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Received from SCORIS Working Group on Non-cardiac Perioperative Morbimortality Evaluation. Brazil.

Submitted on July 28th, 2008 Accepted on November 06th, 2008.

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# Epidemiology and outcomes of non-cardiac surgical patients in Brazilian intensive care units

Epidemiologia e desfecho de pacientes cirúrgicos não cardíacos em unidades de terapia intensiva no Brasil

#### ABSTRACT

**Objectives:** Due to the dramatic medical breakthroughs and an increasingly ageing population, the proportion of patients who are at risk of dying following surgery is increasing over time. The aim of this study was to evaluate the outcomes and the epidemiology of noncardiac surgical patients admitted to the intensive care unit.

Methods: A multicenter, prospective, observational, cohort study was carried out in 21 intensive care units. A total of 885 adult surgical patients admitted to a participating intensive care unit from April to June 2006 were evaluated and 587 patients were enrolled. Exclusion criteria were trauma, cardiac, neurological, gynecologic, obstetric and palliative surgeries. The main outcome measures were postoperative complications and intensive care unit and 90day mortality rates.

**Results:** Major and urgent surgeries were performed in 66.4% and 31.7% of the patients, respectively. The intensive care unit mortality rate was 15%, and 38% of the patients had postoperative complications. The most common complication was infection or sepsis (24.7%). Myocardial ischemia was diagnosed in only 1.9% of the patients. A total of 94 % of the patients who died after surgery had co-morbidities at the time of surgery  $(3.4 \pm 2.2)$ . Multiple organ failure was the main cause of death (53%).

Conclusion: Sepsis is the predominant cause of morbidity in patients undergoing non-cardiac surgery. In this patient population, multiple organ failure prevailed as the most frequent cause of death in the hospital.

**Keywords:** Postoperative complications; Sepsis; Gastrointestinal tract/ physiopathology; Multiple organ failure

# INTRODUCTION

High-risk patients spend a significant amount of healthcare resources. Due to dramatic medical breakthroughs and an increasingly ageing population, the proportion of patients who are at risk of dying following surgery is increasing over time. Several attempts have been made to detect the patients at risk and to reduce postoperative morbidity and mortality by improving perioperative care. (1-6)

Only a few patients undergoing major surgery had an increased risk of severe postoperative complications and high mortality rates. A large observational British study with more than four million surgical patients has shown that this population accounts for only 12.5% of the surgical procedures, but also for more than 80% of the deaths. (7) Despite high mortality rates, fewer than 15% of these patients are admitted to the intensive care unit (ICU).

Studies on postoperative morbidity and mortality in non-cardiac surgical patients are rarely made in Brazilian intensive care units (ICUs). A multicenter study performed in elective patients reported rates of mortality and perioperative complications of 3.4% and 9.1%, respectively. However, the majority of the patients in this study were classified as low risk and, not admitted to an ICU. In a retrospective cohort study of 403 patients older than 55 years, mainly submitted to elective surgeries, the mortality rate was 8.2% and the complication rate was 15.8%. In another study performed with cancer patients, the global ICU mortality rate was 20.3%. As expected, the mortality rate was significantly higher for emergency surgical patients (49.3%) than for scheduled ones (5.7%).

In United Kingdom (UK), the vast majority of post-operative deaths occur in older patients with coexisting serial medical conditions who undergo major surgery. (7) For any given risk level, mortality rates of ICU patients are significantly higher in the UK than in the United States (USA). Under the same estimated risk by Physiological and Operative Severity Score for the Enumeration of Mortality and Morbidity (POSSUM) score, mortality rates for surgical patients are almost five times higher in the UK than in the USA. (11) Accordingly, there are 0.6 ICU beds per 10,000 in-habitants in UK in comparison to 4.4 per 10,000 inhabitants in USA. It is known that the National Health System (SUS) in Brazil has a very low proportion of hospital beds allocated to critical care in relation to the needs of the population. In addition, the resources addressed to public health care are broadly recognized as insufficient.

Our hypothesis is that, similarly to UK, non-cardiac surgical patients in Brazilian ICUs have a high risk of complications and death. The primary objective of our study was to describe the epidemiology and outcomes, and the pattern of postoperative complications of non-cardiac surgical patients admitted in Brazilian ICUs.

