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Differences in serum lactate levels, AKI incidence, and intraoperative fluid therapy based on GDFT and standards in major laparotomy surgery patients

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***Abstract*---**This study aimed to analyze the differences in serum lactate levels and the incidence of Acute Kidney Injury (AKI) in GDFT-based and standard liquid therapy in major laparotomy surgery with general anesthesia at Dr Soetomo Hospital. The type of research and research design used is a randomized clinical trial. The research design is an experimental study design. The observed study variables were then followed during surgery up to 48 hours after surgery for data retrieval and measurement. Patients covered by the study were patients who underwent elective major laparotomy at GBPT of Dr Soetomo Hospital. The results revealed that the administration of crystalloid solutions in the standard group was more than that of the GDFT group, while the administration of colloidal solutions in the standard group was less than that of the GDFT group. Intraoperative fluid balance in the standard group were larger compared to the GDFT group. The standard group had higher levels of postoperative serum lactate than the GDFT group ($p < 0.001$). The incidence of AKI in the standard group was 4 (18.2%) and no AKI incidence was found in the GDFT group. There is an association between an increase in serum lactate levels and the occurrence of postoperative MMR ($r = 0.408$). We

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discovered that the incidence of MMR only occurred in the standard group, which was also associated by an increase in serum lactate levels as a sign of increased tissue hypoperfusion. These findings are considered for the selection of the GDFT technique as a form of intraoperative fluid therapy in patients at high risk for major laparotomy surgery.

***Keywords*---**serum lactate levels, acute kidney injury incidence, intraoperative fluid therapy, goal directed fluid therapy (GDFT), major laparotomy surgery patients.

Introduction

Surgical morbidity and mortality have decreased throughout time due to advancements in surgery and anesthesia. In 2% to 3% of individuals undergoing major surgery, myocardial infarction, stroke, and death are undesirable events. To avoid myocardial infarction, acute kidney injury (AKI), and mortality, it is possible to prevent intraoperatively low arterial blood pressure (BP). During surgery, blood pressure is maintained with the use of fluid therapy and vasoactive medications. The objective of fluid treatment is to increase stroke volume (SV) and treat hypovolemia. In all types of surgical procedures, fluid administration in excess might have negative consequences (Heming et al., 2020). Untreated hypovolaemia leads to reduced organ perfusion, anaerobic metabolism, and lactic acid production. Lactic acid buildup produces metabolic acidosis. As a result of this condition, cell dysfunction and death are possible, and it can escalate to multiple organ dysfunction syndrome (MODS) (Auer et al., 2019). An increase in intraoperative serum lactate (mean 2.7 2, OR 1.44, CI 1.15–1.82) has been associated with increased incidence of postoperative AKI (Mitchell et al., 2018).

A multicenter study by Shah et al in 2020, which examined 22,109 moderate to high risk patients undergoing non-cardiac surgery reveals that 16,561 (74.9%) patients were hypotensive with mean arterial pressure (MAP) <60 mmHg within one minute and 8,463 (38.3%) patients were hypotensive for three to five minutes (Shah et al., 2020). Intraoperative hypotension is common and is associated with major postoperative complications such as myocardial injury, acute kidney injury (AKI) and death. Incident of AKI was found in 2,477 (7.4%) patients who underwent surgery and 82.4% of them occurred within three days postoperatively. Meanwhile, myocardial injury occurred in 770 patients (2.3%), and 926 (2.8%) had postoperative cardiac complications. The study also found 506 (1.5%) patients died within 30 days postoperatively. Patients who were not hypotensive compared with patients who were hypotensive (MAP < 55 mmHg) for more than 20 minutes had a 1.5 times greater risk of AKI or myocardial injury and a nearly doubled risk of cardiac complications (Walsh et al., 2014).

Thus far, intraoperative fluid management has been the focus of much discussion. Some experts recommend administering as few intraoperative fluids as possible, as excessive fluid administration can raise the risk of postoperative complications. Nonetheless, inadequate intraoperative fluid administration leads negative side effects, such as acute prerenal tubular necrosis in the postoperative phase. Intraoperative fluid administration has become the standard of care for all anesthetic surgical procedures. Excess fluid in postoperative patients can result in complications such as lung congestion, decreased tissue oxygenation, slowed wound healing, increased edema, and delayed recovery (Makaryus et al., 2018). Intraoperative fluid management is crucial, as insufficient or excessive fluid resuscitation might have negative impacts. Hypovolemic circumstances can lead to hypoperfusion and multiple organ dysfunction (MODS), whereas hypervolemia can disturb the healing process by causing tissue edema (Bellamy, 2006; Miller et al., 2014). In abdominal surgery, the liberal use of intravenous fluids is associated with a considerable increase in complications when compared to the limited strategy. Patients in the liberal group who received more than six liters of fluid on the day of surgery experienced roughly four kilograms of postoperative weight gain (indicating tissue edema). Patients in the restrictive group who received fewer than four liters of liquids on the day of surgery gained approximately one kilogram at most (Brandstrup et al., 2003). Although, according to one of the findings of the study, Restrictive versus Liberal Fluid Therapy in Major Abdominal Surgery (RELIEF), the group of patients who received restrictive fluids had a significantly higher risk of acute kidney injury than the group that received liberal fluids (8.6% vs. 5%, P 0.001) (Myles et al., 2017).

