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### ORIGINAL INVESTIGATION

# Fluid therapy and pulmonary complications in abdominal surgeries: randomized controlled trial



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#### **KEYWORDS**

Anesthesia; Digestive system surgical procedures; Fluid therapy; Hemodynamic monitoring; Organism hydration status; Postoperative complications

#### Abstract

*Background*: There is no consensus on the most effective strategy for Postoperative Pulmonary Complication (PPC) reduction. This study hypothesized that a Goal-Directed Fluid Therapy (GDFT) protocol of infusion of predetermined boluses reduces the occurrence of PPC in patients undergoing elective open abdominal surgeries when compared with Standard of Care (SOC) strategy.

*Methods:* Randomized, prospective, controlled study, conducted from May 2012 to December 2014, with ASA I, II or III patients undergoing open abdominal surgeries, lasting at least 120 min, under general anesthesia, randomized into the SOC and the GDFT group. In the SOC, fluid administration was according to the anesthesiologist's discretion. In the GDFT, the intervention protocol, based on bolus infusion according to blood pressure and delta pulse pressure, was applied. Patients were postoperatively evaluated by an anesthesiologist blinded to the group allocation regarding PPC incidence, mortality, and Length of Hospital Stay (LOHS).

*Results*: Forty-two patients in the SOC group and 43 in the GDFT group. Nineteen patients (45%) in the SOC and 6 in the GDFT (14%) had at least one PPC (p = 0.003). There was no difference in mortality or LOHS between the groups. Among the patients with PPC, four died (25%), compared to two deaths in patients without PPC (3%) (p = 0.001). The LOHS had a median of 14.5 days in the group with PPC and 9 days in the group without PPC (p = 0.001).

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Study conducted at the Institutional Research Board of Faculdade de Medicina de Botucatu – Univesidade Estadual Paulista on 7<sup>th</sup> May 2012. This study was registered at The Brazilian Registry of Clinical Trials (ReBEC) on 5<sup>th</sup> April 2021, UTN code: U1111-1207-3998, RBR-6ybk8kr, https://ensaiosclinicos.gov.br/rg/RBR-6ybk8kr.

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*Conclusion:* The GDFT protocol resulted in a lower rate of PPC; however, the LOHS and mortality did not reduce.

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#### Introduction

Postoperative Pulmonary Complications (PPC) are one of the main factors affecting morbidity and mortality in the postoperative period, leading to a longer length of hospital stay (LOHS), increased mortality, and rising costs.<sup>1</sup> The PPC incidence range is 6–80%, depending on the presence of risk factors and the definition adopted, including conditions ranging from atelectasis to Acute Respiratory Distress Syndrome (ARDS).<sup>2</sup>

PPC have a high incidence and a negative impact on clinical outcomes, particularly in patients undergoing abdominal surgery; hence, strategies reducing their occurrence should be developed.<sup>3</sup> Thus, Goal-Directed Fluid Therapy (GDFT) has been proposed as a possible intervention, since both "liberal" and "restrictive" strategies are associated with PPC.<sup>4-6</sup> However, there is no consensus on the most effective strategy or protocol for prevention of PPC.<sup>7</sup>

This study hypothesized that a GDFT protocol of infusion of predetermined boluses reduces the occurrence of PPC in patients undergoing elective open abdominal surgeries compared to the standard of care (SOC) volume replacement strategy. The primary outcome was PPC incidence in patients undergoing different intraoperative fluid replacement strategies, while the secondary outcomes included LOHS, renal function, and 30-day mortality.

#### **Methods**

This clinical, randomized, prospective, controlled study was conducted at the Hospital das Clínicas da Faculdade de Medicina de Botucatu (HC-FMB/UNESP) from May 2012 to December 2014. The FMB-UNESP Research Ethics Committee approved it, and the participants provided written informed consent. This study was registered at The Brazilian Registry of Clinical Trials (ReBEC – U1111-1207-3998, RBR-6ybk8kr).

