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Impact of postoperative intravenous fluid administration on complications following elective hepato-pancreato-biliary surgery

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ABSTRACT

Background: The impact of perioperative intravenous fluid administration on surgical outcomes has been documented in literature, but not specifically studied in the context of hepato-pancreato-biliary (HPB) surgery. This study aimed to investigate the impact of postoperative intravenous fluid administration on intensive care unit (ICU), in this subgroup of patients.

Methods: A single-center retrospective cohort of 241 HPB patients was assessed,

focusing on intravenous fluid administration in ICU, during the first 24 hours. Intravenous fluid variables were compared to hospital stay and postoperative complications. Data were assessed using Spearman's correlation test for bivariate correlations and logistic regression for multivariate analysis.

Results: The median volume of intravenous fluid administered in the first 24 hours postoperatively was 4380 mL, of which 2200 mL was crystalloid, 1500 mL colloid and 680 mL "other" fluid. Patients with one or more complications had a higher median total intravenous fluid input (4790 vs. 4300 mL), higher colloid volume (2000 vs. 1500 mL), lower urine output (1595 vs. 1900 mL) and greater overall fluid balance (+3040 vs. +2553 mL) than those without complications. There were correlations between total intravenous fluid volume administered ($r = 0.278$, $P < 0.001$), intravenous colloid input ($r = 0.278$, $P < 0.001$), urine output ($r = -0.295$, $P < 0.001$), positive fluid balance ($r = 0.344$, $P < 0.001$) and length of hospital stay. Logistic regression model was constructed to predict the occurrence of one or more complications; total intravenous fluid volume and overall fluid balance were both independent significant predictors (OR = 2.463, $P = 0.007$; OR = 1.001, $P = 0.011$; respectively).

Conclusions: Administration of high volumes of intravenous fluids in the first 24 hours post-HPB surgery, along with higher positive fluid balance is associated with a higher rate of complications and longer hospital stay. Moreover, lower urine output is associated with longer hospital stay. Whether these are the cause of complications or the result of them remains unclear.

Keywords: Intravenous fluids; Hepato-pancreato-biliary surgery; Postoperative outcome

Introduction

Administering the optimal volume of intravenous fluid perioperatively is a crucial element of preferred outcomes for patients; either excessive or insufficient volumes is associated with harm [1,2]. Inappropriately high positive fluid balance results in physiological dysfunction that affects the cardiopulmonary system [3,4], coagulation cascade [5], gastrointestinal tract [6] and tissue oxygenation [7]. Consequently, the administration of high volumes of intravenous fluid has been associated with both increased postoperative morbidity and increased length of hospital stay [8,9]. In contrast, inadequate intravascular resuscitation risks hypo-perfusion and organ failure [10], leading to equally harmful postoperative complications. Thus, ensuring precise individualised intravenous fluid management in the perioperative period is essential for patients' preferred outcomes.

Hepato-pancreato-biliary (HPB) surgery can be complex, prolonged and involve major shifts of fluids between body compartments. Immediate postoperative care plays a pivotal part in the recovery of these patients and intravenous fluid titration is an easily modifiable component of this. Goal-directed fluid therapy (GDFT) has been suggested as a strategy to individualize the prescription of intravenous fluids in the perioperative period, aiming to deliver the optimal amount of fluid at the right time, according to evidence-based physiological targets [11], aiming for reduced complications, shorter length of hospital stay and overall cost savings [12,13] for patients. Whilst previous GDFT studies have included HPB operations, none have focused specifically on this subgroup [14]. This study aimed to retrospectively review intravenous fluid administration in a single intensive care unit (ICU) in the first 24 hours post-HPB surgery and to assess the correlation of these values with length of hospital stay and postoperative complications.

Methods and patients

Permission for this audit was granted by the hospital's Governance Facilitator. Using the Health Research Authority decision tool (<http://www.hra.nhs.uk/research-community/before-you-apply/seek-advice-and-support/>), this project was classified non-research and therefore did not require NHS Research Ethics Committee approval.

