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Guidelines for potential multiple organ donors (adult). Part III. Organ-specific recommendations

Diretrizes para manutenção de múltiplos órgãos no potencial doador adulto falecido. Parte III. Recomendações órgãos específicas

ABSTRACT

Brain death (BD) alters the pathophysiology of patients and may damage the kidneys, the lungs, the heart and the liver. To obtain better quality transplant organs, intensive care physicians in charge of the maintenance of deceased donors should attentively monitor these organs. Careful hemodynamic, ventilatory

and bronchial clearance management minimizes the loss of kidneys and lungs. The evaluation of cardiac function and morphology supports the transplant viability assessment of the heart. The monitoring of liver function, the management of the patient's metabolic status and the evaluation of viral serology are fundamental for organ selection by the transplant teams and for the care of the transplant recipient.

INTRODUCTION

The relative shortage of organ donors has lead to discussions concerning the use of borderline donors, which increases the relevance of assessing the care of potential donors.

Deceased donors often experience shock and rhabdomyolysis along with an increase in the administration of nephrotoxic drugs or radiology contrasts, which may lead to acute renal failure $(\mathbf{C})^{(1)}(\mathbf{A})^{(2)}(\mathbf{D})$. To maintain adequate function, kidneys should receive appropriate care (\mathbf{C}) . (4,5)

The lungs are particularly sensitive to the pathophysiological changes that occur with brain death and are susceptible to infective agents, inflammatory responses and cardiovascular dysfunction $(\mathbf{D})^{(G)}(\mathbf{C})$. Judicious fluid replacement, protective ventilation, the use of bronchial hygiene physiotherapy and serial lung function studies minimize the loss of transplantable lungs (\mathbf{D}) . (6)

An assessment of the morphology and function of the donor heart are mandatory before heart transplantation (\mathbf{B}). The early correction of hemodynamic and metabolic disorders with the aim of reversing heart dysfunction increases the potential of the organ for transplantation (\mathbf{B}). (9)

An elevated bilirubin, elevated levels of transaminases, or a positive finding by serology for B and C viruses (except if HBsAg-positive), are not absolute contraindications for the transplantation of a donor liver $(\mathbf{C})^{(10\text{-}16)}(\mathbf{A})^{(17)}(\mathbf{C})$. However, an elevation in liver enzymes may be a sign of either hypoperfusion or of the initial immunological response in the setting of subclinical viral hepatitis (\mathbf{C}) .

These factors need not prevent the use of an organ for transplantation. They should, however, alert the maintenance team to act to restore adequate blood flow to the organ. The factors should also be of concern to the transplant team in reference to organ selection and to the care of the transplant recipient (\mathbf{C}) .

OBJECTIVE

These guidelines are aimed at contributing to the institutional coordination of organ transplantation and will provide "real world" guidelines that are appropriate in the Brazilian context for the uniform care of the deceased donor. Ultimately, this aim of this guide is to increase the quality and quantity of transplantable organs.

METHODOLOGY

The Writing and Planning Committee, comprised of young intensive care physicians and intensive medicine residents, conducted an extensive literature review. From this review, they formulated questions and forwarded the questions to all of the authors of this article. These initial questions served as the starting point for receiving suggestions for the formulation of other questions and definitions.

The final questions were revised by the Executive Committee and were returned to the authors to develop the guidelines presented in this article.

The questions guided the literature review, which was conducted using the P.I.C.O. methodology where P stands for the target population, I for the intervention, C for the control or comparative group and O for the clinical outcome.

The retrieved articles were critically analyzed and categorized according to their grade of recommendation and the strength of the presented evidence in the following manner:

- A: More consistent experimental or observational studies.
- B: Less consistent experimental or observational studies.
- C: Case reports (non-controlled studies).
- **D:** Opinions that lack critical evaluation and are based on consensus, physiological trials or animal models.

Given the paucity of evidence from trials involving deceased donors, many of these recommendations were based on comparisons with other clinical conditions. Therefore, physiological, epidemiological and experimental analyses were used.

The seven discussion subgroups were as follows: 1) overview; 2) hemodynamic support; 3) endocrine-metabolic management; 4) mechanical ventilation and pulmonary maintenance; 5) liver maintenance; 6) renal maintenance and 7) heart maintenance. Each subgroup had a coordinator who was responsible for stimulating and guiding the discussions via email. The texts from each subgroup were organized by the Writing and Planning Committee, presented for review by the Executive Committee and were returned to each subgroup for review. The full text was provided to all panel members and discussed in a meeting

held during the XIV South-Brazilian Intensive Care Medicine Congress in May 2001 at Joinville, Santa Catarina, Brazil. The coordinators presented their recommendations at the meeting and discussed the results with conference attendees. Because a large portion of the research that the recommendations were based on was poorly supported, the grade of recommendation was added based on the GRADE system (Grading of Recommendation, Assessment, Development and Evaluation). This system allowed us to classify the quality of the recommendations as STRONG (should be done), WEAK (perhaps should be done) and NONSPECIFIC (there are no advantages or disadvantages). A strong recommendation means that the benefits of an intervention outweigh the risks. A weak recommendation means that the benefits of an intervention are likely to outweigh the risks, although the evidence is weak and more research on the subject is warranted. A nonspecific recommendation means that the benefits and risks of the intervention must be assessed on a caseby-case basis. A strong recommendation should be understood as "recommended" and a weak recommendation as "suggested."

