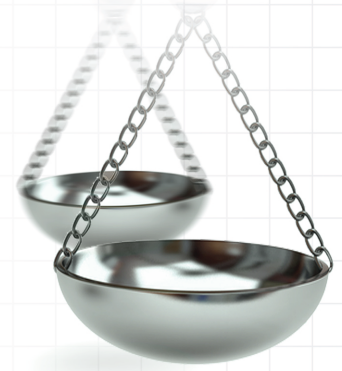




Impact of a goal-directed fluid therapy on length of hospital stay and costs of hepatobiliarypancreatic surgery: a prospective observational study

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Aim: The effectiveness of goal-directed fluid therapy (GDFT) algorithms in improving postoperative outcomes has extensively been suggested. Nevertheless, there is a lack of strong evidence regarding both the clinical impact and the cost-effectiveness of the GDFT protocols. The aim of this study is to evaluate the costs of patients undergoing hepatobiliarypancreatic surgery when a GDFT protocol is applied. **Materials & methods:** Consecutive ASA I-III patients undergoing hepatobiliarypancreatic surgery were included in this prospective observational study. Depending on device availability, patients were handled either by fluid therapy guided by Vigileo monitor-derived hemodynamic variables (Vigileo-GDFT group) or by standard fluid treatment (standard group). Postoperative length of stay and economic costs were analyzed. **Results:** In total, 147 patients were included (71 in the Vigileo-GDFT group and 76 in the standard group). The total hospital length of stay was 13 (median, 1st-3rd quartile, 9-20) days for the Vigileo-GDFT group and 14 (8-21) days for the standard group ($p = 0.58$); no statistically significant differences between the two groups emerged regarding costs and postoperative complications. In both groups, complications were the main contributor to total cost sustained. **Conclusion:** The application of a GDFT algorithm did not reduce the total length of hospital stay and the global costs, which were mainly influenced by the number of complications.

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Keywords: costs • fluid therapy • GDFT • length of hospital stay • postoperative complications

Major abdominal surgery is associated with a relevant systemic inflammatory response and a proportional increase in the tissues' demand for oxygen. If this demand does not correspond with an increase of the cardiac output, organ failure, complications and death can occur, especially in high-risk patients [1-3]. Hepatobiliarypancreatic surgery is considered to be a high-risk procedure with an associated significant morbidity and mortality. If mortality is improving, postoperative morbidity is still substantial [4].

Over 25 years ago, Shoemaker was the first to prove a reduction in morbidity and mortality in patients undergoing major abdominal surgery through the application of a goal-directed fluid therapy (GDFT) [5]. GDFT is a generic term that refers to the management of fluids and hemodynamics based on some parameters, such as stroke volume, cardiac output and/or the transport of oxygen, combined with the clinical evaluation of vital signs, during and immediately following surgery. This approach reduces systemic inflammatory response and increases tissue perfusion and oxygenation [6]. Its effectiveness in terms of clinical outcomes (complications and length of hospital stay) in high-risk surgical patients has been extensively demonstrated [7-9], and GDFT is currently recommended by the NHS in the UK [10], the French Society of Anesthesiology [11] and the Enhanced Recovery After Surgery (ERAS) Society in Europe [12]. However, evidence supporting the clinical effectiveness of GDFT derives from small randomized studies and also includes forms of invasive monitoring. Furthermore, the OPTIMISE [13] study and a

recent Cochrane meta-analysis [14] have shown the benefits in terms of reduction of complications and mortality deriving from such treatment are more marginal than was previously expected. On the other hand, only a few studies have taken into consideration the cost-effectiveness of GDFT showing an actual reduction of costs but with multiple limitations linked to the variability of the kind of device used; the fluid therapy applied in the standard groups and the postoperative period is considered for the evaluation of the outcome [15,16].

