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Efficacy of Biphasic Fluid Therapy in Robot-Assisted Kidney Transplantation

Robot Yardımlı Böbrek Naklinde Bifazlı Sıvı Tedavisi'nin Etkinliği

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ÖZET

Amaç: Perioperatif sıvı tedavisi, nakledilen böbreğin işlevini etkileyen faktörlerden biridir. Bu çalışmada, perioperatif hasta stabilizasyonu ve allograft böbrek fonksiyonları üzerine ikili fazlı sıvı tedavisinin etkinliği değerlendirilmiştir.

Gereç ve Yöntemler: 2015-2017 yılları arasında gerçekleştirilen 65 canlı vericili robot yardımlı laparoskopik böbrek nakli operasyonu verileri retrospektif olarak analiz edildi (16/04/2018, Protokol no 2018-07-13). Hastalar nakil öncesi diyaliz tedavisi alan grup (Grup Preemptif: GP, n=27) ve nakil öncesi diyaliz tedavisi almayan grup (Grup Non-Preemptif: GNP, n=38) olarak bölündü. Tüm vakalarda ikili fazlı sıvı tedavisi kullanıldı (faz 1=vasküler anastomoz öncesi 1-3 ml/kg/s ve faz 2=vasküler anastomoz sonrası 10-12 ml/kg/s). Hastaların hemodinamik ve biyokimyasal durumu, erken ve geç allograft böbrek fonksiyonları değerlendirildi. Veriler istatistiksel olarak gruplar içinde ve arasında karşılaştırıldı.

Bulgular: Tüm hastalarda vasküler anastomoz sonrasında hemodinamik/metabolik stabilite ve diürez elde edildi. Gruplar arasında intravenöz (iv) sıvı toplam miktarında (faz 1'de verilen miktar dışında) fark yoktu, ancak GP'de faz 1' de verilen sıvı miktarı anlamlı olarak daha azdı ($p<0,05$). Ameliyat öncesi kan pH ve HCO3 değerleri GP'de düşüktü, Na+ ve Cl- değerleri yüksekti ($p<0,05$). K+ ve Ca+2 değerlerinde her zaman ve her iki grupta ekstübasyon sonrası pH değerlerinde fark bulunmadı. Ameliyat öncesi kan üre ve kreatinin düzeyleri GP'de anlamlı olarak yüksekti ($p<0,05$), ancak tüm değerler ameliyat sonrası 1. ve 7. günlerde normale döndü. Uzun süreli takipte, her iki grupta da benzer mortalite ve reddetme oranları görüldü.

Sonuç: Sonuçlarımız, canlı vericili robot yardımlı laparoskopik böbrek nakli hastalarında ikili fazlı sıvı tedavisinin hemodinamik/metabolik stabilite ve allograft böbrek fonksiyonlarını elde etmede etkili olduğunu desteklemektedir.

Anahtar Kelimeler: Anestezi, sıvı tedavisi, hemodinamik izleme, böbrek nakli, nakil alıcısı, robot yardımlı cerrahi

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Approval was received for this study from the Health Sciences University Istanbul Bakırköy Dr Sadi Konuk Training and Research Hospital ethics committee (16/04/2018, Protocol no 2018-07-13). The ethical rules of the Declaration of Helsinki were followed in the study protocol.

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ABSTRACT

Objective: Perioperative fluid treatment is among the factors affecting transplant kidney function. In this study, the efficacy of biphasic fluid treatment on per-operative patient stabilization and allograft kidney functions were evaluated.

Material and Methods: Data of 65 robotic living releated donor kidney transplantation performed between 2015-2017 were retrospectively analyzed (16/04/2018, Protocol no 2018-07-13). The patients were divided as preemptive (Group Preemptif: GP, n=27) and non-preemptive group (Group Non-Preemptif: GNP, n=38). Biphasic fluid treatment was used in all cases (Phase 1 = before-vascular anastomosis 1-3 ml/kg/h and phase 2 = after-vascular anastomosis 10-12 ml/kg/h, respectively). Hemodynamic and biochemical status of the patients, early and late allograft kidney function were evaluated. Datas were statistically compared within and between the groups.

Results: Hemodynamic/metabolic stability and diuresis were achieved after vascular anastomosis in all patients. There was no difference in the total amount of iv fluid given between the groups, except that the amount of fluid given in phase 1 was significantly less in GP ($p<0.05$). Pre-operative blood pH and HCO3 values were lower, Na+ and Cl- values were higher in GP($p<0.05$). No difference was found in K+ and Ca+2 values at all times and pH values after extubation in both groups. Pre-operative blood urea and creatinine levels were significantly higher in GP ($p<0.05$) but all decreased to normal on postoperative 1 and 7 days. In long-term follow-up, both groups had similar mortality and rejection rates.

Conclusion: Our results support that biphasic fluid treatment is effective to achieve hemodynamic/metabolic stability and allograft kidney functions in robotic living releated kidney transplantation patients.

Keywords: Anesthesia, Fluid therapy, Hemodynamic monitoring, Kidney transplantation, Transplant recipient, Robot-assisted surgery

INTRODUCTION

Kidney transplantation is the most common parenchymal organ transplantation. It is considered the best treatment method for end-stage renal disease patients because it provides usual living standards by improving short- and long-term outcomes (1). Robot-assisted laparoscopic surgery has been used for living donor nephrectomies as an alternative to open and laparoscopic techniques in kidney transplantation surgery, but there is minimal experience in transplant recipient patients (2).

