Rev Bras Anestesiol. 2020;xxx(xx):xxx–xxx

Sociedade Brasileira de Anestesiologia

Brazilian Journal of ANESTHESIOLOGY

Revista Brasileira de Anestesiologia

SCIENTIFIC ARTICLE

Pulse pressure variation guided fluid therapy during kidney transplantation: a randomized controlled trial☆

Alessandro De Cassai [a,*], Ottavia Bond [a], Silvia Marini [a], Giulio Panciera [a], Lucrezia Furian [b], Flavia Neri [b], Giulio Andreatta [a], Paolo Rigotti [b], Paolo Feltracco [a]

[a] *University of Padova, Department of Medicine – DIMED, Section of Anesthesiology and Intensive Care, Padova, Italy*
[b] *Padua University Hospital, Department of Surgery, Oncology and Gastroenterology, Kidney and Pancreas Transplant Unit, Padua, Italy*

Received 12 November 2019; accepted 15 February 2020

KEYWORDS
Kidney transplantation;
Fluid therapy;
Creatinine;
Urea;
Urine

Abstract

Purpose: Kidney transplantation is the gold-standard treatment for end stage renal disease. Although different hemodynamic variables, like central venous pressure and mean arterial pressure, have been used to guide volume replacement during surgery, the best strategy still ought to be determined. Respiratory arterial Pulse Pressure Variation (PPV) is recognized to be a good predictor of fluid responsiveness for perioperative hemodynamic optimization in operating room settings. The aim of this study was to investigate whether a PPV guided fluid management strategy is better than a liberal fluid strategy during kidney transplantation surgeries. Identification of differences in urine output in the first postoperative hour was the main objective of this study.

Methods: We conducted a prospective, single blind, randomized controlled trial. We enrolled 40 patients who underwent kidney transplantation from deceased donors. Patients randomized in the ''PPV'' group received fluids whenever PPV was higher than 12%, patients in the ''free fluid'' group received fluids following our institutional standard care protocol for kidney transplantations ($10\,mL.kg^{-1}.h^{-1}$).

Results: Urinary output was similar at every time-point between the two groups, urea was statistically different from the third postoperative day with a peak at the fourth postoperative day and creatinine showed a similar trend, being statistically different from the second postoperative day. Urea, creatinine and urine output were not different at the hospital discharge.

Conclusion: PPV guided fluid therapy during kidney transplantation significantly improves urea and creatinine levels in the first week after kidney transplantation surgery.

☆ Congresses: Partial results have have already been presented at Euroanesthesia 2019 (1–3 June 2019).

* Corresponding author.
E-mail: alessandro.decassai@gmail.com (A. De Cassai).

https://doi.org/10.1016/j.bjane.2020.04.022

Please cite this article in press as: De Cassai A, et al. Pulse pressure variation guided fluid therapy during kidney transplantation: a randomized controlled trial. Rev Bras Anestesiol. 2020. https://doi.org/10.1016/j.bjane.2020.04.022

PALAVRAS-CHAVE
Transplante renal;
Fluido terapia;
Creatinina;
Ureia;
Urina

Reposição de volume orientada pela variação da pressão de pulso durante transplante renal: estudo randomizado controlado

Resumo

Objetivo: Transplante renal é o tratamento padrão-ouro na doença renal em estágio terminal. Embora diferentes variáveis hemodinâmicas, tais como pressão venosa central e pressão arterial média, tem sido usadas para orientar a estratégia de reposição volêmica durante a cirurgia, a melhor estratégia ainda não foi determinada. A Variação da Pressão de Pulso (VPP) durante o ciclo respiratório é reconhecida como um bom preditor da resposta à infusão de volume para otimização hemodinâmica perioperatória no centro cirúrgico. O objetivo do estudo foi estudar se a estratégia de reposição de volume orientada por VPP é melhor do que a estratégia liberal de reposição de volume durante cirurgia de transplante renal.O principal objetivo do estudo foi identificar diferença no débito urinário na primeira hora do pós-operatório.

Método: Realizamos estudo prospectivo, uni-cego, randomizado, controlado. Incluímos 40 pacientes submetidos a transplante renal de doador cadáver. Pacientes randomizados para o grupo ''VPP'' receberam volume quando a VPP estava acima de 12%, e os pacientes no grupo ''reposição liberal'' receberam volume de acordo com o nosso protocolo institucional padrão de assistência para transplante renal ($10\,mL.kg^{-1}.h^{-1}$).

Resultados: O débito urinário foi semelhante em todos os tempos nos dois grupos, a ureia foi estatisticamente diferente a partir do terceiro dia do pós-operatório com pico no quarto dia do pós-operatório e a creatinina apresentou tendência semelhante, tornando-se estatisticamente diferente a partir do segundo dia do pós-operatório. Ureia, creatinina e débito urinário não estavam diferentes na alta hospitalar.