The American Society for Enhanced Recovery (ASER) and the Perioperative Quality Initiative (POQI) suggest that the Goal Directed Fluid Therapy (GDFT) protocol should be implemented. However, advanced hemodynamic monitoring equipment is required to improve clinical decision making when using the GDFT method (Thiele et al., 2016). The application of GDFT-based intraoperative fluid therapy has been tested on patients having surgery at Dr. Soetomo Hospital, although it is only recommended for high-risk patients, especially those having open heart surgery. Implementing GDFT at Dr. Soetomo's Regional General Hospital (RSUD) is challenging due to the limitations of sophisticated hemodynamic monitoring technology used in standard practice. As a result, this study aims to analyze the differences in serum lactate levels, the prevalence of MMR, and the number of intraoperative fluid therapy administrations using Goal Directed Fluid Therapy (GDFT) and standards in major laparotomy surgery performed under general anesthesia at Dr. Soetomo Hospital.

Literature Review

Major Laparotomy

According to the consensus in 2020 by the European Surgical Association (ESA), major surgery is a complicated process that might have consequences on the pathophysiological process and the outcome. Comorbidities, the clamping of blood arteries or organ ischemia, a significant risk of intraoperative bleeding, the requirement for the administration of norepinephrine, a lengthy duration of operation, and the requirement for blood product transfusions are all associated with major surgery (David et al., 2020). Laparotomy is a surgical procedure that is performed by making a wide incision in the abdomen in order to get access to the peritoneal cavity. This procedure is also known as celiotomy. A surgical procedure is considered major if there is a danger of blood loss greater than 500 milliliters, considerable fluid changes, and an overnight stay in the hospital following the operation. Malignancies of the stomach, small intestine, colon, and gynecology are the types of operations that fall under the category of major laparotomy operations (Reddy & Rajaratnam, 2020).

Intraoperative Hypotension

Intraoperative hypotension was defined as a decrease in systolic blood pressure (TDS) below 80 mmHg, a decrease in BP more than 20% below baseline, and a combination of definitions consisting of an absolute BP below 100 mmHg and/or a 30% decrease below baseline (Bijker et al., 2007). Organ function might be affected by intraoperative hypovolemia. Peripheral vasoconstriction, which is a result of adaptive mechanisms that occur in a healthy body to maintain blood flow to the heart and brain, produces ischemia in other organs and tissues that need blood flow for postoperative repair. Fasting, the use of intestinal hypertonic preparations, anesthetic drugs, and positive pressure ventilation are some of the conditions that might result in intraoperative hypotension in patients undergoing surgery. Functional intravascular volume deficits are frequently found in anesthetized patients (Bundgaard-Nielsen et al., 2010). Since an excessive rightward shift in the Starling myocardial performance curve has the potential to exacerbate postoperative cardiac morbidity, excessive fluid administration can result in a number of issues following surgery, including an increase in cardiac function performance (Monnet et al., 2016).

Acute Kidney Injury (AKI)

Acute kidney injury (AKI) is a syndrome characterized by the sudden and rapid impairment of kidney function in controlling the composition of body fluids and electrolytes, as well as the creation of metabolic waste products. Etiology, includes renal illness (such as acute interstitial nephritis, glomerular kidney disease, and acute vasculitis), non-specific diseases (such as ischemia and toxic damage), and extrarenal pathology (eg, prerenal azotemia and acute postrenal obstructive nephropathy). AKI is commonplace, risky, and require treatment. Even immediate renal function decline has a poor prognosis. Detection and treatment of AKI as soon as possible can improve outcomes. RIFLE and AKIN are two similar definitions based on SCr and urine output that have been suggested and validated. A single definition is required for practice, research, and public health (Kellum et al., 2012). AKI is defined as an increase in serum creatinine 0.3 mg/dl (≥ 26.5mol/l) in 48 hours or an increase in serum creatinine 1.5 times the baseline in the previous 7 days or a decrease in urine output < 0.5 ml/kg/hour for 6 hours (Kellum et al., 2012).