Minimally invasive surgical techniques together with the subtleties in anesthesia management improve graft function and the recipient's health. Overall increased recipient lifelong and quality of life reduce the need for re-transplantation and thus increase the number of organs available for transplantation (3). However, protecting the allograft kidney during robotic kidney transplantation surgery with the additional problems such as intra-abdominal CO_2 insufflation, inability to reach the patient due to positioning and exaggerated deep Trendelenburg position make anesthesia management of these patients more difficult and challenging. Preemptive transplantation, defined as elective transplantation before the need for chronic dialysis, allows the patient to avoid dialysis entirely and has been applied with increasing frequency in recent years. However, preemptive transplantation patients possibly have excess intravascular volume and metabolic problems (such as hyperuricaemia, hyperkalemia and acidosis) which directly affect perioperative anesthesia management. In 2021, the American Society of Anesthesiologists (ASA) transplant anesthesia committee stated that intraoperative fluid management might affect the outcome of renal transplantation and emphasized that an individualized approach may be the best (4).

Besides the advantages and positive contributions of preemptive renal transplantation and robotic surgery on patients' comfort and allograft kidney function, they both make anesthesia management of these patients more complex. In this clinical study we aimed to investigate the efficacy of biphasic fluid management on hemodynamic/metabolic stability of recipients patients and on allograft kidney function

in both preemptive and non-preemptive robotic kidney transplantation patients.

MATERIAL AND METHODS

Obtaining Patient Data:

This study was designed retrospectively after ethics committee approval (16/04/2018, Protocol no 2018-07-13) of Bakırköy Dr Sadi Konuk Training and Research Hospital and was performed in line with the principles of the Declaration of Helsinki. As a result of power analysis, with an effect size of 0.8, a margin of error of 5%, and a power of 95%, the minimum sample size was 70, with 35 for each group. Between 2015 and 2017, 80 patients who underwent robot-assisted laparoscopic living related donor renal transplantation were screened from the hospital database and patient files. We excluded all cadaveric donor kidney transplantations, 9 patients with missing data, 1 who underwent open surgery and 5 who received peritoneal dialysis before transplantation. A phone call survey was done for long term results. The patients or their relatives are contacted by telephone for 5-year postoperative data.

Definitions

Timeframes: "Phase 1" was defined as the time from clamping the kidney in the donor until it was brought to the recipient, which includes both warm and cold ischemia periods. "Phase 2" was defined as the time from bringing the kidney to the recipient until extubation of the patient, that includes warming an reperfusion period and "Total phase" was defined as the time from opening the vascular access to the patient's recovery (Figure 1).

T0: donor kidney pedicle clamping, T1: induction of anesthesia, T2: before vascular anastomosis, T3: after vascular anastomosis and T4: extubation (Figure 1).

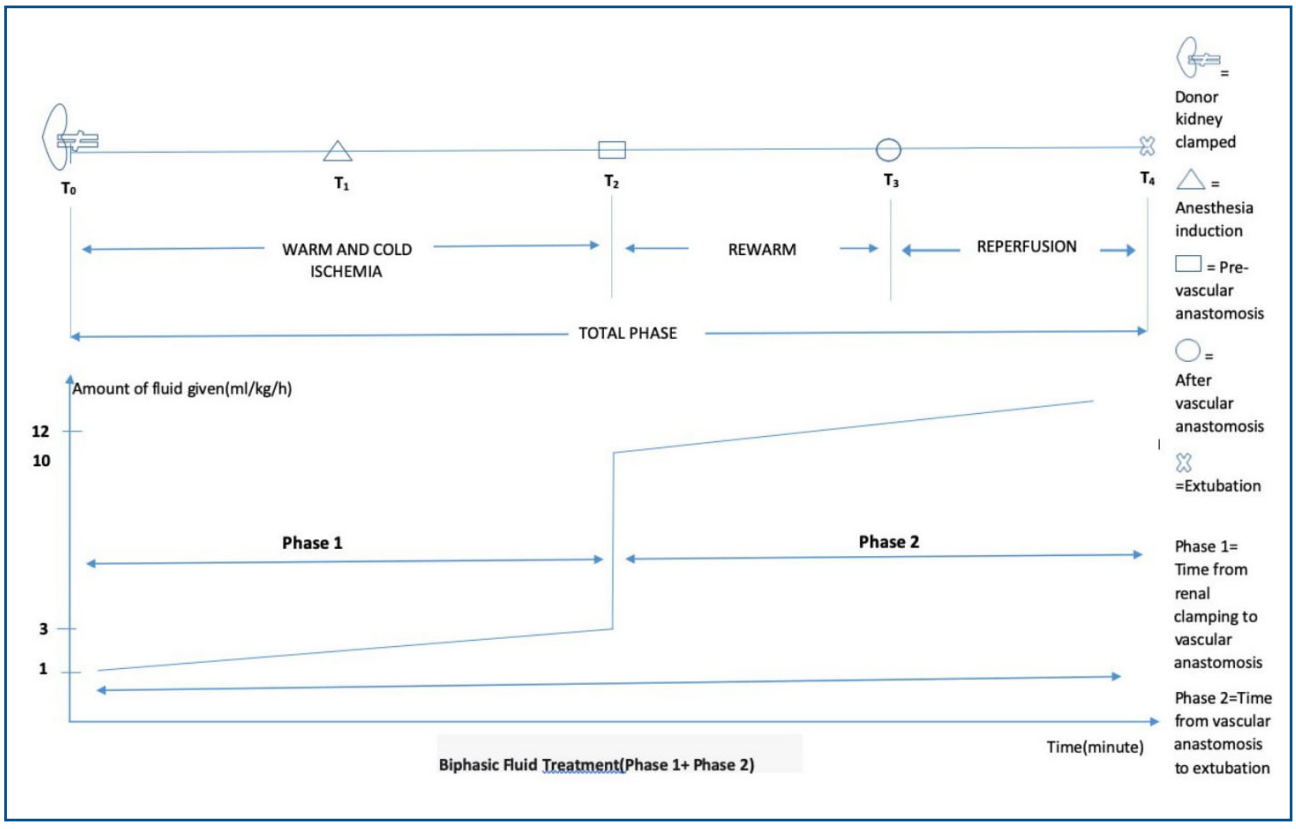

Figure 1. Timeframes

Warm ischemia time refers time period between donor kidney vascular clamping and commencement of cold storage.

