



Impact of goal directed therapy in free flap reconstructive surgery of the head and neck

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Background: Free flap reconstruction of head and neck defects has improved in recent years and multidisciplinary management is necessary to optimize the patient outcome. Few studies have focused on the relation between intraoperative haemodynamic management in free flap reconstructive surgery and the incidence of complications. The aim of the study was to identify patient and intraoperative predictors of postoperative medical and surgical complications. A secondary objective was to investigate the impact of the introduction of a hemodynamic monitoring system on intraoperative fluid and vasopressor management and on complications.

Methods: A retrospective cohort study of patients undergoing free flap reconstruction surgery between 2005 and 2022 was conducted. A multivariate model was developed to evaluate the association between the covariates and the incidence of medical and surgical complications. Then, the population was subdivided according to whether or not invasive hemodynamic monitoring was used. The incidence of complications and intraoperative management of fluids and vasopressors were evaluated using a linear regression model.

Results: The study included 208 patients. Higher intraoperative hemoglobin values at the end of surgery [odds ratio (OR): 0.46, 95% confidence interval (CI): 0.25–0.83, P=0.01] and arterial hypertension (OR: 0.27, 95% CI: 0.08–0.95, P=0.04) were associated with a reduced risk of postoperative surgical complications. Length of postoperative intensive care unit stay (OR: 1.62, 95% CI: 1.30–2.03, P=0.008), tumor stage T1–2 (OR: 3.00, 95% CI: 1.28–6.90, P=0.03), tumor stage T3–4 (OR: 4.41, 95% CI: 3.73–12.3, P=0.006) and a history of arterial hypertension (OR: 3.74, 95% CI: 1.21–11.6, P=0.02) were predictors of medical complications. The use of invasive hemodynamic monitoring was associated with a reduction in intraoperative fluid administration (8.2 vs. 9.5 mL/kg/h, P=0.008), increased use of vasopressors (OR: 2.53, P=0.003) and reduction of the length of hospital stay (20 vs. 23 days, P=0.038).

Conclusions: Our study identifies patient and management-related factors as predictors of postoperative complications and supports the evidence favoring goal-directed intraoperative fluidic management. The introduction of a continuous invasive monitoring system significantly reduced the amount of fluid administered and shortened the hospital length of stay. Further studies are needed to validate precise protocols regarding the use of goal directed therapy.

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Introduction

Background

Large defects in the head and neck caused by resection of advanced tumors, severe facial trauma or deformity can result in dysphagia, phonation, and cosmetic impairment. Microvascular free flaps represent a first choice for head and neck reconstruction after ablative surgery ensuring better functional results and generally higher success rates compared to local and regional flaps (1). However, the duration and complexity of the procedure are significantly greater.

Although success rates of more than 95% (2), complications such as flap failure are still a major concern due to their impact on patient clinical outcome (3,4). A

coordinated multidisciplinary approach throughout the perioperative period is crucial to optimizing healthcare and enhancing patient outcomes. Optimal flap perfusion during the surgical procedure can be achieved by maintaining adequate tissue oxygenation and cardiac output (CO), and intraoperative management of fluids and vasopressors appears to be essential part of a delicate process aimed at maintaining optimal pressure and perfusion during the surgical procedure (5,6). It has been reported that avoiding too liberal or restrictive fluid regimens could be associated with a reduction in morbidity, length of hospital stay and flap thrombosis (7-11). Studies have also been designed to identify clear limits for fluid administration beyond which the risk of surgical complications increases (10,12). The use of vasopressors does not appear to have a significant clinical impact (5), although their use has been shown to be associated with a reduction in flap blood flow in animal models (13), while the use of inotropes, such as dobutamine, appears to improve flap arterial perfusion albeit with reservations (14).

Highlight box

Key findings

- Higher hemoglobin values and arterial hypertension reduce the risk of postoperative surgical complications.
- Length of intensive care unit stay, malignant pathologies and arterial hypertension are predictors of postoperative medical complications.
- The use of invasive hemodynamic monitoring reduces intraoperative fluid administration, increases use of vasopressors and reduces the length of stay.

What is known and what is new?

- In this study, the use of invasive hemodynamic monitoring is associated with a reduction in intraoperative fluid administration, but consequent role of vasopressors is discussed.
- The use of invasive hemodynamic monitoring is associated with an increased administration of vasopressors without a corresponding rise in complication rates. Additionally, it appears to decrease the length of hospital stays.

What is the implication, and what should change now?