# **METHODS**

The institutional review board waived the informed consent requirement. The SCORIS study was a multicenter, prospective, observational, cohort study performed from April 1st through June 31st 2006 in 21 Brazilian ICUs from 18 institutions (eight public and ten private hospitals). The study was designed to describe the epidemiology and clinical outcomes, to evaluate the independent predictors of outcomes, and to

develop our own model to predict the outcome of noncardiac surgical patients in Brazilian ICUs. Due to the large database created, the data presented here will be only that of the first part of the analysis. A total of 885 adult patients submitted to either elective or emergency surgeries admitted to the ICU after operation was evaluated. Of these, 587 were enrolled. Exclusion criteria were trauma, cardiac, neurological, gynecologic, obstetric, and palliative surgeries.

Data were collected based on age, gender, smoking habits (active last year), alcohol abuse, nutritional status, diabetes, renal function, chronic obstructive pulmonary disease, and presence of malignant disease. Cardiopathy was considered in the presence of moderate or severe cardiomegaly, turgescent jugular veins, and use of digitalis, diuretics, antianginal, and antihypertensive drugs. (3) The inability to climb two flights of stairs in a subjective evaluation defined a patient with a low functional capacity 2. Electrocardiogram (EKG) abnormalities included non-sinusal rhythms, frequent ventricular extra-systoles (more than 5/min), O waves, or ST-T segment abnormalities. (3) For the diagnosis of angina, the Canadian Cardiovascular Society (CCS) classification system was used. (2) For the diagnosis of acute myocardial infarction (MI), the presence of typical EKG alteration together with elevated cardiac enzymes and/or segmental wall motion abnormalities on echocardiography exams were considered. Cardiac arrest was defined as the presence of a chaotic cardiac rhythm, or the absence of cardiac rhythm requiring the initiation of any component of the basic or advanced life support. Other clinical predictors of increased perioperative cardiovascular risk were defined according to American College of Cardiology/American Heart Association (ACC/AHA) guidelines. (2) All data have been entered on an electronic case report file (CRF) (Comunicare) and the variables were cross-checked by two authors.

The following procedures were considered major surgeries: laparotomy, enterectomy, cholecystectomy with choledochostomy, vascular, major amputation, any aorta procedure, rectum abdominoperineal resection, pancreatectomy, esophagectomy, and hepatectomy. (3) POSSUM, Acute Physiology and Chronic Health disease Classification System II (APACHE II), Multiple Organ Dysfunction System (MODS), and Sequential Organ Failure Assessment (SOFA) scores were performed. (3,12-14) In the calculation of these scores, the most abnormal values were collected for vital signs and laboratory assessments.

A list of major post-operative complications occurring during hospitalization was prospectively evaluated (Table 1).<sup>(15,16)</sup> All patients were monitored until hospital discharge or death.

# Statistical Analysis

Continuous variables are presented as mean ± standard deviation (SD), and/or median and compared using Student's *t*-test or Mann–Whitney U-test. Categorical variables were reported as absolute numbers (frequency percentages). Morbimortality rates were evaluated with the relative risk (RR) (95% confidence interval (CI)). We considered p < 0.05 as statistically significant.

# **RESULTS**

Eight hundred and eighty-five patients were evaluated. The final pool of patients comprised 587. Of these, 298 were excluded (127 had neurosurgeries; 51, cardiac surgeries; 35, palliative surgeries; 6, gynecologic surgeries; 32, trauma; 34, lost follow-up; 8, age lower than 18 years; and 5, no indication for ICU admission).

Demographics, clinical characteristics, and type of

surgeries of the 587 study patients are depicted in table 2. Major and urgent surgeries were performed in 66.4% and 31.7%, respectively. Median age was 65 years. On the first day of ICU stay, 159 (27%) patients required mechanical ventilation, and 82 (14%) received vasoactive agents. The frequency of baseline conditions is shown in table 3. The most frequent baseline condition was arterial hypertension occurring in almost 60%. A high frequency of cardiopathy was found in 35%. Diabetes was also highly prevalent (20%). The mean number of baseline conditions was 1.9 ± 1.8.