The aim of this study is to evaluate the length of hospital stay and costs of patients undergoing hepatobiliarypancreatic surgery in which a GDFT protocol based on a mini-invasive hemodynamic monitoring system (Vigileo™, Edwards Lifesciences, CA, USA) is used for the management of fluid-therapy as opposed to a standard fluid therapy protocol. The hypothesis is that the use of a GDFT protocol based on a Vigileo system can reduce the length of hospital stay in patients undergoing hepatobiliarypancreatic surgery.

Materials & methods

Ethics, consent & permissions

This prospective observational study was approved by the Ethical Committee of the Regina Elena National Cancer Institute, Rome (Italy) with registration number 89/10, amendment 1. The procedures followed were in agreement with the Helsinki Declaration 1975, revised in Hong Kong 1989. After having obtained written informed consent, consecutive patients (American Society of Anesthesiologists [ASA] I–III candidates) for open hepatobiliarypancreatic surgery who met the inclusion criteria were enrolled in the study. Patients under 18 years of age and patients with hemodynamically significant aortic valve disease and cardiac rhythm disorders were excluded.

Management

Depending on device availability, patients were handled either by a mini-invasive hemodynamic monitoring system for a GDFT (Vigileo–GDFT group) or receiving a fluid therapy (standard group) according to a standardized protocol.

The same team carried out the surgical procedures for both groups and all patients underwent general anesthesia according to a standard protocol. More specifically, patients were premedicated with midazolam 0.01 mg/kg intravenous (iv.). A general anesthesia was induced with fentanyl 2–5 µg/kg, propofol 1.5–2 mg/kg and cisatracurium 0.07 mg/kg iv. After orotracheal intubation, anesthesia was maintained with a mix of sevoflurane/O₂/air. A continuous infusion of cisatracurium 0.06–0.12 mg/kg per hour was also carried out and an additional bolus of fentanyl was administered according to the anesthetic needs and the hemodynamic changes.

All patients were subjected to standard monitoring: continuous electrocardiography, heart rate, invasive blood pressure (with a radial artery catheter), pulse oxymetry (SpO₂), body temperature, hourly diuresis, inhaled and exhaled gas.

A FloTrac/Vigileo system (Edwards Lifesciences, CA, USA, software version 1.14) was applied to the Vigileo–GDFT group to obtain a continuous monitoring of the cardiac index (CI), stroke volume index (SVI) and stroke volume variation (SVV). The CI was maintained at values ≥ 2.5 l/min/m². A fluid therapy protocol was used, which included a basal infusion of crystalloids at 4 ml/kg per hour and bolus of colloids (250 ml of hydroxyethyl starch 130/0.4, HES, in 15 min), if CI < 2.5 l/min/m², SVI < 35 ml/m² and SVV $> 13\%$. In the case of CI < 2.5 l/min/m² and SVI < 35 ml/m² with SVV $< 13\%$, an infusion of dobutamine (3–10 µg/kg per minute) was carried out.

In the standard group, a regimen of fluid therapy through a basal infusion of crystalloids varying from 4 to 7 ml/kg per hour was maintained. Mean arterial pressure (MAP) was maintained between values of 65 and 95 mmHg. Colloid boluses (HES) of 250 ml were administered in 15 min if MAP was $\leq 70\%$ the preinduction value or if diuresis was ≤ 1 ml/kg per hour with a Central Venous Pressure (CVP) < 8 mmHg; when the MAP was $\leq 70\%$ the preinduction value or if diuresis was ≤ 1 ml/kg per hour, despite fluid resuscitation an infusion of inotropic agents (dobutamine 3–10 µg/kg per minute) was carried out. In both groups, patients were transfused with concentrated red cells for hemoglobin values less than 8 g/dl (< 9 g/dl in patients with congestive heart failure or coronary heart disease).

At the completion of surgery, patients were extubated in the operating theater and transported to the intensive care unit (ICU). In the postoperative period, the same standardized regimen of fluid therapy was applied to both groups: total parenteral nutrition up to 3000 ml/day was administered and gradually converted into enteral nutrition after 5–7 days, starting at 10 ml/h to achieve the dose of 60 ml/h, until mouth feeding resumed.