Eight-five adult patients with ASA (American Society of Anesthesiologists) physical status I, II, or III, undergoing elective medium or major open abdominal surgeries (sigmoidectomy, colectomy, hemicolectomy, splenectomy, rectosigmoidectomy, pancreatectomy, intestinal transit reconstruction, abdominoperineal amputation, biliary bypass, gastrectomy, exploratory laparotomy, partial hepatectomy, and gastro-pancreatoduodenectomy) under general anesthesia were included in the present study.

All patients undergoing one of the above-mentioned open surgeries that were booked to last at least 120 min were included. Patients presenting with body mass index > 35 kg.  $m^{-2}$ , pregnancy, chronic obstructive pulmonary disease or bronchial infection, coagulopathies, preoperative renal function changes (creatinine > 1.3 mg.dL<sup>-1</sup>), sepsis or signs of systemic inflammatory response syndrome, symptoms of liver failure, urgent or emergency surgery were not included in the study. Moreover, refusal of study participation, loss of postoperative follow-up, or deviation from the allocated protocol resulted in exclusion from the study. The visual representation of participant flow throughout the study, encompassing enrollment, randomization, and follow-up processes, is depicted in Figure 1.

Anesthesia was induced using sufentanil (0.5–0.7  $\mu$ g.  $kg^{-1}$ ), etomidate (0.3 mg. $kg^{-1}$ ), or propofol (2 mg. $kg^{-1}$ ), according to individual clinical needs. Neuromuscular blockade (NMB) was monitored and maintained continuously using SX TOF-Watch<sup>®</sup> monitor. Rocuronium (0.6 mg.kg<sup>-1</sup>) or cisatracurium (0.2 mg.kg $^{-1}$ ) was administered for muscle relaxation. Anesthesia was maintained with continuous isoflurane inhalation at variable concentrations, according to each procedure and patient, associated with continuous remifentanil infusion (0.1–0.3  $\mu$ g.kg<sup>-1</sup>.min<sup>-1</sup>). NMB was maintained by administering subsequent doses of 20% of the initial amount of the same neuromuscular blocker used for anesthesia induction when the Train-of-Four ratio (TOF) was  $\geq$  2. All patients underwent orotracheal intubation (OTI) and volume-controlled ventilation (tidal volume, 6–8 mL.kg<sup>-1</sup>; positive end-expiratory pressure, 5 cmH<sub>2</sub>O), without recruitment maneuvers and with the necessary respiratory rate to maintain the expired end-tidal CO<sub>2</sub> fraction at 35-40 mmHg. At the end of the surgery, NMB was reversed by administering sugammadex or neostigmine along with atropine, according to the neuromuscular blocker used. Postoperative analgesia was managed with intravenous medications (2 g dipyrone and 100 mg tramadol) 1 hour before the end of the surgery. Rescue morphine was administered in the postanesthesia care unit (PACU) for pain, and the dose was titrated based on the verbal rating scale (0-10). Additionally, antiemetic medications were administered at the end of the procedure (10 mg metoclopramide and 8 mg ondansetron). All patients were monitored with invasive blood pressure, and a central venous line was inserted in accordance with the hospital's standard protocols at the time, which determined the technique and site for central venous catheter insertion, without any influence from our study.

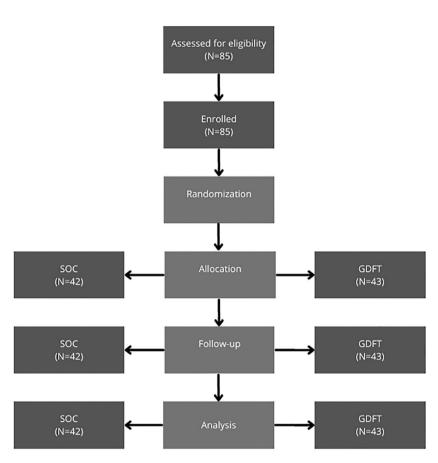
Volume replacement was divided into the following three periods:

- 1) Preoperative: All patients received 5% glucose solution (1  $mL.kg^{-1}.h^{-1}$ ) from fasting until admission to the operating room. Patients undergoing colon preparation additionally received Ringer's Lactate (RL) solution (1 mL.  $kg^{-1}.h^{-1}$ ) until entrance to the operating room.
- 2) Intraoperative: Patients were randomized using computer code generation into two groups: SOC or GDFT. The group allotment was sealed in opaque envelopes that were opened immediately after the patient was monitored and before anesthesia induction.