Lactic Acid

The accumulation of lactate and protons in body fluids causes lactic acidosis, which is frequently associated with a poor clinical outcome. The effects of lactic acidosis are dependent on its severity and clinical state. In the presence of hypovolemia or sepsis, lactic acidosis nearly triples the risk of mortality, and the greater the lactate level, the worse the prognosis. Despite the fact that hyperlactatemia is frequently linked to tissue hypoxia, it can also be produced by other processes. Controlling the triggering circumstance is the only treatment that is successful. Even so, breakthroughs in the identification of the condition's pathophysiological characteristics and cellular dysfunction-causing causes may lead to the development of new treatments. This summary of lactic acidosis stresses its pathophysiological characteristics as well as its diagnosis and treatment (Jeffery & Nicholas, 2014). As a result of impaired mitochondrial oxidation, there is excess and underused lactate synthesis in both generalized and localized tissue hypoxia. Although systemic oxygen delivery is sufficient to prevent hypoxia, microcirculatory failure can result in localized hypoxia and hyperlactatemia. Acidemia decreases hepatic lactate metabolism; severe hypoxia and acidemia can transform the liver into a lactate-producing organ (Jeffery & Nicholas, 2014).

Standard Intraoperative Fluid Therapy

Fluid responsiveness can be predicted by intraoperative monitoring with routine hemodynamic measurements (e.g., noninvasive blood pressure and heart rate) and, in certain cases, with one or more invasive monitors of dynamic hemodynamic parameters (Suminar, 2022). Other typical clinical measures for assessing volume status in conscious patients, such as thirst, weakness, etc., cannot be applied to anesthetized individuals (Joshi, 2020). Regardless of the monitor employed, determining intraoperative intravascular volume status is difficult because cardiovascular reactions to anesthetic medicines, intravascular volume loss owing to surgery, and poor or unknown preoperative volume status are continually changing (Joshi, 2020).

Goal-Directed Fluid Therapy (GDFT)

The concept of Goal Directed Fluid Therapy (GDFT) was introduced in 1983 by Shoemaker and colleagues, who demonstrated that regulating oxygen administration based on physiological goals could reduce mortality in critically ill patients. GDFT is based on optimizing hemodynamic measurements such as pulse, blood pressure, stroke volume (SV), pulse pressure variation (PPV), and stroke volume variation (SVV) utilizing noninvasive cardiac output (CO) monitoring instruments such as pulse-contour arterial waveform analysis, transesophageal echocardiography, or esophageal Doppler. Inotropes and vasopressors are also included in the GDFT protocol (Butterworth et al., 2018). In cardiac surgery, GDFT can reduce mortality and major complications. A randomized controlled trial (RCT) (OPTIMISE, Optimization of Peri-operative Cardiovascular Management to Improve Surgical Outcome) studied the management of GDFT compared with standard treatment in high-risk patients undergoing gastrointestinal surgery. The main results obtained from the OPTIMISE study were complications occurred in 36.6% of the intervention and 43.4% of the usual care group, with an RR of 0.84 (95% CI 0.71 to 1.01; P = 0.07) supports GDFT. A meta-analysis of 38 trials, with 6,595 participants, concluded that GDFT reduced the incidence of postoperative infection (RR 0.81, 0.69 to 0.95) and reduced length of hospital stay (mean reduction 0.79 (95%, CI 0.96 – 0.62 days). GDFT can also help reduce costs associated with postoperative complications. In addition, adequate oxygen delivery before surgery can reduce postoperative morbidity. Current guidelines recommend the use of GDFT in high-risk surgery (Heming et al., 2020).

In patients undergoing major laparotomy surgery, general anesthesia must be administered. Vasodilation owing to general anesthetic medicines, decreased stroke volume due to bleeding, decreased cardiac output due to vagal reflexes, and decreased stroke volume due to the use of mechanical ventilation can all contribute to intraoperative hypotension. Risk variables such as age, ASA status, gender, type of anesthetic, duration of surgery, amount of bleeding, and number of blood products supplied may potentially worsen intraoperative hypotension. Intraoperative hypotension circumstances can result in hypoxia of numerous tissues, leading to an increase in lactate levels, and acute kidney damage (AKI) can occur 48 hours after surgery if the kidneys were hypoxia. Intraoperative fluid administration is a therapy given to treat hypotension due to intravascular fluid loss. This fluid administration can be given based on standard fluid therapy or based on goal directed fluid therapy (GDFT). The concept of intraoperative fluid administration of fluid responsiveness is a concept that has been used in recent years. In this study, we compared GDFT-based intraoperative fluid administration compared to standard fluid therapy. The final results studied were differences in the amount of intraoperative fluid given, and the impact of tissue hypoxia in the standard monitoring group compared to GDFT-based monitoring which showed an increase in serum lactate levels and the incidence of AKI 48 hours postoperatively. This study is designed to test the hypothesis that there are differences in serum lactate levels, the incidence of acute kidney injury (AKI), and the amount of intraoperative fluid administration based on GDFT and standard in major laparotomy surgeries carried out at Dr. Soetomo Surabaya Hospital.