A description of the method for the collection of evidence

The primary database used for the literature review was MEDLINE, which was accessed via the PubMed service. The search was based on the P.I.C.O. methodology of structured questions. Using the MeSH interface (Medical Subject Heading), the following combinations of key words were used: (organ donor OR donor management OR brain death AND recommendation OR consensus), (organ donor OR donor management OR lung transplantation AND mechanical ventilation OR strategies of ventilation), (organ donor OR donor management OR lung transplantation AND fluid challenge OR fluid resuscitation OR positive balance), (organ donor OR donor management OR lung transplantation AND bronchoscopy OR bronchoalveolar lavage), (organ donor OR donor management OR lung transplantation AND pneumoniaventilator associated), (organ donor OR donor management OR lung transplantation AND prevention and control), (braindeath OR organ donor AND renal donation), (renal function AND brain-death organ donation), (brain-death organ donor AND management OR kidney transplantation), (organ transplantation OR donor kidneys OR management donor kidneys), (transplantability AND liver OR hepatic AND donor), (cadaveric donor AND timing AND liver transplantation), (expanding the donor pool AND liver OR marginal donor liver AND outcome OR extended criteria donor AND MELD), (deceased cardiac donor OR non heart beating donor AND brain death donor), and (organ donors AND echocardiographic OR cardiac transplantation OR management of heart donors). The secondary databases used for the literature review included the Cochrane, Ovid and Trip databases.

RENAL MAINTENANCE

What are the recommended measures to ensure the preservation of renal function?

For the maintenance of adequate renal function, which consists of a normal creatinine clearance (> 80 mL/min) and 1 to 3 mL/kg/h urinary output, we recommend a MBP≥ 65 mmHg, a CVP between 6 and 10 cm₂ and diuresis at > 1 mL/kg/h in a deceased donor (C). (4,5) These parameters can be achieved with the vigorous infusion of crystalloid solutions (C). (20) Eventually, the use of excessive fluid infusion becomes of value to avoid the use of vasopressors (D). (21,22) However, no controlled or retrospective studies have been done that specifically address the ideal method of fluid replacement for deceased donors.

The aim of vigorous fluid replacement is to protect the donor kidney. However, the maintenance of renal function may jeopardize lung function and eventually render lungs inappropriate for transplantation (\mathbf{D}). A recent study analyzing the effects of restrictive fluid replacement aimed at improving lung obtention has shown that maintaining hemodynamic parameters within the minimum normal range (CVP < 6 mmHg) to prevent volume overload increased the number of available lungs without reducing the number of available kidneys. Additionally, the graft quality was maintained, in contrast to the graft quality associated with more liberal fluid replacement (\mathbf{C}).

Another alternative to liberal fluid replacement is the use of catecholamines. In addition to their hemodynamic effects, catecholamines such as dopamine have been found to have an anti-inflammatory effect. *In vitro* dopamine reduces IL-8 and chemokine expression in the tubular cells as well as delaying the function of adhesion molecules, such as ICAM-1 and VCAM, and inducing HO-1 expression ($\bf C$). (24-26) A recent study showed that the infusion of low-dose dopamine (4 µg/kg/min) after a diagnosis of brain death and until the organs were removed for transplant reduced the need for immediate post-transplant dialysis in transplant recipients without changing the graft and patient survival rates $\bf B$). (27) However, high-dose dopamine (10 µg/kg/min) and/or norepinephrine may impair organ function because of the vasoconstrictive effect of these substances ($\bf D$). (6)

In our review of the literature, we found no studies that addressed the association between iodine contrasts and nephrotoxicity in deceased donors. We recommend following the guidelines associated with other types of patients (\mathbf{D}) .⁽³⁾

There is no single approach that can be recommended to maintain organ perfusion (**D**).⁽²⁸⁻³⁰⁾ A level of perfusion that is as close as possible to normal perfusion is fundamental for maintaining renal function.

Recommendations

- To maintain the donor's hemodynamic stability (MBP \geq 65 mmHg and urinary output \geq 1 mL/kg/h) (C)^(4,5) by means of fluid replacement, vasopressor drugs and, when required, inotropic drugs (D). ^(6,28-30) **Strong Recommendation**.
- Consider the use of low-dose vasopressors such as dopamine (4 μ g/kg/min) in stable subjects to reduce the need for post-transplant dialysis (**B**). (27) **Weak Recommendation.**

Are changes in creatinine and/or creatinine clearance levels in the donor organ a contraindication for renal transplant?

A baseline creatinine (Cr) of 1.5 mg/dL (\mathbf{D})⁽³¹⁾ or 2 mg/dL (\mathbf{D})⁽³²⁾ is considered at the upper limits for kidneys to be considered appropriate for donation (\mathbf{D}).⁽²⁸⁾ A donor kidney with values rising above these levels is known as an expanded-criteria kidney (ECK).

A donor kidney with a creatinine clearance (CrCl) lower than 50 mL/min alone is considered as an exclusion criterion for transplantation (**D**). However, these kidneys may be considered for a double-renal transplant (**D**). Some research has suggested that CrCl values between 50 and 70 mL/min in ECK donors is an indication for the use of the kidney in double-renal transplantation (**B**). Other research has shown that the use of an ECK donor with a creatinine clearance < 100 mL/min was associated with an increased serum creatinine one year after transplantation (**B**). CrCl < 80 mL/min in kidneys harvested from elderly donors (> 55 years) has been associated with lower rates of renal survival after transplantation (**B**).

Acute renal failure (ARF) is not an absolute contraindication for transplantation of the donor kidney. Several reports have shown that patients with ARF due to rhabdomyolysis will come to have an acceptable creatinine clearance (\mathbf{C}). Successful case series have been reported with ARF donors (\mathbf{C}). Other authors recommend the use of a pre-implant histology assessment as a criterion for using a graft (\mathbf{B}) (\mathbf{C}). There are no controlled studies that address this subject. There may then be a bias in the studies noted above because only the positive series results were published.