Data were collected retrospectively from ICU charts in patients who underwent HPB surgery within a period of 12 months, recorded for a maximum of 24 hours postoperatively or until discharge from ICU, with the use of a pre-defined pro-forma and finally transferred to a computerized database. A total of 365 patients were initially identified as being potentially eligible for the audit; 124 were excluded for reasons including: not being admitted to the ICU on the day of surgery, liver transplantation, under 18 years of age, and inability to access patient records. Complete data was collected for the remaining 241 patients. Postoperative complications were routinely and prospectively collected and graded according to the Clavien-Dindo classification system [15].

Data were assessed for normality using histograms, normality (Q-Q) plots and the Kolmogorov-Smirnov normality test. None of the data were found to be normally distributed therefore were described by median with interquartile range (IQR), 95% confidence interval (CI) and range. Correlation was performed using Spearman's correlation and comparison of independent groups with the Mann-Whitney *U* test. Pearson's Chi-square test with Monte Carlo correction for continuity was used to compare sets of categorical data. Finally, following the removal of outliers by calculating z-scores for each of the continuous data sets being entered (14 cases in total),

logistic regression analysis was conducted. A model was constructed to predict the occurrence of one or more complications, using age, gender, American Society of Anesthesiologists (ASA) grade, total intravenous fluid input, urine output and overall fluid balance as predictors. Statistical significance was determined as $P < 0.05$. Analysis was performed using SPSS software version 23.0 (IBM Corporation, Chicago, IL, USA).

Results

Complete data were collected on 241 patients (146 males; median age 63 years, range 19-84 years); their demographics are shown in Table 1. The median length of ICU stay was 1 (range 1-54) days, whilst for total length of hospital stay this was 10 (range 3-154) days. The median (range) total intravenous fluid volume administered in the first 24 hours postoperatively was 4380 (1000-11585) mL of which 2200 (200-3900) mL was crystalloid, 1500 (0-7000) mL colloid and 680 (0-3054) mL “other” fluid (primarily for the dilution of intravenous drugs) (Fig. 1). Thirty patients received a blood transfusion during the first 24 hours in ICU, whilst fresh frozen plasma was given to three patients, platelets to one of those and additionally to two more. The median urine output in the first 24 hours was 1760 mL, surgical drain loss 200 mL and overall fluid balance +2857 mL (Fig. 1). Central venous pressure (CVP) monitoring alone was used in 124 patients (51.5%), along with other readings of standard monitoring including heart rate and systolic and diastolic blood pressure. Mixed venous oxygen saturation (SVO₂) was used in addition to CVP in 107 patients (44.4%). LiDCO Rapid (LiDCO, London, UK) was used in 10 patients (4.1%) and parameters obtained included stroke volume, stroke volume variation, cardiac output and cardiac output index. Other parameters taken into consideration included age, cardiac and renal comorbidities as

well as measured and ideal body weight. There were correlations between total intravenous fluid volume ($r = 0.278$, $P < 0.001$), positive fluid balance ($r = 0.344$, $P < 0.001$), intravenous colloid volume ($r = 0.278$, $P < 0.001$) and urine output ($r = -0.295$, $P < 0.001$) with length of hospital stay. No correlation was seen between length of hospital stay and intravenous crystalloid volume. ASA grade was correlated to length of hospital stay ($P < 0.001$), and also to volume of colloid received ($P = 0.009$), total intravenous fluid received ($P = 0.011$), urine output ($P = 0.025$) and overall fluid balance ($P = 0.002$).

