the surgical setting. So far, no perioperative cardiovascular risk (such as Goldman, Detsky, and Lee) included COPD and asthma as an independent risk factor.

There is a clear correlation between cardiovascular events and reduced forced expiratory volume in one second (FEV1) out of the perioperative period<sup>345</sup>. In the clinical practice, we know that lung disease in the context of non-cardiac surgery may increase the risk of complications. Such complications are the vast majority of lung. These complications are equally prevalent for cardiovascular and contribute to increased morbidity and mortality of the procedure.

The risk of pulmonary complications in the postoperative period is highly variable and depends on the classifications used. It is accepted that pulmonary complications are responsible for increased perioperative morbidity and mortality are those capable of causing some kind of injury that has clinical relevance. Among these factors, we cite atelectasias, infections, respiratory failure, prolonged mechanical ventilation, bronchospasm and acute exacerbation of chronic lung condition (including chronic bronchitis, pulmonary fibrosis or asthma)<sup>346,347</sup>. Recent data has shown that the incidence of pulmonary complications in the postoperative period in noncardiac surgery is around 7%<sup>348</sup>. These complications are very similar to the incidence of cardiovascular complications, such as acute ischemic events, as observed in a retrospective cohort study with 8930 patients undergoing surgical repair of hip fracture. In this study, there were 2% of cardiovascular complications and 2.6% of pulmonary complications, no significant difference<sup>349</sup>.

Complications that occur postoperatively are usually associated with reduced lung volumes, changes in diaphragmatic function, reduced effectiveness of cough and mucociliary clearance, and possible changes in function of the respiratory center.

Some factors associated with patients have clinical relevance. They are: age, chronic lung disease, asthma, smoking, obesity, obstructive sleep apnea, pulmonary hypertension, congestive heart failure and metabolic diseases.



Age is relevant as an independent perioperative risk after 50 years of age - the risk increases with each decade thereafter<sup>348</sup>. The presence of chronic lung disease or asthma is well controlled clinically<sup>350,351</sup>, even with reduced lung function (e.g., forced expiratory volume in one second (FEV1) less than 1 liter) is not absolute contraindication to any procedure - the risks versus the benefits should be clearly assessed.

Smoking is also an independent risk factor for complications in the postoperative period, even if there is concomitant chronic lung disease, especially in those patients who smoked more than 20 pack-years smoked and in the two months prior to surgery<sup>348,352</sup>. The presence of obstructive sleep apnea can increase the risk of reintubation in the postoperative period, in addition to being associated with hypoxemia<sup>353</sup>.

The presence of pulmonary hypertension, especially if pre-capillary, may confer greater risk in the perioperative period, especially if we consider the interventions that have the greatest impact on cardiopulmonary interaction (surgery with wide variation in volume or restriction of the diaphragm, for example). In our environment, we must pay special attention to those patients with hepatosplenic schistosomiasis, because there is a small incidence of pulmonary hypertension, either pre- or post-capillary<sup>354</sup>. The existence of malnutrition also confers increased risk of pulmonary complications<sup>348</sup>.

The surgical site is the most important factor that determines the risk of pulmonary complications. The closer to the diaphragm, the greater the chance of complications<sup>348</sup>. The long operative time and type of neuromuscular blocker (avoid pancuronium) can also increase the risk of pulmonary complications<sup>355,356</sup>.

From the standpoint of reducing cardiovascular risk, the clinical management of these patients is identical to that of patients without COPD, considering those of higher risk for coronary artery disease or cerebrovascular disease confirmed, patients with diabetes mellitus and chronic renal failure or in situations of high-risk surgeries. Regarding the handling to reduce pulmonary complications, the recommendations are similar to those outside the surgical setting, to optimize pulmonary function and minimize the occurrence of respiratory complications. The optimization of pulmonary function includes the use of antibiotics when active infection is detected and the use of corticosteroids and/or bronchodilators in patients who were already using, or who have residual bronchospasm. Stopping smoking should be recommended, preferably in more than two months before the surgery.

Specialized physical therapy treatment or monitoring is of paramount importance in this context. Patient education regarding lung expansion maneuvers is essential since the preoperative period. The approach with lung expansion maneuvers postoperatively was the only strategy with level of evidence A for the reduction of pulmonary complications in a systematic review of 2006<sup>357</sup>.

There are no validated models of pulmonary risk so far. The cohorts of validation does not validate unequivocally the data initially published. Among them, is the Cardiopulmonary risk index<sup>358</sup>, the Brooks-Brunn risk index<sup>359</sup> Multifactorial index and postoperative respiratory failure is<sup>360</sup>.

