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EDITORIAL

Volemia and kidney transplantation

Volemia e transplante renal

Kidney transplantation is considered the treatment of choice for terminal chronic kidney disease, presenting longer survival than dyalisis.[1] Brazil ranks second in the world in terms of absolute number of kidney transplantations, only behind the United States, but ranks thirty in number of transplantations per million inhabitants. In 2019, there were over six thousand kidney transplants in the country, most from cadaver donors. Despite the expressive number of procedures, demand in Brazil is growing, and in December 2019, over 25 thousand patients were on the waiting list.

In past decades, progress of immunosuppressive therapies and of clinical and surgical care has resulted in longer graft survival, albeit the incidence of graft dysfunction having remained stable, attributed to employment of marginal organs.

Optimized hemodynamic management in the intraoperative period of kidney transplant is associated with improved survival of the transplanted organ.

The volemia of end stage chronic kidney disease patients oscillates between extreme values, with a narrow therapeutic range for fluid replacement. While hypovolemia worsens renal graft perfusion, hypervolemia can lead to complications related to volume overload. Adequate volume replacement decreases perioperative complications, although, there is no consensus on the ideal hemodynamic strategy.[2]

The strategy traditionally adopted for fluid management consists of liberal infusion of crystalloids guided by measurements of Central Venous Pressure (CVP) and Mean Arterial Pressure (MAP). High volume fluid is administered aiming to preserve renal blood flow, because kidney denervation compromises self-regulation mechanisms, and MAP values above 80 mmHg are associated with lower incidence of acute tubular necrosis and early graft dysfunction.[3]

At the end of the 1980's, Shoemaker et al. introduced the concept of hemodynamic goal-oriented cardiovascular supra optimization, which initially was associated with longer survival of high-risk patients.[4] The concept was improved and assessed by clinical trials throughout decades, leading to the concept of Hemodynamic Goal-Directed fluid Therapy (HGDT/GDFT).[5]

HGDT in clinical practice involves adoption of a protocol based on the interpretation of several hemodynamic parameters and administration of fluid and vasoactive drugs, in different associations. HGDT protocols vary as to the type of fluid administered (crystalloids and/or colloids), classes of vasoactive drugs used (vasopressors and/or ionotropes), and the hemodynamic parameters used, acquired by different cardiovascular monitors such as esophageal Doppler, transthoracic bioimpedance and cardiac output monitors, regardless of calibration.[5]

Volemia cannot be adequately predicted by static cardiac pre-load indexes, such as Pulmonary Artery Occlusion Pressure (PAOP), CVP and global end diastolic volume acquired by transpulmonary thermodilution. Pre-load dynamic measurements, such as Pulse-Pressure Variation (PPV) and Sroke-Volume Variation (SVV), can predict fluid responsiveness by analysis of heart-lung interaction triggered by positive pressure ventilation analogously to bedside Frank-Starling curve tests.[6,7]

PPV is the dynamic index more commonly used, showing excellent sensitivity and specificity when under 9% and above 12%.[7] Intermediate values, however, are less accurate in predicting volemia. It should be underscored that the limitations of its use should be respected, given its predictive value depends on correct interpretation. Therefore, PPV measurements should not be adopted in the following scenarios: spontaneous breathing, heart arrythmias, low pulmonary compliance, tidal volume below 8 mL/Kg, intra-abdominal hypertension, and right ventricle failure.[8]

Anesthetic management of major surgery targets reduction of risks and optimization of outcomes. Therefore, HGDT

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aims to reduce perioperative morbidity and mortality.[7] However, HGDT protocols are heterogeneous and the clinical benefit of the strategy remains controversial. While some meta-analyses show that HGDT improves renal perfusion and reduces morbidity and mortality in major surgery,[9,10] others suggest it only has a marginal benefit.[11]

In the present number 70(3) of BJAN, De Cassai A et al assessed, through a prospective randomized trial, performance of HGDT in the cadaver donor kidney transplant perioperative period. PPV guided fluid management strategy was compared to conventional fluid strategy ($10\,mL.Kg^{-1}.h^{-1}$), and similar results were observed regarding urinary output at end of surgery.[12]

HGDT in the kidney transplantation scenario was assessed mainly by observational studies, as for example, Toyoda et al.,[13] and Chin J-H et al.,[14] who showed that SVV is able to predict blood volume during kidney transplants. Prospective clinical trials that have analyzed SVV as part of HGDT protocols showed similar results to conventional therapy.[15] Most studies have approached the efficacy of HGDT in live donor transplants, given cold ischemia time and kidney graft quality can interfere in patient hemodynamic response, acting as a confounding variable for outcome assessment.

Patients submitted to kidney transplant present pathophysiological changes due to chronic kidney disease that can interfere in hemodynamic measurements on which HGDT is based. The presence of arterial-venous fistula leads to enlargement of the left ventricle mass, and increase in pulmonary blood flow and cardiac output, which can affect estimate of stroke volume.[16] Moreover, early stiffening and remodeling of the arterial system in chronic renal patients can influence estimated measurement of SV and affect PPV measurement, as they change the pulse wave propagation rate.[17]

Graft dysfunction, whose concept is variable, may not be the best outcome for assessing HGDT effectiveness, given factors associated with donor, receptor, and organ preservation interfere in the graft dysfunction incidence.[18] Perioperative hemodynamic optimization reduces the incidence of renal hypoperfusion, which is only one of the causes of non-functioning kidney transplant. Perioperative oliguria is a physiological response to surgical stress, and is not a predictor of fluid responsiveness or of kidney function, as demonstrated by Eriksen et al in a porcine model of kidney transplant; therefore, urinary output cannot be an adequate outcome for assessing HGDT effectiveness.[19]

HGDT is a customized optimization strategy whose impact on reduction of surgical mortality is still controversial. Using the strategy during kidney transplant faces challenges related to the cardiovascular adaptations inherent to chronic renal disease that can affect the accuracy of hemodynamic measurements that guide fluid resuscitation of chronic renal patients.

The role of HGDT in kidney transplantation has not yet been well established, and well-designed clinical studies are required to determine its influence on graft dysfunction and on the incidence of postoperative complications. The expressive figures of kidney transplants in Brazil can allow for the development of a research network to make multicenter studies feasible, and with enough power to generate robust conclusions on the subject.

Conflicts of interest

The authors declare no conflicts of interest.

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