Data collection period: May 2012 to December 2014 Location: Surgical center at the Hospital das Clínicas de Botucatu (HC-FMB)

Inclusion criteria: Adult patients ASA I, II, or III, undergoing medium to large open abdominal surgeries with a minimum duration of 120 minutes, in a supine position, under general anesthesia.

Exclusion criteria: BMI > 35 kg/m<sup>2</sup>, pregnancy, COPD or bronchial infection, coagulopathies, preoperative renal function alterations (creatinine > 1.3 mg/dL), sepsis or signs of systemic inflammatory response syndrome, signs of hepatic insufficiency, patients undergoing urgent or emergency surgeries, and those who declined to participate in the study





During the intraoperative period, both groups had identical hemodynamic targets: mean arterial pressure (MAP) of 65-80 mmHg and delta pulse pressure (dPP)  $\leq 12\%$ . Despite these common targets, the methodology for achieving them differed markedly between groups. In the SOC group, anesthesiologists had complete discretion over fluid administration, including the choice of fluid type, volume, and infusion rate. This approach led to a diverse range of infusion strategies and typically resulted in higher overall fluid volumes, reflecting the variability inherent in individual clinical judgment. Conversely, the GDFT group adhered to a strict, predefined protocol. This protocol dictated specific fluid types, volumes, and rates of administration, based strictly on

changes in MAP and dPP. This structured approach aimed to standardize fluid therapy, reduce variability, and potentially mitigate the risks associated with fluid overload in the perioperative period. The detailed GDFT protocol is depicted in Figure 2.

Blood products were available for administration in both groups. Red blood cell (RBC) concentrates were administered when the plasma hemoglobin (Hb) concentration was < 8 g.dL<sup>-1</sup>, except in cardiac patients (< 10 g.dL<sup>-1</sup>). Fresh frozen plasma (FFP), cryoprecipitates, and platelet concentrates were administered according to the plasma fibrinogen concentration and platelet count in the intraoperative and immediate postoperative periods.

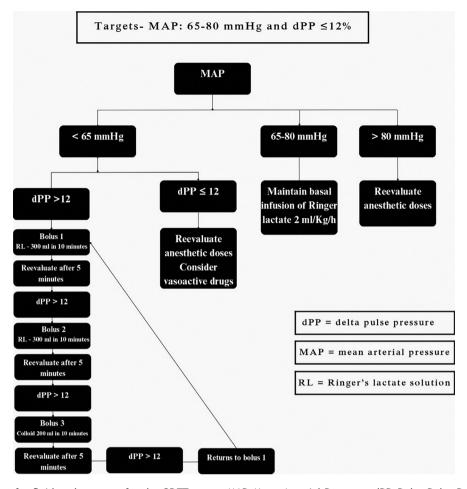


Figure 2 Algorithm for fluid replacement for the GDFT group. MAP, Mean Arterial Pressure; dPP, Delta Pulse Pressure; RL, Ringer's Lactate solution

3) Immediate postoperative: The same fluid infusion regimen used in the intraoperative period was followed for volume replacement at the PACU according to the group. In both groups, the hemodynamic target in this period was limited to changes in MAP since patients were breathing spontaneously.

During the intraoperative and immediate postoperative periods, patients in both groups received a continuous infusion of two mL.kg<sup>-1</sup>.h<sup>-1</sup> of LR to replace insensible fluid losses and diuresis. The diuresis volume was measured using an indwelling urinary catheter after anesthesia induction. The initial volume immediately after catheterization was discarded, and the volumes collected during the surgical procedure were noted.

The total fluid volume administered to each group, type of infusion (crystalloids, colloids, and blood products) and need for vasoactive medications were evaluated. Moreover, the patients were analyzed for the total time MAP and dPP were within the target ranges.