- New and well-dimensioned studies are needed. A standardized protocol regarding the use of goal-directed therapy should be validated in larger cohorts of patients.

Rationale and knowledge gap

Consensus recommendations from the Enhanced Recovery after Surgery Society and the Society for Head and Neck Anesthesia provide guidance on current best practice. Current recommendations regarding intraoperative fluid management encourage achieving a euvoletic state through a zero-balance fluid strategy or the use of intraoperative hemodynamic monitoring to perform goal directed therapy (GDT) (15,16). A recent meta-analysis shows that the introduction of GDT in non-cardiac surgery could reduce mortality, length of hospital stay and some postoperative complications such as infections and anastomotic leaks (17). Nevertheless, there is no clear consensus regarding the use of precise GDT protocols and their applications, and the issue remains an open debate between anesthesiologists and surgeons.

Objective

In this article, we evaluated variables that may affect medical and surgical outcomes by retrospectively analyzing our series of 220 free flap reconstructions in head and neck surgery.

The aim of the present study was to record the medical and surgical complications during the patient's hospital stay and to identify patient and intraoperative predictors of postoperative complications. A secondary objective was to investigate the impact of the hemodynamic monitoring system on intraoperative fluid and vasopressor management and perioperative complications. We present this article in accordance with the STROBE reporting checklist (available at <https://joma.amegroups.com/article/view/10.21037/joma-23-28/rc>).

Methods

Our single-center retrospective cohort study included patients undergoing head and neck free tissue transfer surgery between 2005 and 2022 at Città della Salute e della Scienza University Hospital in Turin (Italy). All patients over 18 years of age reconstructed with free flaps in the head and neck region were included. Patients with incomplete clinical or surgical records were excluded from this study. Data on the intra- and postoperative period were obtained from the hospital electronic medical record and archived in a database with access limited to the authors involved with data analysis.

The primary outcome was the incidence of medical or surgical complications during the patient's hospital stay. Surgical complications were subdivided into major, if they required surgical revision, or minor, according to the Clavien-Dindo classification (18). Medical complications included systemic and organ-specific infections, organ-related complications, and mortality.

The use of an invasive hemodynamic monitoring system (FloTrac™ system, Edwards Lifesciences, Irvine, CA, USA) to guide intraoperative fluid therapy was set as an independent dichotomic variable. FloTrac™ system is based on an algorithm that allows to extrapolate hemodynamic parameters such as CO, cardiac index, stroke volume (SV), stroke volume index (SVI) and stroke volume variation (SVV) from the arterial pressure waveform. All patients received intraoperative fluid maintenance therapy at the discretion of the anesthesiologist. For patients receiving invasive hemodynamic monitoring, additional fluid challenge was performed according to SVV value and inotropes and

vasopressor were started to maintain adequate cardiac index and mean arterial blood pressure. Preoperative variables used as covariates and retrospectively acquired from the medical record, included demographic data, comorbidities, American Society of Anesthesiologists Classification of Physical Status System (ASA-PS) and tumor staging. Intraoperative variables included the volume of fluids administered, volume and type of colloid, use of vasopressor or inotrope, use of packed red blood cells (RBC) and duration of surgery. Postoperative variables included surgical and medical complications, RBC transfusions, intensive care unit (ICU) and hospital length of stay (LOS), and in-hospital mortality.

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the institutional ethical committee of AOU Città della Salute e della Scienza of Torino, Italy on 5 June 2023 (No. 183/2023) and individual consent for this retrospective analysis was waived.

Statistical analysis

Descriptive statistical analysis was performed on the patient's baseline characteristics. Quantitative data were presented with median and interquartile ranges and qualitative data as absolute frequencies and percentages.

We performed a multivariable logistic regression analysis to estimate the association between surgical/medical complications and the following variables: age, ASA score, comorbidities, volume of fluids, use of colloids, use of inotrope or vasopressor, lowest hemoglobin value, invasive hemodynamic monitoring, intraoperative and postoperative RBC transfusions, surgical time, ICU LOS, oncological disease, neck dissection and TNM classification. The goodness of fit of the logistic regression model was evaluated using the Hosmer-Lemeshow test. The results were summarized with odds ratio (OR) and 95% confidence intervals (CIs). Tests were two-tailed and a P value less than 0.05 was considered statistically significant. We applied univariate logistic regression analysis to estimate the relationship between the use of an invasive hemodynamic monitoring system to guide fluid therapy and the incidence of postoperative complications, intraoperative use of colloids, vasopressor or packed RBC and univariate linear regression analysis to estimate the relationship between hemodynamic monitoring, volume of fluids administered and hospital LOS. Statistical analysis was performed using R Statistical Software (version 4.3.0; R Foundation for Statistical

