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# Effects of intraoperative different fluid therapy protocols on postoperative renal functions

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## Abstract

**Purpose** Planning intraoperative fluid therapy in patients undergoing major abdominal surgery is important. It was aimed to define the difference between fluid therapy protocols for renal function, bleeding and postoperative service follow-ups.

**Materials and methods** This is an observational case-controlled prospective study. Sixty patients aged 18–65 years who had undergone pancreatic surgery between December 2023– February 2023 were included in the study. Liberal (Group 1;  $n=30$ ) and targeted fluid therapies (Group 2;  $n=30$ ) were administered to the patients. Liberal fluid therapy was planned with 8–10 ml/kg/h crystalloid infusion. The targeted fluid therapy (TFT) group (Group 2;  $n=30$ ) began with a 2 ml/kg/h crystalloid infusion at the baseline. Additional fluid boluses were given in 250 ml of colloid infused over 10 min if PVI was  $> 13\%$  for at least five minutes. The patients were staged using the KDIGO (Kidney Disease: Improving Global Outcomes) criteria. The amount of bleeding during surgery was recorded for both groups.

**Results** No significant difference was observed in postoperative renal function. A significant difference was observed in the amount of intraoperative bleeding. The amount of bleeding was greater in patients managed with liberal fluid therapy. No significant difference was observed between the groups in the oral intake (hour), drain withdrawal (hour) mobilization (hour) and discharge (day) times and there isn't any statistically significant difference between groups in cost effectivity ( $p>0.05$ ).

**Conclusion** Kidney function was preserved during individualized targeted fluid therapy using non-invasive haemodynamic monitoring parameters.

**Keywords** Pancreatic surgery, Targeted fluid therapy, KDIGO criteria

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## Introduction

Planning ideal intraoperative fluid therapy in patients undergoing major abdominal surgery is critical because of the balance of oxygen supply consumption, fluid–electrolyte balance, adequate tissue perfusion, and prevention of excessive fluid overload [1]. Targeted fluid therapy (TFT) planned with PVI hemodynamic assessments has been associated with better outcomes, including survival [2].

Peroperative adverse effects such as pulmonary, cerebral, peripheral, and periorbital oedema, hypertension, bowel dysfunction, delayed wound healing, dilutional coagulopathy may occur because of excessive and uncontrolled fluid administration. Reduced cardiac output and impaired tissue perfusion, shock and multi-organ failure may result from inadequate fluid replacement [3].

Renal function is sensitive to volume changes, and hypovolemia may increase the risk of postoperative kidney damage [2]. TFT protocols are an effective method for preventing intraoperative fluid overload and insufficiency, as well as reducing postoperative complications in surgical patients [4].

The Pleth Variability Index (PVI) is a non-invasive cardiovascular parameter. It is a measurement based on respiratory changes and arterial pulse pressure. Using the PVI, a patient's intravascular status can be evaluated. This is an effective method for evaluating perioperative fluid therapy in patients without vasoactive agents and vascular pathology. Effective cardiac stabilization can be achieved using less fluid. The PVI correlates with the SPV (systolic pressure variation) and PPV (pulse pressure variation) invasive parameters.

In this study it was aimed to define the difference between fluid therapy protocols for renal function and postoperative service follow-ups.

## Methods

This study was initiated after Ankara City Hospital Clinical Research Ethics Committee No. 2 approved this study (Reference number E2-21-1078) and after receiving informed consent to participant was obtained from all participants. The clinical trial number is NCT06188299 (12.18.2023).