Recommendation

- Assessing the viability of kidneys for transplant should not be based only on changes in Cr and/or CrCl $(D)^{(33)}(B)^{(35)}$. Strong Recommendation.

Should serial serum creatinine measurements and creatinine clearance calculations be performed for all potential donors? How frequently should these calculation be performed?

Serum creatinine (Cr) is an indirect method used for

estimating the rate of glomerular filtration. Some limitations should be considered in reference to the value of this estimation. Cr is a product of muscle metabolism and is distributed in the water volume of the body. The production rate is proportional to the subject's muscle mass. In the critically ill condition of deceased donors, rhabdomyolysis is common and leads to sudden increases in plasma creatinine levels. Conversely, the infusion of large volumes of fluid can dilute Cr and reduce the level in the plasma., The use of Jaffe's method may also interfere with the accuracy of Cr measurements.

The assessment of baseline renal function

A baseline Cr is used in the assessment of all deceased donor kidneys. Its main function is to identify pre-existing renal disease and chronic impairment of glomerular filtration. For these purposes, a baseline Cr is used to calculate the estimated creatinine clearance (CrCl) using the Cockroft-Gault formula.

CrCl is just one parameter that can be used to identify previous renal disease and a family history of renal disease. Other criteria, such as a urinalysis and sediment evaluation is mandatory to rule out glomerular disease (hematuria, proteinuria or cylindruria) or urinary tract infection.

A baseline creatinine of between 1.5 mg/dL (\mathbf{D})⁽³¹⁾ and 2 mg/dL (\mathbf{D})⁽³²⁾ is the maximal tolerable level for renal transplantation. A donor kidney with values rising above these levels is known as an ECK. A Cr > 1.36 mg/dL is associated with late graft function (\mathbf{B}). Lower Cr levels in a donor organ are associated with lower Cr levels in the transplant recipient (\mathbf{C}). (44)

Research has shown that the measurement of CrCl alone failed to strongly correlate with the measurement of renal graft outcome (\mathbf{C}). Other research has shown that CrCl > 70 mL/min was the best discriminator associated with strong renal function at 1 to 12 months after renal transplantation when compared with other scores (\mathbf{D}). A CrCl < 50 mL/min is an exclusion criterion for the use of a renal graft (\mathbf{D}). Transplant recipients of kidneys from higher CrCl donors have higher rates of graft survival, patient survival and renal function (\mathbf{B}).

Serial renal function assessment

Changes in Cr and diuresis volume are used as criteria for diagnosing acute renal injury (ARI) (C)⁽¹⁾(A).⁽²⁾ A deceased donor is exposed to several ARI risk factors, such as shock, rhabdomyolysis, the use of nephrotoxic drugs or radiology contrasts. In a stable setting, Cr is expected to increase daily by 1 mg/dL when glomerular filtration has ceased. However, in a critically ill patient, as previously mentioned, the increased distribution volume may underestimate the real level of variation. Patients with anuria may experience days without a significant change in Cr levels when receiving significant volume expansion

because of Cr dilution. Conversely, with rhabdomyolysis, an increase in Cr may overestimate the amount of kidney damage. Additionally, the ancillary parameter of diuresis volume is higher in deceased donors due to the lack of the effects of the tubular antidiuretic hormone (ADH). These factors should be considered when assessing serial Cr measurements (**C**).⁽¹⁾

There are no studies that suggest when serial Cr measurements should be performed in the setting of the management of the deceased donor. The Canadian Forum on Medical Management to Optimize Donor Organ Potential recommends repeating Cr measurements every 6 hours (**D**),⁽²⁸⁾ but this recommendation was suggested without a rationale. Changes in Cr within 48 hours are used as diagnostic criteria in ARI diagnosis (**A**).⁽²⁾ However, a 48-hour period may not be feasible in the setting of the deceased donor.

There is no indication for the use of CrCl estimated by formulas in the setting of ARI. Its use is indicated for assessing the balance between Cr production and excretion.

Recommendations

- Record a baseline Cr and then repeat the measurement every 24 hours for all potential donors $(\mathbf{D})^{(28)}(\mathbf{B})^{(43)}(\mathbf{C})$. Strong Recommendation.
- Analyze the volume of diuresis and Cr variation in conjunction with the clinical conditions of all potential donors (C). (1) Strong Recommendation.

What are the indications for the use of renal ultrasonography (USG) in the assessment of potential donors?

There is no precise indication for the use of renal USG in the assessment of potential donors. The information obtained from USG is not useful (\mathbf{D}) . (28)

There may be some cases where USG could be useful. When a donor with a family history of renal disease, such as polycystic renal disease or cases of suspected chronic renal disease has an initial increase in the creatinine level, USG could be useful for assessing the size of the kidneys. When available, a total abdominal USG could be useful for ruling out neoplasms.

Recommendation

- Routine renal USGs are not indicated for deceased donors. The use of this test should be evaluated on a case-by-case basis (\mathbf{D}) . (13) **Strong Recommendation**

LUNG MAINTENANCE

How should be gas exchange be monitored? Which tests should be performed? What are the ideal blood gas parameters?

Brain death releases inflammatory mediators and induces a number of hemodynamic changes. Although all solid organs are affected, the lungs are particularly sensitive to the effects of hemodynamic instability. The lungs are additionally susceptible to the effects of resuscitation efforts and changes in capillary permeability $(\mathbf{D})^{(6)}(\mathbf{C})$. Longterm hospitalization in the ICU also exposes the lungs to infective agents. These harmful agents account for the loss of many organs and render less than 20% of multiple organ donors appropriate for transplantation (\mathbf{C}) . Judicious fluid replacement, careful ventilation and serial evaluations minimize the loss of these organs (\mathbf{D}) .

