

Mean Arterial Pressure Control Impact on Early Graft Function in Kidney Transplantation

Böbrek Transplantasyonunda Ortalama Arter Basıncı Kontrolünün Erken Dönem Greft Fonksiyonu Üzerindeki Etkisi

Mustafa Bajraktari¹, Rudin Domi²

¹University of Medicine, Faculty of Technical Medical Sciences, Tirana, Albania

²University of Medicine, Faculty of Medicine, Department of Anesthesia and Intensive Care, Tirana, Albania

ABSTRACT

Objective: For end-stage renal disease, kidney transplantation is the best therapy. Early graft function is critical for kidney transplant success. The purpose of this study was to see how mean arterial pressure (MAP) affected early graft function and biochemical outcomes.

Methods: This was a retrospective study of transplanted patients from live-related donors at the Transplant Center Hospital, Tirana, Albania, between January 2007 and December 2022. The patients divided based on their mean MAP. One group had MAP above 100 mmHg (68 patients). The second group had MAP between 85-100 mmHg (74 patients) and the other group MAP less than 85 mmHg (52 patients). Serum creatinine decrease was observed during the first three post-operative days and the sixth day. For statistical computation, correlation analysis, analysis of variance test (ANOVA), and multivariate analysis technique were used in this study.

Results: On the first, second, and third postoperative days, the first and second groups' mean serum creatinine values were comparable to the third group's mean values. The mean MAP at the time of declamping was 108.64 mmHg for the first group, 95.28 mmHg for the second group, and 80.18 mmHg for the third group. The mean MAP ranged from 78 to 118 mmHg. There was no significant difference between the first two groups on the first, second, third, and sixth postoperative days, but there were significant differences between the first and second groups compared to the third group on the first, second, and third postoperative days.

Conclusion: Early graft function requires a mean MAP greater than 85 mmHg and adequate fluid hydration.

Keywords: Mean arterial pressure, kidney transplantation, creatinine

ÖZ

Amaç: Son dönem böbrek hastalığı için böbrek transplantasyonu en iyi tedavi yöntemidir. Erken greft fonksiyonu böbrek nakli başarısı için kritik öneme sahiptir. Bu çalışmanın amacı ortalama arter basıncının (OAB) erken greft fonksiyonunu ve biyokimyasal sonuçları nasıl etkilediğini görmektir.

Yöntem: Bu retrospektif çalışmaya Ocak 2007 ile Aralık 2022 tarihleri arasında, Arnavutluğun Tiran şehri Transplant Merkezi Hastanesinde canlı donörlerden böbrek transplante edilmiş hastalar dahil edildi. Bir grupta OAB 100 mmHg'nin üzerindeydi (68 hasta). İkinci grupta OAB 85-100 mmHg arasında (74 hasta) ve diğer grupta 85 mmHg'nin altında (52 hasta) idi. Ameliyat sonrası ilk üç gün ve altıncı günde serum kreatinininde düşüş miktarı takip edildi. Bu çalışmada istatistiksel hesaplama için korelasyon analizi, varyans analizi testi (ANOVA) ve çok değişkenli analiz tekniği kullanıldı.

Bulgular: Ameliyat sonrası birinci, ikinci ve üçüncü günlerde, birinci ve ikinci grupların ortalama serum kreatinin değerleri üçüncü grubun ortalama değerleriyle benzerdi. Klempin çıkarılması sırasındaki ortalama OAB birinci grup için 108,64 mmHg, ikinci grup için 95,28 mmHg ve üçüncü grup için 80,18 mmHg idi ve ortalama OAB 78 ila 118 mmHg arasında değişiyordu. Ameliyat sonrası birinci, ikinci, üçüncü ve altıncı günlerde ilk iki grup arasında anlamlı bir fark yokken, ameliyat sonrası birinci, ikinci ve üçüncü günlerde üçüncü gruba kıyasla birinci ve ikinci gruplar arasında anlamlı farklar vardı.

Sonuç: Erken greft fonksiyonu ortalama OAB'nin 85 mmHg'den yüksek olmasını ve yeterli sıvı hidrasyonunu gerektirir.