Conclusões: A terapia orientada por VPP durante transplante renal melhorou de forma significante os níveis de ureia e creatinina na primeira semana pós-transplante renal.

Background and objective

Kidney transplantation (KT) is the gold-standard treatment to End Stage Renal Disease (ESRD). Patients with ESRD receiving KT have a higher survival rate[1] and a lesser healthcare expenditure than patients undergoing dialysis.[2,3]

Recent studies pointed out that an optimized fluid therapy during transplant surgeries is associated with better graft function, possibly by maintaining optimal blood volumes and providing adequate oxygen delivery to tissues:[4–6] inadequate volume infusions during KT could result in acute respiratory failure and prolonged mechanical ventilation,[1] whereas fluid overload is considered to be detrimental for graft perfusion, microcirculation and tissue oxygen delivery.[4] Fluid management during KT is, therefore, a challenge for the anesthesiologist with little to no evidence supporting the proper practice.

In the past few years, different hemodynamic variables like Central Venous Pressure (CVP) or Mean Arterial Pressure (MAP) were proposed as targets for adequate perioperative fluid infusion; however, a recent study demonstrated their poor performance in predicting graft function.[7]

Respiratory arterial Pulse Pressure Variation (PPV) is considered to be a good predictor of fluid responsiveness for hemodynamic optimization in the perioperative setting.[8–11] No study has yet examined a PPV guided hemodynamic optimization during KT.

We hypothesized that a PPV-based fluid management during KT may be as effective as a liberal fluid strategy during KT, ensuring adequate postoperative urine output and being able, at the same time, to avoid fluid overload.

Differences in Urine Output (UO) in the first postoperative hour was the main outcome of this study.

Secondary outcomes were differences in UO, urea and creatinine levels in the first postoperative week, differences in the need of haemodialysis and differences in cardiopulmonary complications rate among the two groups.

Methods

Design

We conducted a prospective, single blind; non inferiority randomized controlled trial with a parallel design and a 1:1 allocation ratio. The study protocol was approved by the Institutional Review Board of Padova (4423/AO/18) and registered on Clinicaltrials.gov (NCT03446196). The study was in accordance with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Every patient enrolled in the trial provided written informed consent to participate.

Subjects and setting

Informed consent to participate to the trial was requested to all individual patients who met inclusion/exclusion criteria.

Please cite this article in press as: De Cassai A, et al. Pulse pressure variation guided fluid therapy during kidney transplantation: a randomized controlled trial. Rev Bras Anestesiol. 2020. https://doi.org/10.1016/j.bjane.2020.04.022

We included every patient with age $\geq$ 18 undergoing kidney transplantation from cadaver. Exclusion criteria were double kidney transplantation, combined kidney-pancreas transplantation, combined liver-kidney transplantation and/or history of heart disease and/or cardiac arrhythmias.

Randomization

Twenty ''Free fluid'' and 20 ''PPV'' cardstocks were prepared by a member of the research team not involved in the clinical setting (GP). He then inserted each cardstock in a different envelope and sealed the envelopes, proceeding to shuffle the sealed envelopes.

At the day of the surgery, after obtaining written informed consent, the patients were randomly assigned by a member of the study (SM) to one of the two groups by opening a randomly chosen envelope.

Anesthesia

All patients underwent standardized general anesthesia, according to the usual practice/protocol at our institution. Anesthesia was induced with propofol 2 $mg.kg^{-1}$ and fentanyl 2 $\mu g.kg^{-1}$. Rocuronium 0.6 $mg.kg^{-1}$ was administered to facilitate tracheal intubation. After tracheal intubation, patients were ventilated with a 40/60 oxygen/air mixture using a pressure-regulated volume-control mode (FLOW-i Ventilator, MAQUET Medical System, Italy). Expiratory tidal volume was maintained at 8 $mL.kg^{-1}$ and PEEP at 5 cmH_2O, adjusting the respiratory rate to keep partial arterial carbon dioxide pressure ($PaCO_2$) at 35-40 mm Hg. Anesthesia was maintained with desflurane at 0.9 Minimum Alveolar Concentration (MAC) to maintain a bispectral index value between 40 and 60, and analgesia was provided through remifentanil continuous infusion in order to achieve a heart rate within $\pm$20% range from the preoperative value. Ultrasound guided central venous catheter was placed in the internal jugular vein and a 20 G catheter was positioned in the radial artery to continuously MAP via a pressure transducer (Edwards Lifesciences, Irvine, CA, USA) and connected to an Endless version MostCareUP (Vytech, Padova, Italy). MostCareUP was used to acquire all hemodynamic variables (specifically PPV). According to our standard care protocol, all patients undergoing KT at our institution should receive only normal saline as crystalloid during KT. Always according to our standard care protocol for KT, by the time of vascular declamping of the graft, an intravenous bolus of 100 mg of furosemide and 80 mL of mannitol 18% should be administered to all recipients. At the end of the surgery, sugammadex 2–4 $mg.kg^{-1}$ total body weight was administered to ensure full reversal (train-of-four ratio = 1.0), depending on the depth of neuromuscular blockade.

