Crystalloid fluids and delayed graft function in kidney transplant: A cohort study

ABSTRACT

Background: Normal saline is commonly used in the perioperative kidney transplant period; its high chloride content can cause hyperchloremic metabolic acidosis giving a possible advantage to balanced electrolyte solutions due to their lower chloride content. The evidence regarding the best practices in fluid management during kidney transplantation and its effect on the incidence of delayed graft function (DGF) is still limited. Materials and Methods: One hundred thirty-eight patients were included and followed up for seven days after surgery. Administered crystalloid type and volume were compared among patients with and without DGF, along with additional patient and surgical variables. To investigate whether intraoperative fluid type/amount influence DGF, patients were categorized into three groups: those who received mainly (>50%) lactated Ringer's solution, normal saline, or plasmaLyte. A logistic regression analysis was used to define variables independently correlated with DGF, and odds ratios (OR) with a 95% confidence interval (CI) were reported. Results: The incidence of DGF was 8.7%. Cold ischemia time independently increased the odds of DGF (OR = 1.006 (95% CI: 1.002-1.011) while fluid type (saline versus PlasmaLyte OR = 5.28, 95% CI: 0.76–36.88) or amount (OR = 1.00, 95% CI: 1.00–1.01) did not significantly modify the odds of DGF. Central venous pressure, systolic blood pressure, and mean arterial pressure were higher in the non-DGF group, but this was not statistically significant (P > 0.05). Significant intraoperative acidosis developed in patients who received normal saline compared to those in PlasmaLyte and lactated Ringer's groups; however, acid-base balance and electrolytes did not vary significantly between the DGF and non-DGF groups. Conclusion: DGF was primarily influenced by surgical factors such as cold ischemia time, whereas intraoperative fluid type or amount did not affect DGF incidence.

Key words: Delayed graft function, intraoperative fluid administration, kidney transplant

Introduction

Kidney transplant is the treatment of choice for patients with end-stage renal disease (ESRD) as the recipients will have an improved life quality with freedom from dialysis.^[1] Despite improvements in renal transplantation outcomes, delayed

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graft function (DGF) still represents a substantial complication and a prognosticator of the patient and graft outcome.^[2] DGF is defined as failure of the transplanted kidney to function normally within the first week after transplantation, necessitating dialysis. The most common cause of DGF is

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acute tubular necrosis (ATN). Any factor that causes graft oxygen consumption-delivery mismatch, like the ischemia time and preservation techniques, may cause ATN.^[3,4] The recipient's hemodynamics and fluid management also affect DGF and long-term transplant outcomes.[5-7] Normal saline has long been considered as the fluid of choice in kidney transplant. However, it was found that the administration of big volumes of normal saline causes a relative increase in plasma chloride ions compared to sodium ions leading to a reduction in the plasma strong ion difference and hence to metabolic acidosis.^[8] Renal vasoconstriction and a lower glomerular filtration rate were observed after infusion of chloride-rich fluids into denervated animal kidneys.^[9] When comparing normal saline with balanced crystalloids in non-kidney transplant patients, there was a greater incidence of serious adverse kidney events following normal saline administration.^[10]

Although balanced electrolyte solutions produce less metabolic acidosis, which is a potential benefit in ESRD, the best fluid practices for kidney transplantation are still not certain.^[11,12]

Materials and Methods

Study participants and design

This study is a retrospective cohort study involving 138 consecutive patients who underwent kidney transplantation between March 2018 and January 2020. Ethical approval was obtained from Institutional Review Board (approval number RC 19/424/R) and the requirement of consent was waived by the ethical committee as all data were collected anonymously from electronic medical records. The study involved adult patients who were receiving a kidney from a living or deceased donor.

Data were retrieved from electronic medical records and included recipient demographics (age, gender, and body mass index (BMI)) as well as comorbid conditions like hypertension, ischemic heart diseases, diabetes mellitus, and liver diseases), kidney-transplant related data as the underlying causes of kidney disease, cold ischemia time (CIT), and warm ischemia time.

Other data related to anesthesia management as monitors, type and volume of fluid administration, and blood products transfusion were collected additionally, whereas laboratory data, such as glomerular filtration rate, urea, creatinine, potassium, sodium, chloride, and bicarbonate, were abstracted. To investigate the effect of fluid type/amount on DGF, patients were categorized into those who received mainly (more than 50%) lactated Ringer's solution, normal saline, or PlasmaLyte.

Intraoperative changes in hemodynamics and arterial blood gases were retrieved from medical records. Additionally, postoperative fluid administration over the first 3 days was reported along with changes in electrolytes and kidney function parameters over the first week after surgery.

Study outcomes

DGF, identified as the need for renal dialysis within 7 days of transplantation, was the primary outcome in this study. Secondary outcomes included the immediate postoperative outcomes as urine output, sodium, potassium, bicarbonate, and chloride levels.

Sampling technique and sample size

A consecutive nonprobability sampling technique was adopted to collect data. *A priori* sample size was calculated, assuming the prevalence of DGF varying around $15\pm10\%$, using power of 80% (beta = 20%) and a level of confidence of 95% (alpha = 0.05), and the minimal sample size was 120.

Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics for Windows, Version 23.0 (Armonk, NY, USA: IBM Corp.). Descriptive statistics of numeric variables were reported as the median and interquartile range [IQR], and categorical variables as frequency and percentage. Mann–Whitney test was used to compare patients with and without DGF and Kruskal–Wallis test was used when comparing patients receiving different fluids. At the same time, Chi-square or Fisher's exact tests were used to test the association between categorical variables. To investigate the associations between DGF and possible risk factors, logistic regression models were used to estimate crude and adjusted odds ratios (OR) with 95% confidence intervals (95% CI). A *P* value of less than 0.05 was considered statistically significant.

Results

Table 1 displays the characteristics of the participating patients; a total of 138 patients were included in the current study, whose median age was 46 [IQR: 31.5,59.5] years, with male majority (64%), nonsmokers (85.6%), and BMI of 28.67 [IQR: 24.59, 32.40] kg/m². The most common cause of ESRD was diabetes (34.1%) followed by hypertension (14.5%); however, 16.7% were with unknown causes. The majority of patients were on hemodialysis (88.5%), 27.4% were insulin-dependent diabetic, 45.3% were hypertensive, and 31.7% had dyslipidemia. On average, the surgery time was

Table 1: Characteristics of Participating Pat	ients
Age (years)	46 [31.5,59.5]
Sex (male)	89 (64.0)
Smoking	
Smoker	16 (11.5)
Ex-smoker	4 (2.9)
Nonsmoker	119 (85.6)
Body Mass Index (kg/m²)	28.67 [24.59, 32.40]
Primary etiology of ESRD	
Diabetes mellitus	47 (34.1)
Hypertension	20 (14.5)
Unknown Othore	Z3 (10.7) 48 (24.8)
	40 (34.0)
Previous dialysis	8 (5.8)
Hemodialysis	122 (88.4)
Peritoneal dialysis	8 (5.8)
Diabetes mellitus	51 (37)
On oral hypoglycemic	20 (14.5)
On insulin	38 (27.5)
Hypertension	116 (84.1)
Liver disease	12 (8.6)
Dyslipidemia	44 (31.7)
Ischemic Heart disease	25 (18.4)
Duration of surgery (minutes)	240 [210,270]
Blood loss (ml)	200 [100,200]
Cold ischemia time (minutes)	240 [210,180]
Warm ischemia time (minutes)	49 [43,57]
Donor type	
Living	103 (74.6)
Deceased	35 (25.6)
Preoperative laboratory parameters	
Sodium (mmol/L)	135 [133,136]
Chloride (mmol/L)	98 [96,102]
rotassium (MMOI/L) Creatining (umol/L)	4.5 [4.2,5] 633 5 [518 8 820 2]
Glomerular filtration rate (mL/min/1.73m ²)	8 [6.10]
	101 001

Data are expressed as frequency (percentage) or as median [Q1, Q3]

240 min [IQR: 210,270], blood loss was 200 ml [IQR: 100,200], cold ischemia time was 240 min [IQR: 210,180], and 74.6% had living donors.