Anahtar sözcükler: Ortalama arteriyel basınç, böbrek nakli, kreatinin

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*Corresponding author: Mustafa Bajraktari • m.bajraktari@live.com

Mustafa Bajraktari © 0000-0002-1333-6043 / Rudin Domi © 0000-0003-4594-7815

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INTRODUCTION

End-stage renal disease (ESRD) can be treated with dialysis or kidney transplantation (1,2). Kidney transplantation is widely regarded as the best replacement therapy for ESRD patients (3). To achieve the highest success in graft function, the main approach to perioperatively management has been the administration of large amounts of fluids guided by the central venous pressure (CVP) (4-6). But this approach can often result in loading excess amounts that can lead to endothelial damage and displacement of excess fluids in the third interstitial space. In recent years, a shift towards a more conservative fluid approach guided by mean arterial pressure (MAP) has shown promise (7). The purpose of this study was to demonstrate how the value of MAP at the moment of declamping and after, would affect the decrease in creatinine values, which is more accurate marker of renal function than urine output, when other conditions, such as the amount of intraoperatively fluids, albumin, or hemotransfusions, were standard in the entire group of patients included in the study. The aim is to better understand the impact of MAP on graft outcomes in patients with specific limitations on CVP measurement.

MATERIAL and METHODS

Study Design and Participants

This was a retrospective study of patients who received renal transplants only from live-related donors at the University of Medicine, Tirana, Albania between January 2007 and December 2022.

Our study included 194 patients, 70 of whom were female (36%) and 124 of whom were male (64%). The patients had an average age of 32 years and a weight of 59.5 kg. The donors were all alive and genetically related to the recipients, with 140 (72%) being female and 54 (28%) being male. Only 18 patients (8.2%) had acute rejection of the allograft, which was not included in this study, and 7 kidney transplants performed by a different team of surgeons were not included in the statistical analysis of serum creatinine values in the early postoperative period.

Data Collection and Analysis

We classified the patients into three groups based on their mean MAP.

Group 1 included 68 patients with MAP >100 mmHg, Group 2 had 74 patients with MAP between 85-100 mmHg, and Group 3 comprised 52 patients with MAP <85 mmHg. The average MAP was measured during declamping, and serum creatinine levels were recorded in the first three postoperative days and on the sixth day.

Numeric variables were expressed using descriptive statistics, such as mean and standard deviation, while categorical variables were presented with absolute and relative values. We employed Chi-square and Fischer's exact tests to compare proportions between categories and Student's t-test for independent samples to compare means of continuous variables. All tests were two-tailed, and the level of significance was set at $p < 0.05$.

Anesthesia Management

The anesthesia induction involved propofol (2-2.5 mg kg⁻¹), fentanyl (2 µg kg⁻¹), and vecuronium (0.1 mg kg⁻¹). Maintenance of anesthesia included sevoflurane (2-2.5%), vecuronium (0.05 mg kg⁻¹), and remifentanyl (0.25-0.35 µg kg⁻¹ h⁻¹). Methylprednisolone (500 mg) was administered 30 minutes before the surgery, followed by a second dose of 100-200 mg immediately after the start of the intervention (total 10 mg kg⁻¹).

Some patients were administered ephedrine, phenylephrine or atropine to maintain adequate MAP after reperfusion, nitroglycerine (NTG) was used to control intraoperative hypertension.

Intraoperative monitoring consisted of peripheral capillary oxygen saturation, electrocardiogram, arterial blood pressure, and end-tidal carbon dioxide (ETCO₂). Invasive blood pressure monitoring was performed, due to the fact that nowadays kidney transplantation is routine and sophisticated monitoring (PPV, SVV, EVLW) are considered in marginal patients.

Fluid Management

During transplantation, all patients received fluid therapy with normal saline (15-20 mL kg⁻¹ h⁻¹) and human serum albumin (20%-50 mL). Furosemide (up to 40 mg) was used immediately after declamping to stimulate diuresis, and 31 patients (16%) received blood transfusions. The hemoglobin level below 7 gr dL⁻¹ was considered as threshold value for transfusion. The aim of the fluid regimen was to maintain MAP and CVP at optimal levels without the need for excessive fluid administration.

Ethical Considerations

This study was conducted following ethical guidelines and was approved by the relevant institutional review board (23/05/2023, No: 34/1). Patient data were handled with strict confidentiality and compliance with data protection regulations.