Intervention protocol

All transplantations have been executed by the same surgical team. Patients randomized in the ''PPV'' group received normal saline whenever PPV was higher than 12%: the volume of fluid given was not predetermined and clinicians were invited to administer fluids until PPV was equal or less than 12%; patients in the ''free fluid'' group received normal saline according to our institutional standard care protocol (10 $mL.kg^{-1}.h^{-1}$ plus and following a fluid replacement for bleeding with saline at 1:1 ratio).

Dynamic variables based on interaction between pulmonary and cardiac cycle, such as PPV, are considered better predictors of fluid responsiveness in patients during general anesthesia and mechanical ventilation[10] when compared to CVP or other static parameters.PPV values higher than 9% and lower than 13% are less reliable than more extreme values in predicting response to crystalloid infusion: in order to avoid this ''gray area'', we chose PPV of $\geq$ 12% as a trigger to increase saline infusion.

Although all patients were connected to the MostCareUP monitor, attending anesthesiologists were blinded to MostCareUP data in the ''free fluid'' group: this was obtained by covering the MostCareUP screen with an opaque blanket.

Postoperative period

All physicians involved in the postoperative care were blinded to treatment group. Postoperative treatment was the same for both groups following the standardized protocols of our transplantation center. Each patient was admitted to the semi-intensive care division of the Transplant Unit and managed with a standardized fluid-therapy protocol, receiving as much fluids as needed in order to equalize UO. Patients received 60 mg of endovenous furosemide every eight hours if UO was less than 0.5 $mL.kg^{-1}.h^{-1}$. Patients underwent dialysis ifUO was less than 0.5 $mL.kg^{-1}.h^{-1}$ with either clinical signs of fluid overload, kalemia greater than 6.5 $mEq.L^{-1}$ or blood urea nitrogen greater than 40 $mmoL.L^{-1}$.

Variables

For each patient we collected the following data: age, sex (F/M), weight (kg), height (cm), Body Mass Index (BMI) ($kg.m^{-2}$), Body Surface Area (m^2), ASA-PS class, dialysis and/or residual diuresis (mL/die); furthermore, we collected parameters related to the transplanted kidney: ischemia time (min), Karpinsky[12] score (0–12) and intraoperative fluids (mL) administered.

MostCareUP records beat to beat values: to facilitate the analysis, we considered four time-points: a) Baseline after tracheal intubation (T0), b) Before arterial anastomosis (T1), c) 15 minutes after arterial anastomosis (T2) and d) After tracheal extubation (T3). At every time-point, a corresponding value of the following variables from the MostCareUP monitor was obtained by averaging a five minutes period: Blood Pressure (BP), Heart Rate (HR), MAP, SpO_2, Cardiac Index (CI), Stroke Volume Index (SVI), arterial Elastance (Ea), Cardiac Cycle Efficiency (CCE), PPV, Stroke Volume Variation (SVV).

We recorded Urine Output (UO) from ureteral anastomosis until the operating room discharge (normally, 30 minutes after extubation) and CVP at operating room discharge.

Please cite this article in press as: De Cassai A, et al. Pulse pressure variation guided fluid therapy during kidney transplantation: a randomized controlled trial. Rev Bras Anestesiol. 2020. https://doi.org/10.1016/j.bjane.2020.04.022