Cold ischemia time refers time period between after cold package till the allograft kidney is brough recipient till reperfusion.

Rewarm time is the period from removal of the kidney from cold storage to vascular anastomosis and reperfusion. During this period the kidney is wrapped in ice until completion of the vascular anastomosis to decrease damage.

Patients were divided into two groups: those who had never undergone dialysis were included into the preemptive group (GP) and those who had undergone hemodialysis were included into the non-preemptive group (GNP). Demographic data (age, gender, weight, height), duration of anesthesia and surgery, preoperative and postoperative day 1 and 7 urea and creatinine values, hemodynamic data such as peak heart rate (HR) and mean arterial pressure (MAP) at time points during surgery and blood gases, (pH, Partial carbon dioxide pressure ($PCO_{2)}$, bicarbonate ($HCO_{3)}$, lactate (Lac), sodium (Na^{+}), potassium (K^{+}), chlorine (Cl^{-}), ionized calcium (Ca^{+2})) values, Phase 1 fluid, Phase 2 fluid, total fluid and urine amounts were recorded.

Biphasic fluid therapy: In cases of robotic kidney transplantation, the period from clamping the kidney in the donor until the kidney is brought into the recipient is defined as "Phase 1" and the period from and of phase 1 to extubation is defined as "Phase 2". Intravenous fluid infusion rate was administered at a rate of 1-3 ml/kg/h in Phase 1 and 10-12 ml/kg/h in Phase 2. This application was defined as biphasic fluid therapy (Figure 1).

Anesthesia Management

A standard anesthesia management is applied to all robotic renal transplantation patients. Electrocardiogram (ECG), peripheral oxygen saturation and non-invasive blood pressure monitoring are routinely performed on every patient. We give 1.5 mg midazolam for premedication, 1000 mg paracetamol for preventive analgesia, 100mg tramadol. If there is an arm with arteriovenous fistula for the dialysis, we protect that arm, wrapping it, and placing a fistula sticker on it. The connections of the arterial monitoring should be checked regularly, there is almost no chance of intervention in case of any separation or in case the trace shows incorrectly. Because we believe that these patients will need these vessels in the future life, we do not routinely insert central venous catheter. Because of increased infection risk, we also do not use any catheter that already in use neither for fluid infusion nor invasive monitorization.

Four vascular accesses are established with a 16-gauge peripheral cannula in both arms. Invasive arterial pressure monitoring is performed with radial artery cannulation using Seldinger technique and arterial blood gas samples are taken regularly. During all these processes, we do not start routine fluid infusion and we just we infuse the volume that required for medication of anesthesia management. During induction, midazolam 0.07-0.1 mg/kg, fentanyl 1-2 mcg/kg, propofol 20-30 mg and atracurium 0.6 mg/kg are administered and patients are orotracheally intubated and connected to the anesthesia device. Partial carbon dioxide pressure (pCO_2) is set to 35-45 mmHg, tidal volume 6-8 ml/kg, frequency 13-15/min, positive end-expiratory pressure (PEEP) 5-7 cmH_2O in PRVC mode on the Maquet Flow-I anesthesia device. Sevoflurane (MAC=0.5) and remifentanil (0.05-0.5 mcg/kg/min) maintain anesthesia. We fixed both arms on the sides and support with gel pads to prevent pressure from being of the operation. The material used to fix the arms should not cause any compression at any point. Any compression point can cause serious injury when the patient position is changed upside down. We use bilateral shoulder supports in our clinic to prevent the patient from slipping out of bed. The place where these supports are placed should be medial so that neither the carotids nor the brachial plexus is compressed. The neck should be in a neutral position so that it does not rotate on either side. The eyes and nose should be saved from the robot arms injury. However, the height of the safety guard should be at the nose level and a maximum of 4-5 cm so that it does

not hit the robot arms. After the lithotomy position is given, a 40-45° deep Trendelenburg position is added. The deep trendelenburg position should be reached intermittently, not all at once. During this period, it is important to choose the appropriate drug and dose to keep the patient's hemodynamics stable. To avoid fluid load, we use only 20-30 mg of propofol during induction of anesthesia and we arrange the max value for sevofloran at 0.5.

Isotonic (0.09 NaCl) infusion, 1 mL/kg/h, is used for maintenance fluid therapy. Following induction, 45.5 mg pheniramine maleate is started, followed by 1-1.5 mg/kg rabbit-derived anti-human thymocyte globulin (ATG) infusion in 250 ml 10% dextrose solution (50 – 100 and 150 mL/h) to be finished until the end of vascular anastomosis. We do not use colloids solution in these group of patients. A 500 mg methylprednisolone bolus is administered before circulation starts in the allograft kidney. We aim to keep the peak heart rate above 45 /min and the mean arterial pressure above 65 mmHg. When the heart rate drops below 45/min, 0.5 mg of atropine is administered. When the mean arterial pressure falls below 65 mmHg, a fluid bolus is given. If there is no response to the fluid response, vasopressor and inotrope is administered.

We routinely apply biphasic fluid therapy. We apply limited fluid therapy in the period between the clamping of the donor kidney, which we describe as phase 1, and anastomosis to the recipient kidney. During the period from vascular anastomosis to extubation, that is, in phase 2, we apply liberal fluid therapy to the patient. Thus, we apply fluid therapy to the patient when necessary. We perform routine blood gases monitoring at regular intervals. 1gr paracetamol and 100mg tramadol are administered for postoperative analgesia. Patients are extubated at the end of surgery when adequate respiration and alertness are achieved. Since these patients are immunosuppressed, they are not admitted to the intensive care unit but sent to the transplantation service.