Conceptual Framework

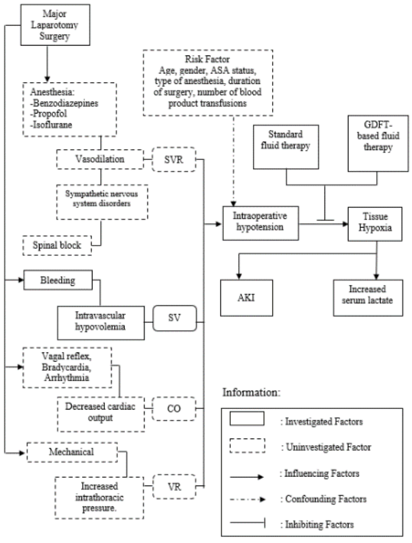

Figure 1. Conceptual Framework

Methods

The type of research and research design used is a randomized clinical trial. The research design is an experimental study design. The research variables were observed and then followed during the operation up to 48 hours after the operation for data collection and measurement. Patients covered by the study were patients who underwent elective major laparotomy at GBPT of Dr Soetomo Hospital. The intended sample in this study were patients who met the following criteria:

- Inclusion criteria:
  - Patients with age > 17 years and < 60 years.
  - American Society of Anesthesiologists (ASA) physical status class II and III.
  - The patient underwent a laparotomy under general anaesthesia.
  - The patient/guardian is willing to sign the informed consent form.
- Exclusion criteria:
  - Patients who refuse to be used as research samples
  - Patients under regional anaesthesia.
  - Patients with pregnancy, acute myocardial infarction, acute/chronic heart failure, pulmonary edema and acute/chronic renal failure.
  - Drop-out patients.
- Drop out criteria:
  - Emergency conditions that occurred during the study such as refractory hypotension or cardiac arrest.
  - The monitoring instrument is not in accordance with the clinical condition so that it requires other supporting examinations.
  - The patient requires postoperative intensive care.
  - Incomplete data.

As for the sample size formula calculation :

$$n = \frac{2\sigma^2 (z_{1-\alpha/2} + z_{1-\beta})^2}{(\mu_1 - \mu_2)^2}$$

Information

n : Minimum sample size
$Z1-\alpha$: Standard normal distribution (table Z) value at an alpha (0.05) = 1.96
$Z1-\beta$: Standard normal distribution (table Z) value at a beta (99% = 1.64)
$\sigma 2$: Estimation of variance in population
$\mu 1 - \mu 2$: Estimated difference in mean value in population 1 and population 2

If SD : 283
Mean 1 : 485
Mean 2 : 791
2075906.88
93636
22.1700 minimum sample size for each group
Equivalent to 22 samples per group

To determine the sample included in the GDFT (G) and standard (S) groups, a systematic random sampling method was used. The sample of odd serial numbers is group G and the sample of even serial numbers is group S. Meanwhile, the independent variable of this study includes: Standard monitoring-based fluid therapy, GDFT-based fluid therapy, intraoperative fluid volume volume, duration of intraoperative hypotension. Meanwhile, dependent variable includes: Serum levellactate, the incidence of AKI. As for cofounding variable in this study that covers: age, gender, American Society of Anesthesiologists (ASA) status, comorbidities, type of anesthesia, duration of surgery, amount of bleeding and number of blood product transfusions. Furthermore, there are research instruments in the form of Data Collection Sheet (research form), Continuous Non-Invasive Arterial Pressure (CNAP): LiDCO, Standard monitoring (pulse oximetry, EtCO2, NIBP, ECG), and Serum lactate and creatinine levels examination. The research carried out at the Integrated Surgery Center (GBPT) of Dr. Soetomo Surabaya Hospital in January – April 2022.