In both groups at the end of surgery, data were collected about the total amount of fluids administered, their breakdown (crystalloid/colloid), the total number of colloid boluses administered, the use of inotropic agents and units of red blood cells transfused.

Measurement

In both groups, the incidence of major abdominal and systemic complications was evaluated by personnel not involved in the intraoperative management of patients and therefore unaware of the protocol used. The major abdominal complications considered were anastomotic leakage, enteric fistulas, perforation, abdominal abscesses (confirmed by computerized tomography); systemic complications were divided into cardiac (electrocardiographic signs or laboratory data of myocardial infarction, angina or arrhythmia), hepatic (persistent alteration in hepatic function tests including bilirubin, prothrombin time, ammonia concentration, aspartate aminotransferase, alanine aminotransferase, gamma glutamyl transferase), respiratory (x-ray findings of airspace or interstitial opacity, lobar consolidation or pleural effusions; severe respiratory failure requiring respiratory support) and renal (oliguria with urine output <0.5 ml/kg per hour for more than 4 h, creatinine increase $>30\%$ of preoperative values, dialysis). Furthermore, the incidence of readmission to the ICU was assessed.

The total length of hospital stay and costs were evaluated for both groups and four categories were identified: pharmaceuticals and consumer goods; costs of hospitalization, including medical and nonmedical personnel and calculated as 'ordinary' or 'extraordinary' hospitalization (ICU); costs of surgical procedures and possible further surgeries; and cost of diagnostic examinations, calculated according to the regional expense lists (price list of the Lazio region).

A dedicated, *ad hoc* developed software (supporting costs evaluation in major abdominal surgery [SCM]) was used to extract and analyze the data regarding the patients enrolled in the study. This software enables registration, conservation and analyses of the clinical data and costs of patients undergoing major abdominal surgery.

Statistical analysis

Data are expressed as mean (standard deviation [SD]) or median (1st–3rd quartiles). Continuous variables with normal and with non-normal distribution (hospital length of stay and costs) were compared with Student's *t*-test and Mann-Whitney U test, respectively. Chi-square or Fisher exact tests were used for categorical variables. A *p*-value < 0.05 was considered significant. We used software version 21 of statistical package for social science (SPSS version 21, IL, USA).

Results

Population

In total, 147 consecutive patients who underwent hepatobiliopancreatic surgery at our institute between 2011 and 2013 were included. Of these, 71 underwent a GDFT protocol based on a mini-invasive hemodynamic monitoring system (Vigileo–GDFT group) and 76 underwent a standard fluid-therapy protocol (standard group). The demographics and perioperative data are shown in [Table 1](#). Hourly hemodynamic variables are presented in [Figure 1](#); the MAP is significantly lower at 2 and 3 h from the start of surgery in GDFT group.

Hospital stay

The length of hospital stay of the Vigileo–GDFT group was 13 (9–20) days (median, 1st–3rd quartile); it was 14 (8–21) days in the standard group ($p = 0.58$). The length of ordinary hospital stay of the Vigileo–GDFT group was 12 (9–19) days, and 12 (8–20) days for the standard group ($p = 0.87$). The length of stay in the ICU was 0 (0–1) days for the Vigileo–GDFT group, and 0 (0–2) days for the standard group ($p = 0.23$; [Table 2](#)).

Costs

In the Vigileo–GDFT group, the costs relating to pharmaceuticals, surgical procedures, hospitalization and diagnostic testing were 55€ (6.5–401); 1517€ (1042–2275); 5700€ (3040–9405); 2019€ (1201–3068), respectively. In the standard group, they were 46€ (31–181); 1706€ (1138–2275); 4940€ (3420–7980); 1868€ (1335–2803), respectively. No significant differences emerged among the four cost categories considered ([Table 2](#)).

Nonsurgical complications (cardiac, respiratory, hepatic and renal) are demonstrated in [Table 2](#), without any significant difference between the two groups.

Table 1. Demographics and perioperative data.