Our patient population had an overall major complication rate of 38.3% and 90-day mortality rate of 20.3%. The prevalence of postoperative complications is shown in table 1. There was a median of 2 complications per patient (2.9 ± 1.9 complications). The most common complications seen were infectious or septic complications (24.7%), extubation failure (10%), and gastrointestinal dysfunction (GID) (8%). Extubation failure was accompanied by a significantly higher risk of death. Mortality rate was almost five times higher for patients with extubation failure (67.8% vs 15.1%; RR 4.48 CI 95% 3.42 - 5.86, p<0,05). Nosocomial infection rates by site were pneumonia 10%, abdominal 5.6%, surgical site infection 5.1%, urinary tract

Table 1 - Definitions and frequency of postoperative complications

Complications	Definition	Frequency
Sepsis/severe sepsis/septic shock	ACCP/SCCM <sup>15</sup>	135 (22.9)
Extubation failure	Failure to extubate in the first 24 hours after the operation or the need for	59 (10.0)
	reintubation within 72 hours after extubation.	
Gastrintestinal dysfunction	Intolerance to feeding after 5 days of the operation or the need for parenteral nutrition	47 (8.0)
Cardiac adverse event	Unexpected cardiac arrest and or acute myocardial infarction	34 (5.6)
Severe bleeding	Transfusion of more than 2 units of RBC or reoperation was necessary	32 (5.5)
Heart failure	Classical signs and symptoms or worsening in relation to the pre-operative status	32 (5.5)
Pulmonary edema	Radiological signs of vascular hypertension and clinical signs of congestion	27 (4.6)
Fistula or anastomosis leak	Abnormal communication between two epithelized surfaces or anastomosis	30 (5.1)
	breakdown requiring reintervention	
Surgical site infection	CDC definitions <sup>16</sup>	30 (5.1)
Shock	Refractory hypotension despite fluid resuscitation and, need for vasoactive agents	24 (4.0)
Nosocomial pneumonia	CDC definitions <sup>16</sup>	10 (1.7)
Urinary tract infection	CDC definitions <sup>16</sup>	10 (1.7)
Venous thromboembolism o	r Confirmed by spiral CT or perfusion scintilography or autopsy	7 (1.2)
pulmonary embolism		
Blood stream infection	CDC definitions <sup>16</sup>	6 (1.0)
Cerebral vascular accident	Confirmed by CT	6 (1.0)

ACCP/SCCM – American College of Chest Physicians/Society of Critical Care Medicine; RBC – red blood cells; CDC – Centers for Disease Control; CT – computed tomography. Results are expressed in N(%)

Table 2 - Demographic and general characteristics of the patients

Variable	Results			
Age (years)	62.4 ± 17 (65)			
Gender (male)	322 (55)			
MODS score	$3.7 \pm 3.1$ (3)			
SOFA score	$5.0 \pm 3.9$ (4)			
APACHE II score	$14.4 \pm 6.4 \ (14)$			
POSSUM score	$36.0 \pm 10.6 (34)$			
Hospital LOS (days)	$16.9 \pm 20.3 (10)$			
ICU LOS (days)	6.1 ±12.0 (2)			
Hospital LOS before surgery (days)	$5.3 \pm 10.1 (1)$			
Invasive mechanical ventilation	150 (25.5)			
Non-invasive mechanical ventilation	9 (1.5)			
Vasoactive drugs	82 (14)			
Elective surgery	401(68.3)			
Urgent surgery	186 (31.7)			
Major surgery	390 (66.4)			
Gastrintestinal surgery	259 (44.1)			
Vascular surgery	135 (22.9)			
Exploratory laparotomy	44 (7,4)			
Orthopedic surgery	39 (6.6)			
Urologic surgery	31 (5,3)			
Head and neck surgery	17 (2,9)			
Liver surgery	9 (1,5)			
Lung surgery	6 (1,0)			
Limb amputation	6 (1.0)			

MODS – Multiple Organ Disfunction System; SOFA – Sequential Organ Failure Assessment; APACHE – Acute Physiologic Chronic Health Evaluation; POSSUM - Physiological and Operative Severity Score for the Enumeration of Mortality and Morbidity Organ; LOS - length of stay, ICU – intensive care unit; Values are presented as mean/mean± standard deviation (median) or N (%)

Table 3 - Baseline conditions

Baseline conditions	Results
Arterial hypertension	349 (59)
Cardiopathy	208 (35)
Câncer	188 (32)
Diabetes	120 (21)
Tabagism (active last year)	118 (20)
Low functional capacity	112 (19)
EKG abnormalities	108 (18)
COPD	87 (15)
Malnutrition	86 (11)
Previous AMI	52 (8,9)
Alcoholism	39 (6.6)
Hemodynamic instability before surgery	39 (6.6)
Previous CVA	37 (6.3)
Liver failure	32 (5.4)
Heart failure (compensate)	30 (4.9)
Angina	19 (3.2)
Heart failure (decompensate)	14 (2.4)
Severe valvopathy	13 (2.2)
Chronic renal failure (need for RRT)	11 (1.9)

EKG-electrocardiogram; COPD-chronic obstructive pulmonary disease; AMI-acute myocardial infarction; CVA-cerebral vascular accident; RRT-renal replacement therapy. Results are expressed as N (%).

infection 1.7% and catheter-related blood stream infection 1.0%.