Table 2 shows the intraoperative fluid administration and changes in hemodynamics and blood gases in patients with and without DGF. Out of 138 patients, 12 patients (8.7%) developed DGF. PlasmaLyte was the most used fluid (100 patients, 74.6%), followed by normal saline (33 patients, 21.4%), whereas only 5 patients received lactated Ringer's solution-all of whom did not develop DGF. Neither intraoperative fluid type nor amount differed significantly between patients with and without DGF (P > 0.05). Central venous pressure (CVP) did not vary significantly between DGF and non-DGF groups at the start of surgery or at reperfusion, whereas by the end of surgery, it was higher among the non-DGF group; however, this difference was not statistically conclusive. On average, patients with DGF had lower systolic blood pressure (SBP) and mean arterial blood pressure (MAP), yet, this variation was not

statistically significant. (P > 0.05). Amongst the two groups, acid-base balance and electrolytes did not differ significantly.

At the end of surgery, laboratory outcomes were compared among different groups of patients according to the type of intraoperative fluid administration [Table 3]. The amount of intraoperative fluids in the three groups were nearly equivalent (median was around 5000 ml, P = 0.95). Significant intraoperative acidosis developed in the normal saline group. Differences among the three groups did not reach statistically significant levels in all the other outcomes.

Table 4 shows the crude and adjusted odds ratios of various factors for developing DGF. Out of all studied factors, five factors had a crude association with risk of developing DGF; having a deceased donor (OR = 3.34; 95% CI = 1.02-11.16), increasing the CIT (OR = 1.003; 95% CI = 1.001 - 1.006), higher blood loss (OR = 1.006; 95%Cl = 1.001-1.011), longer surgery (OR = 1.012; 95%Cl = 1.001-1.022), and intraoperative administration of normal saline (OR = 3.48; 95%) CI = 1.04-11.67). After adjusting these crude associations, an independent association was defined only between DGF and CIT time (OR = 1.006; 95%CI = 1.002–1.011).

The postoperative fluid administration, electrolyte changes, and kidney function parameters among patients with and without DGF are shown in Supplementary File 1. Significant difference between the two groups was evident in some parameters as early as day zero of surgery like the urine output; this discrepancy increased dramatically between the two groups with each day after the surgery as measured by all variables. Fluids administration was adjusted for each patient according to their kidney function, like urine output and creatinine level; therefore, the amount of fluids was significantly lower in the DGF group compared to those without DGF.

Discussion

In a kidney transplant, maintaining intravascular volume primarily with isotonic crystalloid solutions is critical to ensure optimal graft perfusion and avoid DGF, but different crystalloids can affect electrolytes and acid-base balance in various ways, raising the question whether this could affect the patient or the graft outcome.

The current study found no association between the crystalloid type and DGF. In one of the earliest studies comparing normal saline and balanced crystalloid solutions (lactated Ringer's solution) in kidney transplantation, insignificant difference in postoperative serum creatinine taken as a primary

Table	2: Intrao	perative	Fluid	Administration,	Hemodynamics,	and	Arterial	Blood	Gas	Changes	in	Patients	With	and	Without	Delayed
Graft	Function	(DGF)														

	DGF $n = 12$ (8.7)	No DGF <i>n</i> =126 (91.3)	Р
Total fluid (mL)	6000 [5000,6750]	5000 [4500,6000]	0.24
Normal saline	6 (50.0)	27 (21.4)	0.11
PlasmaLyte	6 (50.0)	94 (74.6)	0.11
Lacteted Ringer's	0 (0.0)	5 (4)	0.11
Albumin 5%	3 (25.0)	26 (20.6)	0.72
Packed Red Blood cell transfusion	1 (8.3)	5 (4.0)	0.43
Central Venous Pressure (mmHo)	- ()	- ()	
start	15 [12.18]	12 [9.15]	0.11
At reperfusion	22 [16.26]	18 [15.22]	0.17
End of surgery	14 [10,18]	18 [14,22]	0.05
Systolic Blood Pressure (mmHa)			
start	137 [119.5.158]	146.5 [121.157]	0.41
At reperfusion	127.5 [111.75,132]	127.5 [113,138]	0.55
End of surgery	134 [123,150]	137 [120,154]	0.95
Diastolic Blood pressure (mmHq)			
start	83 [67,91.75]	82.5 [72,95]	0.73
At reperfusion	59.5 [53,66.75]	66 [58,73.75]	0.07
End of surgery	69 [56.25,72]	65 [59,77]	0.85
Mean Arterial Pressure (mmHg)			
start	101.5 [84,122]	106 [91,126]	0.37
At reperfusion	82.5 [74.5,86]	88 [77.25,86]	0.11
End of surgery	89.5 [85.5,98.25]	90 [78,102]	0.98
рН			
start	7.47 [7.39,7.49]	7.43 [7.39,7.47]	0.22
At reperfusion	7.38 [7.29,7.45]	7.40 [7.37,7.43]	0.81
End of surgery	7.30 [7.26,7.48]	7.39 [7.34,7.43]	0.07
pCO2(mmHg)			
start	34.9 [33.88,40.78]	35.3 [31.65,37.25]	0.78
At reperfusion	38.1 [35.2,40.2]	34.55 [32.38,36.58]	0.05
End of surgery	41.1 [34.6,45.6]	36.3 [34.4,39.1]	0.06
Bicarbonate (mmol/L)			
start	25.7 [21.7,26.4]	22.9 [20.5,24.9]	0.10
At reperfusion	23.8 [20.3,25.3]	21 [19,23.2]	0.09
End of surgery	21.5 [19,22.8]	21.6 [19.2,22.8]	0.95
Base Excess			
start	2.7 [-3.7,3.3]	-1 [-3.5,1]	0.19
At reperfusion	0.1 [-6.6,0.9]	-3.3 [-5.7, -1.1]	0.24
End of surgery	-4.4 [-6.6, -2.8]	-3.3 [-6, -1.7]	0.39
Potassium (mmol/L)			
start	4.0 [3.6,4.9]	4.2 [3.7,4.6]	0.83
At reperfusion	4.2 [3.9,6.0]	4.4 [3.9,4.9]	0.78
End of surgery	4.3 [4.1,4.8]	4.5 [4.0,4.9]	0.51
Sodium (mmol/L)			
start	135.9 [134.5,137.2]	135.8 [133.9,137.8]	0.69
At repertusion	137.4 [133.6,138.7]	134.4 [132.3,136.5]	0.11
End of surgery	137.2 [134.1,138]	134.2 [133,130.3]	0.06
Blood glucose (mmol/L)	0.0.14.0.7.71	5 0 (4 0 7 0)	0.00
start	b.3 [4.6,/./]	5.9 [4.8,7.9]	0.88
At repertusion	/.4 [5./,δ.δ]	0.5 [5.3,8.9] 7.0 [5.9,10]	0.63
End of surgery	ö.9 [b.2,10.9]	/.ម [១.୪,IU]	U.64

Data are expressed as frequency (percentage) or as median [01, 03] DGF=Delayed graft function

outcome was found between the two groups; some patients in the saline group developed moderate hyperkalemia and metabolic acidosis, which required intervention and the study was stopped early due to safety concerns, concluding that although normal saline does not detrimentally affect renal function in kidney transplant patients, lactated Ringer's solution seemed safe and superior.^[11] This safety was challenged by another group of investigators who used the same study design, due to the development of hypercoagulability, vascular graft thrombosis, and graft loss in the lactated Ringer's solution group despite lower serum potassium level and less acidosis.^[13] Hadimioglu *et al*.^[12] found that normal saline, lactated Ringer's solution, and PlasmaLyte can all be used safely in kidney transplants, with PlasmaLyte