Operational Framework

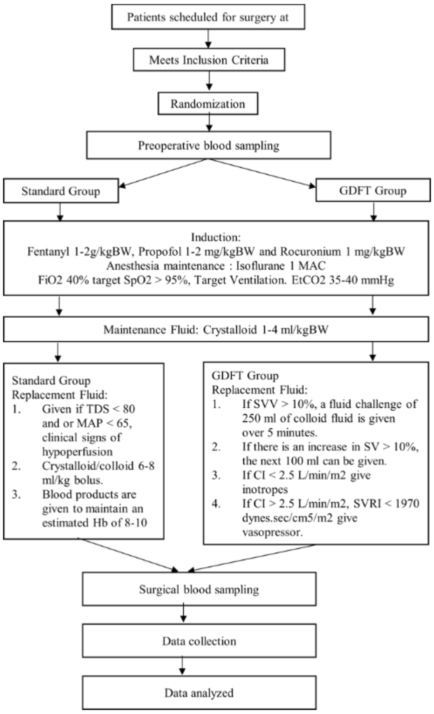

Figure 2. Research Framework

A special Data Collection Sheet is used to collect data. In addition, the data/research results are presented as tabulations and texts/writings that explicate graphs/diagrams. In this study, a two-group difference test with an independent sample t test will be performed on the details relating to the amount of fluid, lactate levels, the incidence of AKI, and hypotension, if the data satisfy the normal distribution assumption. The normality test was carried out by Saphiro Wilk because the sample size was less than 50. If the data did not adhere to the normal distribution, the Mann Whitney test will be applied. The chi square test was conducted on the nominal scale. 0.05 is used as the level of significance. Spearman's correlation test was used to determine the existence of a correlation.

Results and Discussions

Results

There were 44 patients who were the subjects of this study. Based on Table 1, the demographic characteristics of the subjects include: age with a mean of 44.64 (±8.62 years, as many as 3 (6.8%) patients are men, as many as 41 (93.2%) are woman, average body weight 56.16 (±10.02) kg, with an average BMI of 23.94 (±4.15). There were no significant differences between the two groups (Table 1). Meanwhile, there were significant differences in the characteristics of comorbid anemia, preoperative lactate anemia, preoperative serum lactate and duration of intraoperative hypotension (Table 2).

Table 1
Demographic characteristics of research subjects

Category	Total	Standard	GDFT	P-value
Age, years. Mean (±SD)	44,64 (±8,62)	45,64 (±8,57)	43,64 (±8,76)	0,448
Gender				
Man, n (%)	3 (6,8%)	2 (9,1%)	1 (4,5%)	1,000
Woman, n (%)	41 (93,2%)	20 (90,9)	21 (95,5%)	1,000
Body weight, kg. Mean (±SD)	56,16 (±10,02)	56,5 (±11,09)	55,82 (±9,07)	0,251
BMI, kg/m^2. Mean (±SD)	23,94 (±4,15)	24,36 (±4,80)	23,51 (±3,45)	0,501

Table 2
Clinical, laboratory and intraoperative characteristics of research subjects

Category	Total	Standard	GDFT	P-value
PS ASA				
ASA 2, n (%)	30 (68,2%)	14 (68,2%)	16 (72,7%)	0,440
ASA 3, n (%)	14 (31,8%)	8 (31,8%)	6 (27,3%)	0,440
Comorbid				
Hypertension, n (%)	18 (40,9%)	9 (40.9%)	9 (40,9%)	1,000
DM, n (%)	7 (15,9%)	4 (18,2%)	3 (13,6%)	1,000
Anemia, n (%)	12 (27,3%)	9 (40,9%)	3 (13,6%)	0,042
Hypoalbumin, n (%)	7 (15,9%)	4 (18,2%)	3 (13,6%)	0,680
Preoperative Laboratory				
Lactate, mmol/L. Mean (±SD)	1,41(±0,33)	1,49 (0,068)	1,33 (0,071)	0,036
Creatinine, mg/dL. Mean (±SD)	0,70 (±0,10)	0,72 (0,017)	0,68 (0,02)	0,179
Intraoperative				

Operation duration, minutes. Mean (±SD)	179,32 (±56,66)	178,64 (±15,13)	180,0 (±8,36)	0,447
Bleeding, ml. Mean (±SD)	854,55 (±420,94)	850,0 (±99,89)	859,1 (±80,69)	0,759
Hypotension Period				
< 5 minutes, n (%)	31 (70,3%)	12 (54,5%)	19 (45,5%)	0,021
5-10 minutes, n (%)	13 (29,5%)	10 (86,4%)	3 (13,6%)	0,021

Differences in intraoperative fluid administration, fluid outflow and fluid balance in research subjects

The provision of crystalloid solutions was higher in the standard group than in the GDFT group, whereas the provision of colloid solutions was lower in the standard group (Table 3). The administration of blood product transfusions did not differ significantly between the two groups. The standard group received more intraoperative fluids than the GDFT group, but the difference is not significant (Table 3). The intraoperative fluid balance of the standard group was significantly greater than that of the GDFT group (Table 3).