Infectious complications occurred in 24.7% of the patients. Of these 22.9% had sepsis (5.3%, sepsis, 3.0%, severe sepsis and, 14.6%, septic shock). We evaluated the temporal pattern of the occurrence of sepsis at specific time intervals, 1 through 3 days, 4 through 7 days, and 8 through discharge or death (32%, 22.5%, and, 45.5%, respectively) (Figure 1). The highest incidences were 1 through 3 days or later than 8 days after the operation. The risk of pneumonia was higher after 8 days (4.6%) in comparison to 1 to 4 days and 4 to 8 days (2.6% for both periods) (Figure 1).

Other frequent complications were congestive heart failure in 5.5% of the patients, severe bleeding in 5.5%, and pulmonary edema in 4.6%. Myocardial ischemia was diagnosed in only 1.9%.

ICU mortality rate was 15%. Overall in-hospital mortality rates were 16.7% at 30 days, 19.7% at 60 days, and 20.3% at 90 days after surgery (Figure 2). A total of 94 % of the patients who died after surgery

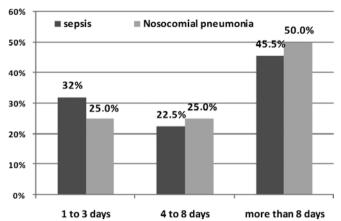


Figure 1. Temporal pattern of the occurrence of sepsis and nosocomial pneumonia at specific time intervals.

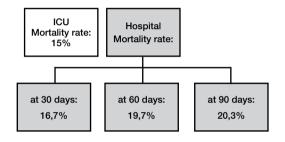


Figure 2. Intensive care unit and in-hospital mortality rates.

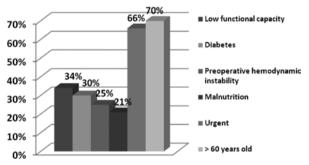


Figure 3. Characteristics of the patients who died after surgery.

had significant medical co-morbidities at the time of surgery  $(3.4 \pm 2.2)$ .

In the case of the patients who died, 66% underwent urgent surgeries, 70% were older than 60 years of age, and 46% older than 70 years of age (Figure 3). A total of 34% patients had previous low functional capacity, 30% had diabetes, 25% had preoperative hemodynamic instability, and 21% had malnutrition. A total of 69.3% of the patients had septic shock, 29.5% had pneumonia, 23.8% had GID, 19.3% had severe bleeding, and 18% had pulmonary edema. Main causes of death in the ICU were multiple organ failure (MOF) in 53%% of the patients, sudden death in 14.9%, and refractory shock in 6.8%. The distribution of in-hospital mortality rates according to the number of baseline conditions in patients undergoing or not to major surgeries is shown in table 4. Mortality rates were three times higher for major surgeries than for moderate surgeries in patients with two or less baseline conditions (p<0.05).

Mortality rates increased in all groups (moderate or major surgery, elective, or urgent surgery) according to the number of associated conditions. Patients undergoing urgent surgeries had significant higher hazards of death (relative risk of 3.32 for patients without baseline conditions, 5.38 for patients with one or two baseline conditions and 2.5 for those with three or more baseline conditions, p<0.05 for all). Likewise, patients undergoing major surgeries were at a significantly higher risk. A total of 123 patients had urgent major surgeries. Overall mortality rate for these patients was 54%, for those without baseline conditions, 43.8%, and 55.1% for those with one or more baseline conditions (RR 1.26 CI 95% 0.70-2.25). Peritonitis was found in 51% of the major urgent surgeries cases.