Table	3:	End	of	Surgery	Laboratory	Parameters	According	to	Intrao	perative	Fluid	Type
							_					

	Normal saline	PlasmaLyte	Lactated Ringer's solution	Р
Fluid administration amount (mL)	5250 [4750,6000]	5125 [4550,6000]	5000 [4000,7500]	0.95
Urine at end of surgery (mL)	500 [232.5,812.5]	500 [250,850]	500 [240,830]	0.81
pH at end of surgery	7.39 [7.30,7.43]	7.39 [7.34,7.43]	7.4 [7.4,7.4]	0.66
Sodium bicarbonate end of surgery (mmol/L)	20.3 [19.1,22.1]	21.9 [19.2,22.8]	21.6 [21.6,22.1]	0.39
Base excess at the end of surgery	-5.3 [-6.9, -2.7]	-3.2 [-5.9, -1.7]	-2.2 [-2.6, -1.7]	0.25
Acidosis (base excess change)	-4.0 [-0.2, -8.9]	-2.40 [-1.47, -3.1]	-2.4 [-1.5, 3.1]	0.03
Potassium at the end of surgery (mmol/L)	4.5 [4.2,5.1]	4.5 [4.1,4.9]	3.1 [3,3.7]	0.11
Sodium at the end of surgery (mmol/L)	134.1 [133.2,136.7]	134.2 [133.1,137]	135 [132.7,136.1]	0.99
Blood glucose at the end of surgery (mmol/L)	9.3 [7,12]	7.6 [5.7,9.6]	8.9 [6.8,11]	0.12

Data are expressed as median [Q1, Q3]

Table 4: Univariate	and Multivariate	Association of DGF	With Patient-Related	and Surger	v-Related Factors
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	Crude Odds Ratios (95%CI)	Adjusted Odds Ratio
Age	0.99 (0.95-1.03)	
Body mass index (kg/m²)	1.03 (0.93-1.14)	
Sex (female versus male)	1.86 (0.56-6.12)	
Preoperative ejection fraction	1.156 (0.865-1.545)	
Hypertension	0.95 (0.194-4.678)	
Diabetes mellitus	1.24 (0.37-4.14)	
Liver diseases	0.95 (0.112-8.066)	
Dyslipidemia	0.72 (0.184-2.791)	
Deceased donor versus living related	3.34 (1.02-11.16) *	0.43 (0.04-5.16)
Cold ischemia time (minutes)	1.003 (1.001-1.006) *	1.006 (1.002-1.011) *
Warm ischemia (minutes)	1.004 (0.99-1.01)	
Total fluid volume (mL)	1.00 (1.00-1.01)	
Normal saline versus PlasmaLyte	3.48 (1.04-11.67) *	5.28 (0.76-36.88)
Received albumin (yes versus no)	1.28 (0.32-5.08)	
Blood loss (mL)	1.006 (1.001-1.011) *	1.005 (0.99-1.01)
Red Blood Cells transfusion (yes versus no)	2.19 (0.23-20.4)	
Duration of surgery (minutes)	1.012 (1.001-1.022) *	1.001 (0.981-1.022)

*P less than 0.05. Data are expressed as Odds Ratio (95% Confidence Interval)

tending to have the best metabolic profile. In this study, significant intraoperative acidosis developed in the normal saline group and in the immediate postoperative serum chloride level was considerably higher. Kim *et al.*^[14] found a significantly higher serum chloride in the normal saline group, but postoperative urine output, serum creatinine, and graft failure were not significantly different between the groups. A Cochrane meta-analysis was uncertain whether lower chloride solutions had more advantage compared to normal saline in terms of improved graft outcomes.^[15]

The intraoperative crystalloid volume was similar in patients who developed or did not develop DGF, and this was similar to the findings of a recent multicenter pilot study.^[16] In the present study, CVP was slightly elevated at the end of surgery in the non-DGF group, but this was not statistically conclusive. Studies on CVP as a volume guide in kidney transplant showed inconsistent results, with many studies advising maximal hydration^[17] and high CVP to ensure good graft function,^[18] whereas other studies observed an association between high CVP and DGF^[5] and advised against supranormal volume loading, especially in cardiac patients with poor myocardial function.^[19] As a result, the target CVP in a kidney transplant seems elusive, keeping in mind the intraoperative factors that may alter its readings leading to incorrect decision making. These factors include operating table position, which is not always flat and the surgeon may left or right tilt it to have more access to the iliac vessels, the pressure effect of surgical retractors on the abdominal viscera and venous return, and the positive pressure ventilation during the procedure that can also affect venous return.^[20] Systematic reviews revealed a weak correlation between CVP and blood volume, as well as CVP's inability to predict hemodynamic responses to a fluid challenge.^[21,22]

Although statistically insignificant, the current study patients with DGF had an average lower SBP and MAP. Blood pressure targets and thresholds are different between studies.^[5,23] Campos *et al*.^[5] found that MAP more than 93 mmHg led to greater graft survival. In a previous study, Tóth *et al*.^[24] observed a significantly higher MAP in patients with good graft function. Unfortunately, since the ideal measurement to assess kidney microcirculation is still unknown, these associations do not mean that increasing blood pressure restores renal function. Furthermore, the ideal MAP that prevents acute kidney injury during different medical conditions is unknown.^[25]

Fluid requirements among transplant patients are highly variable and traditional parameters such as heart rate, blood pressure, CVP, pulmonary artery pressure, and urine output to direct fluid therapy in kidney transplantation are not very reliable. An individualized approach tailored for each patient's physiologic needs will be more beneficial than a standardized algorithm.^[25]

The incidence of DGF in our study was 8.7%, which corresponds with other published literatures that show an incidence of 1%–18% with living donors, and 10%–60% with deceased donors kidney transplant.^[26,27] In accordance with other researches, CIT was independently associated with DGF. CIT is one of the most crucial predictors of short- and long-term graft survivals.^[28] There is a significant proportionate escalation in the risk of graft failure for each added hour of CIT and shortening of CIT will reduce DGF rates and the occurrence of acute rejection and graft loss.^[29]

Despite the known limitation of the retrospective design and the relatively small sample size of the study, the detailed reporting of perioperative variables and outcomes adds to the strengths of our study. Moreover, we are planning for a future larger prospective study to confirm our results and clarify the definitive effect of fluid management on DGF.

Declaration of patient consent

Consent was waived by the ethical committee as all data were retrieved anonymously from electronic medical records.

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Conflicts of interest

There are no conflicts of interest.

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Supplementary F	ile 1	: Postoperative	fluid a	dministration,	electrolytes	and	kidney	function	parameters	changes,	over	the	first	week