Routine tests and procedures for the assessment of lungs from a deceased donor include the following: pulse oxymetry, serial arterial blood gases, tracheal cannula suction, chest radiography, bronchoscopy and bronchoalveolar lavage (**D**). (28) Target blood gas levels for the maintenance of lungs for transplantation are as follows: $SaO_2 \ge 95\%$ and $PaO_2 \ge 80$ mmHg; or PaO₂ > 300 mmHg with FiO₂ of 100% and PEEP of 5 cmH₂O; or PaO₂/FiO₂ \geq 300 mmHg (**D**). (28) Acidosis should be corrected with sodium bicarbonate or by increasing the rate of ventilation (PaCO 2 between 30 and 35 mmHg) for a pH > 7.2 (C). (48) Some studies have shown that it is possible to transplant organs from donors with more severe changes if the changes were not associated with other risk factors (C). (49-51) Blood gas measurements should be repeated at least every 6 hours and/or whenever oxymetry monitoring or ventilation parameters have changed. Some articles have shown that the rate of graft failure is higher in this group. However, other studies show no differences. This improvement should be sustained (C). (50,51) Other mandatory tests include: 1) Chest radiography: preferably with the head of the bed at 45° and with ventilation tidal volume of 12 mL/kg body weight (use this volume during the test only). Radiographic studies should be done less than 6 hours before organ extraction (C). (51) 2) A bronchoscopy should be performed as a part of the multi-organ donor assessment and for the collection of bronchoalveolar lavage fluid specimen(**B**). (52,53)

Recommendations

- Continuous pulse oxymetry monitoring, arterial blood gases every 6 hours, and chest radiography every 24 hours $(\mathbf{D})^{(28)}$ (\mathbf{C}) . Strong Recommendation.
- The ideal blood gas parameters are as follows: $SaO_2 \ge 95\%$ and $PaO_2 \ge 80$ mmHg or $PaO_2 > 300$ mmHg with FiO_2 of 100% and PEEP of 5 cmH $_2$ or $PaO_2/FiO_2 \ge 300$ mmHg (**D**). (28) **Strong Recommendation**.
- Even when these target values are not achieved, lung donation is not contraindicated. **Strong Recommendation**.

Once all of the above criteria are met, when is bronchoscopy indicated?

The respiratory management of a potential donor is frequently complicated by pulmonary injuries such as the following: neurogenic pulmonary edema, respiratory infections, pulmonary bleeding and traumatic pulmonary injury (\mathbf{D})^(6,54,55) (\mathbf{C}). The development of atelectasis secondary to the supine position of the deceased donor, the prolonged period of mechanical ventilation and aggressive fluid resuscitation are frequent causes of hypoxemia. If these conditions are not corrected, there is up to a 30% reduction in the likelihood of the feasibility of transplanting these lungs (\mathbf{D}). (57)

The objectives of bronchoscopy in a donor are as follows: to assess the bronchial anatomy; to evaluate and remove endobronchial foreign bodies; to identify and assess aspirated material for possible infection; and to clear secretions (**D**.^(6,57,58) The performance of an early bronchoscopy is an important factor in the aggressive management of potential donors. Studies have shown that the performance of a bronchoscopy, along with frequent pulmonary suction (respiratory physical therapy) and pulmonary expansion ventilation techniques (using PEEP), results in a significant increase in both the quality of the donor organs and in the number of transplantable organs $(\mathbf{D})^{(29)}(\mathbf{C})$. (56,59-62) A bronchoscopy can be performed either by a local hospital physician or by the transplant team surgeon (D). (28) During the bronchoscopy, respiratory fluids should be collected (bronchoalveolar lavage fluid) for Gram staining and cultures with the aim of guiding eventual antibiotic therapy (\mathbf{D}). (28,57)

In donors presenting with evidence of gas exchange abnormalities and radiographic evidence of unilateral lung injury, a therapeutic bronchoscopy may support a contralateral lung assessment with the aim of avoiding the discarding of a potential donor organ and of contributing to graft survival (**D**). (6,29,57,63)

Recommendations

- A bronchoscopy is indicated for all potential lung donors $(\mathbf{D})^{(29)}(\mathbf{C})$. Strong Recommendation.
- If a bronchoscopy cannot be performed at the hospital of origin, clinicians should inform the team responsible for removing the organs that this test could not be performed. In these circumstances, the procedure will be performed by the organ removal team (\mathbf{D}) . Strong Recommendation.

Which bronchial hygiene procedures should be used?

The aims of bronchial hygiene physiotherapy are to prevent atelectasis and to improve the pulmonary gas exchange of mechanically ventilated critically ill patients (\mathbf{D}). The recommended procedures are as follows: low-pressure tracheal suction (\mathbf{D}), essential critically ill patients (\mathbf{D}).

positioning every 2 hours $(\mathbf{D})^{(28)}$ and pulmonary expansion techniques (\mathbf{D}) . There are few studies concerning bronchial hygiene for deceased donors. Many of our recommendations are taken from the guidelines associated with other clinical conditions.