Table 4 - The distribution of in-hospital mortality rates according to the number of baseline conditions in patients submitted or not to major surgeries or urgent/emergent surgeries

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N of baseline conditions	No	Yes	RR	CI 95%
Major surgery				
0	4 (5.4%)	13 (16.2%)	3.01	1.02-8.81
1-2	7 (8.5%)	47 (24.9%)	2.91	1.37-6.17
≥3	7 (19.4%)	43 (34.0%)	1.76	0.86-3.56
Urgent/emergent surgery				
0	8 (6.9%)	9 (23.0%)	3.32	1.37-8.00
1-2	16 (8.5%)	38 (45.7%)	5.38	3.18-9.08
≥3	19 (19.4%)	31 (48.4%)	2.50	1.55-4.02

N – number; RR – relative risk; CI - Confidence interval

# **DISCUSSION**

Postoperative complications are a significant source of morbidity and mortality for patients undergoing non-cardiac surgery. Our study found a high incidence of complications in this population (38.3%). The most common complication was sepsis affecting 23% of the overall population and 73% of those who died. The vast majority of deaths after non-cardiac surgery was due to MOF.

We found an incidence of 24.7% of infection in which 23% of the patients developed sepsis. This rate is a little higher than that observed in a European study including over 4,500 patients with a prevalence of ICU-acquired infection of 20.6%. Sepsis is a major public health problem in Brazilian ICUs and mortality rates range from 47% to 52%. An even higher rate of 28% of the patients presenting septic complications but with a similar temporal pattern of distribution was reported after intra-abdominal operations. (23)

Extubation failure was the second most common complication (10%). Mortality rate was almost 5 times higher for patients with extubation failure in our study. Rates of over 12% of extubation failure were reported in similar populations of high risk patients; and often results in 12 additional days of mechanical ventilation and a higher mortality. Comparatively, lower extubation failure rates, 4.7% and 1.8% respectively, were observed after on-pump coronary artery bypass grafting or in a heterogeneous group of patients admitted to either an ICU or a high dependency unit of a tertiary hospital. (25, 26)

The third most common postoperative complication (8%) was GID. Likewise, in a retrospective analysis of 2,588 adult patients admitted to the ICU, GID was identified in 9.7% of all patients. (27) In a diverse group of elective, moderate risk surgical procedures in which postoperative complications occurred in 27% of the patients, 51% of the complications were related to the gastrointestinal tract. (28) On the other hand, gastrointestinal complications occurred in only 2.5% of patients undergoing cardiac surgery. (29) Gastrointestinal failure represents a relevant clinical problem followed by an increased mortality, longer ICU stay, and mechanical ventilation. Nevertheless, the lack of a consensus definition of GID is a major limiting factor of research in the area.

It was previously suggested that cardiac complications are the most relevant type of morbidity after non-cardiac surgery<sup>(30)</sup>. In our study, cardiac morbidity

was less common than infectious complications. Cardiac adverse events (CAE) defined as unexpected cardiac arrest and/or acute MI occurred in 5.6% of the patients. Of these 68% died. Only 11 patients (1.9%) had documented MI (1.9%). In another study, MI was diagnosed in 4% of the patients with a very strict monitoring protocol 23. In a cohort of 183,069 noncardiac surgical patients, CAE occurred in 1.3% of the patients, and among these, 59.4% expired. (31) Of note, this study excluded most cardiac-specific risk factors such as angina and recent MI as independent predictors of CAE. Patients who underwent emergency vascular surgery are particularly at risk of CAE, but this seems to have been converted into late mortality from MOF. (32) Heart failure was also a frequently encountered complication after major surgeries and its frequency (5.5%) is in accordance with previous reports. (33,34) Elderly patients with chronic HF who underwent major surgical procedures had substantially higher risks of operative mortality and hospital readmission than other patients, including those with coronary disease, admitted for the same procedures. (35,36)

The incidence of pulmonary edema (PE) in our casuistic was 4.5%. PE may have many causes in ICU patients. Fluid overload is probably the main one. Recent studies suggest that current fluid strategies may result in excessive administration of fluids. Accordingly, a study comparing different intravenous fluid regimens in the perioperative period of major elective gastrointestinal surgeries found a similar incidence of 5.5% of patients presenting pulmonary edema in the conventional group. (37) No cases were observed in patients with the restricted regimen aimed at maintaining preoperative body weight. Yet, there are a substantial proportion of patients with diastolic dysfunction and prone to sudden development of pulmonary congestion (flash PE). (38) Non-cardiogenic pulmonary edema may also be due to acute lung injury secondary to sepsis or Transfusion Related Acute Lung Injury (TRALI), a serious and under diagnosed complication of blood transfusion.