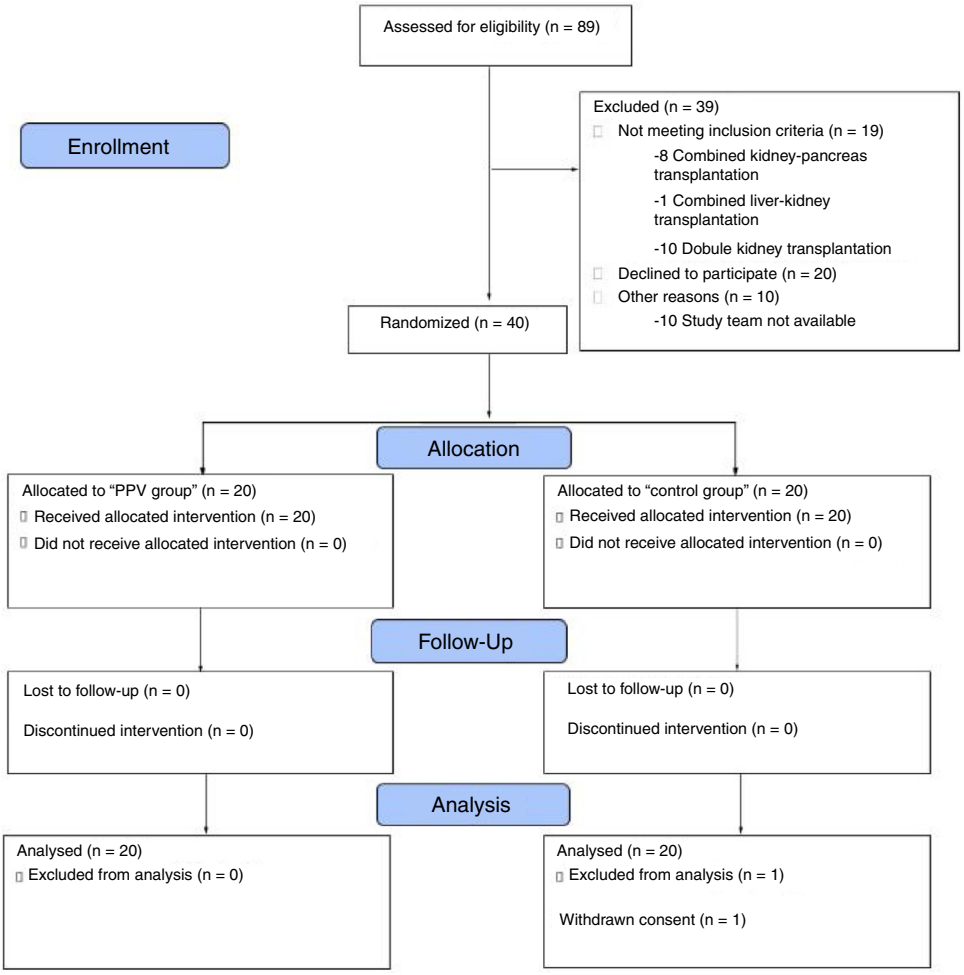

Fig. 1 CONSORT flow-chart.

Blinding

Patients, surgeons, ward clinicians and the statisticians were blinded to group allocation.

Statistical analysis

To determine the required sample size, we considered the UO in the first postoperative hour to be 852 ± 170 mL.[13] We considered a 20% difference of UO in the first hour after transplantation in the intervention group to be statistically significant. The required sample size to detect the aforementioned UO difference with a power of 85%, a significance level of 0.05 and considering a 1:1 allocation ratio was of 36 patients. We expected to lose 10% of the patients during the follow-up, and for this reason we chose to include 40 patients in the study. Normal distribution of quantitative variables was analyzed using the Shapiro-Wilk test. Variables were compared using the two-tailed Student' *t*-test when variables were normally distributed, and the Mann-Whitney *U* test when they were non-normally distributed. Continuous variables are presented as mean ± Standard Deviation (SD) and 95% Confidence Interval (CI). Median, first and third quartile values are reported for non-normally distributed variables. Variables presented as percentage were compared between groups using the Chi-Square test or the Fisher exact test, when appropriate.

All statistical analyses were conducted using R version 3.4.0 (2017-04-21); p-values < 0.05 were considered statistically significant, Prism (GraphPad Software, San Diego, CA, USA) was used to create the artworks. We followed the CONSORT guidelines[14] to report this trial.

Results

A total of 89 patients underwent KT from deceased donor at our institution from March 10, 2018 to January 1, 2019; nineteen of them were excluded because they did not meet the inclusion criteria (Fig. 1), leaving 70 patients available. Of them, 20 were excluded because they refused to participate, and 10 patients were not enrolled because the research team was not available on the day of the procedure. Forty patients were enrolled in the study, 1 of them withdrew consent after the randomization process resulting in 39 patients (20 patients in PPV group and 19 patients in ''free fluid'' group) included in the current analysis.

All donors and recipients were white; there weren't non-heart-beating donors. All KT were single-kidney trans-

Please cite this article in press as: De Cassai A, et al. Pulse pressure variation guided fluid therapy during kidney transplantation: a randomized controlled trial. Rev Bras Anestesiol. 2020. https://doi.org/10.1016/j.bjane.2020.04.022

Table 1 Demographic data.