Def $n = 12 (s, f_1)$ No Def $n = 12 (s, 13, s)$ P Bay 0 135 [133, 13, 8] 134 [132, 136] 0.33 Day 1 135 [123, 13, 8] 134 [132, 136] 0.33 Day 3 131 5 [122, 138, 3] 137 [134, 138] 0.33 Day 4 135 [122, 138, 3] 137 [134, 138] 0.01 Day 5 132 [130, 138, 8] 137 [134, 138] 0.01 Day 6 135 [122, 138, 3] 134 [132, 137] 0.09 Day 6 135 [128, 3, 138] 137 [134, 138] 0.01 Day 6 135 [128, 3, 138] 138 [134, 138] 0.01 Day 7 133 [127, 134, 8] 134 [132, 137] 0.09 Day 1 9 [168, 104, 8] 103 [100, 107] 0.03 Day 1 9 [168, 104, 8] 103 [100, 107] 0.01 Day 4 9 [168, 104, 8] 103 [100, 107] 0.01 Day 5 55 [54, 100, 8] 100 [101, 107] 0.01 Day 6 95 [122, 98, 8] 106 [101, 100] 0.01 Day 6 95 [122, 98, 8] 106 [103, 108]				
Sadum (mmol(1) Day 0 (155 [153,137,8] (144 [132,156] (154 [131,137,8] (154 [132,136] (154 [132,136] (154 [131,137,8] (157 [134,138] (DGF $n = 12$ (8.7)	No DGF <i>n</i> =126 (91.3)	Р
bay 0 135 [133,1378] 134 [122,156] 0.33 Day 1 135 [123,138] 134 [122,156] 0.30 Day 2 132 [123,138] 136 [123,138] 0.21 Day 3 135 [123,138] 137 [124,138] 0.01 Day 4 132 [123,138] 137 [124,138] 0.01 Day 6 135 [127,1348] 134 [132,138] 0.03 Day 7 1325 [127,1348] 134 [132,138] 0.03 Day 7 1355 [127,1348] 136 [100 [107,107] 0.06 Day 1 96 [98,104,5] 100 [100,107] 0.07 Day 2 100 [58,103,5] 100 [106,112] <0.01	Sodium (mmol/L)			
by 1 133 [132,188] 134 [123,18] 034 [122,138] 032 Day 3 1315 [123,188,1] 137 [134,138] 0.01 Day 4 13.1 [123,188,1] 137 [134,138] 0.01 Day 4 13.1 [123,188,1] 137 [134,138] 0.01 Day 4 13.1 [123,188,1] 137 [134,138] 0.03 Day 7 123 [123,180] 137 [134,138] 0.03 Day 7 123 [127,134,134] 131 [134,138] 0.03 Day 7 123 [127,134,134] 131 [132,138] 0.03 Day 1 91 [98,10,45] 100 [97,101 0.07 Day 2 100 [98,10,5] 110 [107,113] <0.01	Day 0	135 [133.137.8]	134 [132,136]	0.33
by 2 133 [12,138] 136 [13,136] 0.22 by 3 131 [12,318,3] 137 [134,139] 0.01 by 4 131,3 [12,3,18,3] 137 [134,139] 0.01 by 6 132 [12,3,18,3] 137 [134,139] 0.01 by 6 132 [12,3,134,3] 137 [134,139] 0.01 by 7 133 [12,3,134] 133 [13,137] 0.02 by 7 133 [12,3,134,3] 139 [13,137] 0.02 by 7 193 [13,0,13] 105 [10,0,107] 0.07 by 2 100 [38,104,5] 101 [07,113] <0.01	Day 1	133 [132,136.8]	134 [132,136]	0.80
bw 3 115 [172,13,18.8] 137 [134,138] 0.01 bw 4 135 [172,13,18.3] 137 [134,138] 0.01 bw 5 132 [121,13,18.3] 137 [134,138] 0.01 bw 6 135 [122,13,13,0] 135 [134,138] 0.03 bw 7 135,5 [122,13,13,0] 135 [134,138] 0.03 bw 7 135,5 [122,13,13,0] 135 [124,13,13] 0.03 bw 7 105 [123,13,13,0] 101 [105,112] -0.01 bw 3 96,5 [93,10,15] 110 [107,113] -0.01 bw 4 96 [94,101] 108 [106,112] -0.01 bw 5 95,5 [93,99,75] 100 [103,108] 0.01 bw 6 95,5 [93,99,75] 100 [103,108] 0.01 bw 7 96,5 [92,99,75] 100 [103,108] 0.01 bw 7 96,5 [93,99,75] 100 [103,108] 0.01 bw 1 5 [34,3,5,1] 4,3 [35,4,6] 4,3 [3,5,4,6] 0.01 bw 1 5 [34,3,5,1] 4,1 [3,4,4,7] -0.01 0.01 bw 2 4,1 [3,4,4,2] <td< td=""><td>Day 2</td><td>133 [132,138]</td><td>136 [133,138]</td><td>0.32</td></td<>	Day 2	133 [132,138]	136 [133,138]	0.32
bay 4 (315) 12(33,136,3] (37) [134,138] -0.01 Day 5 121 [120,136,8] (33) [134,138] 0.03 Day 6 113,12(23,136,1) (33) [134,138] 0.03 Day 7 123,5[12,1,13,4] (31) [134,138] 0.03 Day 1 19,15 [18,105,1] (10) [17,103] 0.25 Day 1 19,15 [18,105,1] (10) [17,103] 0.26 Day 2 100 [19,103] (10) [17,103] 0.01 Day 2 100 [19,112] (-0.01) 0.01 Day 4 96 [16,101] (10) [10,101] (-0.01) Day 5 95 [18,1018] (10) [10,101] (-0.01) Day 6 95 [18,293,9] (10) [10,103] (-0.01) Day 6 95 [18,293,9] (10) [10,103] (-0.01) Day 7 96 [12,52,2] 4.1 [4,4,4,5] (0.13) Day 1 5 [47,52,1] 4.1 [13,4,4,7] (-0.01) Day 2 4.1 [3,4,4,5] (-0.01) (-0.01) Day 1 5 [47,52,1] 4.1 [13,4,5,1] (-0.01)	Day 3	131.5 [128,136.8]	137 [134,139]	0.01
by 5 122 [120,188] 137 [134,138] 0.01 by 6 131 [128,158] 131 [134,138] 0.03 Day 7 133.5 [12.8,158] 131 [134,138] 0.03 Day 0 101.5 [18,106.5] 100 [17,103] 0.26 Day 1 99 [98,104.5] 100 [17,103] 0.26 Day 3 96.5 [14,30.1] 100 [16,112] -0.01 Day 3 96.5 [14,30.1] 100 [16,112] -0.01 Day 4 96 [14,101] 100 [16,112] -0.01 Day 5 95.5 [12,9.50] 100 [16,10] -0.01 Day 4 96 [14,101] 100 [16,112] -0.01 Day 5 95.5 [12,9.53] 100 [16,10] -0.01 Day 6 95.5 [12,9.54] 41 [18,45] -0.01 Day 7 86.5 [12,9.54] 41 [18,45] -0.01 Day 1 5 [41,52] 41 [18,45] -0.01 Day 3 41 [18,45] -0.01 -0.01 Day 4 41 [18,45] -0.01 -0.01 Day 5 41 [18,45] </td <td>Day 4</td> <td>131.5 [129.3,136.3]</td> <td>137 [134,139]</td> <td><0.01</td>	Day 4	131.5 [129.3,136.3]	137 [134,139]	<0.01