Table 1 Summary of baseline characteristics

Variables	Median [IQR]/N [%]
Age (years)	61 [50–70]
ASA score	
1	19 [9]
2	129 [62]
3	60 [29]
4	0
Obesity (BMI >30 kg/m ²)	20 [10]
Alcohol abuse	24 [12]
Tobacco use (or cessation <1 year)	76 [37]
Chronic pulmonary disease	16 [8]
Diabetes	25 [12]
Dyslipidaemia	32 [15]
Hypertension	70 [34]
Ischemic heart disease	6 [3]
Chronic kidney disease	7 [3]
Hepatobiliary disease	11 [5]
Coagulation disorders	9 [4]
Invasive haemodynamic monitoring	132 [63]
Volume of fluids (mL/kg/h)	8.3 [6.5–10]
Use of colloids	133 [64]
Hydroxyethyl starch	77 [37]
Albumin	71 [34]
Use of inotrope or vasopressor	112 [54]
Norepinephrine	59 [28]
Dopamine	49 [24]
Ephedrine	25 [12]
Phenylephrine	8 [4]
Dobutamine	2 [1]
Lowest intraoperative hemoglobin (g/dL)	8.2 [7.4–9.3]
Intraoperative use of packed red blood cells	90 [43]
Duration of surgery (minutes)	550 [480–640]
Length of stay (days)	20 [6–29]
ICU admission	187 [90]
ICU length of stay (days)	2 [2–4]

IQR, interquartile range; ASA, American Society of Anesthesiologists; BMI, body mass index; ICU, intensive care unit.

Computing, Vienna, Austria).

Results

In the study period, 220 patients underwent free flap reconstructive surgery of head and neck. Twelve were excluded due to age under eighteen years or missing documentation and 208 (92 female and 116 males) were included. The median age at surgery was 61 years, ranging from 19 to 86 years. The baseline characteristics of the study population are presented in *Table 1*.

Out of all patients, 72.1% underwent surgery for malignant tumor resection. The remaining 27.9% were diagnosed with non-malignant conditions, including keratocysts or other cysts (8.6%), ameloblastomas (5.8%), osteonecrosis and osteomyelitis (3.4%). Additionally, some patients required secondary reconstruction after cancer resection (8.2%) or due to trauma (1.9%). Reconstruction was performed by an osteo-myo-cutaneous or bony fibular (n=87), radial forearm (n=50), anterolateral femoral (n=35), latissimus dorsi (n=27), iliac crest (n=3) or rectus abdominis (n=6) flap. A titanium reconstruction plate was used in 60 patients. Tracheostomy was performed in 167 cases (80.3%), while unilateral or bilateral neck dissection was required in 136 patients (65.4%). The average duration of surgery was 550 minutes.

Postoperative complications

A total of 106 (51%) subjects experienced at least one medical or surgical complication (*Table 2*) with no significant differences between the baseline characteristics of the two subgroups.

Major surgical complications, requiring readmission to the operating room and including total flap necrosis or hemorrhage occurred in 32 (15%) patients, while minor surgical complications, not requiring revision surgery, occurred in 73 (35%) patients.

Medical complications, mainly represented by infections, postoperative pulmonary complications and cardiovascular complications, occurred in 49 (24%) patients. Pneumonia was the most common infection, followed by urinary tract and bloodstream infections. More than half of the patients required postoperative RBC transfusions. Overall mortality was 1.4%.

As reported in *Table 3*, the multivariate model developed for the analysis of postoperative complications showed that a history of arterial hypertension (OR: 0.27, 95% CI: 0.08–

Table 2 Summary of postoperative complications

Complications	N [%]
Major surgical complications	32 [15]
Flap necrosis	18 [9]
Hemorrhage	14 [7]
Minor surgical complications	73 [35]
Partial flap failure	6 [3]
Flap dehiscence	47 [23]
Surgical site infection	20 [10]
Medical complications	49 [24]
Infections (pneumonia, sepsis/septic shock, UTI)	26 [13]
Pulmonary complications (respiratory failure, prolonged mechanical ventilation, pleural disorders)	20 [10]
Renal complications (acute kidney injury, acute renal failure)	3 [1]
Cardiovascular complications (new onset arrhythmias, myocardial injury, cardiac arrest)	12 [6]
Hematologic complications (deep vein thrombosis, pulmonary embolism)	3 [1]
Cerebrovascular accident	2 [1]
Delirium	9 [4]
Gastrointestinal tract complications	5 [2]
Mortality	3 [1.4]
Postoperative blood transfusions	133 [64]

UTI, urinary tract infection.