	PPV (n = 19)	FF (n = 20)	*p*
Age	55.42 (SD = 12.72)	50.55 (SD = 10.79)	0.205
Sex	5F / 14M	4F / 16M	0.716
Weight(kg)	72.26 (SD = 9.64)	74.80 (SD = 13.82)	0.512
Height (cm)	170.26 (SD = 6.37)	169.40 (SD = 10.50)	0.759
BMI (kg. m^{-2})	25.34 (SD = 3.13)	25.86 (SD = 2.80)	0.584
BSA (m^2)	1.84 (SD = 0.15)	1.87 (SD = 0.22)	0.580
ASA-PS	3 (IQR = 0)	3 (IQR = 0)	0.992
Residual dieresis (mL.d^{-1})	350 (IQR = 1100)	250 (IQR = 850)	0.465
Preoperative dialysis	95.0%	94.8%	0.992
Etiology			
Diabetes	36.8%	30.0%	0.654
Glomerulonefritis	15.7%	10.0%	0.534
Other	47.5%	60.0%	0.610

PPV, Pulse Pressure Variation group; FF, Free Fluid group; BMI, Body Mass Index; BSA, Body Surface Area; ASA-PS, The American Society of Anesthesiologists Physical Status; SD, Standard Deviation; IQR, Inter-Quartile Range; *p*-value < 0,05 are marked with an asterisk (*).

plantation. Demographic variables were homogeneous between the two groups (Table 1).

KT preoperative and intraoperative data are shown in Table 2. Patients in the PPV group received less intraoperative fluids (p = 0.010). Intraoperative hemodynamic variables are summarized in Table 3. Statistical differences between groups were found in SVI at T1 (p = 0.012), in PPV at T2 (p = 0.033) and in MAP at T3 (p = 0.038).

Fig. 2 shows the trend of blood urea and creatinine during the first postoperative week and at hospital discharge.

UO and consequently the amount of fluids administered were similar inthe first (''PPV group'': 2520 mL [IQR = 2632 mL] versus ''free fluids'' group: 1950 mL [IQR = 2463 mL], p = 0.890) and the subsequent postoperative days in the first week between the two groups. Urea was statistically different from the third Postoperative Day (POD) with a peak at fourth POD. Creatinine showed a similar trend, being statistically different from the second POD. Urea, creatinine and UO were not different at hospital discharge.

Three patients in ''PPV group'' (15.8%) and five patients in ''free fluids'' group (25%) required postoperative dialysis (p = 0.694). Five patients in ''free fluid group'' (25%) and two patients in ''PPV group'' (10.5%) had clinical and radiographic signs of fluid overload and needed oxygen therapy (p = 0.410). No patient had signs of myocardial ischemia in the perioperative period. There was no difference in cumulative furosemide dose between the two groups (p = 0.456). No patient needed vasoactive drugs in the postoperative period.

Length of stay was not different among the groups (PPV group: 12 days; IQR = 3.5; free fluid group 12.5 days, IQR = 6.25; p = 0.207).

Discussion

The study was designed to show a 20% difference in UO during the first post-transplant hour: as we found none, the hypothesis was rejected.

For this reason, the main finding of our study is that a PPV strategy is as adequate as a free fluid strategy in maintaining UO in patients undergoing KT.

Although median UO in the PPV group was almost twice when compared to the ''free fluids'' group, this difference did not reach statistical significance. The main explanation for this finding may be linked to the relatively small sample size itself. The study used[13] to determine sample size investigated KT from living donors, while our study investigated KT from deceased donors. Longer ischemia time, donor and kidney status may have played a role by increasing variability in the early UO. For this reason, more studies with a larger population will be needed to further investigate whether a PPV fluid strategy may be more effective than a free fluid strategy to maintain UO in patients undergoing KT.

Interestingly, another study that used a Goal Directed Therapy (GDT) for fluids did not find any difference in the early UO.[15]

In our study, patients in ''PPV group'' required less fluid during the surgery. Although there were no differences in respiratory and cardiac complications, it is known that KT patients are at a higher risk for fluid overload in the postoperative period.[4]

Furthermore, the ''PPV group'' had lower urea and creatinine levels in the first week after transplantation, which again could be possibly justified by fluid overload, which is known to be related to worse graft perfusion, microcirculation and tissue oxygen delivery.[4]

There were little statistical differences between intraoperative hemodynamic parameters among the groups: indeed, only SVI after induction of general anesthesia, PPV after arterial anastomosis and MAP at extubation reached a statistically significant difference.

While a higher SVI and a lower PPV in the ''PPV group'' could be the result of a tailored fluid GDT, MAP difference after extubation may be the result of fluid overadministration with ''free fluid'' patients lying in the upper part of the Frank-Starling curve.

Observed differences in MAP (82.30 vs. 92.80 mmHg) may have played little or no role on the graft function, as Tóth[16] suggested. In his study, Tóth[16] observed stable creatinine

Please cite this article in press as: De Cassai A, et al. Pulse pressure variation guided fluid therapy during kidney transplantation: a randomized controlled trial. Rev Bras Anestesiol. 2020. https://doi.org/10.1016/j.bjane.2020.04.022

Table 2 Preoperative and intraoperative data.