Bay 6 13.15.1[28.3,36] 135 [134,313] 0.03 Day 7 13.5 [124,3,134] 131 [133,137] 0.09 Chioride (mmalk) 0.00 0.07 0.07 0.07 Day 0 10.15 [98,106.5] 100 [97,103] 0.26 0.07 0.07 Day 3 95.5 [94,30.15] 110 [107,113] <0.01	Day 5	132 [130,136.8]	137 [134,138]	0.01
Bay 7 135.5 [127.8 [134.6] 134 [133.137] 0.09 Chorde (manu/L) Bay 0 10.15 [58,106.5] 100 [97,103] 0.26 Day 1 99 [98,3,104.5] 100 [10,017] 0.07 Day 2 100 [39,103.5] 100 [10,5,112] <0.01	Day 6	131.5 [128.3,136]	135 [134,138]	0.03
Chioria (mmol.) Day 0 (1) [15, 193, 106.5] [10, 109 [17, 103] 0.28 Day 1 99 [18.3, 104.5] [10, 105.5] 103 [100, 171] 0.07 Day 3 95 5 [193, 105.5] 109 [105, 112] 0.01 Day 4 96 [194, 101] 199 [105, 112] 0.01 Day 5 95 5 [193, 105, 103] 100 [101, 113] 0.01 Day 6 95 5 [193, 105, 103] 100 [101, 103] 0.01 Day 6 95 5 [193, 105, 103] 0.01 Day 7 95 95 5 [193, 105, 103] 0.01 Day 7 95 95 5 [193, 105, 103] 0.01 Day 7 95 95 2 [193, 103] 106 [103, 103] 0.01 Day 7 0 96 18 [293, 8] 106 [103, 103] 0.01 Day 7 0 96 18 [293, 8] 0.05 [103, 104] 0.03 Day 1 5 [14, 5, 2] 4.4 [4, 4] 0.33 Day 1 5 [14, 5, 2] 4.4 [4, 4] 0.33 Day 1 5 [14, 5, 2] 4.4 [4, 4] 0.33 Day 1 5 [14, 5, 2] 4.4 [4, 4] 0.33 Day 1 5 [14, 5, 2] 4.4 [4, 4] 0.33 Day 1 5 [14, 5, 2] 4.4 [1, 34, 4] 0.37 Day 6 3 3 [3, 3, 4] 4.1 [3, 4, 4] 0.37 Day 6 3 3 [3, 3, 3] 4.1 [3, 4, 4] 0.37 Day 7 3 3 5 [3, 3, 3] 4.3 [3, 4, 6] 0.01 Day 7 3 3 5 [3, 3, 3] 4.3 [3, 4, 6] 0.01 Day 7 3 3 5 [3, 3, 3] 4.3 [3, 4, 6] 0.01 Day 7 3 3 5 [3, 3, 3] 4.3 [3, 4, 6] 0.01 Day 7 3 2 0.01 [12, 2] 0.02 Day 1 17, 5 [163, 2, 2] 0.01 [16, 2, 2] 0.02 Day 1 17, 5 [163, 2, 2] 10 [16, 2, 2] 0.02 Day 2 2.05 [18, 2, 4] 19 [17, 2, 1] 0.01 Day 3 2.05 [18, 2, 4] 19 [17, 2, 1] 0.01 Day 4 2.15 [19, 3, 2, 5] 10 [16, 5, 2] 0.01 Day 7 2.25 [18, 2, 4] 19 [17, 2, 1] 0.01 Day 7 2.25 [18, 2, 4] 19 [17, 2, 1] 0.01 Day 7 2.25 [18, 2, 4] 19 [17, 2, 1] 0.01 Day 7 2.25 [18, 2, 4] 19 [17, 2, 1] 0.01 Day 7 2.25 [18, 2, 4] 19 [17, 2, 1] 0.01 Day 7 2.25 [18, 2, 4] 19 [17, 2, 1] 0.01 Day 7 2.25 [18, 2, 4] 19 [17, 2, 1] 0.01 Day 7 2.25 [18, 2, 4] 19 [17, 2, 1] 0.01 Day 7 2.25 [18, 2, 4] 19 [17, 2, 1] 0.01 Day 7 2.55 [19, 3, 77, 8] 19 32 [71, 6], 1] 0.01 Day 7 2.55 [19, 3, 77, 8] 19 32 [71, 6], 1] 0.01 Day 7 3 502 [19, 3, 77, 8] 19 32 [71, 6], 1] 0.01 Day 7 3 502 [19, 3, 77, 8] 19 32 [71, 6], 1] 0.01 Day 7 3 502 [19, 3, 77, 8] 19 52 [71, 8] 0.01 Day 7 4 503 [23, 13, 9] 0.01 Day 7 4 503 [24, 15, 103] 74 55 [50, 3] 0.01 Day 7 4 503 [24, 153, 8] 0.01 [74, 543] 0.01 Day 7 4 503 [24, 153, 8] 0.01 [74	Day 7	133.5 [127.8,134.8]	134 [133,137]	0.09
by 0 101.5 [98.706.5] 100 [97.103] 0.26 by 1 99 [98.3,104.5] 103 [100,107] 0.07 by 2 100 [98,103.5] 109 [105,112] <.0.01	Chloride (mmol/L)			
by 1 99 [06.3,104.5] 103 [100,107] 0.07 by 3 96 5,194.3,101.5] 109 [105,112] <0.01	Day 0	101.5 [98,106.5]	100 [97,103]	0.26
by 2 100 [B0 (03.5] 109 [105.112] <0.01	Day 1	99 [98.3,104.5]	103 [100,107]	0.07
Dy 3 965 [94,3,101.5] 110 [107,113] -0.01 Dy 4 96 [94,101] 109 [106,112] -0.01 Dy 5 95,5 [92,99,8] 100 [101,10] -0.01 Dy 7 95,5 [92,99,8] 106 [103,108] -0.01 Dy 7 95,5 [92,99,8] 106 [103,108] -0.01 Dy 7 95,5 [92,99,8] 40 [104,10] -0.01 Dy 7 95,5 [93,99,7] 41,4 [4,4,6] 0.13 Dy 1 54,7,5 2] 43,14,4,7] -0.01 Dy 2 47,1 [4,3,5,4] 43,13,9,4,6] -0.01 Dy 4 41,13,6,4,2] 41,13,8,4,5] -0.01 Dy 5 41,36,4,5] 41,13,8,4,5] -0.01 Dy 6 35,13,4,3,9] 41,13,8,4,5] -0.01 Dy 7 36,13,3,3,9] 21,13,2,4,5] -0.01 Dy 7 36,13,3,3,9] 113,2,9,1 0.01 Dy 7 20,116,2,2] 0.02 0.01 Dy 1 15,12,2,0 20,116,2,2] 0.01 Dy 0 15,12,2,0 <td< td=""><td>Day 2</td><td>100 [98,103.5]</td><td>109 [105,112]</td><td>< 0.01</td></td<>	Day 2	100 [98,103.5]	109 [105,112]	< 0.01
by 4 86 [94,101] 109 [106,112] -0.01 by 5 95,5 [94,100,8] 109 [104,110] -0.01 by 7 95,5 [94,90,8] 107 [103,108] -0.01 by 7 95,5 [94,90,8] 107 [103,108] -0.01 by 0 16 [47,5,2] 4.3 [4,4,7] -0.01 by 2 4.7 [4,5,5,4] 4.3 [3,9,4,6] -0.01 by 4 4.1 [3,6,4,2] 4.3 [3,9,4,6] -0.01 by 7 4.3 [3,9,4,6] 4.3 [3,9,4,6] -0.01 by 4 4.1 [3,6,4,5] 4.1 [3,8,4,5] -0.01 by 7 3.5 [3,3,3] 4.1 [3,8,4,5] -0.01 by 7 3.5 [3,2,3] 4.1 [3,8,4,5] -0.01 by 7 3.5 [1,2,4] 19 [1,7,2] 0.01 by 7 2.5 [1,2,2] 2.0 [1,8,2] 0.01 by 7 2.5 [1,2,4] 19 [1,7,2] 0.01 by 4 2.1 [19,3,2,5] 19 [1,7,2] 0.01 by 4 2.5 [18,2,4] 19 [17,5,2] -0.01 by 5 2.3 [2,0,2,5]<	Day 3	96.5 [94.3,101.5]	110 [107,113]	< 0.01