ICU mortality rate was 15%. Overall mortality rates were 15%, 19.7%, and 20.3% at 30, 60, and 90 days after hospital admission. A quarter of the deaths occurred after ICU discharge and 15% of the deaths after day 30. The vast majority of deaths after surgery were due to MOF (53.4%). A national audit of 1029 ICU patients in Ireland found an ICU mortality rate of 17.6%. [39] Interestingly, in an Italian ICU, mortality rate in patients admitted after scheduled surgery was much lower (2.4%) but the rate of complications was

very similar (36%) to the mixed population of elective and urgent surgeries included in our cohort. (40) However, comparison is difficult due to the lack of definitions for the complications reported in this study. In a prospective study performed in a German University Hospital postoperative ICU, mortality rate was 9%. (41) In another German multi-center study, the most frequent causes of perioperative death were myocardial failure (33.7%) and multi-organ-failure (19.2%). (42)

Major surgical trauma increases oxygen requirements from an average of 110 ml min<sup>-1</sup> m<sup>-2</sup> at rest to an average of 170 ml min<sup>-1</sup> m<sup>-2</sup> in the postoperative period. (43) This increase in oxygen demand is normally met by increases in cardiac output and tissue oxygen extraction. Very frequently, the high-risk patients are unable to spontaneously elevate their cardiac output to match the demand. Thus, they are more likely to develop oxygen debt and as a consequence of MOF. In agreement with this scenario, a total of 94% of the patients who died after surgery had significant medical co-morbidities (median 3), particularly cardiovascular pathology, and two-thirds have had urgent surgeries, 34% low functional capacity, 70% were older than 60 years of age, and 46% older than 70 years of age (Figure 1). These results are very similar to the previous findings reported in UK by the National Confidential Enquiry into Perioperative Deaths (NCEPOD). (44)

Some limitations of our study are the relatively small number of patients and ICUs. But despite the continental proportions of our country all regions were represented. Surveillance of complications by independent individuals at each of the study centers was not a requirement. Thus, it is possible that the number of complications have been underestimated. Nevertheless, complications had strict predefined criteria.

# **CONCLUSION**

In conclusion, sepsis is the predominant cause of morbidity and mortality in patients undergoing non-

cardiac surgery. The vast majority of deaths were due to MOF. The compromised physiologic reserves in combination with extensive surgery, followed by MOF from which recovery is prolonged, seem to be a hallmark of these high-risk patients. In order to significantly improve survival, a well-orchestrated and multidisciplinary approach with emphasis on prevention of complications and organ support will be necessary.

# **RESUMO**

**Objetivo:** Devido aos avanços da medicina e ao envelhecimento da população, a proporção de pacientes em risco de morte após cirurgias está aumentando. Nosso objetivo foi avaliar o desfecho e a epidemiologia de cirurgias não cardíacas em pacientes admitidos em unidade de terapia intensiva.

**Métodos:** Estudo prospectivo, observacional, de coorte, realizado em 21 unidades de terapia intensiva. Um total de 885 pacientes adultos, cirúrgicos, consecutivamente admitidos em unidades de terapia intensiva no período de abril a junho de 2006 foi avaliado e destes, 587 foram incluídos. Os critérios de exclusão foram; trauma, cirurgias cardíacas, neurológicas, ginecológicas, obstétricas e paliativas. Os principais desfechos foram complicações pós-cirúrgicas e mortalidade na unidade de terapia intensiva e 90 dias após a cirurgia.

**Resultados:** Cirurgias de grande porte e de urgência foram realizadas em 66,4% e 31,7%, dos pacientes, respectivamente. A taxa de mortalidade na unidade de terapia intensiva foi de 15%, e 38% dos pacientes tiveram complicações no pós-operatório. A complicação mais comum foi infecção ou sepse (24,7%). Isquemia miocárdica foi diagnosticada em apenas 1,9%. Um total de 94% dos pacientes que morreram após a cirurgia tinha co-morbidades associadas  $(3.4\pm2.2)$ . A principal causa de óbito foi disfunção de múltiplos órgãos (53%).

**Conclusão:** Sepse é a causa predominante de morbidade em pacientes submetidos a cirurgias não cardíacas. A grande maioria dos óbitos no pós-operatório ocorreu por disfunção de múltiplos órgãos.

**Descritores:** Complicações pós-operatórias; Sepse; Trato gastrintestinal/fisiopatologia; Insuficiência de múltiplos órgãos

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