The risk of pulmonary complications in the perioperative period is related to three main factors: the clinical conditions, the type and duration of surgery. There is yet a widely validated model for preoperative evaluation of pulmonary complications.

In short, according to the recently published guidelines of the European Society of Cardiology, there is no recommendation for specific management of cardiac risk in patients with COPD and asthma<sup>36</sup>.

Recommendations for the use of perioperative corticosteroids:

#### **Degree of Recommendation IIa**

- Patients with asthma.

#### **Degree of Recommendation IIb**

- Patients with COPD or interstitial lung diseases.

### **9.7. Smoking**

Smoking is the leading cause of preventable death worldwide, contributing directly to at least 20% of all deaths, about 200,000 deaths a year in Brazil. A considerable number of deaths is attributed to neoplasms, but heart and lung diseases account for most of the tobacco-related mortality. The treatment of smoking cessation, along with other restrictive measures to exposure to tobacco products should therefore be a priority target for preventive measures at different levels of performance of health services.

In the context of secondary and tertiary prevention of cardiovascular events, especially heart disease, smoking cessation represents a risk reduction of death and recurrence of severe events (36% and 32% respectively) of magnitude higher than the pharmacological measures widely advocated in international guidelines, such as beta-blockers (23%), angiotensin-converting enzyme inhibitors (23%), lipid management (29%) and platelet aggregation (15%)<sup>361</sup>. In the specific case of chronic obstructive pulmonary disease (COPD), gradually evolving and incapacitating disease that affects about 10 to 15% of the adult population<sup>362</sup>, smoking cessation is still the only measure capable of modifying its natural history, and together with supplemental oxygen for those patients already suffering from chronic respiratory failure, reducing their mortality<sup>363</sup>.

Admissions constitute moments of opportunity to raise awareness of the patient to quit smoking, and facilitate the monitoring of nicotine with drawal symptoms and follow the narrow tolerance and efficacy of treatments. The medical teams should take advantage of a hospital admission of a smoker not only as a time to implement measures for adaptation to restrictive regulations of smoke-free environments, but also to address more actively the question of individual smoking, searching, evaluating, advising, treating and monitoring these patients.

Reducing the risks of mortality and postoperative complications in different smokers also has a special role in the scenario of perioperative care, given the significant impact of smoking on postoperative healing rates of infection, respiratory, cardiovascular, orthopedic complications, and other. The history of smoking is associated with longer stays in intensive care units (ICU) postoperatively and longer hospitalizations<sup>364-366</sup>, in spite of this, little is approached along the smoking preoperative patient, which is partly due

to unfamiliarity with the doctors or the optimum timing of smoking abstinence. Recognizing the best moment to address the issue of smoking and start treatment as early as possible can translate into meaningful reductions in clinical and surgical complications and reduce costs to the health system.

### 9.7.1. Smoking Cessation During Hospitalization

Currently there are two main aspects concerning the imposition of smoking cessation treatment to hospitalized patients: focus on the individual and on the institutional dimension. The first is based on the premise that frequently the disease responsible for admission may have been caused or exacerbated by smoking, or that the continued consumption of cigarettes can lead to serious clinical outcomes in the short, medium and long term regardless of the cause or diagnosis of hospitalization. In addition, smoking cessation during hospitalization offers an opportunity to access more readily withdrawal symptoms, titer drug doses in a safer manner and monitor more reliably the effectiveness of the therapeutic program as a whole. Regarding the institutional aspect, in turn, the adequacy of hospitals to the restrictive legislation to the consumption of smokeless tobacco products requires that they comply with the rules banning smoking in these environments. On the other hand, programs of quality certification and accreditation of health services not just assume compliance with laws, but also the existence of a structured program for smoking cessation treatment to patients and staff.

The reasons that drive a patient to stop tobacco consumption during the hospitalization, which are part of your health care or even merely resulting from the condition of staying in an environment free of tobacco, should be used as an important step, which will promote supportive care and monitoring necessary to keep the patient continuously abstinent. It should be noted also that if these efforts do not organize themselves in a structured program that involves the identification of smokers at admission, the institution of therapeutic interventions (informational, cognitive-behavioral and drug), monitoring during hospitalization and follow-up post-discharge, such efforts lose their effect in the medium and long term.