Statistical Method

The data collected in the study was analyzed with GraphPad V5.0 software. The homogeneity of the data of the groups was evaluated by the Shapiro-Wilk test. The Student's t-test was used for homogeneous pairwise group comparisons. The Mann-Whitney U test evaluated nonhomogeneous pairwise comparisons. The frequency and percentage values of categorical variables were compared by the Chi-square test. In statistical representation, mean and standard deviation were used if the data were homogeneous. Median and interquartile range (Q25-75), number and percentage values were used for the non-homogeneous ones. Values with $P < 0.05$ were considered statistically significant. Intragroup comparisons were made with repeated Manova tests. Dunnet's multiple comparison tests detected significant differences between periods (Post hoc analysis). Values with $P < 0.017$ were considered statistically significant.

RESULTS

Total of 65 patients of which 27 GP pts, 38 GNP pts were included the study. There were 11 and 14 female patients and mean ages were 40 and 41 years in GP and GNP respectively. There was no statistically significant difference between the groups in demographic characteristics such as age, height, and gender. Preoperative blood Urea (152mg/dl vs 80 mg/dl) and Cr (7,04 mg/dl vs 5,72 mg/dl) respectively) values and total urine volume during the operation (650ml vs 400ml) were statistically significantly higher and the amount of fluid given in Phase 1 was statistically significantly lower (350ml vs 800ml) in GP compared to GNP ($p < 0.05$, Table 1). There was no statistically significant difference between the duration of anesthesia, duration of surgery, the amount of fluid given during Phase 2 and total fluid amounts of both groups, blood urea and Cr values on postoperative day 1 and 7 ($p>0.05$). Mean, SD, median, interquartile range (Q25-75), number and percentage of patients and p values of all parameters belonging to the groups are shown in Table 1.

Table 1. Age, height, preop Cr, preoperative and postoperative 7th day urea-creatinine Phase1 iv amount of fluid administered, total fluid, total urine amount of the patients in the preemptive group and the nonpreemptive group

Peroperatif	GP (n=27)	GNP (n=38)	U value	P value
Patients Data	**Mean ± SD and median (IQR_{25-75})**	**Mean ± SD and median (IQR_{25-75})**		
Female no (%)	11 (40,74%)	14 (36,84%)		0,9524 £
Age (year)	41(30-55)	40(29-50,5)	485,5	0,7192 *
Height (cm)	168(158-171)	167,5(160-171)	513	0,9947 *
Weight (kg)	68(60-78)	65,5(55,75-75,75)		0,4732 Ψ
Preop Cr	7,040(6,420-7,700)	5,725(4,448-7,085)	320,5	0,0106 *
Preop BUN	152 (137-174)	80(62,5-99,25)	174,5	< 0,0001 *
Anesthesia time, (minute)	313 ±56,59	307,6±47,07		0,6806 Ψ
Surgical time, (minute)	275,9±45,06	269,5±49,00		0,5937 Ψ
Postop day 1 urea	67,47±23,49	61,32±24,02		0,3089 Ψ
Postop day 7 urea	66(46-83)	61(45,50-78,25)	475	0,6175 *
Postop day 1 Cr	2,23(1,76-2,73)	2,49(1,725-3,308)	438	0,3213 *
Postop day 7 Cr	1,22(1,04-1,72)	1,25(0,9475-1,51)	436	0,3084 *
Phase 1 fluid amount (mL)	350 (300-500)	800(687,5-1000)	55,5	< 0.0001*
Phase 2 fluid amount (mL)	2409±764,1	2082±806,3		0,104 Ψ
Total amount of fluid(mL)	4000(3500-5000)	3775(3000-4225)	369	0,0551 *
Perop total amount of urine (mL)	650(400-1000)	400(250-500)	267,5	0,0011 *

Mann Whitney U test:*, Student T test : Ψ, Chi-Square test : £

The mean± SD/median IQR25-75 and p values of all parameters of both groups are shown in Table 2. The pH values of GP patients were found to be statistically significantly lower in the T1, T2 and T3 (7.32 ± 0.07, 7.29 ± 0.09, 7.24 ± 0.08) periods compared to GNP (7.36 ± 0.06, 7.35 ± 0.06, 7.29 ± 0.06) ($p < 0.05$). However, pH values were similar in the T4 period (7,24 ± 0,07 vs 7,27 ± 0,06.). PCO_2 values were statistically significantly higher in GNP compared to GP in the T1 period (P=0.007). In GNP, blood Na and Cl^- values were statistically significantly lower than GP values in all periods (approximately 3.5 meq/dL for Na and 6 meq/dL for Cl^-. GNP HCO_3 values were statistically significantly higher (approximately 3 meq/dL). There was no difference between the K^+ and Ca^{+2} values of both groups in all periods. Although a statistically significant difference was found between the lactate values of the T3 period, it was not considered clinically significant. Both groups had similar lactate values at other time points (Table 2). The mean and standard deviation values of T1 vs T2 and T1 vs T3 for HR in GP patients were calculated as 88 ± 15 vs 66 ± 13 and 88 ± 15 vs 73 ± 8 1/min, respectively and the differences were statistically significant ($p < 0.0001$, Figure 2-A). The T1 vs T4 mean and standard deviation values were 88 ± 15 vs 83 ± 16 1/min and were not statistically significant ($p>0.017$, Figure 2-A). T1 vs T2, T3 and T4 mean and standard deviation values for MAP in GP patients were 122 ± 90 vs 81 ± 17, 94 ± 19 and 101 ± 17 mmHg, respectively and the differences were not statistically significant ($p>0.017$, Figure 2-B). The analysis performed for GNP, T1 vs T2 and T1 vs T3 mean and standard deviation values for HR were calculated as 90 ± 17 vs 76 ± 15 and 90 ± 17 vs 81 ± 12 1/min, respectively and the differences were statistically significant (p values $p < 0.0001$ and 0.0013, respectively,

Figure 2-C). The T1 vs T4 mean and standard deviation values were 90 ± 17 vs 96 ± 16 1/min and were not statistically significant ($p > 0.017$ Figure 2-C). The T1 vs T2 mean and standard deviation values for MAP of GNP patients were calculated as 104 ± 16 vs 84 ± 13 and the difference was statistically significant ($p < 0.0001$, Figure 2-D). T1 vs T3 and T4 mean and standard deviation values were calculated as 104 ± 16 vs 100 ± 19 and 107 ± 15, respectively. However, the differences were insignificant ($p > 0.017$, Figure 2-D).