Of the 241 patients, 137 had no complications, 69 developed one complication, 25 developed 2 separate complications, and 10 developed 3 or more distinct complications. When looking into the first complication each patient developed, wound infection was the commonest one ($n = 20$, 19%), followed by chest infection (18, 17%), bile leak (13, 13%), pancreatic leak (11, 11%) and delayed gastric emptying (10, 10%). Fig. 2 summarizes the above and also presents complications with lower incidence in this cohort. A further subgroup analysis was done between patients with no complications and patients with complications independently of the number of complications. Colloid volume, total intravenous fluid volume and positive fluid balance were greater and urine output volume was lower in the subgroup of patients that developed complications as compared to those that didn't, whilst crystalloid and other fluid volumes were similar between these subgroups (Table 2). According to the Clavien-Dindo classification system, 71 patients had a minor postoperative complication (defined as grade 1 or 2) and 38 had a major postoperative complication (defined as grades 3-5). There were no differences in the volume of intravenous fluid received by those with or without minor complications. However, those patients with major complications had greater overall positive fluid balance (3373 vs. 2665 mL, $P = 0.011$) and lower urine output (1395 vs.

1810 mL, $P = 0.001$). Whilst there was a trend for a greater number of patients with one or more complications as ASA grade increased, this was not statistically significant (35.0% in ASA 1, 41.0% in ASA 2, 50.7% in ASA 3 and 60% in ASA 4; $P = 0.263$). The type of operation, i.e. hepatic resection or pancreatic resection, was not significantly correlated with postoperative morbidity, thus further stratification according to this parameter was not deemed necessary. Creation of any type of anastomosis was correlated with postoperative complications ($P = 0.001$).

Amongst different outcomes, complications and hospital stay were correlated with the method of guidance of fluid administration. Complications as classified according to the Clavien-Dindo system were correlated with the followed method ($P = 0.009$). Although in parameters with more than one groups the interpretation of this finding is challenging, based on Fig. 3, it can be argued that the combined use of CVP and SVO_2 was associated with relatively higher number of more severe complications, while the use of LiDCO was associated with fewer complications. Moreover, patients monitored with a combination of CVP and SVO_2 tended to have longer hospital stay than any of the two methods alone (12 days versus 9 days for CVP versus 9 days for LiDCO) ($P = 0.01$). Median hospital stay for patients monitored exclusively with CVP was 9 days (IQR 6-14 days), patients monitored with LiDCO had a median length of hospital stay of 9 (7-10) days too while patients monitored with both CVP and SVO_2 had a median stay of 12 (8-20) days. However, a causative relation cannot be securely established.

A test of the full logistic regression model against a constant model was statistically significant ($\chi^2 = 19.7$, $P = 0.006$, degrees of freedom = 2), indicating that the predictors reliably distinguished between those patients with and those without complications. Within the model, total intravenous fluid volume and calculated 24 hours fluid balance were both predicative (OR = 2.463, $P = 0.007$; OR = 1.001, $P = 0.011$;

respectively) whilst the other predictors did not reach statistical significance (Table 3).

Discussion

This retrospective study of patients who underwent elective HPB surgery demonstrated a consistent association between high positive fluid balance in the first 24 hours postoperatively and both increased length of hospital stay and the occurrence of postoperative complications. Both total volume of intravenous fluid administered and urine output were independently correlated with length of hospital stay. The use of colloids, but not crystalloids, was associated with longer hospital stay and a higher rate of postoperative complications. In this series, there was very limited use of cardiac output monitoring postoperatively and in the majority of cases intravenous fluid administration was guided by CVP and SVO₂.

The median overall volume of fluid received in the first 24 hours postoperatively (not including intraoperative input) was 4480 mL, which for a 70 kg person was 64 mL/kg per day. This falls outside of the maintenance fluid volume of 25-30 mL/kg per day recently recommended by the National Institute for Health and Care Excellence and is likely to dramatically exceed the accompanying recommendations for sodium and chloride prescriptions of 1 mmol/kg per day [16]. The reason for the relatively high volume of fluid given postoperatively in this ICU setting is unclear but may be related to the mode of patient monitoring used. CVP was monitored in 95.9% of the patients in this study yet this method of assessing intravascular fluid responsiveness lacks an evidence base [17]. The advent of readily available devices that measure cardiac output in a non-invasive manner has revolutionized hemodynamic monitoring of high-risk patients in ICUs [18]. Despite this, only 7.9% of the patients had a cardiac output

monitor used for their fluid optimization postoperatively and this may be a factor that influenced the findings of this study.