Central venous blood samples (1.5 mL) were collected from all patients immediately before anesthesia induction and every hour until PACU discharge to assess central venous oxygen saturation ( $ScvO_2$ ). Arterial blood samples were collected to evaluate Hb and lactate levels. Renal function was analyzed based on the perioperative urine output and plasma markers (creatinine, Neutrophil Gelatinase-Associated Lipocalin [NGAL], and cystatin C) assessed before anesthesia induction, 48 hours, and 5 days after surgery.

The patients were postoperatively evaluated by an anesthesiologist blinded to the group allocation. The following PPC were assessed: pneumonia, unscheduled postoperative OTI, and pulmonary thromboembolism. Moreover, LOHS and 30-day mortality were also studied. We also evaluated LOHS and mortality among patients who developed PPC regardless of the groups they were initially allocated.

#### **Statistical analysis**

Study data were collected by multiple evaluators and transcribed into an individual evaluation form explicitly developed for this purpose.

The sample size was calculated based on data from previous studies on PPC. An absolute 30% reduction in overall PPC was considered clinically significant, requiring approximately 66 patients for a Type I error of 0.05 and 80% test power. We decided to include 85 patients in the randomization to ensure the minimum sample size even with a loss of 25%. Initially, descriptive analyses included calculating means and standard deviations for quantitative variables and frequencies and percentages for qualitative variables,

Table 1	Comparison between	groups for	demographic and	d clinical	variables and	surgical duration.
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	Gro	ups	
	SOC (n = 42)	GDFT (n = 43)	
Variable	Mean $\pm$ SD	Mean $\pm$ SD	<i>p</i> -value
Age (years) <sup>a</sup>	$\textbf{49.1} \pm \textbf{11.0}$	$\textbf{49.1} \pm \textbf{13.9}$	1.00
Weight (kg) <sup>a</sup>	$\textbf{68.8} \pm \textbf{14.7}$	$\textbf{69.8} \pm \textbf{16.3}$	0.77
Height (cm) <sup>a</sup>	$\textbf{164.4} \pm \textbf{9.5}$	$\textbf{165.4} \pm \textbf{9.5}$	0.63
Total surgical duration (min) <sup>a</sup>	$\textbf{270.2} \pm \textbf{114.5}$	$\textbf{250.7} \pm \textbf{92.2}$	0.39
Variable	n (%)	n (%)	<i>p</i> -value
Sex <sup>b</sup>			
Male	22 (52)	21 (49)	0.91
ASA			
lp	11 (26)	7 (16)	0.39
II <sup>b</sup>	26 (62)	31 (72)	0.44
III <sup>c</sup>	5 (12)	5 (12)	1.00
Morbidities	n (%)	n (%)	<i>p</i> -value
Diabetes Mellitus <sup>b</sup>	5 (12%)	6 (14%)	0.97
Systemic Arterial Hypertension <sup>b</sup>	8 (19%)	15 (35%)	0.16
Alcoholism <sup>c</sup>	4 (9.5%)	4 (9.3%)	1.00
Smoking <sup>b</sup>	12 (28.6%)	12 (27.9%)	0.86

SOC, Standard of Care; GDFT, Goal-Directed Fluid Therapy; SD, Standard Deviation; ASA, American Society of Anesthesiologists classification – patient's physical status.

<sup>a</sup> Student *t*-test for independent samples.

 $^{\rm b}\,$  Chi-Square test at 5% for association between categorized variables.

<sup>c</sup> Fisher's exact test.

stratified by group. For the quantitative variables with normal distribution, the Student's *t*-test was used to compare independent samples. A generalized linear model with gamma distribution was used for variables without normal distribution. Count data variables were compared according to a generalized linear model with Poisson distribution or negative binomial distribution, depending on the extra variation found. Qualitative variables were compared between groups using the difference of proportions test. Associations between qualitative variables and groups were compared using the chi-square and/or Fisher's exact test.

Quantitative variables repeated over time with normal distribution were analyzed by an adjusted repeated measures model followed by the adjusted Tukey multiple comparison test. Variables without normal distribution were analyzed using the same model, adjusted considering a gamma distribution, followed by the Wald multiple comparison test.