	PPV (n = 19)	FF (n = 20)	*p*
Karpinskyscore	0 (IQR = 3)	0 (IQR = 2.25)	0.561
Ischemia Time (min)	815.42 (SD = 245.19)	782.65 (SD = 233.75)	0.671
Duration (min)	200 (IQR = 65)	245 (IQR = 75)	0.067
Fluids (mL)	1921 (SD = 522.63)	2517 (SD = 819.38)	0.010*
Diuresis (1st hour)	60 (IQR = 180)	37.5 (IQR = 166.25)	0.895
Length of Stay (d)	12 (IQR = 3.5)	12.5 (IQR = 6.25)	0.207

PPV, Pulse Pressure Variation group; FF, Free Fluid group; SD, Standard Deviation; IQR, Inter-Quartile Range; d, day; min, minutes; *p*-value < 0,05 are marked with an asterisk (*).

Table 3 Intraoperative hemodynamic variables.

		T0	T1	T2	T3
HR (bpm)	FF	70.96 ± 13.98	74.37 ± 14.85	74.07 ± 16.28	83.17 ± 19.77
	PPV	69.02 ± 16.26	66.67 ± 13.59	70.19 ± 13.34	76.22 ± 14.58
MAP (mmHg)	FF	75.32 ± 11.45	81.39 ± 11.35	77.36 ± 10.03	92.80 ± 13.48*
	PPV	78.70 ± 9.52	86.76 ± 12.40	78.32 ± 10.87	82.30 ± 16.14*
CI (L. min^{-1}. m^{-2})	FF	2.25 ± 0.39	2.28 ± 0.50	2.40 ± 0.56	2.78 ± 0.57
	PPV	2.40 ± 0.36	2.59 ± 0.41	2.41 ± 0.46	2.47 ± 0.67
SVI (mL. m^{-2})	FF	33.93 ± 10.22	32.30 ± 10.48*	34.25 ± 10.15	35.91 ± 11.86
	PPV	37.93 ± 11.23	40.34 ± 9.56*	35.96 ± 10.44	34.85 ± 13.04
SVV (%)	FF	12.24 ± 4.64	9.08 ± 3.98	10.48 ± 4.50	14.03 ± 7.23
	PPV	12.87 ± 5.78	9.11 ± 4.44	11.13 ± 5.01	13.50 ± 4.96
PPV (%)	FF	11.66 ± 6.96	7.33 ± 4.71	8.14 ± 5.38*	13.91 ± 7.93
	PPV	13.17 ± 7.99	5.54 ± 4.01	5.10 ± 2.58*	10.66 ± 7.19
Ea (mmHg)	FF	1.30 ± 0.37	1.51 ± 0.54	1.30 ± 0.46	1.55 ± 0.47
	PPV	1.24 ± 0.42	1.32 ± 0.41	1.34 ± 0.30	1.48 ± 0.51
PPV/SVV (units)	FF	1.07 ± 0.73	0.87 ± 0.50	0.88 ± 0.59	1.11 ± 0.46
	PPV	1.21 ± 0.92	0.66 ± 0.37	0.57 ± 0.35	0.85 ± 0.49
CCE	FF	-0.09 ± 0.30	0.09 ± 0.24	0.07 ± 0.31	-0.07 ± 0.29
	PPV	-0.11 ± 0.31	-0.01 ± 0.31	-0.03 ± 0.40	-0.04 ± 0.36

PPV, Pulse Pressure Variation group; FF, Free Fluid group; *p*-value < 0.05 are marked with an asterisk (*).

levels in patients with a MAP between 80 and 100 mmHg, but an increase in creatinine in patients with MAP < 80 mmHg.

The most effective perioperative fluid strategy in kidney transplantation is actually unknown.[6] Standard parameters used in the intraoperative setting, such as BP, HR and CVP, resulted to be inadequate in predicting graft function after KT.[7]

Historically, a CVP-based strategy has been used to drive volume expansion during kidney transplantation; however, CVP is poorly related to actual blood volume and has little ability to predict the hemodynamic response to a fluid challenge.[17]

Although an aggressive volume expansion strategy targeting a CVP between 10 mmHg and 15 mmHg[1] has been suggested in order to improve renal blood flow and better graft outcomes, this strategy has several downsides. An elevated CVP leads to a worse graft function,[18,19] and excessive fluid administration could lead to pulmonary edema, myocardial ischemia and even increase mortality.

Two previous studies investigated a goal-directed fluid therapy during KT:[15,20] both Cavaleri et al.[15] and Corbella et al.[20] applied a Stroke Volume (SV) optimization protocol with different objectives. Cavaleri[15] aimed to show a reduction in early complications after KT using a FloTrac™/EV1000 monitor, while Corbella[19] aimed to evaluate if the use of esophageal doppler monitoring would alter the amount of fluids given during KT.