Overall positive fluid balance was associated with increased length of hospital stay and was higher in those patients with postoperative complications scored using the Clavien-Dindo grading system. Although the correlation between positive fluid balance and length of hospital stay was not strong ($r = 0.344$, $P < 0.001$) it was statistically significant and demonstrates that this could contribute to the complex process of developing postoperative complications. Overall fluid balance was also one of the two significant predictive factors in the logistic regression model (the other being total intravenous fluid administration). What is not clear from a study of this nature, however, is the nature of any causal linkage between intravenous fluid volumes and outcome. There are perfectly rational arguments to explain i) an excess of intravenous fluid leads to pathology; and ii) the occurrence of complications for other reasons necessitates additional intravenous fluid as part of their management. The statistical associations and differences demonstrated in this cohort provide no insight into which direction these factors (intravenous fluid administration and complications) correlate with but do confirm that the relationship is significant. Weight gain due to a more liberal approach to fluid administration is associated with higher rates of postoperative complications [8,19]. Daily weight measurement may therefore be an important prognostic indicator in perioperative patients.

The type of intravenous fluid used in ICUs and perioperatively has also come under close scrutiny recently [20,21]. Whether crystalloid or colloid should be used in GDFT protocols [22], the possible harm associated with hydroxyethyl starch [23] and the composition of crystalloid solutions [24] have all been topics of extensive discussion. In this single-center study, the only colloid available postoperatively in the

ICU was Gelofusine (4% succinylated gelatin in 0.9% saline), as a result of departmental policy. Thus, whilst not formally recorded, it can be mentioned that all colloid administered in the data capture time was Gelofusine. The data demonstrated that there was an association between volume of colloid received by patients and postoperative outcomes, whilst this correlation was absent for crystalloids. The reason for this is not clear but could either be the result of the colloid substance itself (succinylated gelatin) or the increased sodium and chloride loads in the gelatin's carrier solution (154 mmol/L of sodium and 120 mmol/L of chloride) as compared to the Hartmann's solution (131 mmol/L and 111 mmol/L; respectively) the commonest crystalloid used in the ICU studied. Of note, a chloride liberal approach to intravenous fluid use in critically ill patients has been shown to be associated with an increased incidence of acute kidney injury [25]. Thus, whilst no definitive conclusions can be drawn from this study regarding the effect of a specific fluid type on postoperative outcomes, gelofusine administration was associated with more complications and an increased length of hospital stay when compared to crystalloids.

The risks of inappropriate administration of intravenous fluids in those surgical patients requiring ICU postoperatively are likely to be greater than in those patients designated for ward level care [26]. High-risk surgical patients represent one end of the spectrum of surgical patients, either by virtue of their concomitant comorbidities or the nature of their surgery; the margin for clinical error in this cohort is therefore small [27]. Most patients undergoing HPB surgery fall into the high-risk category and the findings of this study highlight that there is a demonstrable correlation between excessive fluid given within 24 hours of surgery and relevant perioperative outcomes. With knowledge that postoperative complications reduce longevity and quality of life [28,29], it is imperative that morbidity in the immediate postoperative period is minimised. Different

strategies have been proposed to rationalise the volume of intravenous fluid given in the perioperative period, whilst ensuring that oxygen delivery is sufficient to maintain an optimal level of systemic oxygen delivery. GDFT is perhaps the most widely accepted technique for delivering fluid optimally to high risk surgical patients, however, strategies described as “liberal” or “restrictive” intravenous fluid administration have also been put forward [30]. Terminology surrounding the latter two approaches has caused confusion over the years and depending upon their precise definition studies can yield conflicting results [8,9]. GDFT involves titrating small boluses of intravenous fluid (250 mL) against stroke volume measured on a cardiac output monitor in order to optimise intravascular haemodynamics on an individual basis. Adopting this approach to fluid prescription post-HPB surgery could lead to a reduction in overall intravenous fluid administered and consequent improvement in outcomes [31]. It should be noted though, that when using GDFT there is a risk of harm in some patient subgroups if the overall intravenous fluid input remains high [32].