All analyses were performed using SAS software 9.3 for Windows, with a significance level set at 0.05 for all tests.

#### Results

The study analyzed 85 patients, 42 in the SOC group and 43 in the GDFT group. No patients were excluded from the study due to loss of follow-up, protocol deviation, or any other reason.

#### **Patient characteristics**

The groups were homogeneous for anthropometric parameters, sex, total surgical duration, patient's physical status, and presence of previous morbidities. The main comorbidities in both groups were smoking, systemic arterial hypertension, diabetes mellitus, and alcoholism, with no statistically significant differences (Table 1). The profile of surgeries and the profile of patients who were reintubated according to the groups are described in Tables 1 and 2 in the Supplementary Material.

#### Volume loss and intraoperative volume replacement

The groups were homogeneous for total intraoperative bleeding volume. Despite the fluid balance at the end of the surgery being less positive in the GDFT group than in the SOC group, the difference was not statistically significant. There was a statistically significant decrease in the total volume infused in the GDFT patients due to the smaller amount of crystalloids administered. The volume of synthetic colloids, RBC, and FFP administered during surgery was similar between the groups (Table 2).

#### **Blood gas data**

Lactate values increased over time and were statistically similar in both groups, except at 120 min, when lactate was higher in the SOC group. This was probably due to the exogenous administration of lactate, which was present in the LR and infused in greater volume in this group of patients. The ScvO<sub>2</sub> values increased during surgery compared to the preoperative values in both groups and returned to the baseline values before PACU discharge. Compared to the preoperative values, Hb levels decreased in both groups during different periods but without statistically significant differences between them during the same period. Blood data are

	Groups		
	SOC (n = 42)	GDFT (n = 43)	
Variable	${\sf Mean}\pm{\sf SD}$	$\text{Mean} \pm \text{SD}$	<i>p</i> -value
Total volume infused (mL) <sup>a</sup>	$4879.9 \pm 2147.3$	$3810.4 \pm 2126.9^{*}$	0.02
Ringer's lactate solution (mL) <sup>a</sup>	$3901.2 \pm 1475.1$	$2982.9 \pm 1524.0^{*}$	0.006
Voluven <sup>®</sup> 6% (mL) <sup>1a</sup>	$\textbf{737.8} \pm \textbf{383.2}$	$\textbf{779.7} \pm \textbf{565.1}$	0.71
Voluven <sup>®</sup> 6% (mL.kg <sup>-1</sup> ) <sup>a</sup>	$\textbf{10.7} \pm \textbf{5.9}$	$\textbf{10.8} \pm \textbf{6.6}$	0.94
Red blood cells (mL) <sup>b</sup>	$\textbf{484.4} \pm \textbf{298.3}$	$\textbf{348.6} \pm \textbf{146.0}$	0.08
Fresh frozen plasma (mL) <sup>b</sup>	$296.1 \pm 139.8$	$\textbf{245.2} \pm \textbf{80.1}$	0.37
Losses (mL) <sup>b</sup>	$5062.9 \pm 3287.5$	$\textbf{4364.5} \pm \textbf{2920.6}$	0.29
Fluid balance (mL) <sup>a</sup>	$1566.8 \pm 1546.9$	$1025.6 \pm 1443.1$	0.10
Intraoperative bleeding $(mL)^{b}$	$\textbf{1283.2} \pm \textbf{959.7}$	$1100.1 \pm 851.1$	0.34

**Table 2** Data regarding the total volume infused, total volume of crystalloids (Ringer's lactate solution) and colloids (Voluven<sup>®</sup>) infused, red blood cells count, fresh frozen plasma administered, total volume losses, fluid balance, and intraoperative bleeding in the studied groups.

SOC, Standard of Care; GDFT, Goal-Directed Fluid Therapy; SD, Standard Deviation.

<sup>a</sup> Student *t*-test for independent samples.

<sup>b</sup> Generalized linear model with gamma distribution to compare two groups.

described in Graphs 1, 2 and 3 provided in the Supplementary Material.