The differences between T1 vs T2 mean and standard deviation values for pH were not statistically significant in between-group evaluations of GP patients ($p=0.04$, Table 3). The T1 vs T3 and T1 vs T4 pH mean and standard deviation values were statistically significant ($p < 0.0001$, Table 3). Differences between T1 vs T2 mean and standard deviation values for Cl^- were not considered statistically significant. However, the differences between chloride mean and standard deviation values at times T1 vs T3 and T1 vs T4 were statistically significant ($p < 0.0001$, table 3), similar to the periods in pH values. HCO_3 mean values decreased by approximately 1 meq/L in each period (from T1 to T4) after the T1 period. Therefore, the differences between HCO_3, T1, T2, T3 and T4 mean and sd values were considered statistically significant ($p < 0.017$, Table 3). For potassium, only the difference between T1 vs T2 mean and standard deviation values was statistically significant ($p=0.0001$, Table 3). The differences between the value of potassium in T1 and the other periods (T3 and T4) were not statistically significant. No statistically significant difference was found between the periods for sodium and lactate. Although a statistically significant difference was found between all period values for free calcium, it was not considered clinically significant because it was within normal limits.

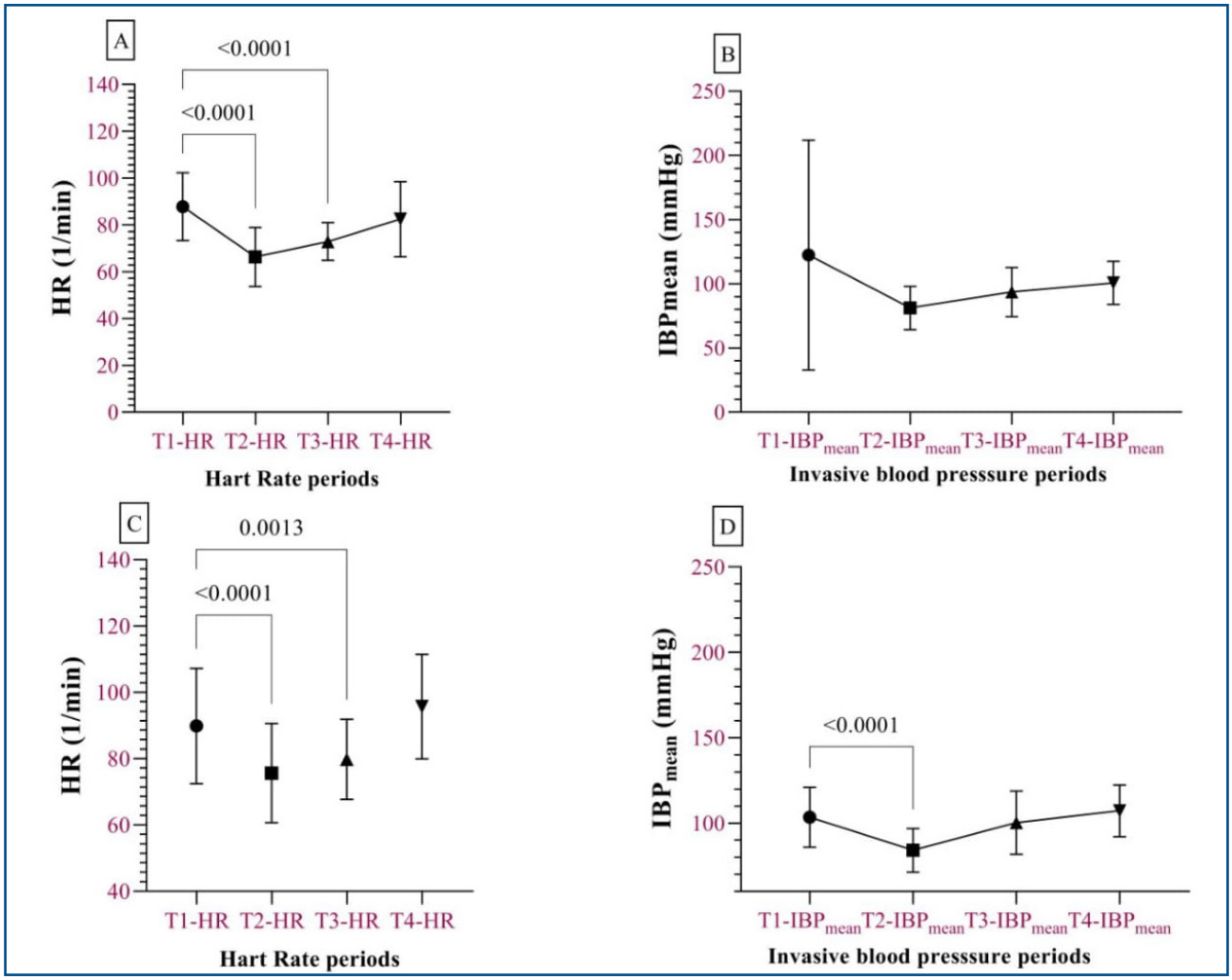

Figure 2. Comparison of GP (A – B) and GNP (C – D) HR and IBP mean results.