RESULTS

The surgical interventions for kidney transplants were con-

Table I: Clinical and Demographic Data of the Study Groups

Characteristics	Group 1 (n=68)	Group 2 (n=74)	Group 3 (n=52)	p
Recipient gender (M/F, n/%)	43/25 (63/37)	47/27 (64/36)	34/18 (65/35)	0.96
Recipient age (y)	36.48 ± 18.74	37.24 ± 16.66	36.78 ± 18.82	0.90
Hemodialysis (n/%)	53 (78)	62 (83.7)	43 (82.6)	0.64
Time spent on dialysis (y)	3.4 ± 2.04	3.1 ± 1.14	3.2 ± 1.16	0.62
Type of transplantation (SKT/DKT, n/%)	68 (100%) SKT	74(100%) SKT	52 (100%) SKT	
Donor gender (M/F, n/%)	19/49 (28/72)	22/52 (30/70)	14/38 (26/74)	0.38
Donor age (y)	48.28 ± 11.62	49.14 ± 9.16	46.84 ± 10.46	0.86

Values are mean ± Standard Deviation or median (min-max), and p-value <0.05 is considered significant. **n:** number; **M:** Male; **F:** Female; **y:** years; **SKT:** Single kidney transplantation; **DKT:** Dual kidney transplantation.

Table II: Baseline Characteristics of Patients

Characteristics	Group 1	Group 2	Group 3	p
BMI	23.64 ± 4.25	21.92 ± 3.44	22.66 ± 4.84	0.27
ASA (II/III)	12/56	13/61	8/44	0.93
Duration of surgery (h)	1.54 ± 0.82	1.58 ± 1.12	1.52 ± 0.94	0.74
MAP (mmHg)	112.64 ± 14.24	94.78 ± 6.22	78.42 ± 6.04	0.0001
HR (bpm)	82.5 ± 22.48	86.42 ± 18.6	79.84 ± 23.43	0.08

Data are displayed as mean ± SD or n. **BMI:** Body mass index; **ASA:** American Society of Anesthesiologists; **h:** Hours; **MAP:** Mean arterial pressure; **HR:** Heart rate; **bpm:** Beats per minute.

Table III: Average MAP at the Time of Declamping

Group	MAP (mmHg)	Patients number
Group 1	>100	68
Group 2	85 <MAP< 100	74
Group 3	< 85	52
Total		194

MAP: Mean arterial pressure.

ducted from January 2007 to December 2022. We excluded 18 patients who experienced acute allograft rejection and seven cases performed by a different surgical team from the statistical analysis. All three study groups demonstrated comparable clinical and demographic characteristics, including age, sex distribution of recipients and donors, body mass index (BMI), and American Society of Anesthesiologists (ASA) class, Table I, Table II.

During declamping, we measured the MAP, Table III, and serum creatinine levels were assessed on the first three postoperative days and the sixth day, Table IV. There were no significant differences in serum creatinine concentrations between the three groups before surgery. In the first three days after surgery, all groups experienced a significant decrease in serum creatinine levels, with no notable variation in the rate of reduction among the first two groups (MAP >100 mmHg and MAP between 85-100 mmHg). However, the third group, with

a mean MAP of <85 mmHg during declamping, demonstrated a notably slower decrease in serum creatinine levels (p<0.05).

DISCUSSION

This retrospective study, with its large sample size and single-center design, provides robust evidence for the importance of MAP in anesthesia management during kidney transplant surgeries. Mean arterial pressure was evaluated as the primary guide in renal transplant hemodynamic management in our study. The impossibility of measuring CVP in 34 patients was the reason for using MAP rather than CVP and MAP together. The inability to measure CVP was due to the high risks of placing central venous catheters in these patients, which included the presence of thrombi or narrowing of the central veins as a result of long-term use of catheters for hemodialysis.

Maintaining optimal MAP levels, specifically above 85 mmHg at the time of declamping and postoperatively, was associated with a rapid decrease in serum creatinine levels during the first three days after surgery. This observation suggests that adequate MAP values contribute to enhanced graft perfusion and function, leading to improved renal transplant success. The rapid decline in serum creatinine levels in patients with MAP >100 mmHg and MAP between 85-100 mmHg further supports the notion that MAP plays a significant role in graft function (8).