#### Renal function

The groups were homogeneous for the urinary output, both in absolute values and in mL.kg<sup>-1</sup>.h<sup>-1</sup>, and for the other parameters used to assess renal function (Table 3). There was a statistical difference in the NGAL values in the SOC group during different periods (preoperative < postoperative day 2 = postoperative day 5) (Graph 4 in the Supplementary Material).

#### Protocol efficiency

The intervention protocol was as efficient as the SOC in restoring the circulating volume lost intraoperatively when evaluating the pre-established protocol targets, albeit with less infused fluids (Table 2). Data referring to MAP and dPP are described in Table 3.

#### Postoperative complications

The volume replacement protocol based on bolus infusion resulted in a low rate of postoperative and pulmonary complications. Nineteen patients (45%) in the SOC group, compared to 6 (14%) in the GDFT group, had at least one postoperative complication (p = 0.003). There was a statistically significant difference between the SOC and GDFT groups regarding PPC (36% vs. 2%; p = 0.001). The groups were homogeneous in the individual analyses of other complications (renal, cardiovascular, infectious, and surgical) (Table 4).

The groups did not differ in the need for vasoactive drugs, including ephedrine, metaraminol, or noradrenaline. Ephedrine was the most commonly used medication in both groups.

#### Comparison between patients with and without PPC

The incidence of PPC in this study was 19%. In total, sixteen patients presented with at least one PPC. Among these

Table 3 Data referring to episodes of hypotension (MAP < 65 mm.Hg), hypovolemia (dPP > 12%), and urinary output in the studied groups.

	Gro	pups	
	SOC	GDFT	
	$Mean\pmSD$	$Mean \pm SD$	<i>p</i> -value
% Time with MAP < 65 mmHg during surgery <sup>a</sup>	$\textbf{16.8} \pm \textbf{18.7}$	$\textbf{16.7} \pm \textbf{15.2}$	1.0
dPP episodes > 12% <sup>b</sup>	$\textbf{45.4} \pm \textbf{19.6}$	$\textbf{49.0} \pm \textbf{22.4}$	0.43
% Time with dPP $> 12\%$	$\textbf{21.5} \pm \textbf{21.6}$	$\textbf{18.2} \pm \textbf{15.2}$	0.47
Urinary output (mL) $c^{3c}$ in the intraoperative period	$\textbf{583.8} \pm \textbf{426.3}$	$\textbf{465.3} \pm \textbf{296.4}$	0.10
Urinary output $(mL.kg^{-1}.h^{-1})^{c}$ in the intraoperative period	$\textbf{1.9} \pm \textbf{1.0}$	$\textbf{1.6} \pm \textbf{0.9}$	0.15

SOC, Standard of Care; GDFT, Goal-Directed Fluid Therapy; MAP, Mean Arterial Pressure; dPP, Delta Pulse Pressure; SD, Standard Deviation. <sup>a</sup> Generalized linear model with negative binomial distribution for comparison of two groups.

<sup>b</sup> Student *t*-test for independent samples.

 $^{\rm c}\,$  Generalized linear model with gamma distribution for comparison of two groups.

Postoperative complications	SOC (n = 42) (%)	GDFT (n = 43) (%)	<i>p</i> -value
Pneumonia	4 (10%)	0	0.12
Non-predicted postoperative OTI	14 (33%)	1 (2%)	0.0005
Surgical wound infection	2 (5%)	0	0.46
Abdominal wall dehiscence	2 (5%)	0	0.46
Anastomosis dehiscence	2 (5%)	2 (5%)	1.0
Surgical retreatment	5 (12%)	4 (9%)	0.97
ICU admission	16 (38%)	9 (21%)	0.13
Deep vein thrombosis	0	1 (2%)	1.0
Pulmonary thromboembolism	1 (2%)	1 (2%)	1.0
Cardiac arrhythmias	1 (2%)	1 (2%)	1.0
Acute kidney injury	1 (2%)	2 (5%)	1.0
Need for dialysis	0	1 (2%)	1.0
Sepsis/septic shock	2 (5%)	3 (7%)	1.0
Bleeding	1 (2%)	0	1.0
Death up to 30-days	4 (10%)	2 (5%)	0.43

Table 4Comparison between groups for postoperative complications. Results are presented according to the number of<br/>patients who had the complication.