Dyp 5 95 5 [94,100.8] 100 [104,100] <0.01 Dyp 7 95 [92,93.8] 006 [103,108] 0.01 Dyr 7 95 [92,93.8] 006 [103,108] 0.01 Dyr 0 45 [4,05.2] 44 [4,4,6] 0.33 Dyr 1 5 [4,7,5.2] 4,3 [3,4,6] 0.43 [3,4,5] 0.01 Dyr 2 4,3 [3,3,4] 4,3 [3,4,5] 0.13 0.01 Dyr 5 4,1 (3,6,4,2] 4,1 [3,6,4,5] 0.01 0.01 Dyr 4 4,3 [3,3,4] 4,1 [3,6,4,5] 0.01 0.01 Dyr 5 4,1 (3,6,4,2] 4,1 [3,6,4,5] 0.01 0.01 Dyr 4 15,5 (3,3,3) 4,1 [3,6,4,5] 0.01 0.01 Dyr 5 4,1 (3,6,4,5] 0.01 0.01 0.01 Dyr 4 15,5 (3,2,3) 0.1 [13,2,0] 0.01 Dyr 5 2,1 [2,2,1 0.01 0.01 Dyr 4 2,1 [18,2,2] 19 [17,2,0] 0.01 Dyr 5 2,1 [2,2,5] 20 [18,2,2] 0.01 Dyr 4	Day 4	96 [94,101]	109 [106,112]	< 0.01
by 6 95,5 [93,99,75] 107 [103,109] -0.01 Putssim (mmol/L) 0.01 Day 0 5 [4,0,5,2] 4.4 [4,4,6] 0.01 Day 0 5 [4,0,5,2] 4.3 [3,9,4,6] -0.01 Day 2 4.7 [4,3,5,4] 4.3 [3,9,4,6] -0.01 Day 4 4.1 [3,6,4,2] 4.3 [3,9,4,6] -0.01 Day 5 4.1 [3,6,4,5] 4.1 [3,8,4,6] 0.01 Day 4 4.1 [3,6,4,5] 4.1 [3,8,4,5] -0.01 Day 5 3.5 [3,3,3] 4.3 [3,9,4,6] -0.01 Day 6 3.5 [1,2,3] 4.1 [3,8,4,5] -0.01 Day 7 3.5 [1,2,3] 4.3 [3,9,4,6] -0.01 Day 7 3.5 [1,2,4] 19 [1,7,2] 0.01 Day 1 17.5 [16,3,20] 20 [18,2,2] 0.01 Day 2 2.0 5 [18,2,4] 19 [17,5,21] 0.01 Day 4 2.1 5 [19,3,2,55] 19 [17,5,21] 0.01 Day 5 2.3 [2,02,55] 2.0 [18,5,22] 0.01 Day 4 5.5 [Day 5	95.5 [94,100.8]	108 [104,110]	< 0.01
Dey 7 96,5 [92,96,8] 106 [103,108] 0.01 Potassium (mm0/L) Day 1 5 [47,57] 4.4 [4,46] 0.13 Day 2 4.7 [4,35,41] 4.3 [33,46] <0.011 Day 3 4.3 [33,46] 4.3 [33,45] 0.19 Day 4 4.1 [3,6,42] 4.1 [3,8,45] 0.011 Day 5 4 [3,6,42] 4.1 [3,8,45] 0.011 Day 6 3.5 [34,3,3] 4.3 [3,3,45] 0.011 Day 7 3.6 [3,3,3] 4.3 [3,3,45] 0.011 Day 6 3.5 [17,21] 20 [18,21] 0.38 Day 1 17.5 [18,320] 201 [18,21] 0.01 Day 4 2.1 [3,4,25] 19 [17,20] 0.011 Day 4 2.1 [3,22,5] 19 [17,52] 0.021 Day 6 2.4 [21,28] 20 [18,22] 0.011 Day 4 2.1 [3,4,45] 0.011 0.021 Day 5 2.3 [20,255] 20 [18,22] 0.011 Day 4 2.4 [21,28] 20 [18,22] 0.011 <	Day 6	95.5 [93,99.75]	107 [103,109]	< 0.01
Petassium (mmol/L) 0 4.6 [4.0.5.2] 4.4 [4,4.6] 0.13 Day 1 5 [4.7.5.2] 4.3 [3.4.6] -0.01 Day 2 4.7 [4.3.5.4] 4.3 [3.3.4.6] -0.01 Day 3 4.3 [3.3.4.6] 4.3 [3.3.4.6] 0.01 Day 4 4.1 [3.8.4.2] 4.1 [3.8.4.4] 0.57 Day 5 4.3 [3.3.4.6] 4.3 [3.3.4.5] -0.01 Day 7 3.6 [3.3.3] 4.1 [3.8.4.5] -0.01 Day 7 3.6 [3.3.3] 4.3 [3.3.4.5] -0.01 Day 7 3.6 [3.3.2] 20 [18.21] 0.02 Day 0 15.5 [17.21] 20 [18.21] 0.01 Day 4 2.5 [19.2.4] 19 [17.20] 0.01 Day 3 2.0 5 [19.2.4] 19 [17.20] 0.01 Day 4 2.1 5 [19.3.25.5] 20 [18.22] 0.02 Day 5 2.3 [20.25.5] 2.0 [18.22] 0.02 Day 4 2.5 [19.2.4] 19 [17.52] 0.01 Day 5 2.3 [20.25.5] 2.0 [18.22] 0.01 Da	Day 7	96.5 [92,99.8]	106 [103,108]	0.01
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	Potassium (mmol/L)			
Day 1 5 [4,7,52] 4,3 [3,4,47] -0.01 Day 2 4,7 [4,52,4] 4,3 [3,9,4,6] -0.01 Day 3 4,3 [3,9,4,6] 4,3 [3,9,4,5] 0.019 Day 4 4,1 [3,6,4,2] 4,1 [3,8,4,4] 0.57 Day 6 3,5 [3,4,3,9] 4,1 [3,8,4,5] -0.01 Day 7 3,5 [3,3,3,9] 4,3 [3,8,4,6] -0.01 Day 7 3,5 [3,3,3,9] 4,3 [3,8,4,6] -0.01 Solium bicarbonate (mmol/L) U 15,5 [17,21] 20 [18,22] 0.38 Day 1 17,5 [16,3,20] 20 [18,22] 0.01 0.01 Day 2 20,5 [19,24] 19 [16,5,20] 0.14 Day 3 20,5 [19,24] 19 [17,52,1] -0.01 Day 4 21 [51,3,25,5] 20 [16,22] 0.02 Day 5 23 [20,25,5] 20 [16,22] 0.02 Day 6 24 [21,28] 20 [18,52] 0.01 Day 4 651,5 [423,74,8] 290 [19,3,43,13] -0.01 Day 4 513,5 [35,6,72,3] 93 [7,1,8,14,28]	Day 0	4.6 [4.0.5.2]	4.4 [4.4.6]	0.13
Day 2 4.7 [4.3,5.4] 4.3 [3.9.4,6] -0.01 Day 3 4.3 [3.9.4,6] 4.3 [3.9.4,6] 0.19 Day 4 4.1 [3.6,4.2] 4.1 [3.8,4.4] 0.57 Day 5 4 (3.6,4.3] 4.1 [3.8,4.5] 0.01 Day 6 3.5 [3.4,3.9] 4.3 [3.9.4,6] 0.01 Day 7 3.5 [3.3,3.9] 3.3 [3.9.4,6] 0.01 Day 1 15.5 [17.21] 20 [18.22] 0.38 Day 1 15.5 [18.20] 0.14 0.02 Day 2 20.5 [18.24.8] 19 [15.5.20] 0.14 Day 3 20.5 [18.24.8] 19 [17.5.21] -0.01 Day 4 2.15 [13.2.5.5] 19 [17.5.21] -0.01 Day 3 2.0 5 [18.22] 2.0 [18.2.2] -0.01 Day 4 2.15 [13.2.25.5] 19 [17.5.21] -0.01 Day 5 2.3 [20.2.5.6] 2.0 [18.2.2] -0.01 Day 4 5.5 [40.2.7.74.8] S.5 [40.4.8.400] 0.16 Day 1 5.5 [5.62.774.8] 2.90 [19.3.43.1] -0.01 D	Day 1	5 [4 7 5 2]	4 3 [4 4 7]	< 0.01