Table 3
Comparison of intraoperative fluid, fluid output and fluid balance in research subjects

	Standard Mean (±SD)	GDFT Mean (±SD)	P-value
Incoming Liquid			
Crystalloid	1543.18 (±737,321)	1115.91 (±208.38)	.011
Colloid	95.45 (±180,548)	236.36 (±268,231)	.044
Blood product transfusion	182,091 (±267.353)	111.0 (±254,087)	.434
Liquid Out			
Blood loss	850 (±468,534)	859(±378,480)	.759
Urine production	295.45(±143.849)	294.32 (±89,620)	.990
Total Liquid			
Incoming liquid	1820.73 (±943,644)	1421.05 (±463,281)	.076
Liquid balance	675.27 (±469.262)	267.64 (±264.394)	.002

Differences in serum lactate levels in pre and postoperative blood in research subjects

Distribution of pre- and post-operative serum lactate data on abnormal research subjects using the Shapiro-Wilk normality test with p value = 0.000, so that statistical significance was carried out by the Mann-Whiteney test. Serum lactate levels in pre and postoperative blood were significantly different with p = 0.036 and p < 0.001 (Table 4). Likewise, the serum lactate delta in the two groups was significantly different with p value = 0.029 (Table 5).

Table 4
Pre and postoperative serum lactate levels in research subjects

Fluid therapy	Standard	GDFT	P value
	Mean (±SD)	Mean (±SD)	
Preoperative lactate	1,48 (±0,32)	1,32 (±0,33)	0.036
Postoperative lactate	2,08 (±0,65)	1,63 (±0,62)	< 0.001

Table 5
Analysis of differences in serum levels of lactate pre and postoperative standard and GDFT groups

Fluid therapy	Standard		GDFT		P value
	Mean	SD	Mean	SD	
Preoperative lactate	0.60	0.54	0.30	0.49	0,029

Distribution and characteristics of research subjects with postoperative AKI

There were 4 (18.2%) patients experiencing postoperative AKI in the standard group, whereas none of the patients had AKI in the GDFT group (Table 6).

Table 6
Distribution of postoperative AKI incidence in research subjects

Group	AKI		Normal		P-value
	n	(%)	n	(%)	
Standard	4	18.2	18	81.8	0,036
GDFT	0	0	22	100	

Table 7
Research subjects with AKI characteristic

Code	L/P	ASA	Comorbid	Postoperative lactate	ΔLactate	Hypotension
STD01	P	3	DM, hypokalemia, obesity st 1	3.5	1.1	10
STD05	P	3	Pleural effusion, anemia, hypoalbumin, underweight	2.8	1.3	8
STD10	P	3	Pleural effusion, anemia, hypoalbumin, underweight	2.6	1.2	9
STD18	P	2	Hypertension, overweight	1.9	0.7	8

Based on the data above, research subjects with postoperative AKI had the following characteristics, namely female patients, between the ages of 22-59, had three ASA levels of 3 and one patient was ASA 2, two out of four had comorbid anemia, delta lactate with a range of 0.7- 3.5 mmol/L and had periods of hypotension lasting 8 to 10 minutes (Table 6).

The relationship of delta lactate with the incidence of AKI in research subjects

There is a relationship between serum lactate delta and the incidence of AKI using Spearman's test with p value = 0.006; with a correlation coefficient of 0.408. The greater the change in serum lactate levels, the higher the incidence of AKI with sufficient correlation strength (Table 8).

Table 8
The relationship between pre- and postoperative changes in lactate levels on the incidence of AKI in research subjects

Characteristics	Lactate		p value	r value
	Mean	SD		
AKI	1.1	0.141	0.006	0.408
No AKI	0.385	0.081		

Discussion

Analysis of Standard Intraoperative Fluid Administration and GDFT

The amount of intraoperative crystalloid solution in the standard group was greater than that in the GDFT group with p value = 0.011, while the amount of colloid solution in the standard group was smaller than the GDFT group with p value = 0.044. These findings are similar with previous research that discover the amount of crystalloid solution in the control group was more than in the GDFT group, while the amount of colloid solution was less in the standard group compared to the GDFT group (Sujatha et al., 2019).