Some studies $(\mathbf{D})^{(57)}$ have recommended that tracheal suction be performed with closed suction circuits. However, recent meta-analytical research involving living critical patients failed to show any significant difference regarding the incidence of mechanical ventilation-associated pneumonia when using closed suction circuits (\mathbf{A}) . (65,66)

To reduce pulmonary aspiration, some protocols for donor management have recommended raising the head of the bed to at least 30° and to maintaining the tracheal tube balloon pressure at close to 25 cm $H_2O(\mathbf{C})^{(53)}(\mathbf{D})^{(57)}(\mathbf{C})$. (67) A semiseated position (the head of the bed raised to between 30° and 45°) has been found to reduce the incidence of mechanical ventilation-associated pneumonia and will likely reduce the bronchial aspiration of contaminated oropharyngeal material (A). (68-70) We infer that these recommendation will have similar beneficial effects in the setting of the deceased donor. Another strategy to prevent subglottic secretions from entering the lower respiratory tract is the maintaining of optimal tracheal tube balloon pressure. Balloon pressures below 20 cmH₂O have been shown to increase the risk of pneumonia while pressures above 30 cmH₂O have been shown to increase the risk of ischemic tracheal injury (B).(71-73)

When potential donors develop atelectasis, especially when he atelectasis is associated with hypoxemia, postural drainage is recommended along with ventilatory alveolar recruitment and therapeutic bronchoscopy (**D**). ⁽⁶⁴⁾

Recommendations

- The tracheal tube should be suctioned only in the presence of tracheal secretions. Follow decubitus positioning every 2 hours (\mathbf{D}). ^(28,57,58) Keep the head of the bed raised to between 30° and 45° (\mathbf{A}). ⁽⁶⁸⁻⁷⁰⁾ Keep the tracheal tube balloon pressure between 20 and 30 cmH2O (\mathbf{B}). (71-73) **Strong Recommendation**.

How should volume therapy be managed in a potential lung donor?

The maintenance of a potential donor includes the challenge of restoring or maintaining hemodynamic stability. Hypovolemia is a frequent occurrence and should be aggressively treated. However, fluid overload may result in pulmonary edema, which may render the donor organ unfit for transplantation (**D**). (74) Intravenous fluids must then be carefully monitored. This is especially important for potential lung donors. The lungs may be injured during sympathetic hyperactivity and become increasingly susceptible to pulmonary edema and

capillary leakage. Although hypovolemia should be corrected, the excessive administration of fluids should be avoided. Fluid replacement should be judicious with the aim of maintaining a euvolemic status. The Lung Work Group (D)(48) recommends that a pulmonary artery catheter be inserted to assist with fluid management and to assure good tissue perfusion. Measurements obtained from the pulmonary artery will assist clinicians in maintaining a central venous pressure (CVP) of 6-8 mmHg and a pulmonary wedge pressure (PCWP) of 8-12 mmHg. Recent studies have shown that a CVP > 7 mmHg in a deceased donor, even after heart dysfunction was ruled out, was associated with a poorer clinical outcome, a prolonged period of mechanical ventilation and an increase in the rate of mortality rate for patients receiving lung transplants (C). (75) The findings of this research were additionally supported by an observational study where patients who were initially considered unacceptable as lung transplant donors became effective donors after an aggressive fluid restriction strategy (previous fluid balance: 4.1 ± 1.3 L versus -1.7 \pm 0.8 L; p < 0.008; and previous CVP: 11.3 \pm 0.9 mmHg versus 6.7 ± 0.4 mmHg (**D**). (76) However, hypovolemic deceased donors in general have more systemic inflammation and less viable transplantable organs (C). (77,78)

Although the monitoring of CVP and PCWP are recommended by some researchers, the accuracy and usefulness of the measurements remains uncertain (\mathbf{C}) . (79) Although ventricular filling pressures are the preferred method for assessing cardiovascular responsiveness, recent evidence suggests that CVP and PCWP measurements exhibit low sensitivity and specificity $(\mathbf{C})^{(80)}(\mathbf{B})$. (81-83) More accurate methods should be chosen to assess the variables of dynamic cardiovascular volume responsiveness $(\mathbf{B})^{(81,82,84)}$ (see the hemodynamic management section).

Recommendations

- Use volume expansion techniques in potential lung donors when appropriate. Avoid fluid overload (**C**). (78) Maintain adequate tissue perfusion to avoid the loss of potential donor organs because of hypovolemia (**C**). (77,78) **Strong Recommendation**.

HEART MAINTENANCE

Are echocardiography and/or pulmonary artery catheter (PAC) monitoring needed to assess heart transplantability?

The assessment of the morphologic and hemodynamic status of the heart is essential for heart transplant and should be performed as soon as consent is obtained for the donation (B).⁽⁸⁾ An echocardiogram provides information concerning ventricular contractility, interventricular septum thickness, the presence of an intracardiac shunt, valve disease and, with the use of the Doppler, the flow velocity of the anterior

descending coronary artery. This assessment is particularly important for donors with coronary disease risk factors (**C**). (85) Invasive hemodynamic monitoring with a PAC increases the number of available heart transplants as compared with donors who were not monitored with a PAC without affecting the amounts of infused fluid or the vasopressors administered (**B**). (9)

Recommendations

- An echocardiogram should be performed on all potential heart donors to assess the morphologic and functional status of the heart $(B)^{(8)}(C)$. Strong Recommendation.
- Consider using a pulmonary artery catheter in all potential heart donors (B). (9) Weak Recommendation.

Which invasive hemodynamic monitoring methods (PAC) or echocardiographic parameters are considered ideal for assessing the donor heart?