One of the limitations of this study was that intraoperative fluid data was not collected, therefore the overall volume for the first 24 hours did not include this. The purpose of the study was to assess postoperative practice; however, knowledge of intraoperative fluid administration may have shed further light on the association between fluid balance and outcomes. In a study of acute normovolemic hemodilution prior to pancreaticoduodenectomy (the operative procedure in 66% of the patients in the current study), the mean volume of intravenous fluid given to the control group intraoperatively was 3900 mL [33]. Of note, this study reported higher rates of pancreatic anastomotic complications in patients given large volumes of intravenous fluids. Thus, it seems that both intraoperative and postoperative fluid regimens have an important influence on complication rates. Other unmeasured factors such as

intraoperative blood loss and packed red cell administration and length of surgery could also have influenced outcomes. Another limitation is the minimal use of cardiac output monitoring in the guidance of fluid management as well as the lack of a strict protocol regarding frequency of CVP and SVO₂ measurement and subsequent modification of fluid administration, however, this represents the current practice in a large proportion of ICUs. Finally, further stratification for anastomosis was not attempted, although it was correlated with outcomes, because of the heterogeneity within this category (biliary, pancreatic, gastro-enteric anastomosis and combinations) which requires a significantly higher number of patients to detect differences. Despite its limitations, this study is one of the very few focusing on the group of HPB operations, presents outcomes on a large cohort with adequate representation of subgroups and provides adequate support for the need of further investigation in this field in order to get robust answers in the aforementioned questions.

In conclusion, higher volumes of intravenous fluid, in particular the colloid solution Gelofusine, given in the first 24 hours postoperatively were associated with increased complications and prolonged hospital stay. The present study suggests that CVP or SVO₂ monitoring alone, and more accurate documentation of fluid balance could possibly lead to improvement of outcomes. Overall, larger, multi-center studies are required to examine confounding factors and assess the usefulness of specific hemodynamic parameters following elective HBP surgery.

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Table 1

Participant demographics.

Variables	Data (<i>n</i> =241)
Gender (Male)	146 (60.6%)
Age (yr)	63 (19-84)
ASA grade	
ASA 1	20 (8.3%)
ASA 2	144 (59.8%)
ASA 3	69 (28.6%)
ASA 4	5 (2.1%)
ASA unobtainable	3 (1.2%)
Type of operation	
Pancreatic resections	72 (29.9%)
Hepatic resections	124 (51.5%)
Other	45 (18.7%)
Anastomosis performed	100 (41.5%)

Table 2

Comparison of patients with and without postoperative complications.

Fluid type	Without complications (<i>n</i> = 137)	With complications (<i>n</i> = 104)	<i>P</i> value
Colloid (mL)	1500 (500-2500)	2000 (1000-2750)	0.020
Crystalloid (mL)	2200 (1900-2500)	2200 (1950-2500)	0.886
Other (mL)	680 (451-964)	700 (430-960)	0.933
Total (mL)	4300 (3470-5410)	4790 (3900-5799)	0.030
Urine output (mL)	1900 (1315-2360)	1595 (1150-2110)	0.004
Overall fluid balance (mL)	+2553 (1110-3756)	+3040 (1995-4466)	0.004

Data are presented as median (interquartile range).

Table 3

Details of multivariate logistic regression for development of complications.