#### Degree of Recommendation I

- Hospitalized patients should be actively approached regarding their history and smoking status. Smokers should be questioned regarding their intention to stop smoking and nicotine withdrawal symptoms; Level of Evidence C;
- Nicotine replacement therapy should be initiated in hospitalized smokers who experience withdrawal symptoms; Level of Evidence C ;
- Patients treated during hospitalization should be followed up by at least one month after discharge to remain abstinent. Level of Evidence B.

### 9.7.2. Smoking Cessation in the Preoperative

The negative impacts of smoking on surgical outcomes are multifactorial being mainly due to the direct effects of carbon monoxide (CO) and nicotine and increased oxidative stress and inflammation. Carbon monoxide and nicotine increase heart rate, blood pressure and tissue oxygen demand,

and reduce its carrying capacity. Nicotine, because of its vasoconstrictor effect, increases the risk of tissue ischemia in the surgical and other territories, such as coronary<sup>367</sup>.

The irritating and proinflammatory effect of many components of cigarette smoke on the airways also increases the susceptibility of smokers to respiratory infections, local complications in lung surgery healing and longer periods on mechanical ventilation<sup>368</sup>.

Cigarette smoking is also associated with the need for larger doses of anesthetics and neuromuscular blockers<sup>369</sup>, increased incidence of thromboembolic events and slowness of reparative processes in orthopedic surgery<sup>370</sup>.

Patients candidates for surgery are usually more motivated to quit smoking and are therefore susceptible to a therapeutic approach for this. With the regulation of hospitals (and other enclosed spaces in public and private use) and smoke-free environments and the increasingly widespread availability of effective therapeutic resources to help patients quit smoking, the preoperative becomes therefore a key moment for smoking cessation before an elective surgical procedure.

For too long there has been controversy regarding the ideal period of smoking cessation prior to surgery, which was due in large part to methodological heterogeneity of studies evaluating different moments of smoking cessation, the difficulty of controlling confounding variables in the samples patients, wide variation in the time of follow-up and multiplicity of outcomes.

A review of prospective studies on the impact of smoking cessation in the preoperative period on the occurrence of postoperative complications (respiratory, infectious diseases, mortality and length of stay) and published by Cropley Theadom<sup>371</sup> in 2006 concluded that although there is no major methodological limitation of the studies evaluated, there are many benefits of smoking cessation before surgical admissions, and that this benefit is greater the longer the period of abstinence. It is noteworthy also that there is not an ideal time to recommend a preoperative smoking cessation in term of reduction of surgical complications and risk in the medium and long term, thus smoking cessation should not be postponed based on the assumption that it increases risks if done less than two months after surgery.

A cohort study evaluating recent retrospective data from 7990 pulmonary resection surgeries for cancer published in 2009 concluded that the risk of mortality and respiratory complications after lung resection were higher in smokers and clearly reduced by smoking cessation in the preoperative period. We were unable to identify the ideal interval between smoking cessation and surgery, which strengthened the recommendation for counseling (and treatment) for smoking cessation regardless of proximity to surgery. This corroborates the results of the study published in 2001 by Nakagawa et al.<sup>372</sup>, in which there is clear and growing risk reduction of postoperative complications from four weeks of preoperative smoking cessation.

#### Degree of Recommendation I

- Smoking cessation reduces surgical complications in this subpopulation, clinical research and patients in the

preoperative evaluation should be encouraged to quit smoking regardless of the time to operation; Level of Evidence A;

- The therapeutic intervention should always include cognitive-behavioral approach with or without pharmacological treatment; Level of Evidence A.

#### Degree of Recommendation IIa

- Any first-line pharmacological option (nicotine replacement therapy, bupropion and varenicline) alone or combined (nicotine gum or transdermal associated with nicotine gum or bupropion in combination with transdermal nicotine gum or lozenge) may be used in this population, respecting individual contraindications, but there is more evidence in favor of nicotine replacement therapy; Evidence Level B.

#### 9.7.3. Therapeutic Strategies and Outcomes

As in general situations, the treatment of nicotine dependence in patients candidates for surgery and inpatients is based on cognitive-behavioral interventions (brief approach, individual counseling, provision of informational materials and group therapy) systematized or not and pharmacological support. Because of the peculiarity of these specific cases aimed at smoking cessation and control of symptoms of nicotine withdrawal in a short period of time, the resource available is almost always the nicotine replacement therapy (NRT) alone or combined. We recommend the usual schemes of prescription of transdermal nicotine (6 to 8 weeks of 21 mg/24h or 15 mg/16h, 2 weeks of 14 mg/24h or 10 mg/16h and 2 weeks of 7 mg/24h or 5 mg/16h, according to the presentation chosen) associated with ad libitum rapid replacement forms (in Brazil nicotine is available in tablets and chewing gum, both in the presentations of 2 and 4 mg per unit) for episodes of craving.