The following factors contribute to the failure of transplanted hearts: left ventricular systolic dysfunction (an ejection fraction of less than 50%) (\mathbf{B});^(8,86) changes in structure caused by variances in contractility (C);(85) reduced coronary flow as determined by Doppler studies (C)(85); and prolonged organ ischemia (D). (87) Both echocardiography and PAC monitoring are used to identify hearts that are suboptimal candidates for transplantation (B).(8) Echocardiographic assessment of the left ventricular ejection fraction assists in predicting which organs are viable for transplantation (B). (8) A morphological assessment assists in identifying structural changes that may preclude the use of the organ (C).(85) Hemodynamic monitoring with a PAC allows for the sequential assessment of pharmacological interventions and can assess whether circulatory changes in the a potential donor have been reversed, which improves the outcome for the heart transplant recipient (B). (9) The management of a potential donor through the use of a reanimation protocol corrects and promotes hemodynamic stability (systolic blood pressure > 90 mmHg; wedge pressure \leq 15 mmHg; cardiac index \geq 2.5 L/min/m²) and assists in the management of metabolic disorders. This protocol may reverse heart dysfunction and increase the chances of the viability of a donor organ by up to 30% D. (88,89) In a series of 49 cases of potential deceased donors with left ventricular ejection fraction (LVEF) lower than or equal to 50% who were initially considered inappropriate for transplant, the use of the animation protocol improved LVEF in 38 cases (78%), and 34 of these donor hearts were successfully transplanted (C). (90)

Recommendations

- The ideal parameters for the donor heart are as follows: a left ventricular ejection fraction > 50% ($\bf B$); (8) no variance in structure or contractility ($\bf C$); (85) a cardiac index > 2.5 L/min/

 m^2 and a PCWP ≤ 15 mmHg (**D**).^(88,89) Even when these target values are not achieved, heart transplantation may not be contraindicated. **Strong Recommendation**.

- Consider inserting a PAC to monitor efforts at attempting to reverse cardiac dysfunction (CI < 2.5 L/min/m^2 and PCWP $\leq 15 \text{ mmHg}$) and increase the chances of increasing the viability of the donor organ (B).^(8,9) Weak Recommendation.

Do increases in biomarker values contraindicate the transplantation of the donor heart?

Serum troponin levels alone should not be used as a basis for rejecting a donor heart for transplantation (\mathbf{D}) . (28)

An increase in cardiac enzymes is common in potential deceased donors. Although an increase is related to worsening myocardial dysfunction and transplant failure, it is not necessarily indicative of coronary disease. An increase in the levels of cardiac enzymes alone neither identifies coronary disease or serves as a basis for rejecting the donor heart for transplantation. An increase in cardiac enzymes should be assessed for a correlation with persistent myocardial dysfunction (**D**). (91)

Recommendation

- Transplantation of a donor heart is not contraindicated based on an increase in cardiac biomarkers alone. The variance in the biomarkers should be assessed for a correlation with persistent myocardial dysfunction (**D**). Strong **Recommendation**.

In which conditions should potential heart donors undergo cineangiocoronariography?

During the last three decades, the upper age limit for donors has increased. The increased rate of mortality for patients receiving hearts from older donors has raised questions concerning donor selection (C). (92)

Overall, cineangiocoronariography should be performed on male donors greater than 45 years of age and on female donors greater than 50 years of age. Factors such as cocaine use or the atherosclerotic risk factors of hypertension, diabetes, smoking, dyslipidemia or a positive family history should be considered as an indication for performing cineangiocoronariography even in younger donors (\mathbf{C}) .

Cineangiocoronariography can also be indicated when heart dysfunction is verified in donors by echocardiography or with invasive hemodynamic monitoring. It should be noted that segmental left ventricular (LV) dysfunction is frequently seen in patients with brain injuries without the presence of coronary disease (C). (93)

Because cineangiocoronariography is not widely available in Brazil, the loss of donor organs could occur if all potential donors were required to have cineangiocoronariography. When

cineangiocoronariography is not available, men greater than 45 years of age and women over the age 50 should be considered as potential donors for acute high risk recipients (**D**). (91)

The use of "marginal" organs for transplant is acceptable, particularly for acute high risk recipients (\mathbf{C}). Even organs with mild to moderate coronary artery disease can be used for transplantation, and myocardial revascularization may be performed during or after transplantation (\mathbf{C}). (95)

Recommendations

- Indications for cineangiocoronariography include the following:

Potential male donors greater than 45 years of age and female donors greater than 50 years of age. (D). (89)

Young donors with a previous history of drug abuse (i.e. cocaine) or with atherosclerotic risk factors, such as systemic arterial hypertension, diabetes mellitus, smoking, dyslipidemia or family history (**D**).⁽⁸⁹⁾

Cineangiocoronariography should not be performed based on an increase in cardiac enzyme levels alone (C). Strong Recommendation.

- The unavailability of cineangiocoronariography does not rule out the organ viability. **Strong Recommendation**.

LIVER MAINTENANCE

Which blood chemistry variables should be monitored in liver donors? Is there any serology change which would preclude or complicate the donation of a liver?

Patients diagnosed with brain death frequently experience hydroelectrolytic disorders, particularly hypernatremia. Hypernatremia may be a predictor of primary liver graft failure. The exact mechanism for this is not known, but it is presumed to be related to hepatocyte edema and the subsequent exacerbation of the injury mediated by reperfusion. A serum sodium greater than 160 mEq/L should be corrected before explantation. However, there is no evidence that higher sodium levels contraindicate using the donor organ (C). (96-99)

Changes in potassium level should be corrected to maintain cardiovascular viability, but these changes do not impact the viability of the donor liver. No human studies have shown unfavorable outcomes for patients receiving livers from hyperkalemic donors (C).

An increase in transaminases and bilirubin may be indicative of liver ischemia from hypoperfusion, or the increase may be a sign of subclinical viral hepatitis. This does not preclude the use of the donor organ for transplantation, but the transplant team should monitor the patient postoperatively for complications or for viral hepatitis (\mathbf{C}) .