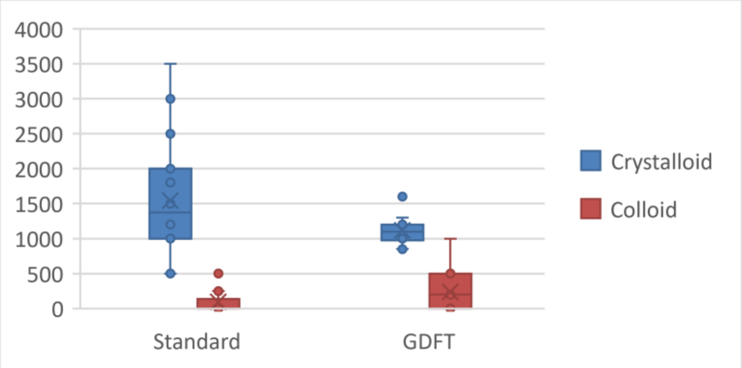

Figure 3. Comparison of intraoperative administration of crystalloid and colloid solutions in the standard and GDFT groups

Total fluid balance in the standard group was greater than that in the GDFT group with p = 0.002. In a study conducted by Sujatha et al, showed that the intraoperative fluid balance in the control group had a more positive fluid balance than the GDFT group which was clinically and statistically significant (Sujatha et al., 2019). Provision of standard / traditional fluid therapy does not have adequate ability to assess and direct fluid therapy. A healthy patient can lose 25% of blood volume before a decrease in blood pressure or an increase in pulse rate occurs, whereas a more sensitive monitor will show a decrease in stroke volume and gastric mucosal pH, which will indicate ischemia (Doherty & Buggy, 2012). Meanwhile, stroke volume is used as an indication of fluid response in the GDFT technique. This fluid therapy management uses an algorithm to maximize cardiovascular contractility according to the Frank-Starling curve using a colloid bolus as an intervention (Doherty & Buggy, 2012).

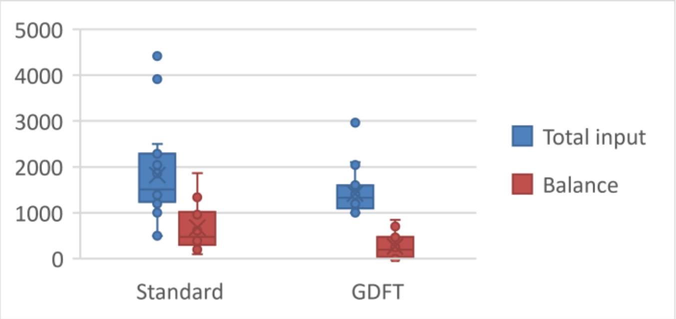

Figure 4. Comparison of total fluid and intraoperative fluid balance in standard and GDFT groups

Analysis of Differences in Serum Lactate Levels in Pre and Postoperative Blood in Research Subjects

Pre and postoperative lactate serum levels were significantly different in the two groups. Even so, the difference in preoperative serum lactate in the two groups was not clinically significant because it was still within the normal range (< 2 mmol/L). Meanwhile, postoperative serum lactate in the standard group was higher than in the GDFT group with p value < 0.001, this result indicated that the tissue hypoperfusion condition in the standard group was greater than in the GDFT group. Furthermore, Cesur et al showed that serum lactate levels in standard fluid therapy were greater than with GDFT (Cesur et al., 2019). In another study by Deng et al, serum lactate concentrations were significantly lower in patients on GDFT fluid therapy (MD – 0.21 mmol/L, CI (-0.39, -0.03), P = 0.02) (Deng et al., 2018). Laktat is the result of anaerobic glycolysis of pyrivate (Embden-Meyerhof pathway). The primary source of lactate in the body is skeletal muscle, which generates about 20 mmol/kgBW on a daily basis. In generalized or localized tissue hypoxia, lactate is overproduced and not utilized as a result of impaired oxidation at the mitochondrial level (Jeffery & Nicholas, 2014). GDFT uses a patient fluid responsiveness approach by measuring hemodynamic changes according to the Frank-Starling curve (Kendrick et al., 2019). GDFT is aimed at optimizing oxygen delivery to tissues using physiological targets related to cardiac output and fluid administration (Butterworth et al., 2018).