Table IV: Serum Creatinine Decreasing Values

Group/ average MAP	Cr: preop	Cr: 1 st day postop	Cr:2 nd day postop	Cr:3 rd day postop	Cr:4 th day postop	Cr:5 th day postop	Cr:6 th day postop
1 / 108.64	6.42 ± 3.6	3.96 ± 0.9	2.01 ± 0.8	1.74 ± 0.6	-	-	0.78 ± 0.6
2 / 95.28	5.86 ± 3.2	3.88 ± 1.2	2.36 ± 1.2	1.69 ± 0.9	-	-	0.76 ± 0.8
3 / 80.18	6.04 ± 2.6	4.64 ± 1.1	3.58 ± 1.3	2.36 ± 1.2	-	-	0.92 ± 1.2
p-value	0.655	<0.001	<0.001	<0.001			0.370

Data are displayed as mean ± SD. **MAP:** Mean arterial pressure; **Cr:** Serum creatinine; **preop:** Preoperative; **postop:** Postoperative.

Our results align with existing studies that highlight the impact of arterial hypotension on early graft dysfunction, particularly acute tubular necrosis (9). The proper reperfusion of the transplant graft in the early postoperative period is crucial for graft survival, and MAP emerges as a vital factor in achieving this outcome (10-12).

Our study highlights the critical role of MAP in early graft function during renal transplantation. Maintaining MAP above 85 mmHg at the time of declamping and beyond is associated with a rapid reduction in serum creatinine levels, indicating improved graft outcomes.

The use of albumin in all patients, as a stabilizer of hemodynamic parameters by increasing the volume of the vascular bed with fluid and decreasing the administration of fluids liberally, was another aspect of our study. Albumin in conjunction with a conservative fluid approach contributed to stable hemodynamics, reduced the need for excessive fluid administration, and avoided the interstitial edema formation.

By maintaining a given MAP without the need for excessive fluid administration, albumin facilitated stable hemodynamics, which in turn promoted diuresis and improved early graft function (10,13,14). This highlights the significance of using albumin as part of perioperative fluid therapy to optimize graft outcomes (15,16).

Furthermore, our study revealed the adverse effects of blood transfusions on graft function. We discovered a relationship between blood transfusions and an increased risk of transplant rejection or chronic failure. Minimizing blood transfusions whenever possible is crucial, as they were associated with an increased risk of graft rejection or chronic dysfunction. This finding emphasizes the importance of judicious blood management strategies to enhance graft success rates (17).

By elucidating the relationship between MAP and serum creatinine values, our results offer valuable insights into optimizing perioperative care and enhancing graft success rates. The urinary output and creatinine levels in the blood serum are usually used to assess the function of the kidney graft in the first few days after the intervention, but in specific cases we

can also use other markers of renal function which are much more sensitive such as NGAL, cystatin c, IL 18, and KIM1, which show us the dysfunction within the first two hours. We know that the early function of the graft, which is expressed by the decrease in creatinine values, is critical for the success of the renal transplant.

The retrospective nature of our study limited the ability to calculate the sample size, but the inclusion of a substantial number of patients from a single center enhanced the reliability of our results. Additionally, the inability to measure CVP in some patients necessitated the use of MAP as the primary hemodynamic indicator. This study contributes unique insights into cases CVP measurements are not feasible, and reliance on MAP as the main hemodynamic indicator becomes necessary.

In conclusion, our research underscores the crucial role of MAP in the early function and success of renal transplants. Maintaining MAP above 85 mmHg during declamping and postoperatively, in conjunction with the use of albumin and conservative fluid therapy, can significantly improve graft outcomes. Implementing these findings in clinical practice may enhance patient care and contribute to better long-term outcomes in renal transplantation.

Overall, our study provides valuable evidence for optimizing anesthesia management during kidney transplant surgeries and highlights the importance of MAP as a key determinant of graft success. The results offer actionable insights for clinicians, leading to enhanced patient outcomes and potentially advancing the field of renal transplantation.

But the special feature of this study was that all interventions, 194, were performed by the same team of surgeons and anesthesiologists, which increases the reliability of the results obtained (14). To our knowledge and after consulting the literature, we have not found a similar study from a single center and with 194 patients enrolled.

CONCLUSION

In conclusion, this retrospective study provides valuable insights into the role of MAP in the early function of kidney

allografts during renal transplantation. The present study underscores the critical importance of maintaining MAP above 85 mmHg to ensure early graft function. The adoption of a more conservative fluid approach, supported by albumin administration, proves beneficial in maintaining hemodynamic stability without compromising the need for excessive fluid volume. Our findings emphasize the significance of MAP as a primary hemodynamic indicator, particularly in cases where CVP measurement is not feasible.