	All patients		Pancreas		Liver	
	Standard (n = 76)	Vigileo GDFT (n = 71)	Standard (n = 23)	Vigileo GDFT (n = 21)	Standard (n = 53)	Vigileo GDFT (n = 50)
Age, mean (SD)	64.5 (11.3)	63.6 (10.8)	65.7 (8.4)	64.7 (9.2)	64 (12.4)	62.2 (11.5)
Sex, M/F	44/32	42/29	17/6	13/8	27/26	29/21
BMI, mean (SD)	25.8 (4.3)	25.9 (4.9)	28 (5.2)	24 (4.5) [†]	24.8 (3.5)	26.6 (4.9)
ASA, I/II/III	3/47/26	3/46/22	0/14/9	0/17/4	3/33/17	3/29/18
Co-morbidity, n (%):						
– Hypertension	46 (60.5%)	46 (64.8%)	18 (40%)	11 (25%)	28 (27.2%)	35 (34%)
– COPD	17 (22.4%)	22 (31%)	6 (13.6%)	7 (15.9%)	11 (10.7%)	15 (14.6%)
– Diabetes	27 (35.5%)	26 (36.6%)	11 (25%)	8 (18.2%)	16 (15.5%)	18 (17.5%)
– Metastatic	20 (26.3%)	5 (7%) [†]	5 (11.4%)	1 (2.3%)	15 (14.6%)	4 (3.9%) [†]
– Cardiac failure	18 (23.7%)	16 (22.5%)	6 (13.6%)	5 (11.4%)	12 (11.7%)	11 (10.7%)
– Neurologic	2 (2.6%)	3 (4.2%)	1 (2.3%)	0	1 (1%)	3 (2.9%)
P-POSSUM operative score, mean (SD)	17.2 (4.8)	17.9 (4.7)	16.8 (5.5)	16.9 (6.7)	18.1 (4.8)	18.4 (4.9)
P-POSSUM physiology score, mean (SD)	19.9 (5.5)	21.8 (6.7)	18.1 (5.6)	19.1 (6.1)	22.1 (5.3)	23 (5.9)
Surgery duration, min, mean (SD)	321 (34)	324 (35)	355 (40)	341 (41)	285 (31)	291 (29)

[†]p < 0.05.

ASA: American Society of Anesthesiologists; COPD: Chronic obstructive pulmonary disease; F: Female; GDFT: Goal-directed fluid therapy; M: Male; P-POSSUM: Portsmouth Physiologic and Operative Severity Score for the enumeration of mortality and morbidity; SD: Standard deviation.

Table 2. Main postoperative data: hepatobiliopancreatic surgery.

Postoperative data	Standard group (n = 76)	Vigileo-GDFT (n = 71)	p-value
Minimum one complication, n (%)	25 (32.9)	17 (23.9)	0.23
>1 complication, n (%)	12 (15.8)	10 (14.1)	0.77
Surgical complications among the complications, n (%)	16 (21.1)	12 (21.1)	0.66
Nonsurgical complications among complications, n (%):	23 (30)	20 (28)	0.53
– Cardiac	3 (13)	4 (20)	0.54
– Respiratory	4 (20)	4 (20)	0.43
– Hepatic	2 (8.7)	1 (5)	0.65
– Renal	2 (8.7)	2 (10)	0.74
Total days of hospital stay, median (1st–3rd quartile)	14 (8–21)	13 (9–20)	0.58
Ordinary days of hospital stay, median (1st–3rd quartile)	12 (8–20)	12 (9–19)	0.87
Days of intensive care, median (1st–3rd quartile)	0 (0–2)	0 (0–1)	0.23
Cost of pharmaceuticals (€), median (1st–3rd quartile)	55 (6.5–401)	46 (31–181)	0.15
Cost of surgery (€), median (1st–3rd quartile)	1517 (1042–2275)	1706 (1138–2275)	0.53
Cost of hospitalization (€), median (1st–3rd quartile)	5700 (3040–9405)	4940 (3420–7980)	0.44
Cost of testing (€), median (1st–3rd quartile)	2019 (1201–3068)	1868 (1335–2803)	0.58

GDFT: Goal-directed fluid therapy.