Day 3 143 [3.9.4.6] 43 [3.9.4.5] 0.19 Day 4 4.1 [3.6.4.2] 4.1 [3.8.4.5] 0.57 Day 5 43 [3.9.4.6] 4.1 [3.8.4.5] 0.67 Day 6 3.5 [3.4.3.9] 4.1 [3.8.4.5] 0.01 Day 7 3.6 [3.3.9] 4.3 [3.9.4.6] 0.01 Sodium bicathonate (mmol/L) U 0 19.5 [17.21] 20 [18.22] 0.38 Day 1 1.7 5 [16.3.20] 20 [18.21] 0.02 0.02 Day 2 20.5 [18.24] 19 [17.20] 0.01 Day 4 21.5 [19.3.25.5] 19 [17.20] 0.01 Day 5 21 [20.25.5] 20 [18.22] 0.02 Day 6 2.4 [21.26] 20 [18.22] 0.02 Day 6 2.4 [21.26] 20 [18.22] 0.01 Day 7 20.5 [18.27] 19 [18.22] 0.84 Creatinine (µmol/L) 0 541.5 [49.4,3/47.8] 507.5 [40.4,8.640] 0.16 Day 1 561.5 [423.794.8] 290 [19.3,43.13] <0.01	Day 2	4 7 [4 3 5 4]	4 3 [3 9 4 6]	< 0.01
Day 4 4.1 [36,4.2] 4.1 [36,4.2] 4.1 [36,4.4] 0.57 Day 5 4 (36,4.5] 4.1 [38,4.5] 0.01 Day 6 3.5 [64,3.3] 4.3 [34,4.5] 0.01 Day 7 3.8 [3.3.3] 4.3 [3.4.6] 0.01 Day 7 3.8 [3.3.3] 4.3 [3.4.6] 0.01 Day 7 3.8 [3.3.3] 2.3 [3.4.6] 0.01 Day 1 17.5 [16.3.20] 20 [16.22] 0.38 Day 1 2.7 [16.24.8] 19 [16.5.20] 0.14 Day 3 20.5 [18.24] 19 [17.5.21] 0.01 Day 4 21.5 [19.3.25.5] 19 [17.5.21] 0.02 Day 5 23 [20.25.5] 20 [18.22] 0.02 Day 6 24 [21.26] 20 [18.22] 0.02 Day 7 20.5 [18.22] 19 [17.5.21] 0.01 Day 6 24 [21.26] 20 [18.22] 0.02 Day 7 20.5 [18.22] 19 [18.22] 0.84 Creatinie (µmol/L) E 12 [18 [39.343.3] 0.01 Day 2	Day 3	4 3 [3 9 4 6]	4 3 [3 9 4 5]	0 19
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	Day 4	4 1 [3 6 4 2]	4 1 [3 8 4 4]	0.57
Day 6 3.5 [3,3,3] 4.1 [3,8,4,5] <0.01 Day 7 3.6 [3,3,3] 4.3 [3,9,4,6] <0.01	Day 5	4 [3 6 4 5]	4 1 [3 8 4 5]	0.87
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	Day 6	3 5 [3 4 3 9]	4 1 [3 8 4 5]	< 0.01
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	Day 7	3 6 [3 3 3 9]	4 3 [3 9 4 6]	< 0.01
Solumi Dearboriate (Inition) 9.5 [17,21] 20 [18,22] 0.38 Day 1 17.5 [16,3,20] 20 [18,21] 0.02 Day 2 20.5 [18,24.8] 19 [16,520] 0.01 Day 3 20.5 [19,24] 19 [17,21] <0.01	Sodium biographonata (mmal/L)	0.0 [0.0,0.0]	10 [0.0, 1.0]	\$0.01
$\begin{array}{c c c c c c c c c c c c c c c c c c c $		10 5 [17 21]	20 [19 22]	0.20
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	Day 0	19.5 [17,21]	20 [10,22]	0.30
bay 220.5 [19,24.6]19 [17,20]0.14bay 320.5 [19,24]19 [17,57]<0.01	Day I	17.5 [16.3,20]	ZU [16,Z1] 10 [16 E 20]	0.02
bay 3 $20.3 [19,24]$ $19 [17,20]$ 0.01 bay 4 $21.5 [19,3,25.5]$ $19 [17,521]$ 0.01 bay 5 $23 [20,25.5]$ $20 [18,22]$ 0.02 bay 6 $24 [21,26]$ $20 [18,5,22]$ 0.02 bay 7 $20.5 [18,22]$ $19 [18,22]$ 0.84 Creatione (µmol/L)Day 0 $541.5 [494,374.8]$ $290 [199,3,431.3]$ <0.01 Day 0 $541.5 [494,374.8]$ $290 [199,3,431.3]$ <0.01 Day 2 $546.5 [350,5,827.5]$ $127 [89,5,222]$ <0.01 Day 3 $513.5 [36,727.2]$ $98.5 [74.8,159]$ <0.01 Day 4 $568 [421.3,752.8]$ $93 [71.8,142.8]$ <0.01 Day 4 $568 [421.3,752.8]$ $93 [71.8,142.8]$ <0.01 Day 6 $471.5 [374.5,779.5]$ $92 [70.5,125]$ <0.01 Day 7 $606.5 [358.5,888]$ $100 (75,141.8]$ <0.01 Day 1 $8 [6,10.5]$ $20 [12,31]$ <0.01 Day 1 $8 [6,10.5]$ $20 [12,31]$ <0.01 Day 3 $10.5 [6.3,15.3]$ $61 [42.8,91.3]$ <0.01 Day 3 $10.5 [6.3,15.3]$ $61 [42.3,91.3]$ <0.01 Day 3 $10.5 [6.3,15.3]$ $61 [42.8,91.3]$ <0.01 Day 4 $8 [7,13.3]$ $74.5 [49,91.3]$ <0.01 Day 5 $9 [7,13.3]$ $74.5 [49,91.3]$ <0.01 Day 6 $9.5 [7,13.$	Day 2	20.5 [10,24.0]	19 [10.5,20]	0.14
Day 4 21.3 (19.3,23.3)19 (17.3,21)<0.01Day 5 23 (20,25.5) 20 (18.22)0.02Day 6 24 (21,26) 20 (18.5,22)0.03Creatinie (µm0/L) 0.16 0.16 0.16 Day 0 541.5 (494.3,747.8) 507.5 (404.8,640)0.16Day 1 651.5 (422,784.8) 290 (199.3,431.3)<0.011	Day 3	20.5 [19,24]	19 [17,20] 10 [17 E 21]	U.UI
Day 5 2.3 [20,25.3] 2.0 [16,22] 0.02 Day 7 20.5 [18,22] 19 [18,22] 0.01 Day 7 20.5 [18,22] 19 [18,22] 0.84 Creatinine (µmol/L) 0.16 0.16 Day 0 541.5 [494,3,747.8] 507.5 [404.8,640] 0.16 0.16 Day 1 651.5 [423,784.8] 290 [199.3,431.3] <0.01	Day 4	21.5 [19.3,25.5]	19 [17.3,21]	< 0.01
Day 0 24 [21,26] 20 [16.3,22] < < < <	Day 5	23 [20,23.3]	20 [10,22]	0.0Z
Day / Z05 [16,22] D16 [16,22] 0.04 Creatinine (µm0/L) E E E Day 0 541.5 [494.3,747.8] 507.5 [404.8,640] 0.16 Day 1 651.5 [423,784.8] 290 [199.3,431.3] <0.01	Day o	24 [21,20]	20 [10.3,22]	< 0.01
Creatinine (µmol/L) Soft 1.5 [494.3,747.8] Soft 5 [404.8,640] 0.16 Day 0 651.5 [423,784.8] 290 [199.3,431.3] <0.01		20.3 [10,22]	19 [10,22]	0.04
Day 0 541.5 [494.3,747.8] 507.5 [404.8,640] 0.16 Day 1 651.5 [423,764.8] 290 [199.3,431.3] <0.01	Creatinine (µmol/L)			
Day 1 651.5 [423,784,8] 290 [199.3,431.3] <0.01	Day U	541.5 [494.3,747.8]	507.5 [404.8,640]	0.16
Day 2 546.5 [350.5,87.5] 127 [89.5,222] <0.01	Day 1	651.5 [423, /84.8]	290 [199.3,431.3]	< 0.01