This is an observational case-controlled prospective study. Patients below the age of 18 years, presenting with cardiac arrhythmia, a cardiac ejection fraction of less than 30%, pulmonary pathology that precluded the generation of tidal volume in excess of 6 ml/kg, hepatic and renal dysfunction, and American Society of Anaesthesiologists (ASA) physical status ASA-3 were excluded from the study. Sixty patients aged 18–65 years who had undergone pancreatic surgery between December 2023– February 2023 were included in the study. Patients received either liberal (under MAP 65; Group 1;  $n=30$ )

or targeted fluid therapy (Group 2;  $n=30$ ) according to the clinician's preference. Liberal fluid therapy was planned with 8–10 ml/kg/h crystalloid infusion. The goal-directed fluid therapy group (Group 2;  $n=30$ ) began with a 2 ml/kg/h crystalloid infusion at the baseline. PVI measurements were followed by Masimo SET version V7.1.1.5 pulse oximetry (Masimo Co., Irvine, California), which was used to continuously, automatically, and non-invasively measure plethysmographic variations throughout the respiratory cycle. Additional fluid boluses were given in 250 ml of colloid infused over 10 min if PVI was  $>15\%$  for at least five minutes. It was used 0.9% NaCl and succinylated gel (Gelofusine®, B. Braun). Patients whose mean arterial pressure could not be brought to 65 mmHg despite a PVI value of 13% or less were administered nor-epinephrine. Gray zone of PVI is 13–9. Values under 9 indicate fluid overload.

After providing 100% oxygen support with a mask for 3 min, lidocaine (1–1.5 mg/kg), propofol (2–3 mg/kg) (propofol 1%, Fresenius, Germany), remifentanyl (1 µg/kg) (Ultiva®, GSK, USA), and rocuronium (0.6–1.2 mg/kg) (Esmeron®, MSD, Germany) were administered intravenously (iv) during induction. After waiting for sufficient myorelaxation, patients were intubated endotracheally. During maintenance anesthesia, 0.05–0.25 µg/kg/min remifentanyl infusion and 2–2.5% sevoflurane (Sevorane®, liquid 100%, Abbvie, England) were administered with a 50:50% medical air: O<sub>2</sub> mixture according to the IBW.

The basal ventilation tidal volume was set to 6–8 ml/kg, the frequency was 12, and the fraction of inspired oxygen (FiO<sub>2</sub>) was 50%. However, the ET-CO<sub>2</sub> (End-Tidal Carbon Dioxide) was maintained between 35 and 40 mmHg by changing the respiratory rate and inspiration expression ratio. The peak pressure remained below 38 cmH<sub>2</sub>O. At the end of surgery, 2 mg/kg of sugammadex (Bridion®, MSD, Netherlands) was used to reverse the residual effects of the intraoperative muscle relaxant. This was done according to the intravenous IBW.

The patients' systolic arterial pressure (SAB), diastolic arterial pressure (DAP), mean arterial pressure (MAP), peak heart rate (PHR), oxygen saturation (SO<sub>2</sub>), and end-tidal CO<sub>2</sub> (ETCO<sub>2</sub>) values were followed throughout the operation and recorded at five-minute intervals. Systolic and diastolic blood pressures were recorded for all patients before and after intubation and before and after extubation. All patients' creatinine, BUN, and potassium values were recorded at 0, 1, 24, 48 and 72 h postoperatively. Patients were staged according to the KDIGO criteria. The amount of bleeding during the operation was recorded for both groups. In our study, lactate concentrations were followed by blood samples taken from patients.

All analyses were performed in SPSS v23 (SPSS Inc., Chicago, IL, USA). Compliance control of normally

**Table 1** The amount of bleeding and the distribution of the amount of fluid administered according to the groups

	Group 1	Group 2	
	Median (IQR)	Median (IQR)	p-value
Amount of Bleeding (cc)	500(0-1500)	325(0-1800)	0,038
Amount of Crystalloid (cc)	3500(2000–6000)	2800(2000–4000)	<b>0,003</b>
Amount of Colloid (cc)	500(0-1000)	500(0-1000)	0,637
Total Fluid (cc)	4600(3000–7000)	3525(2000–4800)	<b>0,008</b>

Mann–Whitney U test results were considered significant at  $p < 0.05$ .

distributed numerical data was performed with the Shapiro–Wilk test. None of the variables met the assumption of a normal distribution. Continuous numerical variables were analysed with the Mann–Whitney U test. The mean, standard deviation, median, minimum, and maximum values of these variables are given. Chi-square analysis was performed for categorical variables. The frequency and percentage values of these variables are given and  $p$  values  $< 0.05$  were considered to indicate statistical significance.