Parameters	Bivariate	Multivariate analysis	
	<i>P</i> value	OR (95% CI)	<i>P</i> value
Type of operation	0.883		
Anastomosis performed	0.001		
Age	0.622		
Gender	0.086		
ASA score	0.396		
Volume of infused colloids	0.020		
Volume of infused crystalloids	0.886		
Volume of other types of infused fluids	0.933		
Total volume of infused fluids	0.030	2.463 (1.437-4.219)	0.007
Volume of blood loss	0.001		
Urine output	0.004		
Documented 24 h fluid balance	0.312		
Calculated 24 h fluid balance	0.004	1.001 (1.001-1.002)	0.011
Discrepancy in documented and calculated fluid balance	0.001		
Optimization method	0.054		

Volume of blood loss: estimated blood loss during the studied 24 h postoperatively;

Documented 24 h fluid balance: the 24 h fluid balance documented on the daily ICU chart;

Calculated 24 h fluid balance: the 24 h fluid balance as calculated upon revision of collected data;

Optimization method: the monitoring method, including CVP, LiDCO, CVP/SVO₂.

Figure legends

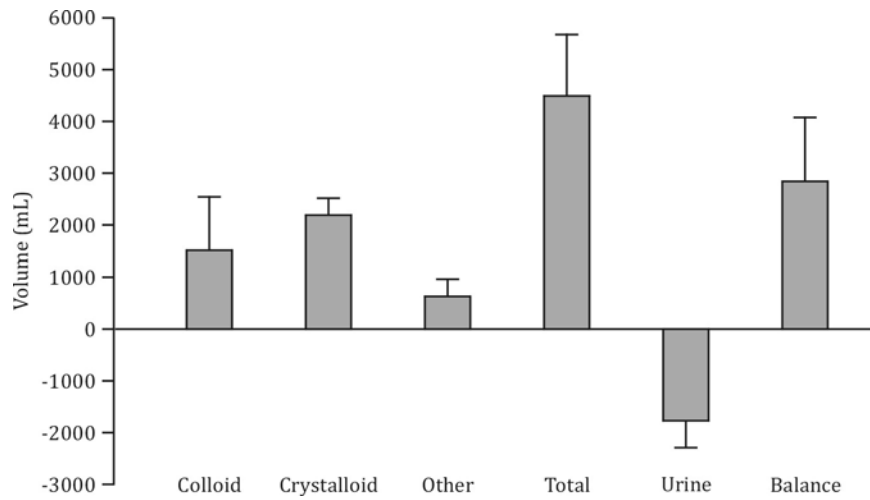


Fig. 1. Fluid volumes measured in the first 24 hours postoperatively (median \pm interquartile range).