Table 2. pH, CO2, HCO3, K, Na, Cl, Ca, lactate values of the T1, T2, T3 and T4 periods ofthe patients in the preemptive group and the non-preemptive group

Arterial blood gas values		GP (n=27)	GNP (n=38)	U/X2	P value
		Mean ± SD or median (IQR_{25-75})	Mean ± SD or median (IQR_{25-75})		
pH,	T1	7.32 ± 0.07	7.36 ± 0.06		0.0007Ψ
	T2	7.29 ± 0.09	7.35 ± 0.06		0.0015Ψ
	T3	7.24 ± 0.08	7.29 ± 0.06		0.009Ψ
	T4	7.24 ± 0.07	7.27 ± 0.06		0.0797Ψ
CO_2, mmHg	T1	36 ± 5	42 ± 5		0.0007Ψ
	T2	39 ± 6	40 ± 5		0.7483Ψ
	T3	41 ± 5	43 ± 5		0.3567Ψ
	T4	43 ± 7	45 ± 8		0.5227Ψ
HCO_3, meq/L.	T1	19.8 ± 3.7	23.4 ± 2.7		< 0.0001Ψ
	T2	18.8 ± 3.7	21.9 ± 3.1		0.0004Ψ
	T3	17.1 (14.9-19.1)	19.8 (18.2-21.0)	272	0.0025*
	T4	16.5 (15.7-19.1)	19.6 (17.5-20.7)	277	0.0017*
K, meq/L	T1	4.4 (4.0-4.9)	4.5 (4.1-4.9)	484.5	0.7089*
	T2	4.8 ± 0.8	4.8 ± 0.9		0.7367Ψ
	T3	4.4 ± 0.7	4.5 ± 0.6		0.5861Ψ
	T4	4.5 ± 0.6	4.6 ± 0.7	444.5	0.3647*
Na, meq/L	T1	138 (135-139)	134 (132-136)	260.5	0.0007*
	T2	137 (134-138)	134 (131-135)	290.5	0.0029*
	T3	138 (135-140)	134 (133-136)	237	0.0002*
	T4	138 (136-141)	135 (132-136)	220	< 0.0001*
CL, meq/L	T1	109 (104-114)	102 (100-106)	238	0.0002*
	T2	111 (106-115)	105 (102-110)	324	0.012*
	T3	115 ± 6	110 ± 4	272	< 0.0001*
	T4	115 (111-119)	109 (106-112)	202.5	< 0.0001*
Lactate, meq/L	T1	0.96 ± 0.29	1.1 ± 0.49		0.0977Ψ
	T2	1.00 (0.80-1.20)	1.20 (0.88-1.50)	386	0.0912*
	T3	1.00 (0.60-1.30)	1.15 (0.90-1.53)	339.5	0.021*
	T4	1.20 (0.90-1.70)	1.35 (1.10-1.90)	386.5	0.0928*
Ca, meq/L.	T1	1.14 ± 0.08	1.12 ± 0.08		0.4257Ψ
	T2	1.10 ± 0.08	1.08 ± 0.08		0.2388Ψ
	T3	1.07 ± 0.10	1.08 ± 0.09		0.7987Ψ
	T4	1.08 ± 0.08	1.10± 0.09		0.4914Ψ

Mann Whitney U test: *, Student T test : Ψ

For pCO_2, the difference between T1 vs T2 and T3 periods was not statistically significant, while the difference between T1 vs T4 mean and standard deviation values was statistically significant, but it was not considered clinically significant because it was within normal limits (Table 3). The differences between the mean and standard deviation values of T1 vs T2, T1 vs T3 and T1 vs T4 times for Cl^- were statistically significant in the intragroup evaluations of GNP patients ($p < 0.0001$, table 4). Basal HCO_3 mean values were higher in all periods compared to the preemptive group values and there was a further decrease (approximately 1.3meq/L) from T1 to T4. Therefore, the differences between the mean and sd values of HCO_3 T1 vs T2, T3 and T4 were statistically significant ($p < 0.0001$, Table 4). The differences between the mean and standard deviation values of T1 vs T3 and T1 vs T4 times for pH were also statistically significant ($p < 0.0001$, table 4). No statistically significant difference existed between all period values for potassium, sodium, free Ca^{+2} and pCO_2 (Table 4). Although a statistically significant difference was found between T1 and T4 periods for lactate, it was not considered clinically significant because it was between normal limits. The last 5 years' follow-up data were compared with Fisher's exact test.

By phone call survey, we were able to reach all patients or their relatives. Mean postransplant folloup period was 5.6 (5.1- 6.8) years. There was total of 4 patients died and 7 rejections on both groups. In GP, 1 patient was died because of heart failure and there were 4 rejections while 22 patients are on follow up. In GNP, 3 patients were died, one because of MI and 2 of Covid-19 infection and ther were 3 rejection while 32 of them are on follow up.

The number and percentages of nonsurvival and kidney rejections and p values of GP and GNP patients were calculated as 1 (4 %) vs 3 (8 %) p=0.37 and 4 (15 %) vs 3 (8 %) p=0.18, respectively.

Table 3. pH, pCO2, HCO3, K, Na, Cl, Ca, lactate values of GP at T1, T2, T3 and T4. Repeated MANOVA and multiple comparisons tests were used for statistical comparison.