The measuring of transaminases, bilirubin, alkaline

phosphatase, gamma-glutamyl transferase, INR (International Normalized Ratio) and prothrombin time every 6 hours is recommended with no clear rationale (**D**). (28,101)

Hyperglycemia is not a contraindication for liver transplantation. However, hyperglycemia can affect perihepatocyte osmolarity. Hypoglycemia may also impact liver neoglucogenesis and may indicate liver damage (\mathbf{D}) . (102)

A liver from an HBsAg positive donor should not be used for transplantation (\mathbf{C}). Other serologies are not absolutely excluded for liver explant, but the donor organ should be rated as of borderline quality. Anti-HBsAg positive donors may have their livers safely used, as the infection is not transmitted to the recipient (\mathbf{C}). However, there is a disease transmission risk for anti-HBc IgG positive donors (\mathbf{C}). The possibility of a liver transplant in this setting is dependent on the recipient's anti-Hbs status. If the recipient is anti-Hbs positive, the liver can be used because the recipient's own surface antibodies will prevent the reactivation of hepatitis $\mathbf{B}(\mathbf{C})^{(16)}(\mathbf{A})$. If the recipient's status is negative, antiviral drugs and immunoglobulin should be used (\mathbf{C}).

Livers from hepatitis C donors can be safely used in HCV (+) recipients. A liver biopsy should always be performed because bridging fibrosis organs should not be used (C). (18)

Recommendations

- Measure serum sodium, potassium and blood glucose levels at least every 6 hours (**D**). (28,101) **Weak Recommendation.**
- Measure transaminases (AST/ALT), bilirubin and APT levels at least every 24 hours (**D**). (28,101) **Weak Recommendation.**
- Maintain serum sodium below 160 mEq/L (C). (96-99) **Strong Recommendation**.
- Liver donation from C and B viruses positive serology potential donors (except if HBsAg positive) is not contraindicated (\mathbf{C}). (10-12,18) **Strong Recommendation**.

RESUMO

A morte encefálica induz várias alterações fisiopatológicas que podem causar lesões em rins, pulmões, coração e figado. Portanto, a atuação do intensivista durante a manutenção do potencial doador falecido exige cuidados específicos com estes órgãos visando sua maior viabilidade para transplantes. O manejo hemodinâmico cuidadoso, os cuidados ventilatórios e de higiene brônquica minimizam a perda de rins e pulmões para o transplante. A avaliação da condição morfológica e funcional do coração auxilia na avaliação do potencial transplantável deste órgão. Por fim, a avaliação da função hepática, assim como o controle metabólico e a realização de sorologias virais são fundamentais para a orientação das equipes transplantadoras na seleção do órgão a ser doado e no cuidado com o receptor.

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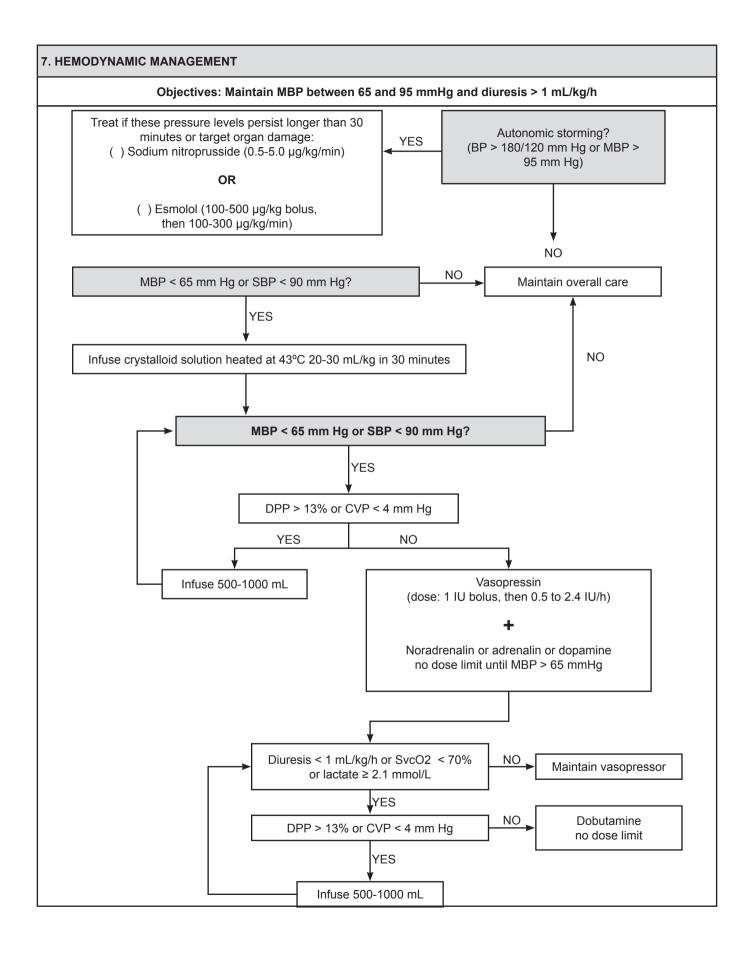
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PATIENT LABEL