Our findings emphasize the importance of maintaining optimal MAP levels, along with the use of albumin and conservative fluid management, to improve graft outcomes. Furthermore, it is important to minimize blood transfusions whenever possible, as they have been associated with increased risks of graft rejection and chronic dysfunction. This study contributes valuable insights into the anesthesia management of kidney transplant surgeries, offering a novel perspective on MAP's impact on early graft outcomes. Implementing these anesthesia management strategies may enhance patient care and contribute to better long-term results in renal transplantation.

As a retrospective study conducted at a single center with a considerable sample size, our results provide a robust foundation for future investigations and could potentially influence clinical practices in renal transplantation. By focusing on the interplay between MAP and serum creatinine levels, we have shed light on an essential aspect of graft success and overall patient well-being. Implementing the knowledge gained from this research may lead to improved patient outcomes and enhanced transplant success rates in the future.

AUTHOR CONTRIBUTIONS

Conception or design of the work: MB

Data collection: MB

Data analysis and interpretation: MB, RD

Drafting the article: RD, MB

Critical revision of the article: RD

Other (study supervision, fundings, materials, etc): RD

The author (MB, RD) reviewed the results and approved the final version of the manuscript.

REFERENCES

- Nargesi AA, Lerman LO, Eirin A. Mesenchymal stem cell-derived extracellular vesicles for kidney repair: Current status and looming challenges. *Stem Cell Res Ther* 2017;8(1):273.
- Diaz G, O'Connor M. Cardiovascular and renal complications in patients receiving a solid-organ transplant. *Curr Opin Crit Care* 2011;17(4):382-9.
- Jin J, Wang Y, Shen Q, Gong J, Zhao L, He Q. Acute kidney injury in cancer patients: A nationwide survey in China. *Sci Rep* 2019;9(1):3540.
- Spiro MD, Eilers H. Intraoperative care of the transplant patient. *Anesthesiol Clin* 2013;31(4):705-21.
- 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(5):1440-6.
- Chaumont M, Racape J, Broeders N, et al. Delayed graft function in kidney transplants: Time evolution, role of acute rejection, risk factors, and impact on patient and graft outcome. *J Transplant* 2015;2015:163757.
- 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(3):807-9.
- Chaumont M, Racape J, Broeders N, et al. Delayed graft function in kidney transplants: Time evolution, role of acute rejection, risk factors, and impact on patient and graft outcome. *J Transplant* 2015;2015:163757.
- 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(5):1440-6.
- Loutzenhiser R, Griffin K, Williamson G, Bidani A. Renal autoregulation: New perspectives regarding the protective and regulatory roles of the underlying mechanisms. *Am J Physiol Regul Integr Comp Physiol* 2006;290(5):R1153-67.
- Webber A, Hambleton J, Chami A, et al. Mean arterial blood pressure while awaiting kidney transplantation is associated with the risk of primary nonfunction. *Transplantation* 2012;93(1):54-60.
- Chappell D, Jacob M, Hofmann-Kiefer K, Conzen P, Rehm M. A rational approach to perioperative fluid management. *Anesthesiology* 2008;109(4):723-40.
- Van Loon E, Bernards J, Van Craenenbroeck AH, Naesens M. The causes of kidney allograft failure: More than alloimmunity. A viewpoint article. *Transplantation* 2020;104(2):e46-e56.
- Gill J, Dong J, Rose C, Gill JS. The risk of allograft failure and the survival benefit of kidney transplantation are complicated by delayed graft function. *Kidney Int* 2016;89(6):1331-6.
- Ferris RL, Kittur DS, Wilasrusmee C, et al. Early hemodynamic changes after renal transplantation: Determinants of low central venous pressure in the recipients and correlation with acute renal dysfunction. *Med Sci Monit* 2003;9(2):CR61-6.
- Hod T, Isakov O, Patibandla BK, et al. Posttransplantation hypomagnesemia as a predictor of better graft function after transplantation. *Kidney Blood Press Res* 2020;45(6):982-95.
- Böhmgig GA, Eskandary F, Doberer K, Halloran PF. The therapeutic challenge of late antibody-mediated kidney allograft rejection. *Transpl Int* 2019;32(8):775-88.