Although aims and methods of these studies were different from ours, similarities in results appear self-evident: a lesser intraoperative fluid volume administration[20] and a better seven day mean serum creatinine levels compared to the control group.[15]

Our study has several limitations we need to discuss. One of the greatest is the monocentric nature of the study itself. Secondly, we evaluated KT only from deceased donors where enrolling living donors may have reduced biases related to organ ischemia. Furthermore, we considered hemodynamic parameters only during the intraoperative timeframe. However, we recognize that many factors in the postoperative period (especially hemodynamics) may have played a role in early graft function. Moreover, only cardiovascular complications were evaluated: it could have been more appropriate to also evaluate neurological, abdominal and infectious complications.

Further studies are needed to identify the best fluid management strategy during KT, especially randomized controlled trial comparing different GDT strategies.

Please cite this article in press as: De Cassai A, et al. Pulse pressure variation guided fluid therapy during kidney transplantation: a randomized controlled trial. Rev Bras Anestesiol. 2020. https://doi.org/10.1016/j.bjane.2020.04.022

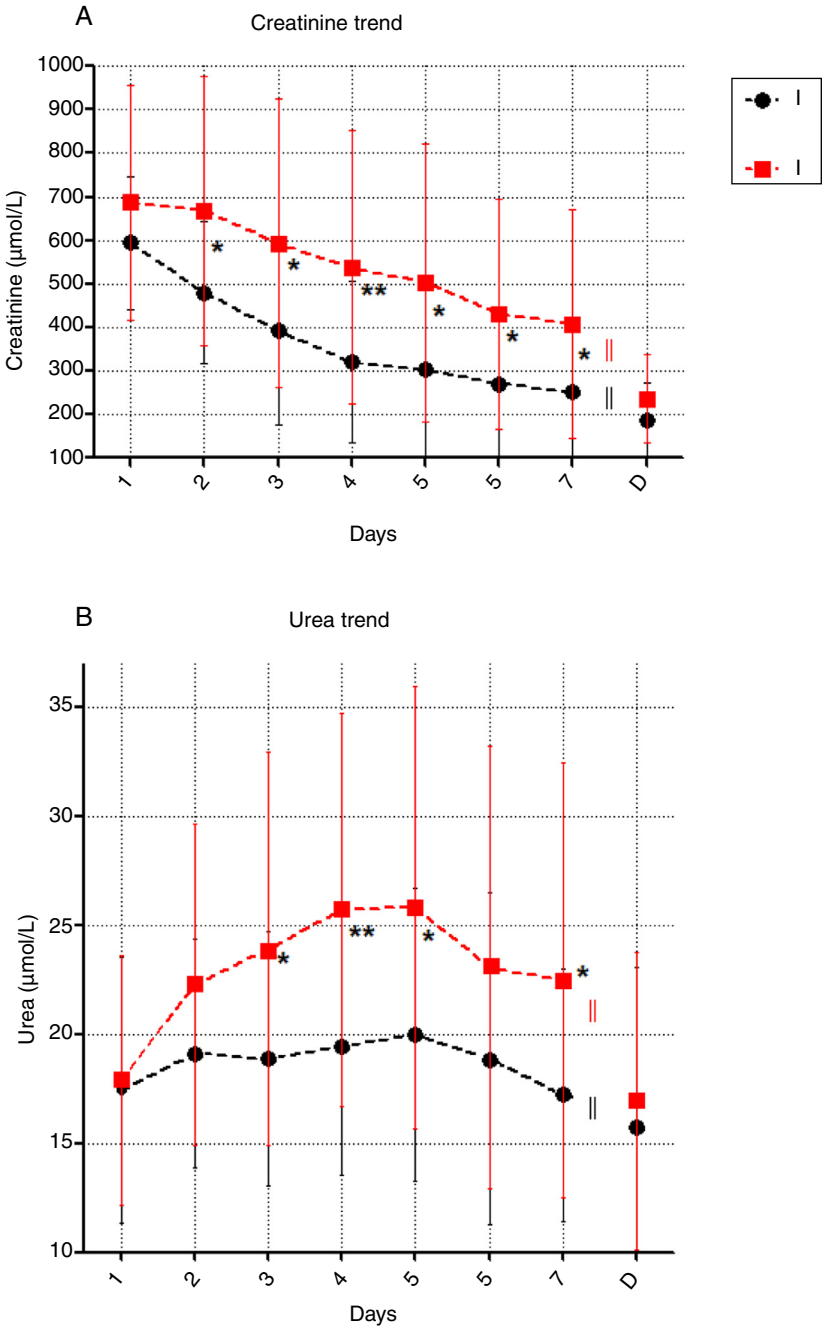

Fig. 2 Panel A: Means and confidence intervals of creatinine in the first postoperative week. Panel B: Means and confidence intervals of urea in the first postoperative week. D: Hospital discharge. *p-value < 0.05, **p-value < 0.01.