Prospective studies evaluating the effectiveness of the implementation of a structured service of counseling, cognitive-behavioral approach, pharmacological support and follow-up of hospitalized smokers showed high success rates of about 35% to 44% in six months<sup>373,374</sup> and approximately 33% in 12 months, and studies have shown success rates exceeding 50% within a year in hospitalized coronary patients<sup>375</sup>. Any combination of NRT with non-nicotine drug (such as bupropion) or the option for monotherapy with varenicline

is theoretically acceptable, although there are specific studies supporting these special situations. The use of individualized doses of nicotine replacement in order to achieve plasma nicotine levels closer to the arterial concentrations of active smoker and aimed at better control of withdrawal symptoms in heavy smokers has been tested and proved to be quite safe until doses exceeding 42 mg per day<sup>376-379</sup>, which persist even in individuals smoking.

In the specific situation of hospitalized patients, we propose the treatment according to the following flowchart:

#### 9.7.4. Conclusions

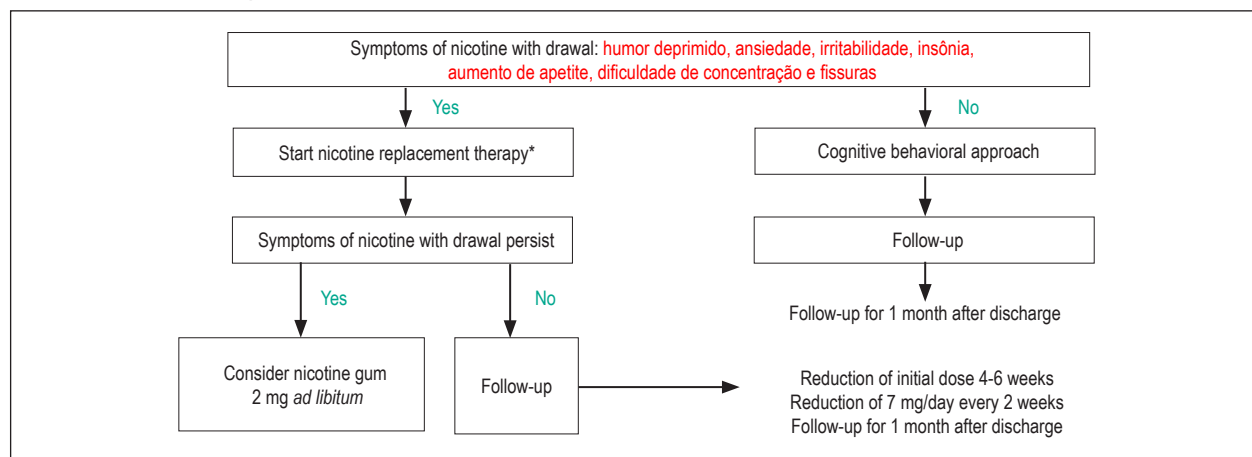
There is a consistent body of evidence substantiating smoking cessation in subpopulations of patients and candidates for surgical procedures. This intervention is extremely effective and less costly.

Hospital admissions and medical visits for surgical risk assessment and perioperative care should include the approach of active smoking, researching, advising, treating and monitoring these patients.

In general, therapeutic strategies differ little from the routines suggested in consensus for the general populations; there is, however, a certain predilection for nicotine replacement therapy. Nicotine replacement therapy is safe and effective in cardiac patients, even in those at high risk, which includes stable coronary heart disease (Level of Evidence A). Nicotine replacement therapy should not be routinely prescribed to patients with a history of acute coronary syndrome at high risk of recent (less than six weeks) coronary disease and patients with complex ventricular arrhythmias (Level of Evidence C). Treatment with individualized doses in order to achieve better control of withdrawal symptoms are safe and well tolerated (Evidence Level B), although there is no solid evidence that it offers higher success rates in the long term.

There is no clear superiority of nicotine replacement therapy on the population over bupropion in hospitalized patients and the studies are controversial to point out additional benefits (beyond the control of withdrawal symptoms) of a drug treatment program of counseling and behavioral approach alone (Level of Evidence B).

Flowchart 2 - Treatment of hospitalized smokers.



\* Less than 20 cigarettes/day: 14 mg patch; 20-30 cigarettes/day: 21 mg patch; 31-40 cigarettes/day: 21 mg + 7 mg patch; > 40 cigarettes/day: 21 mg + 14 mg patch.

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