GP (n=27)	T1 vs T2	p	T1 vs T3	p	T1 vs T4	p
	Mean ± SD		Mean ± SD		Mean ± SD	
PH	7.32 ± 0.07 vs 7.29 ± 0.09	0.04	7.32 ± 0.07 vs 7.24 ± 0.08	<0.0001	7.32 ± 0.07 vs 7.24 ± 0.07	<0.0001
pCO_2, mmHg	36 ± 5 vs 39 ± 6	0.07	36 ± 5 vs 41 ± 6	0.03	36 ± 5 vs 43 ± 7	0.003
HCO_3, meq/L	19.8 ± 3.7 vs 18.8 ± 3.7	0.004	19.8 ± 3.7 vs 17.5 ±3.3	<0.0001	19.8 ± 3.7 vs 17.4 ± 2.6	0.0003
K^+, meq/L	4.5 ±0.7 vs 4.8 ± 0.8	0.0001	4.5 4.5 ±0.7 vs 4.4 ± 0.7	0.8	4.5 ± 0.7 vs 4.5 ± 0.6	0.9
Na^+, meq/L	137 ± 4 vs 136 ± 3	0.002	137 ± 4 vs 138 ± 3	0.3	137 ± 4 vs 139 ± 3	0.03
Cl^-, meq/L	109 ± 6 vs 110 ± 7	0.06	109 ± 6 vs 115 ± 6	<0.0001	109 ± 6 vs 115 ± 5	0.0001
Ca^{+2}, meq/L	1.14 ± 0.08 vs 1.10 ± 0.08	0.0003	1.14 ± 0.08 vs 1.07 ± 0.10	0.0006	1.14 ± 0.08 vs 1.08 ± 0.08	0.0007
Lactate, meq/L	0.96 ± 0.29 vs 1.01 ± 0.44	0.8	0.96 ± 0.29 vs 1.01 ± 0.43	0.8	0.96 ± 0.29 vs 1.30 ± 0.62	0.007

Table 4. pH, pCO2, HCO3, K, Na, Cl, Ca, lactate values of GNP, at T1, T2, T3 and T4 periods. Repeated MANOVA and multiple comparisons tests were used for statistical comparison.

GNP (n=38)	T1 vs T2 Mean ± SD	p	T1 vs T3 Mean ± SD	p	T1 vs T4 Mean ± SD	p
PH	7.36 ± 0.06 vs 7.35	0.4	7.36 ±0.06 vs 7.29 ±0.06	<0.0001	7.36 ±0.06 vs 7.27 ±0.06	<0.0001
pCO_2, mmHg	42 ± 5 vs 40 ±5	0.05	42 ± 5 vs 43 ±5	0.7	42 ± 5 vs 45 ± 8	0.08
HCO_3, meq/L	23.4 ± 2.7 vs 21.9 ±3.1	<0.0001	23.4 ± 2.7 vs 20.0 ±3.6	<0.0001	23.4 ± 2.7 vs 19.4 ± 2.7	<0.0001
K^+, meq/L	4.47 ± 0.6 vs 4.8 ± 0.9	0.8	4.47 ± 0.6 vs 4.5 ± 0.6	0.6	4.47 ± 0.6 vs 4.6 ± 0.7	0.6
Na^+, meq/L	134 ± 3 vs 133 ± 4	0.02	134 ±3 vs 134±3	0.7	134 ±3 vs 135 ±4	0.3
Cl^-, meq/L	103 ± 4vs 106 ± 5	<0.0001	103 ± 4 vs 110 ±4	<0.0001	103 ± 4 vs 109 ± 5	0.0001
Ca^{+2}, meq/L	1.12 ± 0.08 vs 1.08 ±0.08	0.001	1.12 ±0.08 vs 1.07 ±0.09	0.005	1.12 ±0.08 vs 1.10 ± 0.9	0.3
Lactate, meq/L	1.1 ± 0.5 vs 1.28 ± 0.6	0.4	1.1 ± 0.5 vs 1.33 ± 0.6	0.2	1.1 ± 0.5 vs 1.50 ± 0.5	0.003

DISCUSSION

Our results showed that the "biphasic fluid management" regime in robotic kidney transplantation is an effective method to achieve per-operative hemodynamic/metabolic stability and allograft function. Our study group is unique because of both, it consists of preemptive cases besides non-preemptive cases and all recipient procedures were performed using robotic surgery.

As known, transplant candidate patients have severe the metabolic condition including acidosis, hyperkalemia and hypervolemia, which make anesthesia management more difficult. On the other hand, anesthesia management of robotic surgery is also more challenging because of related factors such as patient position, intraabdominal CO_2 insufflation. In with this context in our series, perioperative hemodynamic stability and urine output was achieved after vascular anastomosis in all patients. There was no difference in the total amount of fluid given per-operatively between the two groups, except that the amount of fluid given in phase 1 was significantly less in GP. Not surprisingly, preoperative blood pH values were more acidotic, blood Na^+ and Cl^- values were significantly higher and HCO_3 values were significantly lower in GP.

Preoperative blood urea and creatinine levels were significantly higher in GP ($p < 0.05$) but all decreased to normal levels in both groups on postoperative days 1 and 7. In the five-year long-term follow-up, both groups had similar mortality and renal rejection rates, which are less.

The first objective of anesthesia management in kidney transplantation surgery is to provide hemodynamic and metabolic stability throughout the operation and also provide an "optimal" condition for allograft kidney when vascular anastomosis is completed. Because it's a minimally invasive option and has some advantages, robotic surgery has been gaining popularity and increasingly used in kidney transplantation in recent years (5). Robotic kidney transplantation has been associated with a lower risk of surgical site infection, less symptomatic lymphoceles and less postoperative pain (6). On the other hand, it is necessary to protect the patients who already have high comorbidities of ESRD from both possible complications such as hypervolemic heart failure and pulmonary oedema and some complications specific to robotic surgery such as increased intracranial pressure due to deep Trendelenburg position. In

our clinical practice, we believe we can overcome this problem by, using biphasic fluid treatment. We avoid fluid replacement except for the mandatory volumes of drugs used in induction during phase 1 as detailed before. We also limit intra-abdominal pressure levels to 8-12 mmHg.

Many variables can affect the function of the allograft kidney. Among these variables, ischemia and intraoperative hypotension are both very important. Clinical studies showed that avoiding ischemia is essential and avoiding intraoperative hypotension is also important and these vital measures support allograft kidney function (4). In other words, minimizing ischemic damage during the warm/cold ischemic phase and rewarming of a transplanted kidney and providing adequate perfusion after vascular anastomosis are the most critical factors to achieve allograft function. Therefore, intravenous fluid management becomes essential to maintain intravascular volume during transplant surgery and a dynamic fluid therapy is generally recommended according to mean arterial pressure measurements (7-9). Ischemia and/or reperfusion injury is thought to be a critical risk factor for both early and late graft dysfunction (10). It is known that delayed diuresis after reperfusion of transplanted kidney usually affects long-term outcomes of allograft, indicating possibly shorter graft functioning life and increased rejection rate (11, 12). For this reason, minimizing reperfusion damage by obtaining adequate mean arterial pressure with well-planned fluid management, positively affects graft function in the short and long term (13).