Summary

A PPV based strategy is as adequate as a liberal fluid management during KT and may prevent fluid overload.

Conflicts of interest

The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

References

1. Lemmens HJ. Kidney transplantation: recent developments and recommendations for anesthetic management. Anesthesiol Clin North America. 2004;22:651–2.
2. Joyce AT, Iacoviello JM, Nag S, et al. End-stage renal disease-associated managed care costs among patients with and without diabetes. Diabetes. 2004;27:2829–35.
3. Kontodimopoulos N, Niakas D. Overcoming inherent problems of preference-based techniques for measuring health benefits: an empirical study in the contest of kidney transplantation. BMC Health Services Research. 2006;6:3.

Please cite this article in press as: De Cassai A, et al. Pulse pressure variation guided fluid therapy during kidney transplantation: a randomized controlled trial. Rev Bras Anestesiol. 2020. https://doi.org/10.1016/j.bjane.2020.04.022

4. De Gasperi A, Narcisi S, Mazza E, et al. Perioperative fluid management in kidney transplantation: is volume overload still mandatory for graft function? Transplant Proc. 2006;38:807–9.
5. Aulakh N, Garg K, Bose A, et al. Influence of hemodynamics and intra-operative hydration on biochemical outcome of renal transplant recipients. J Anaesthesiol Clin Pharmacol. 2015;31:174.
6. Calixto Fernandes MH, Schricker T, Magder S, et al. Perioperative fluid management in kidney transplantation: a black box. Crit Care. 2018;22:14.
7. Bacchi G, Buscaroli A, Fusari M, et al. The influence of intraoperative central venous pressure on delayed graft function in renal transplantation: a single-center experience. Transplant Proc. 2010;42:3387–91.
8. Benes J, Chytra I, Altmann P, et al. Intraoperative fluid optimization using stroke volume variation in high risk surgical patients: Results of prospective randomized study. Crit Care. 2010;14:R118.
9. Buettner M, Schummer W, Huettemann E, et al. Influence of systolic-pressure-variation guided intraoperative fluid management on organ function and oxygen transport. Br J Anaesth. 2008;101:194–9.
10. Cannesson M. Arterial pressure variation and goal-directed fluid therapy. J Cardiothorac Vasc Anesth. 2010;24:487–97.
11. Lopes MR, Oliveira MA, Pereira VO, et al. Goal-directed fluid management based on pulse pressure variation monitoring during high-risk surgery: a pilot randomized controlled trial. Crit Care. 2007;11:R100.
12. Karpinski J, Lajoie G, Cattran D, et al. Outcome of kidney transplantation from high-risk donors is determined by both structure and function. Transplantation. 1999;67:1162–7.
13. Othman MM, Ismael AZ, Hammouda GE. The impact of timing of maximal crystalloid hydration on early graft function during kidney transplantation. Anesth Analg. 2010;110:1440–6.
14. Boutron I, Altman DG, Moher D, et al. CONSORT Statement for Randomized Trials of Nonpharmacologic Treatments: A 2017 Update and a CONSORT Extension for Nonpharmacologic Trial Abstracts. Ann Intern Med. 2017;167:40–7.
15. Cavaleri M, Veroux M, Palermo F. Perioperative goal-directed therapy during kidney transplantation: an impact evaluation on the major postoperative complications. J Clin Med. 2019;8:80.
16. Tóth M, Réti V, Gondos T. Effect of recipients' perioperative parameters on the outcome of kidney transplantation. Clin Transplant. 1998;12:511–7.
17. Campos L, Parada B, Furriel F. Do intraoperative hemodynamic factors of the recipient influence renal graft function? Transplant Proc. 2012;44:1800–3.
18. Marik PE, Baram M, Vahid B. Does central venous pressure predict fluid responsiveness? A systematic review of the literature and the tale of seven mares. Chest. 2008;134:172–8.
19. Baxi V, Jain A, Dasgupta D. Anaesthesia for renal transplantation: An Update. Indian J Anaesth. 2009;53:139–47.
20. Corbella D, Toppin PJ, Ghanekar A. Cardiac output-based fluid optimization for kidney transplant recipients: a proof-of-concept trial. Can J Anaesth. 2018;65:873–83.

Please cite this article in press as: De Cassai A, et al. Pulse pressure variation guided fluid therapy during kidney transplantation: a randomized controlled trial. Rev Bras Anestesiol. 2020. https://doi.org/10.1016/j.bjane.2020.04.022