OTI, Orotracheal Intubation; ICU, Intensive Care Unit; SOC, Standard of Care; GDFT, Goal-Directed Fluid Therapy.

patients, four died (25%) compared to two deaths among those patients who presented no PPC (3%) (p = 0.001). The LOHS had a median of 14.5 days in patients with PPC and 9 days in those without PPC (p = 0.001).

#### **Discussion**

This study showed that the GDFT was more effective in reducing the incidence of PPC than the SOC. This could be attributed to a smaller fluid volume administered in the perioperative period in the GDFT group, specifically of crystalloids (approximately 1000 mL less in our intervention group). Although the difference in volume is not highly expressive at first, our results align with some previously published data. For example, we want to draw attention to a relevant finding in the study by Corcoran and colleagues that compared three fluid delivery groups: restrictive, liberal, and GDFT.<sup>4</sup>

Corcoran's study<sup>4</sup> highlights that patients in the liberal fluid group received significantly larger intraoperative and total perioperative fluid volumes than those in the restrictive group, with a notable difference of approximately 1,570 mL. The disparity resulted in higher complications, including pneumonia and pulmonary edema, in the liberal groups. Conversely, patients in the GDFT group, which received a similar fluid volume compared with the volume administered to the patients in the liberal group, also experienced fewer cases of pneumonia.

This observation supports the notion that the mere volume of fluid administered may not be the sole determinant of postoperative complications. Instead, the timing, quality, and route of fluid administration, exemplified by goaldirected strategies, can be pivotal in mitigating complications. In line with the literature, a judicious and goaldirected approach to fluid management may significantly impact postoperative outcomes more than the absolute volume of fluid infused.<sup>4</sup>

PPC are prevalent postoperative complications associated with increased LOHS and short- and long-term mortality.<sup>8</sup> In the US, over one million PPC are estimated to occur yearly, with approximately 46,200 related deaths and 4.8 million extra hospitalization days.<sup>9</sup> In patients undergoing abdominal surgery, PPC represent an additional cost of USD 30,000 per patient and 6-9 extra hospitalization days.<sup>10</sup> The incidence of PPC in the present study was 19%, corroborating literature reports. In the LAS VEGAS observational study conducted in 146 hospitals in 29 countries, the ARISCAT score correlated with an increased risk of PPC in surgical patients. Patients with an ARISCAT score  $\geq$  26 showed a PPC incidence of 19.2% and in-hospital mortality of 1.7%, while those with a score < 26 showed a PPC incidence of 7% and in-hospital mortality of 0.2%.<sup>11</sup> Patel et al reported a PPC incidence of 12% in patients undergoing major abdominal surgery. Moreover, the hospital stay was more extended (10 vs. 3 days), and 30-day mortality was higher (12.5% vs. 0%) in those with PPC than in those without, indicating that PPC are common and significantly affect patient outcomes. Therefore, strategies to reduce the incidence are necessary.<sup>3</sup>

The development of PPC seems to be related to local lung physiologic changes associated with anesthesia and the inflammatory effects of major surgeries, as well as mechanical ventilation.<sup>12</sup> Therefore, multidisciplinary interventions could reduce PPC incidence, such as fluid administration management, preoperative oxygenation, blood loss control, duration of anesthesia, and protective ventilatory strategies.<sup>2</sup>

The present study analyzed a fluid therapy intervention based on strong scientific evidence that administering excess fluids in the perioperative period contributes to the onset of PPC, leading to ARDS.<sup>13,14</sup> Both liberal and more restrictive fluid resuscitation strategies were associated with complications. A systematic review<sup>7</sup> suggests that perioperative GDFT can improve postoperative recovery after major abdominal surgery. However, the most effective GDFT strategy has yet to be determined. The strategy described in the present study could be a viable option because it efficiently maintained the hemodynamic parameters within the predetermined range, similar to the SOC strategy, but requiring a smaller volume of crystalloid administration.