0.95, $P=0.04$) and higher intraoperative hemoglobin values at the end of surgery (OR: 0.46, 95% CI: 0.25–0.83, $P=0.01$) were associated with a reduced risk of major surgical complications. In this study, a history of alcohol abuse and postoperative RBC transfusions appear to be linked with a higher risk of major surgical complications, although this correlation does not reach statistical significance. Length of postoperative ICU stay (OR: 1.62, 95% CI: 1.30–2.03, $P=0.008$) and a history of arterial hypertension (OR: 3.74, 95% CI: 1.21–11.6, $P=0.02$) were strong predictors of postoperative medical complications. Patients with microsurgical reconstructions with oncological etiology had a greater number of complications than non-oncological patients. The risk of complications was greater with higher tumor stage (T1–2: OR: 3.00, 95% CI: 1.28–6.90, $P=0.03$; T3–4: OR: 4.41, 95% CI: 3.73–12.3, $P=0.006$). Intraoperative use of hydroxyethyl starch (HES) was associated with an increased risk of postoperative medical complications, but didn't reach statistical significance.

The intraoperative median volume of fluids administered

was 8.3 (interquartile range, 6.5–10) mL/kg/h. Colloids have been administered to 133 (64%) patients: 71 received albumin and 77 HES; in 15 cases both albumin and HES were administered. Ninety patients required RBC transfusions and more than half of the patients received either vasopressors or inotropes for hemodynamic support.

No significant correlation was observed between the volume of fluids administered, the use of colloids, RBC transfusions, amines and the occurrence of medical or surgical complications as none of the factors reached statistical significance (*Table 3*).

In 145 (69.7%) patients intraoperative fluidic management was based on data from the invasive hemodynamic monitoring system (FloTrac™ system). In this study, the utilization of the FloTrac system (*Table 4*) was associated with a decrease in the volume of administered fluids (*Figure 1A*) and an increase in the use of amines, without a definitive impact on reducing postoperative medical or surgical complications. However, its adoption was correlated with a notable reduction in length of hospital stay (20 *vs.*

Table 3 Multivariate regression analysis of risk factors for postoperative complications