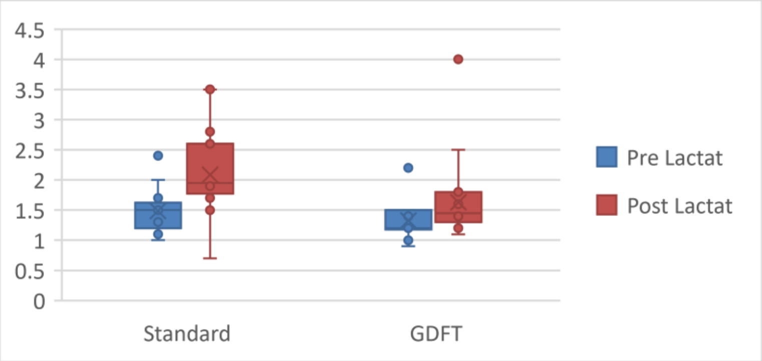

Figure 5. Comparison of Pre and Postoperative Lactate Serum on Research Subjects

Analysis of the incidence of AKI in research subjects

In this study, the incidence of AKI in the standard group was 18.2%, whereas it was not found in the GDFT group. The prevalence of AKI in this study was higher than in previous studies, which reported that administration of fluids by the standard method was 9.9% (Sujatha et al., 2019). In a meta-analysis by Giglio et al, it was found that GDFT improves renal perfusion and oxygenation in high-risk patients undergoing major laparotomy and orthopedic surgery (Giglio et al., 2019). However, Zhao et al did not find a beneficial effect of GDFT on kidney function. This could be due to differences in patients, GDFT protocol and study design in each study (Zhao et al., 2022). In current investigation, there were 4 subjects in the standard fluid therapy group who experienced AKI, in all 4 subjects a 5-10 minute period of intraoperative hypotension was found. These results are in line with previous research which found a decrease in MAP from 55 to 59 mmHg for more than 5 minutes was statistically at risk for AKI (adjusted odds ratio, 1.65; 95% CI, 1.21-2.25; P = 0.002) (Walsh et al., 2013).

Analysis of the Relationship between Increased Serum Lactate and AKI Incidence in Research Subjects

According to the findings of this particular research project, there was a correlation between increased levels of serum lactate and the occurrence of AKI, and the correlation coefficient was adequate. The likelihood of developing AKI is equal to the difference of the change in serum lactate levels, which means the greater the change in serum lactate levels will increase the incidence of AKI. According to Radovic et al, an increase in serum lactate levels in patients with AKI after major surgery was revealed. Furthermore, absolute lactate levels could serve as a reliable biomarker of AKI in cardiac surgery patients at low risk for AKI with an odds ratio (OR) of 2.7 [1.4-4.9] 24 hours after CPB. Serum lactate concentration 4 mmol/L increases risk of AKI (OR 6.3 [1.9–20.5]) (Radovic et al., 2019). Likewise, Wang et al found that there was a relationship between an early-phase increase in serum lactate and the incidence of AKI in patients with severe brain injury (Wang et al., 2022).

Conclusion

Based on statistical analysis and discussion, the researchers came to the following conclusions in this study:

- In the standard group, crystalloid solutions were administered at a higher rate than in the GDFT group, while colloidal solutions were administered at a lower rate. Intraoperative fluid balance in the standard group were higher compared to the GDFT group.
- The standard fluid therapy group had a higher postoperative serum lactate level, whereas the GDFT group had a lower serum lactate level. Therefore, tissue hypoperfusion that occurred in the standard group was greater.
- The incidence of AKI in the standard group was 4 (18.2%) and there was no AKI incidence in the GDFT group.
- There is an association between increased serum lactate levels and the incidence of postoperative AKI, hence the higher the increase in serum lactate levels, the greater the incidence of AKI.

Suggestion

Based on the findings and conclusions, following suggestion may be taken into account:

- Consider the GDFT technique in performing intraoperative fluid management in high-risk patients to reduce the occurrence of AKI.
- A standard GDFT fluid therapy protocol is required in high-risk patients undergoing surgery.
- Carry out further restrictions for further research samples so that there is no bias in the research sample.
- Conducted a follow-up multicenter study with a larger sample to determine differences in serum lactate, the incidence of AKI and the relationship between serum lactate levels and the incidence of AKI in patients undergoing major laparotomy surgery with standard fluid therapy and GDFT.

Research Limitations

This research does have some restrictions on its implementation. First, despite the fact that research on the topic has been limited, the subjects of the study discovered a significant difference in comorbid preoperative anemia. Previous studies also have revealed that lower hemoglobin levels during surgery can increase the risk of postoperative acute kidney injury (AKI). Anemic conditions can reduce oxygen delivery to the kidneys, especially in the susceptible renal medulla (Mitchell et al., 2018), which means that it can be biased in this study. Because oxygen delivery is related to hemoglobin concentration, anemic conditions can reduce oxygen delivery to the kidneys. Furthermore, there weren't that many people involved in this study, and it was only conducted at one specific area, so it's possible that the results can't be generalized to the general public. In spite of these limitations, it is expected that this research will serve as a reference for future research concerning changes in serum lactate levels and the incidence of AKI carried on by intraoperative fluid administrations.

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