Although PPC incidence reduced with the intervention, the length of hospital stay did not decrease significantly. The median LOHS were 11.1 (SD = 6.2) and 11.5 (SD = 6.5) in the SOC and GDFT groups, respectively (p = 0.58). These results corroborate the POEMAS study,<sup>15</sup> wherein the average hospitalization duration was 10.5 days and 11.5 days in the group receiving conventional volume replacement and that receiving GDFT, respectively (p = 0.87).

In the present study, the mortality rate did not differ significantly between the SOC and GDFT groups (9.5% vs. 4.6%; p = 0.433). This result corroborates the POEMAS study<sup>15</sup> results as well, wherein the mortality rate was 5.7% and 4.2% in the usual volume replacement group and the GDFT group, respectively, without a statistically significant difference.

However, the analysis of patients with and without PPC showed a statistically significant difference for LOHS and mortality. Patients with and without PPC were hospitalized for 14.5 days and 9 days, respectively (p = 0.001), while the mortality rates were 25% and 3%, respectively (p = 0.01). Both results corroborate the findings of Dimick et al. who reported that PPC occurrence increases the LOHS by 6–9 days,<sup>10</sup> and those of Khuri et al., who reported a 30-day mortality rate of 22% and 2% in patients with and without PPC, respectively.<sup>16,17</sup>

The Enhanced Recovery After Surgery Plus (ERAS+) protocol was created based on increasingly robust evidence of the importance of perioperative lung care. It added a few steps to the ERAS protocol, mainly focused on lung-related issues such as oral hygiene, increased physical activity, breathing exercises, and educational videos for patients and families. These measures reduced the PPC incidence in patients undergoing major surgeries (oncologic resections) from 18.7% to 10.5% (p = 0.017) immediately after implementation. Despite the favorable results, the ERAS+ required training for an entire multidisciplinary team and those explicitly hired to conduct the protocol. Conversely, the intervention proposed in the present study is easier to implement, consisting of a single intervention performed by the anesthesiologist, therefore minimizing the need for extensive staff training, equipment, or unusual medications.

The limitations of this study include being a single-center study, implying the use of the same team of surgeons and anesthesiologists and the analysis of a specific group of patients undergoing abdominal surgery. These characteristics may limit the generalizability of the results to other populations and clinical contexts. Moreover, the data was collected almost a decade ago, when the ERAS protocols were not the SOC in most of the health care centers in Brazil. However, this may still be the reality of many hospitals worldwide where the costs of implementing this multidisciplinary bundle of interventions may be challenging. Finally, the intervention used in our study was limited to the intraoperative and early postoperative periods. PPC were multifactorial complications, and fluid replacement, among other interventions implemented in the later postoperative period, may have contributed to the results encountered in

the present study. Therefore, future multicenter studies with larger samples and extended periods of observation are needed to confirm and extend the findings of this study.

#### Conclusion

The GDFT intervention proposed in this study is based on the infusion of predetermined volume boluses, and it significantly reduced the incidence of PPC; however, the LOHS and mortality did not reduce. Although further studies are warranted to evaluate this strategy in different scenarios or larger populations, it seems a viable option for perioperative fluid management, allowing for easy implementation and good results compared to SOC fluid replacement. Moreover, the implementation of this strategy can be done without extra staff training or additional equipment and medications.

#### Authors' contributions

Gabriel Isaac Pereira de Castro: Conception and design of the study, acquisition of data, analysis and interpretation of data; drafting the article, and revising it critically for important intellectual content.

Renata Sayuri Ansai Pereira de Castro: Drafting the article, and revising it critically for important intellectual content.

Rodrigo Moreira e Lima: Conception and design of the study, acquisition of data, analysis and interpretation of data; drafting the article and revising it critically for important intellectual content.

Bruna Nogueira dos Santos: Drafting the article, and revising it critically for important intellectual content.

Lais Helena Navarro e Lima: Conception and design of the study, acquisition of data, analysis and interpretation of data; drafting the article, and revising it critically for important intellectual content.

#### **Declaration of competing interest**

The authors declare no have conflicts of interest.

#### Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.bjane.2024. 844500.

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