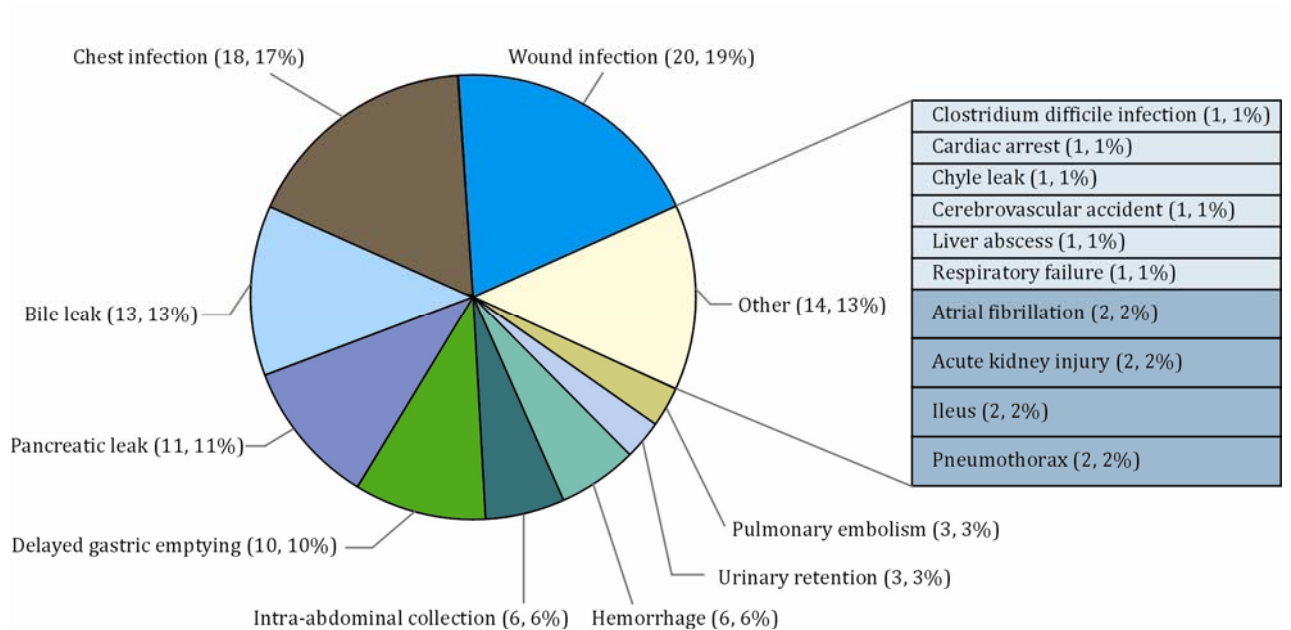


Fig. 2. Incidence of first per patient complication.

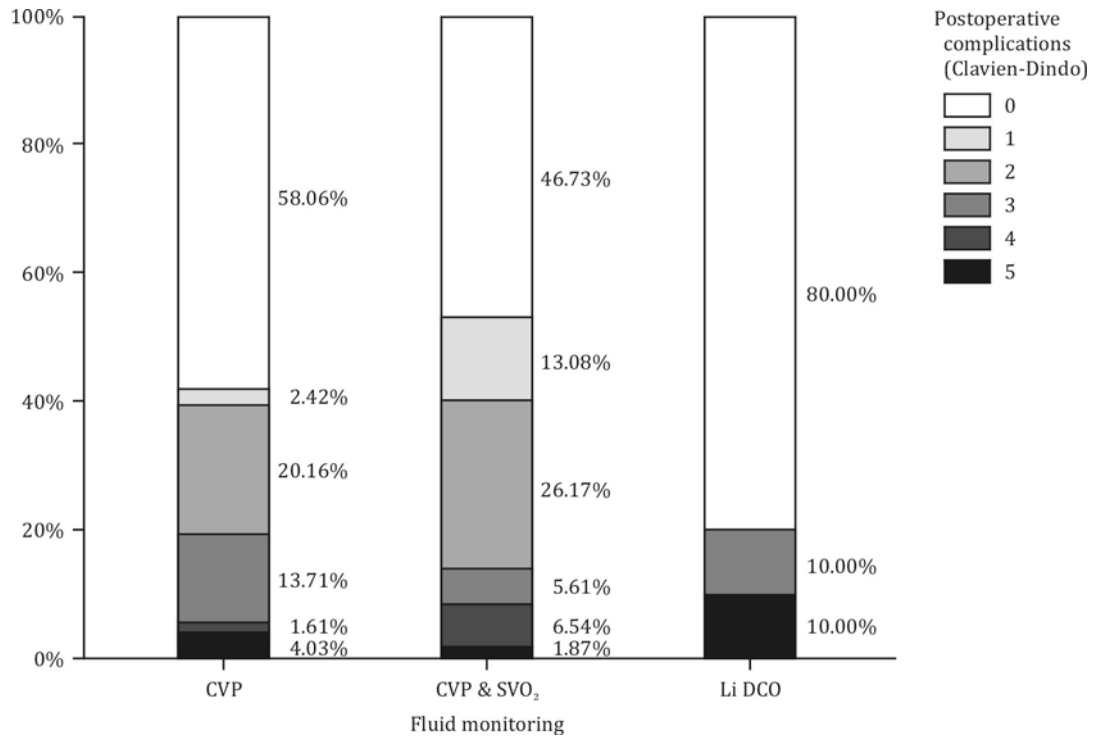


Fig. 3. Distribution of complications, according to Clavien-Dindo classification, across groups of different fluid administration monitoring.

CVP: central venous pressure; SVO₂: venous oxygen saturation.