Therefore, an analysis was carried for subgroups regarding the single surgeries: hepatic and pancreatic. No statistically significant differences emerged in the end points considered (Tables 3 & 4).

The total amount of fluids administered intraoperatively was 8784 ± 1103 ml in the standard group and 5140 ± 1218 ml in the Vigileo-GDFT group ($p < 0.001$). Dosage of dobutamine was statistically significant higher in the Vigileo-GDFT group: 5.0 ± 1.1 in the standard group and 9 ± 0.9 µg/kg per minute in the Vigileo-GDFT group ($p < 0.001$). No significant differences emerged regarding units of red blood cells transfused (Table 5).

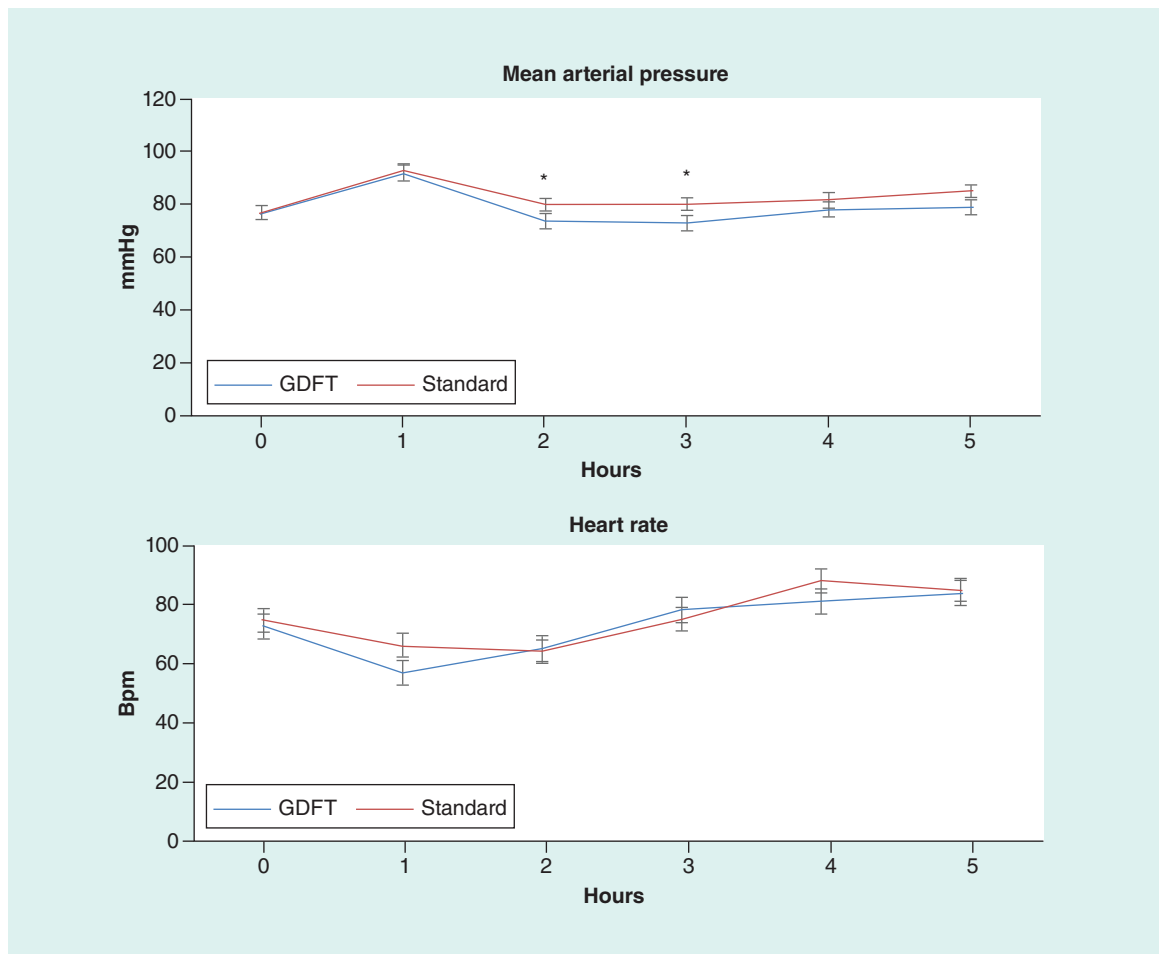


Figure 1. Hourly hemodynamic variables.