Day 3 513.5 [356, 722.3] 98.5 [74.8, 159] <0.01	Day 2	546.5 [350.5,827.5]	127 [89.5,222]	< 0.01
Day 4 568 [421.3,752.8] 93 [71.8,142.8] <0.01	Day 3	513.5 [356,722.3]	98.5 [74.8,159]	< 0.01
Day 5 505.5 [409.3, b51.5] 94.5 [73, 13.5] <0.01	Day 4	568 [421.3, /52.8]	93 [/1.8,142.8]	< 0.01
Day 6 47.15 (374.5,779.5) 92 [70.5,125) <0.01	Day 5	505.5 [409.3,651.5]	94.5 [73,133.5]	< 0.01
Day 7 bbb.5 [358.5,858] 100 [7,5,141.8] <0.01 GFR (mL/min/1.73 m²) <t< td=""><td>Day 6</td><td>4/1.5 [3/4.5,//9.5]</td><td>92 [70.5,125]</td><td>< 0.01</td></t<>	Day 6	4/1.5 [3/4.5,//9.5]	92 [70.5,125]	< 0.01
GFR (mL/min/1.73 m²) Day 0 8 [8,11.5] 10 [8,13] 0.17 Day 1 8 [6,10.5] 20 [12,31] <0.01	Day /	606.5 [358.5,888]	100 [75,141.8]	<0.01
$\begin{array}{c ccccc} Day 0 & 8 \ [8,11.5] & 10 \ [8,13] & 0.17 \\ Day 1 & 8 \ [6,10.5] & 20 \ [12,31] & <0.01 \\ Day 2 & 8 \ [7,14.8] & 50 \ [27,75] & <0.01 \\ Day 3 & 10.5 \ [6.3,15.3] & 67 \ [42.8,91] & <0.01 \\ Day 4 & 8 \ [7,3,13.8] & 74.5 \ [48,91.3] & <0.01 \\ Day 5 & 9 \ [7,13] & 74.5 \ [50.3,91.3] & <0.01 \\ Day 6 & 9.5 \ [7,13.3] & 74 \ [52,90] & <0.01 \\ Day 7 & 8 \ [7,13.3] & 71.5 \ [46,89.5] & <0.01 \\ Urine output (mL) \\ End of surgery & 70 \ [13.8,307.5] & 500 \ [262.5,850] & <0.01 \\ Day 0 & 370 \ [35,1390] & 4800 \ [2710,6325] & <0.01 \\ Day 1 & 540 \ [65.5,1105] & 6537 \ [4590,9157] & <0.01 \\ Day 2 & 60.05 \ [85,990] & 4930 \ [3552,6296.3] & <0.01 \\ Day 3 & 542.5 \ [153.8[2013.8] & 4335 \ [3282.5,5577.5] & <0.01 \\ Day 4 & 997.5 \ [144.5,1800] & 4010 \ [2940,5160] & <0.01 \\ Day 5 & 980 \ [88.8,2276.3] & 3550 \ [2450,4620] & <0.01 \\ Day 6 & 977.5 \ [15,2147] & 2600 \ [1670,4050] & <0.01 \\ Day 7 & 1490 \ [206,2526] & 2690 \ [1422,3790] & 0.03 \\ \end{array}$	GFR (mL/min/1.73 m ²)			
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	Day 0	8 [8,11.5]	10 [8,13]	0.17
Day 2 8 [7,14.8] 50 [27,75] <0.01 Day 3 10.5 [6.3,15.3] 67 [42.8,91] <0.01	Day 1	8 [6,10.5]	20 [12,31]	<0.01
Day 310.5 [6.3,15.3]67 [42.8,91]<0.01Day 48 [7.3,13.8]74.5 [48,91.3]<0.01	Day 2	8 [7,14.8]	50 [27,75]	<0.01
Day 48 [7.3,13.8]74.5 [48,91.3]<0.01Day 59 [7,13]74.5 [50.3,91.3]<0.01	Day 3	10.5 [6.3,15.3]	67 [42.8,91]	< 0.01
Day 5 9 [7,13] 74.5 [50.3,91.3] <0.01 Day 6 9.5 [7,13.3] 74 [52,90] <0.01	Day 4	8 [7.3,13.8]	74.5 [48,91.3]	<0.01
Day 6 9.5 [7,13.3] 74 [52,90] <0.01 Day 7 8 [7,13.3] 71.5 [46,89.5] <0.01	Day 5	9 [7,13]	74.5 [50.3,91.3]	< 0.01
Day 7 8 [7,13.3] 71.5 [46,89.5] <0.01 Urine output (mL) End of surgery 70 [13.8,307.5] 500 [262.5,850] <0.01	Day 6	9.5 [7,13.3]	74 [52,90]	< 0.01
Urine output (mL) 500 [262.5,850] <0.01 Day 0 370 [35,1390] 4800 [2710,6325] <0.01	Day 7	8 [7,13.3]	71.5 [46,89.5]	< 0.01
End of surgery70 [13.8,307.5]500 [262.5,850]<0.01Day 0370 [35,1390]4800 [2710,6325]<0.01	Urine output (mL)			
Day 0370 [35,1390]4800 [2710,6325]<0.01Day 1540 [65.5,1105]6537 [4590,9157]<0.01	End of surgery	70 [13.8,307.5]	500 [262.5,850]	< 0.01
Day 1 540 [65.5,1105] 6537 [4590,9157] <0.01 Day 2 600.5 [85,990] 4930 [3552,6296.3] <0.01	Day 0	370 [35,1390]	4800 [2710,6325]	< 0.01
Day 2 600.5 [85,990] 4930 [3552,6296.3] <0.01 Day 3 542.5 [153.8[2013.8] 4335 [3282.5,5577.5] <0.01	Day 1	540 [65.5.1105]	6537 [4590.9157]	< 0.01
Day 3 542.5 [153.8[2013.8] 4335 [3282.5,5577.5] <0.01 Day 4 997.5 [144.5,1800] 4010 [2940,5160] <0.01	Day 2	600.5 [85.990]	4930 [3552.6296.3]	< 0.01
Day 4 997.5 [144.5,1800] 4010 [2940,5160] <0.01 Day 5 980 [88.8,2276.3] 3550 [2450,4620] <0.01	Day 3	542.5 [153.8[2013.8]	4335 [3282.5.5577.5]	< 0.01
Day 5 980 [88.8,2276.3] 3550 [2450,4620] <0.01 Day 6 977.5 [115,2147] 2600 [1670,4050] <0.01	Day 4	997.5 [144.5.1800]	4010 [2940.5160]	< 0.01
Day 6 977.5 [115,2147] 2600 [1670,4050] <0.01 Day 7 1490 [206,2526] 2690 [1422,3790] 0.03	Day 5	980 [88.8.2276.3]	3550 [2450.4620]	< 0.01
Day 7 1490 [206,2526] 2690 [1422,3790] 0.03	Day 6	977.5 [115.2147]	2600 [1670.4050]	< 0.01
	Day 7	1490 [206,2526]	2690 [1422,3790]	0.03

Contd...

Supplementary File 1: Contd...

	DGF $n = 12$ (8.7)	No DGF <i>n</i> =126 (91.3)	Р
Normal Saline (mL)			
Day 0	711 [351.5,1957]	2060 [1507,2385]	0.01
Day 1	684.5 [325,1831]	3665 [2767.5,4978.8]	< 0.01
Day 2	27.5 [0,658.7]	2350 [1480,3247]	< 0.01
Half normal saline (mL)			
Day O	140 [0,687]	1750 [972,2270]	<0.01
Day 1	300 [45,742.5]	3270 [1967,4305]	<0.01
Day 2	0 [0,270]	1140 [0,1785]	<0.01