For the long-term result of our patients, we also did phone call survey and we found that there was no difference in renal rejection and mortality rate between the groups. On mean 5 years follow up of the present series, there was total of 4 patients died. One patient in the GP group died of heart failure, one in the GNP group died of MI and the other two died of covid 19 pneumonia. We believe the long-term results of our series are comparable with literature. Since the clinical status of renal transplant candidate patients may vary between hypovolemia and hypervolemia, fluid management of these patients also has a narrow safety range (14). Since the allograft kidney is denervated and its autoregulation is impaired, intraoperative fluid management should be organized to keep graft perfusion optimal while avoiding hypovolemia or hypervolemia after reperfusion (15). Allograft rejection may be caused by many factors, such as surgical kidney removal or damage during transplantation, injury during transport between donor and recipient and suboptimal allograft perfusion in the intraoperative and postoperative periods (16). A study by Fernandes et al. argued that the "flow-directed fluid" approach as a fluid therapy regimen in renal transplantation was more effective than other conventional methods (17). In their transplantation consensus, the ASA transplant committee stated that intraoperative fluid management could affect kidney transplantation outcomes and made recommendations to help anesthesiologists dealing with kidney transplant recipients. The best method of assessing fluid status is still controversial. However, it has been emphasized that an individualized approach may be the best (4). Similar to general recommendation, we have determined that hemodynamic and metabolic stability were achieved with close monitoring of arterial blood gas values and MAP in patients who were on restricted fluid therapy (phase 1) until vascular anastomosis. At the same time, the possible side effects of lithotomy and deep Trendelenburg position which had to be performed during robotic surgery, could also be compensated. During robot-assisted surgical procedures, it is necessary to combat the metabolic and respiratory difficulties caused by the deep Trendelenbug position as well (18). Intra-abdominal CO_2 insufflation and CO_2 retention with deep Trendelenburg may lead to a rapid decrease in pH and dangerous hyperkalemia (19). Both conditions are much more dangerous for patients with end-stage renal disease than normal healthy individuals because these patients are often at borderline acidosis and hyperkalemia. More importantly, preemptive cases have more severe metabolic status, as our results showed that the initial pCO_2 values and Ph values at T1,2,3 were lower in GP than in GNP, peroperative management of these patients becomes more complicated. The most crucial factor here is that GP patients are the patients with renal failure who had never been on dialysis and therefore have developed a compensation mechanism prone to metabolic acidosis. Metabolically, HCO_3 values were significantly lower in GP at all times for the same reason. In phase 1, HCO_3 values decreased

more because Cl^- values increased more due to 0.9% NaCl infusion (350 vs 800 mL) in GNP compared to GP (20). Preemptive kidney transplantation has been accepted as an ideal treatment method (21,22). Uremic toxins are better cleared with a functioning kidney allograft. The survival benefit may be greater than with maintenance dialysis treatment. Another reason may be chronic dialysis's regression of the inflammatory and/or oxidative process (23). In our study, GP patients' admission urea and Cr values were significantly higher concerning not being on dialysis. However, there was no difference between GP and GNP patients regarding early post-transplant laboratory results (day 1, day 7 urea, Cr). Both decreased to almost the same values (day1 and day 7 respectively, urea:66 and 61, Cr:1.22 and 1.25).

In fluid selection in renal transplantation, it has been argued that crystalloids should be the first choice over colloids (24). Hadimioğlu et al. Showed that all three crystalloids (isotonic, ringer lactate, plasmalyte) could be used safely in fluid management in renal transplantation (25). According to The European Renal Best Practice (ERBP, 2017) guidelines, there is no conclusive evidence that giving any fluid other than isotonic NaCl to renal transplant recipients during surgery positively affects the clinical course of the patient and the graft (26). A survey conducted in 2002 showed that 83% of transplant centres used more than 90%0,9% NaCl in renal transplantations. The reason for this preference is the belief that solutions containing potassium may potentially exacerbate hyperkalemia (27). Contrary to this belief, some studies on renal transplantation have shown that potassium concentrations increased during surgery with isotonic (0.9% NaCl) (28). Another study showed that isotonic use increased potassium levels postoperatively but not intraoperatively (29). In our study, although isotonic was used as the fluid in both groups, no significant change was determined in the follow-up of potassium values in intra-group blood gases during the perioperative period. The increase in Cl^- values in intra-group evaluations was insignificant in parallel with the administration of less fluid during Phase 1 in GP but significant during the other Phase 2 period, supporting that it is related to the isotonic we used. Despite the effect of the increase in Cl^- values on the metabolic status of the patients, it was observed that it did not cause any adverse effects on short-term hemodynamic responses and urea-creatinine values on postoperative days 1 and 7. Therefore, we think that a 0.9% NaCl solution, which has a known metabolic acidosis effect, does not have a negative effect on the allograft kidney in the short term.

The limitation of this study is that it is a single-center, retrospective study, and the number of cases relatively small. The second limitation is that we did not perform advanced hemodynamic monitoring during operation, because a conventional advanced monitorization as in open surgery is difficult during robotic surgery.

The survival rate of living kidney transplant patients is relatively high. However, this chance depends on the long-term function of the allograft kidney. In this study investigated the efficacy of biphasic fluid management in a unique patient's group which includes both preemptive and non-preemptive cases and all recipient kidney transplantations were performed by robotic surgery. Our results supported that biphasic fluid management regime is effective to achieve hemodynamic/metabolic stability of recipient patients and allograft kidney functions in robotic kidney transplantation patients.

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