*p < 0.05

GDFT: Goal-directed fluid therapy.

Table 3. Main postoperative data: hepatic surgery.

Postoperative data	Standard (n = 53)	Vigileo-GDFT (n = 50)	p-value
Minimum one complication, n (%)	13 (24.5)	8 (16)	0.28
>1 complication, n (%)	6 (11.3)	5 (10)	0.83
Surgical complication among the complications (Clavien-Dindo ≥3), n (%)	8 (15.1)	7 (14)	0.87
Total days of hospital stay, median (1st–3rd quartile)	10 (7–15)	10 (8–13.5)	0.72
Total days of ordinary hospital stay, median (1st–3rd quartile)	10 (7–15)	10 (7–13)	0.7
Days of intensive care, median (1st–3rd quartile)	0 (0–1.5)	0 (0–0.25)	0.9
Cost of pharmaceuticals (€), median (1st–3rd quartile)	64.5 (25.5–64.5)	35.5 (28.7–67.7)	0.3
Cost of surgeries (€), median (1st–3rd quartile)	1138 (916–1896)	1422 (948–1990)	0.5
Cost of hospital stay (€), median (1st–3rd quartile)	3800 (3040–6080)	3990 (3325–5700)	0.74
Cost of testing (€), median (1st–3rd quartile)	1468 (1082–2233)	1489 (1201–1976)	0.72

GDFT: Goal-directed fluid therapy.

Postoperative complications

In accordance with the Clavien-Dindo Classification [16], 71% (105/147) of the patients did not exhibit any postoperative complications; 42 patients (28.5%) experienced grade I–V postoperative complications without any statistically significant difference between the two groups. 28 patients (19%) experienced postoperative complica-

Table 4. Main postoperative data: pancreatic surgery.

Postoperative data	Standard (n = 23)	Vigileo–GDFT (n = 21)	p-value
Minimum one complication, n (%)	12 (52.2)	9 (42.9)	0.53
>1 complication, n (%)	6 (26.1)	5 (23.8)	0.86
Surgical complication among the complications (Clavien-Dindo ≥ 3), n (%)	8 (34.8)	5 (23.8)	0.42
Total days of hospital stay, median (1st–3rd quartile)	22 (16–59)	19 (16–36)	0.18
Total days of ordinary hospital stay, median (1st–3rd quartile)	21 (15–27)	19 (14.5–30.5)	0.4
Days of intensive care, median (1st–3rd quartile)	2 (0–4)	0 (0–1.5)	0.09
Cost of pharmaceuticals (€), median (1st–3rd quartile)	15 (0–982)	61 (46–596)	0.34
Cost of surgeries (€), median (1st–3rd quartile)	2275 (1517–2654)	2086 (1706–2465)	0.89
Cost of hospital stay (€), median (1st–3rd quartile)	9120 (6840–16,340)	7220 (6270–11,590)	0.13
Cost of testing (€), median (1st–3rd quartile)	3070 (2336–4861)	2669 (2304–4307)	0.18

GDFT: Goal-directed fluid therapy.

Table 5. Fluid amount, red blood cells transfused, inotropes and vasopressors.