**Results**

There was no difference in demographic data between the groups. There was no significant difference between the groups in terms of the blood pressure measured for all patients. ( $p > 0.05$ ). A significant difference was observed in the amount of intraoperative bleeding. The amount of bleeding was greater in patients managed with liberal fluid therapy (Table 1).

No significant difference was observed in postoperative renal function. The patients were staged according to the KDIGO criteria, and no significant difference was observed between the groups ( $p = 0.26$ ) (Table 2).

The patients were analysed according to the postoperative service follow-ups. No significant difference was observed between the groups in the oral intake (hour), drain withdrawal (hour) mobilization (hour) and discharge (day) times and there isn't any statistically significant difference between groups in cost effectivity ( $p > 0.05$ ) (Table 3).

BUN and creatinine levels were not significantly different between the groups ( $p > 0.05$ ). Group 2s' urine output

**Table 2** Staging of patients according to KDIGO criteria

	Group 1			Group 2		
	Count	Column N %		Count	Column N %	p value
KDIGO Staging	0	17	70,80%	21	80,80%	0,26
	1	2	8,30%	0	0,00%	
	2	4	16,70%	2	7,70%	
	3	1	4,20%	3	11,50%	

Fisher's exact test was considered significant at  $p < 0.05$ .

**Table 3** Postoperative service follow-ups

	Group 1	Group 2	
	Median [min-max]	Median [min-max]	p-value
Oral Intake (hour)	24(6–72)	16(6–72)	0,82
Drain withdrawal (hour)	96(48–312)	96(0–168)	0,459
Mobilization (hour)	8(6–16)	8(6–16)	0,649
Cost (TL)	7881(3393–11534)	7565(714-14263)	0,608
Discharge (day)	7(4–14)	6(2–12)	0,494

\*\* Mann–Whitney U test results were considered significant at  $p < 0.05$ .

was significantly higher than the group1 (Figs. 1, 2 and Table 4).

**Discussion**

In this study, we concluded that there was no significant difference between different fluid therapies and postoperative renal functions.

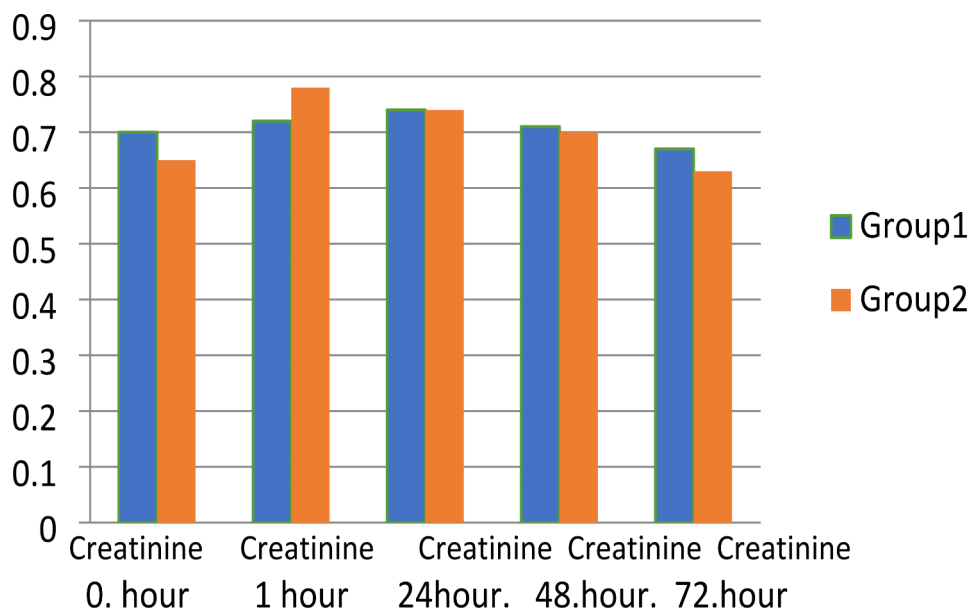
A recent clinical trial, the RELIEF study, showed no significant difference in mortality between restrictive and free fluid therapy groups for patients following major abdominal surgery [5]. Another study suggested that administering more fluid is associated with biomarkers indicating endothelial damage and glycocalyx damage, and other factors may be responsible for the results of the RELIEF study [6].