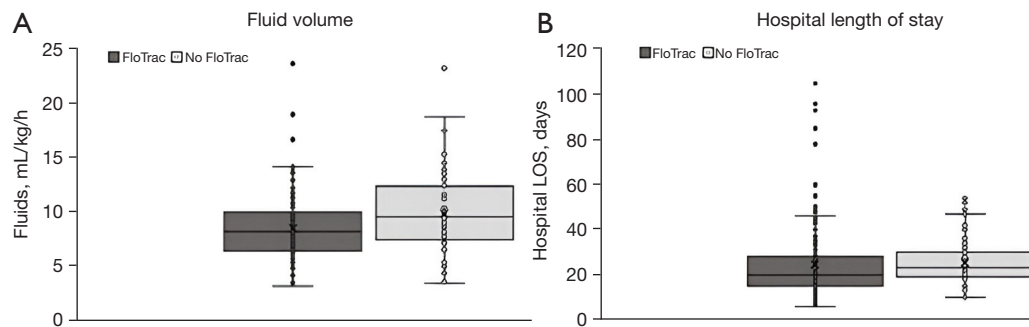
Variables	Surgical complication		Medical complication	
	Odds ratio (95% CI)	P value	Odds ratio (95% CI)	P value
ASA score	0.67 (0.22–1.97)	0.46	1.43 (0.47–4.35)	0.53
Age	1.02 (0.98–1.07)	0.28	0.99 (0.95–1.04)	0.74
Obesity	4.62 (0.66–32.3)	0.12	0.81 (0.12–5.49)	0.83
Alcohol abuse	3.72 (0.96–14.4)	0.06	0.94 (0.22–4.11)	0.94
Tobacco use	0.89 (0.25–3.11)	0.85	0.76 (0.23–2.55)	0.66
Chronic pulmonary disease	2.2 (0.36–13.6)	0.39	2.79 (0.49–15.9)	0.25
Diabetes	0.25 (0.03–2.33)	0.23	0.35 (0.06–2.00)	0.24
Hypertension	0.27 (0.08–0.95)	0.04*	3.74 (1.21–11.6)	0.02*
Ischemic heart disease	9.81 (0.38–256)	0.17	1.73 (0.06–47.6)	0.74
Chronic kidney disease	7.52 (0.72–78.5)	0.09	4.78 (0.42–54.4)	0.21
Hepatobiliary disease	0.91 (0.11–7.38)	0.93	6.47 (0.64–65.4)	0.11
Coagulation disorders	0.01 (0.001–15.9)	0.99	0.04 (0.001–3.75)	0.15
Volume of fluids	1.09 (0.94–1.28)	0.24	0.98 (0.83–1.17)	0.86
Hydroxyethyl starch	0.39 (0.13–1.17)	0.09	2.67 (0.95–7.47)	0.06
Albumin	0.75 (0.25–2.18)	0.59	2.26 (0.78–6.53)	0.13
Use of inotrope/vasopressor	0.71 (0.26–1.97)	0.51	1.61 (0.57–4.51)	0.37
Lowest intraoperative Hb	0.46 (0.25–0.83)	0.01*	1.26 (0.8–1.97)	0.32
Use of packed red blood cells	0.36 (0.09–1.34)	0.13	1.38 (0.38–5.04)	0.63
Invasive haemodynamic monitoring	0.94 (0.33–2.70)	0.91	1.44 (0.46–4.51)	0.54
Duration of surgery	1.00 (0.99–1.00)	0.14	1.00 (1.00–1.30)	0.08
ICU length of stay	1.06 (0.96–1.17)	0.26	1.62 (1.30–2.03)	0.008*
Oncological disease	1.42 (0.21–9.47)	0.72	0.11 (0.01–2.17)	0.15
Neck dissection	0.43 (0.09–2.06)	0.29	0.44 (0.09–2.17)	0.32
Postoperative transfusions	3.00 (0.82–11.0)	0.10	2.59 (0.76–8.81)	0.13
TNM (T1–2)	3.75 (0.42–33.9)	0.24	3.00 (1.28–6.90)	0.03*
TNM (T3–4)	2.13 (0.26–17.2)	0.48	4.41 (3.73–12.3)	0.006*
TNM (N0–1)	0.45 (0.06–3.50)	0.48	0.69 (0.07–7.30)	0.76
TNM (N2–3)	0.28 (0.02–3.04)	0.48	0.76 (0.06–9.41)	0.83

*, $P < 0.05$ was considered statistically significant. CI, confidence interval; ASA, American Society of Anesthesiologists; Hb, hemoglobin; ICU, intensive care unit.

Table 4 Univariate logistic regression analysis. Impact of FloTrac™ on intraoperative hemodynamic management, postoperative complications and hospital LOS

Variables	No FloTrac™	FloTrac™	Odds ratio (95% CI)	P value
Volume of fluids (mL/kg/h), median [IQR]	9.5 [7.5–11.6]	8.2 [6.4–10]		0.008*
Use of colloids, N [%]	31 [49]	59 [41]	0.71 (0.39–1.28)	0.256
Use of inotrope or vasopressor, N [%]	31 [49]	103 [71]	2.53 (1.37–4.66)	0.003*
RBC transfusions, N [%]	25 [40]	62 [43]	1.14 (0.622–2.07)	0.680
Total complications, N [%]	36 [57]	72 [50]	0.74 (0.41–1.34)	0.321
Medical complications, N [%]	16 [25]	33 [23]	0.866 (0.435–1.721)	0.412
Surgical complications, N [%]	24 [38]	53 [37]	0.936 (0.508–1.724)	0.832
Hospital LOS (days), median [IQR]	23 [19–30.5]	20 [15–28]		0.038*

*, P<0.05 was considered statistically significant. LOS, length of stay; CI, confidence interval; IQR, interquartile range; RBC, red blood cell.

**Figure 1** Comparison between standard monitoring and use of FloTrac™ on volume of fluids administered (A) and hospital LOS (B). LOS, length of stay.

23 days, P=0.038) (Figure 1B).

Discussion

Key findings

In the present work, we analyzed patient and perioperative management characteristics and their association with postoperative medical and surgical complications. It emerged that a history of arterial hypertension and the presence of higher hemoglobin values at the end of surgery seem to reduce the risk of major postoperative surgical complications. A potentially protective role of arterial hypertension on flap failure rate has been previously described by Crawley *et al.* (19); this association, however, is partly offset by the potentially harmful role of a history of arterial hypertension on postoperative medical complications and warrants additional investigation,

especially considering the retrospective and single-center design of the study.