	Standard group (n = 76)	GDFT group (n = 71)	p-value
Crystalloid volume replacement (ml), mean (SD)	6587 (1004)	3895 (987)	<0.001
Colloid volume replacement (ml), mean (SD)	1927 (316)	1245 (283)	<0.001
Total volume replacement (ml), mean (SD)	8784 (1103)	5140 (1218)	<0.001
Red blood cells transfused (unit)	3	2	0.43
Dobutamine ($\mu\text{g/kg/min}$), mean (SD)	5 (1.1)	9 (0.9)	<0.001
Norepinephrine ($\mu\text{cg/kg/min}$), mean (SD)	0.08 (0.02)	0.06 (0.01)	0.4

GDFT: Goal-directed fluid therapy; SD: Standard deviation.

Table 6. Complications costs: hepatobiliopancreatic surgery.

Complication costs	No surgical complications (n = 119)	With surgical complications (n = 28)	p-value
Cost of pharmaceuticals (€), median (1st–3rd quartile)	7 (0–43)	401 (145–1431)	0.024
Cost of surgeries (€), median (1st–3rd quartile)	1454 (948–1896)	2496 (2085–3649)	<0.001
Cost of hospital stay (€), median (1st–3rd quartile)	4180 (3040–6460)	11,400 (8265–20,900)	<0.001
Cost of testing (€), median (1st–3rd quartile)	1602 (1201–2402)	4078 (2994–6605)	<0.001

tions of Clavien-Dindo grade ≥ 3 and needed surgical reintervention; this group of patients required significantly higher costs of pharmaceuticals, surgeries, hospital stay and diagnostic testing (Table 6).

Discussion

An optimal intraoperative fluid administration plays a crucial role for such a high-risk procedure like hepatobiliopancreatic surgery, avoiding both overhydration with edema and underhydration and tissue hypoxia. Both pancreatic and liver resections, burdened by high morbidity and mortality, generate mechanical and inflammatory stimuli associated to increased stress response, oxygen demand and an increased rate of complications and death. Despite the importance of an appropriate fluid balance, studies on GDFT remain inconclusive.

In this study, we assessed whether the application of a GDFT protocol guided by the minimally invasive Vigileo monitoring system can induce an advantage in terms of costs in the context of hepatobiliopancreatic surgery. To this end, we prospectively compared two groups of patients undergoing hepatobiliopancreatic surgery. Data of patients receiving a GDFT protocol, according to the availability of the Vigileo device, were compared with those of patients who received fluid therapy according to a standardized protocol. Our results showed that the application of a GDFT protocol does not provide benefits in terms of clinical outcome (length of hospital stay) and costs.

Randomized clinical studies and meta-analyses published in the first decade of the 21st century have highlighted the importance of the application of an intraoperative GDFT protocol aimed to reduce postoperative complications and the length of stay for major abdominal surgery [18,19].

Berger *et al.*, in a systematic review, identified goals for perioperative fluid administration targeting of which appeared to be associated with less postoperative complications and shorter ICU/length of hospital stay [20]. Guest *et al.* studied the impact of GDFT within the perioperative period showing a minimum potential cost-saving of 31% [15], and, in a retrospective study, Benes *et al.* concluded that the use of stroke volume variation and Vigileo/FloTrac system showed not only a substantial improvement in morbidity but was associated with an economic benefit [21].

Conversely, an analysis on high-risk patients undergoing major gastrointestinal surgery showed that the use of a therapeutic algorithm of cardiac output-guided hemodynamic does not reduce complications and mortality within 30 days compared with a treatment commonly used in clinical practice [22]. Furthermore, a meta-analysis of 23 clinical studies has shown that GDFT is not superior to a standard fluid therapy regimen in patients undergoing major abdominal surgery [23].

Nevertheless, recent analysis has failed to demonstrate the effectiveness of a GDFT within the context of the ERAS protocol [24]. The optimal perioperative fluid management is an important component of the ERAS protocols, in this context fluid management is considered within a continuum through the different preoperative, intraoperative and postoperative phases [24].