Forget et al., observed no difference in the occurrence of postoperative kidney disease with targeted fluid therapy [7].

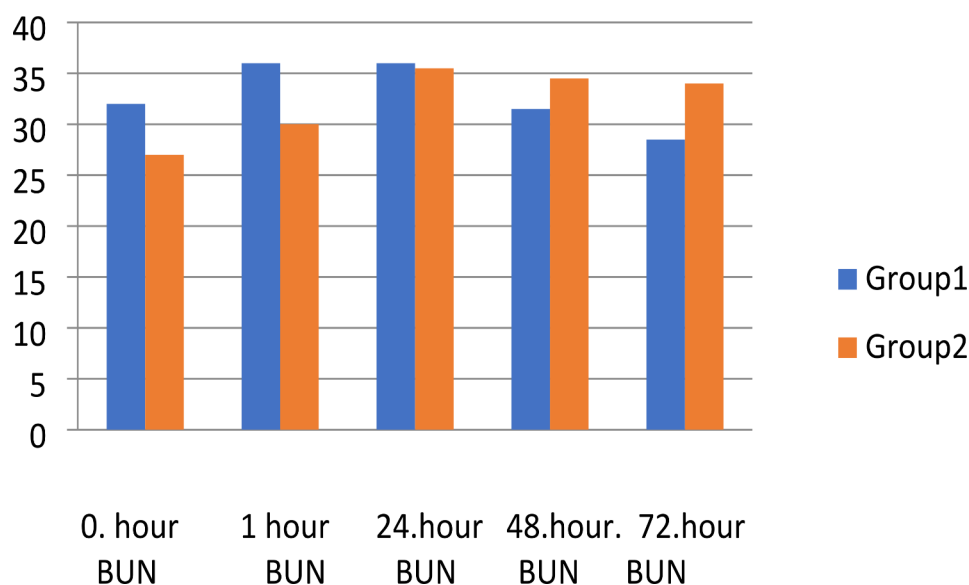
In a previous study, PVI-guided fluid management resulted in less perioperative administration of crystalloids and lower lactate levels during and after major abdominal surgery [7]. Hemodynamic parameters were stable, and lactate levels were lower in gynecological surgery patients who were followed up for PVI [8].

In a study by Çevikalp et al., the “pleth variability index” (PVI) provided more accurate results in evaluating the intravascular volume of the patient compared to fluid resuscitation based on central venous pressure monitoring of fluid therapy [9]. Delayed graft function has been associated with a PVI  $> 9$  in renal transplantation patients [10].

In morbidly obese patients who underwent laparoscopic Roux-en-Y gastric bypass (RYGB) surgery, there



**Fig. 1** Graph showing the relationship between creatinine median values and groups



**Fig. 2** Graph showing the relationships between the median BUN concentration and the groups

was no difference between the inflow and outflow creatinine values in the group with PVI monitoring and those who underwent fluid resuscitation with mean arterial pressure monitoring [11].

In orthopedic surgery, no difference was found in acute postoperative renal failure in fluid treatment structured with PVI follow-up. ( $p=0.808$ ) [12]. In accordance with the literature, no difference in acute renal damage was found in this study.

In this study revealed that bleeding was greater in the group that received liberal fluid therapy. In a previous study by Gottin et al., targeted and restrictive fluid

protocols were associated with a lower incidence of complications than liberal fluid protocols [13].

A study comparing liberal and restrictive fluid therapy revealed that a positive fluid balance might be associated with damage to the endothelium and glycocalyx layers [5]. The greater amount of bleeding in the liberal fluid protocol group was associated with dilution of coagulation factors and damage to the endothelium and glycocalyx layer.