Date	Time	ORGAN DONOR CHECK-LIST			
		1. Was the first brain death test performed	? ()YES()NO		
		2. Was the transplant center informed?	() YES () NO		
		3. RECORD ON PRESCRIPTION:			
	Maintain enteral/parenteral nutrition support - 15 to 30% of the energy calculated from baseline energy expenditure according to the Harris-Benedict equation () SIM () NÃO				
Raise he	ead of bed	1 to ≥ 30°	()SIM()NÃO		
Change	decubitus	s positioning every 2 hours	()SIM()NÃO		
The trac	heal tube	should be suctioned only in the presence of tr	acheal secretions () SIM () NÃO		
Keep the	e endotra	cheal tube balloon pressure between 20 and 3	0 cmH ₂ O () SIM () NÃO		
Arterial o	catheteriz	ation <u>(iMBP, DPP)</u>	()SIM()NÃO		
Central venous catheterization (CVP, SvcO ₂) () SIM (
Vesical o	catheteriz	ation (diuresis control)	()SIM()NÃO		
Insert central thermometer			()SIM()NÃO		
Blood glucose every 6 hs (maintain between 140 and 180 mg%;			call if > 180 mg%) () SIM () NÃO		
Methylprednisolone 15 mg/kg every 24 hours			()SIM()NÃO		
Levothyroxine 300 μg enteral every 24 hours () SIM () NÃ0					
4. SCHE	DULE SA	AMPLING FOR TESTS			
() Tests	s every 6	hours: Hemoglobin, platelets, PT, blood gas,	blood glucose, Na ⁺ , K ⁺ , Ca ⁺⁺ , Mg ⁺⁺ , PO ₄ ⁻		
()Tests every 24 hours: blood urea nitrogen, creatinine, CKMB + troponin (heart donor), AST + ALT + AF + Bilirubins (liver donor), Chest X-ray					
() Tests once: Blood culture 2 samples, urinalysis, urine culture, blood typing, serologies, amylase (pancreas donor)					
() If bleeding: PT, aTTP, fibrinogen and platelets					
5. CENTRAL TEMPERATURE CONTROL					
Infuse only fluids warmed to 43°C Do not use HME filters. Use a heated humidifier					
	PRE	() Temperature >35°C EVENTION OF HYPOTHERMIA	() Temperature < 35°C TREATMENT OF HYPOTHERMIA		
() Heat	room air		() All preventing measures		
() Infus	() Infuse only fluids warmed to 43°C		() Gastric and colonic irrigation with fluids at 43°C		
() Use thermal blankets		ankets	() Fluids at 43°C in a central vein (150-200 mL/h)		
() Use heated humidifier					
6. MECHANICAL VENTILATION					
	Ne	ormal lung () YES () NO	ALI or ADRS () YES () NO		
Volume or pressure controlled mode Tidal volume (TV) 5-8 mL/kg ideal bodyweight Tune FiO_2 to achieve blood gas $PaO_2 \ge 60$ mmHg and/or $SatO_2 \ge 90\%$ PEEP 8-10 cm H ₂ O		5-8 mL/kg ideal bodyweight eve blood gas PaO₂ ≥ 60 mmHg and/or SatO₂ O	Volume or pressure controlled mode TV 5-8 mL/kg ideal bodyweight Tune FiO_2 to achieve blood gas $PaO_2 \ge 60$ mmHg and/or $SatO_2 \ge 90\%$ Tune PEEP according to $SatO_2$ and hemodynamics P plateau < 30 cm H_2O		
P platea	u < 30 cm	n H ₂ O	Recruitment maneuvers/Prone position/Inhaled NO		



8. ASSESS FLUID BALANCE A	ND ENDOCRINE-METABOLIC	ASPECTS				
Maintain urinary output between 0.5 and 3 mL/kg/h Maintain serum Na ⁺ between 130 and 150 mEq/L Maintain normal serum magnesium, phosphorus, calcium and potassium levels Maintain pH > 7.2						
() If diuresis > 4 mL/kg/h	→	DDAVP 1-2 µg IV bolus every 4 hours				
() Se hypernatremia (>150 mEq	/l) 	Glucose 5% or Saline 0.45%				
() If hypernatremia and hypovole	emia 	Lactated Ringer's solution as volume expansion				
() If blood glucose > 180 mg/dL	→	Continued insulin infusion				
9. ASSESS BLOOD TRANSFUS	SION					
Hb <u>≤</u> 7 g/dL		() SIM () NÃO	() Transfuse red blood cells			
Hb < 10 g/dL and hemodynamic	instability	() SIM () NÃO				
Significant active bleeding associ (< 100,000/mm³)	iated with platelet count	()SIM()NÃO	()Transfuse platelets			
Platelet count < 50,000/mm³ with procedure	high bleeding risk and/or invas	()SIM()NÃO	() Hansiuse platelets			
High bleeding risk		()SIM()NÃO	Transfuse fresh plasma if INR > 1.5			
Before invasive procedure		() SIM () NÃO				
Significant active bleeding		()SIM()NÃO				
High bleeding risk		()SIM()NÃO	Transfuse cryoprecipitate if fibrinogen < 100 mg/dL even after fresh plasma transfusion			
Before invasive procedure		() SIM () NÃO				
Significant active bleeding		() SIM () NÃO				
10. ASSESS INFECTION						
() Repeat cultures if infection is	clinically suspected					
() Maintain or start deceased do	nor antibiotic therapy if clinicall	y indicated				
() Inform the receptor on the cul	ture results and schedule main	tenance of antibiotic t	therapy for the receptor			
() In all lung donors perform bronchoscopy by the time of the organ removal, collecting samples for bacterioscopy and culture						
11. HEART ARRHYTHMIAS MA	NAGEMENT					
() Tachyarrhythmias - treat as gu	uided by AHA guidelines					
() Bradyarrhyhmias	Adrenalin (2-10 μg/min) or dopamine (5-10 μg/kg/min)					
(Atropine is ineffective)	If low cardiac output or hypotension - provisional transcutaneous pacemaker followed by intravenous pacemaker					
	Treat as guided by AHA guidelines					
	Initially start CPR maneuvers and transport to the surgery room for removing viable organs					
() Cardiorespiratory arrest	Consider installing a double-balloon catheter for renal preservation, or starting extracorporeal circulation via femoral access, if transference to the surgery room is not feasible or the removal team is unavailable					
	Give 500 IU/kg sodium heparin during initial CPR maneuvers, whenever immediate organ removal and/or perfusion is considered					
Nurse Signature:						
Physician	Signature:					

Maintenance guidelines for potential multiple organ deceased donors

Coordinator: Glauco Adrieno Westphal

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