Our results, focused on open surgery of pancreas and liver, could partly be explained considering the population involved in the study: we defined ASA III patients as high-risk patients. They were 48/147 (32.6%) in total, and therefore the majority of patients treated belonged to a low-medium-risk class. GDFT may be more important in a high-risk surgery population than in a relatively healthy population: Jammer *et al.* investigated if high-risk surgical patients could benefit from SVV-guided fluid therapy, but the question remained open [25]. Lastly, studies in the field of ERAS application protocol showed that patients arrive in the operating room without a significant deficit of fluids; this condition aids in the intraoperative management of fluid therapy. Therefore, the effectiveness of GDFT may be less evident within an ERAS program. Our results seem to further reduce the impact of a GDFT cardiac output-guided algorithm on the clinical and economic outcomes considered and we could speculate that patients at low or moderate risk with a proper preoperative fluid balance do not derive additional benefit from the use of a mini-invasive hemodynamic monitoring system.

Furthermore, the incidence of postoperative complications did not seem influenced by the type of fluid therapy applied. A total of 42 patients (28.4%) developed complications in the postoperative period considered (28 days); 17 patients of the Vigileo GDFT group and 25 patients from the standard GDFT group. No difference was observed between the two study groups. More than half of the postoperative complications were of a surgical nature. These complications had a high impact on the costs of the four categories considered: pharmaceuticals, procedures, hospital stay and diagnostic testing. In patients with surgical complications, the increase of cost due to such complications reached statistical significance.

In our study, dobutamine has been mainly administered in the GDFT group. Increase the supply of oxygen in surgical patients at high risk during the perioperative period showed considerable advantages [26]. To obtain adequate tissue oxygenation, boluses of fluids may not be sufficient. The use of vasopressors and inotropes has proved important in integrating GDFT protocols [8]. Dobutamine, a positive inotropic agent and peripheral vasodilator, can play a crucial role in achieving effective tissue oxygenation.

Currently, to our knowledge, no study has analyzed the economic outcomes of a GDFT protocol in hepatobiliary-pancreatic surgery globally. The main limit of our study is that it is a prospective observational study in which the allocation of patients in the groups depended on the availability of the Vigileo device in the hepatobiliary-pancreatic operating room. A randomized controlled trial is needed to confirm our results and it should only consider a high-risk patient population (e.g., ASA $\geq$ III) to clarify whether the lack of economic and clinical benefits of a GDFT based on a mini-invasive hemodynamic monitoring system found in our trial is due to the relatively health state of patients (ASA I–II). Furthermore, the length of hospital stay, which we used as a clinical outcome parameter, is conditioned by different clinical factors besides the GDFT.

Conclusion

Our results suggest that an appropriate fluid therapy could be more effective on high-risk patients with evident fluid balance alterations, rather than on relatively healthy patients; moreover, from a cost-saving perspective, the

advantages of a proper fluid therapy seem to be offset by surgical complications, which are the main determinants of costs.

Summary points

- Hepatobiliopancreatic surgery is considered to be a high-risk procedure and is associated with a relevant systemic inflammatory response and an increased stress response, oxygen demand and an increased rate of complications and death.
- An optimal intraoperative fluid administration plays a crucial role, avoiding both overhydration with edema and underhydration and tissue hypoxia.
- Despite the importance of an appropriate fluid balance in hepatobiliopancreatic surgery, studies on GDFT remain inconclusive.
- Our results showed that the application of a GDFT protocol does not provide benefits in terms of clinical outcome (length of hospital stay) and costs.
- To obtain adequate tissue oxygenation, boluses of fluids may not be enough and dobutamine can play a crucial role in achieving effective tissue oxygenation.
- Our study shows that an appropriate fluid therapy could be more effective on high-risk patients with evident fluid balance alterations, rather than on relatively healthy patients.
- Surgical complications seem to have a determinant impact on the considered costs reaching statistical significance.
- This is a prospective observational study. A randomized controlled trial is needed to confirm our results.

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Availability of data & materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Financial & competing interests disclosure

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No writing assistance was utilized in the production of this manuscript.

Ethical conduct of research

The authors state that they have obtained appropriate institutional review board approval or have followed the principles outlined in the Declaration of Helsinki for all human or animal experimental investigations. In addition, for investigations involving human subjects, informed consent has been obtained from the participants involved.

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