It has been highlighted in the literature that the administration of substantial quantities of fluid may potentially result in the exacerbation of bleeding due to the development of secondary coagulation disorders. In individuals

**Table 4** BUN, Creatinine, and urine output of the groups

Variables	Group1	Group2	p-value
	Median(IQR)	Median(IQR)	
Creatinine 0.hour	0.7(0.41–1.45)	0.65(0.36–0.93)	0.252
Creatinine 1.hour	0.72(0.44–1.94)	0.78(0.48–1.19)	0.975
Creatinine 24.hour	0.74(0.39–2.55)	0.74(0.1–1.75)	0.748
Creatinine 48.hour	0.71(0.38–2.19)	0.7(0.4–2.26)	0.991
Creatinine 72.hour	0.67(0.33–1.84)	0.63(0.41–2.36)	0.399
BUN 0.hour	32(13–73)	27(8–79)	0.206
BUN 1.hour	36(17–62)	30(12–68)	0.08
BUN 24.hour	36(17–90)	35,5(11–83)	0.357
BUN 48.hour	31.5(19–91)	34,5(9–66)	0.352
BUN 72.hour	28.5(17–108)	34(10–64)	0.542
Urine output (mL)	600(400–850)	1150(750–1800)	<b>0.012</b>

\*\* Mann-Whitney U test results were considered significant at  $p < 0.05$

who are not pregnant and have experienced significant blood loss, the implementation of restrictive fluid management has been demonstrated to prevent the progression to a state of dilution coagulopathy [14].

Another investigation examined the impact of haemodilution on the results of global coagulation tests and clotting factors. The findings revealed a notable decline in the levels of dilution-dependent coagulation factors and aPTT, exhibiting a nearly linear reduction. The measurement of critically low activities for coagulation factors and a critically low level of fibrinogen at dilutions of between 60 and 75% indicates a notable decrease in the examined substances [15].

In their study, Bickell et al. compared the coagulation parameters in patients with penetrating torso injuries who were treated with either immediate or delayed fluid resuscitation. The patients who received immediate fluid administration exhibited diminished levels of haemoglobin, platelet count, PT and APTT in contrast to those who received delayed fluid administration [16].

On the contrary, the superiority of restrictive fluid resuscitation in women with mild postpartum haemorrhage has not been proven, it does not increase the need for blood transfusion, alter coagulation parameters or cause an increase in adverse events. It can be considered as an alternative treatment option to liberal fluid resuscitation [17].

However in a large systematic metaanalysis, the postoperative rebleeding did not differ in both groups: RR, 0.76 (95% CI, 0.28–2.06). The study concluded that a restrictive fluid policy in elective surgery, in comparison to a liberal fluid policy, resulted in a 35% reduction in patients with complications. It is therefore recommended that a restrictive fluid policy should be advised as the preferred fluid management policy [18]. In this study, the PVI-guided targeted fluid therapy protocol was associated with less bleeding.

Our study had several limitations. Although we included all patients who underwent pancreatic surgery in our hospital within a particular time period, our sample size was limited to 60 patients. Four patients died during the course of the study, all of whom were undergoing liberal fluid therapy. The mortality rate was not significant since the sample size is small. In addition to these parameters, we looked at lactate follow-up in patients, but we primarily evaluated the parameters for the KDIGO criteria.

## Conclusion

In conclusion, targeted fluid therapy does not impair postoperative renal functions, and not enhanced the recovery however optimization of tissue perfusion in high-risk surgical procedures should be based on an individualized targeted fluid therapy approach.

## Author contributions

ATDÖ and HG: reviewed the manuscript NT and UCE: collecting data. KY and YY: Prepared figures and tables. EÖ and CC: Writing main manuscript.

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## Data availability

Data is provided within the manuscript.

## Declarations

### Ethics approval and consent to participate

Ankara City Hospital Clinical Research Ethics Committee No. 2 approved this study (Reference number E2-21-1078). All the authors declare their approval of the Helsinki Declaration.

### Consent for publication

Informed consent to participant was obtained from all participant.

### Competing interests

The authors declare no competing interests.

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