Postoperative medical complications, on the other hand, seem to be significantly increased in patients with hypertension, in the case of locally advanced tumors or, as conceivable, in case of prolonged ICU stay (20). It is to be emphasized that, unlike previous studies (8-10,12), our study did not identify variables such as age and comorbidities to be risk factors for postoperative complications and did not show any correlation between administered fluid volume and complication rates. Regarding amine and colloids, our study shows that their use is not associated with an increase in flap failure or postoperative complications. The study, however, appears to show a potentially harmful role of starch use despite the correlation not being statistically significant.

Use of the FloTrac™ system did not result in a reduction in patient postoperative complications; it was, however, associated with a significant reduction in the

hospital LOS. Thus, we confirmed that the use of an invasive hemodynamic system is beneficial in both limiting the amount of fluids administered and reducing the hospital stay.

Strengths and limitations

This study reports features and outcomes of 220 patients undergoing free flap reconstructive surgery of the head and neck region, aiming to assess potential risk factors from both anesthesiological and surgical perspectives and their correlation with medical and surgical complications in a multidisciplinary context.

The study has certain limitations. Although the results are consistent with existing literature evidence, their interpretation is constrained by the study's retrospective and monocentric design, with a relatively small patient cohort. Finally, it is difficult to rule out the potential impact of confounding factors such as the surgeon's learning curve, modifications in surgical technique, and perioperative anesthesiological management. The relatively low number of patients and their heterogeneity hinder the identification of the most effective perioperative management. Future prospective studies are needed to confirm these associations.

Comparison with similar researches

Microvascular free flap reconstruction of head and neck district are complex surgical procedures characterized by a potentially high risk of perioperative complications. Evidence from the literature show that a better multidisciplinary perioperative management leads to an improvement in flap survival and a decrease in the complication rates (2). Different studies have evaluated the impact of comorbidities on the outcome of patients undergoing free flap transfer, identifying several risk predictors such as age, comorbidity indices, smoking, intraoperative hemoglobin values, and perioperative fluid management (8-10).

Explanations of findings

Predictors such as hemoglobin values and ICU LOS could potentially be modified with preoperative strategies including Patient Blood Management (21) and postoperative admission to Surgical Step-down Units.

While there is evidence that both restrictive and liberal intraoperative fluid regimens are associated with increased postoperative complications (12,22), our study did not show

any correlation between administered fluid volume and complication rates. It is noteworthy, however, that in our study the majority of patients received intraoperatively a large amount of fluids and only a few achieved a "near zero" fluid balance and the study's retrospective and single-center design may restrict the generalizability of these findings. Regarding amine and colloids, our finding is consistent with analogous results that have been reported by other authors (12,22-26), suggesting against the hypothesis that vasopressors could increase the rate of flap failure due to impaired microcirculation and flap hypoperfusion.

The introduction of an invasive hemodynamic monitoring system, as previously pointed out by Tapia *et al.* (27) and Funk *et al.* (28), radically modifies the intraoperative hemodynamic management leading to a decrease in fluid administration and an increase in the use of vasopressors or inotropes. Our finding is consistent with existing evidence on GDT (17,23).

Implications and actions needed

New and well-dimensioned studies are needed to identify the most effective hemodynamic and fluid management in microvascular head and neck reconstruction. A standardized protocol for goal-directed therapy should be validated on larger cohorts of patients to improve outcomes.

Conclusions

Given the growing number of procedures that are based on the use of reconstructive techniques with free flaps, an accurate perioperative management has become of the utmost importance in order to increase the surgical success rates and decrease postoperative complications. Our study confirms the role of some patient-related and management-related factors associated with the development of postoperative complications. The early identification of these risk factors could be important in optimizing the perioperative management of patients.

We did not observe a statistically significant difference on the primary outcome between patients monitored with FloTrac™ and those who received usual care. This study supports the growing evidence favoring a goal-directed fluid management over liberal approaches reporting a correlation between continuous invasive monitoring systems and a significant reduction in the volume of administered fluids and hospital LOS. Nevertheless, further prospective studies are necessary to yield conclusive insights.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at <https://joma.amegroups.com/article/view/10.21037/joma-23-28/rc>

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <https://joma.amegroups.com/article/view/10.21037/joma-23-28/coif>). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the institutional ethical committee of AOU Città della Salute e della Scienza of Torino, Italy on 5 June 2023 (No. 183/2023) and individual consent for this retrospective analysis was waived.

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