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ORIGINAL RESEARCH

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Impact of goal-directed hemodynamic therapy on perioperative outcomes in head and neck free flap surgery: A before-and-after pilot study

Justine Philteos[1] | Stuart A. McCluskey[2,3] | Sophia Emerson[2,3] | George Djaiani[2,3] | David Goldstein[1] | Sabri Soussi[2,4]

[1]Department of Otolaryngology—Head and Neck Surgery, University Health Network, University of Toronto, Toronto, Ontario, Canada

[2]Department of Anesthesiology and Pain Medicine, University of Toronto, Toronto, Ontario, Canada

[3]Department of Anesthesia and Pain Management, Toronto General Hospital, University Health Network, Toronto, Ontario, Canada

[4]Department of Anesthesia and Pain Management, Toronto Western Hospital, University Health Network, Toronto, Ontario, Canada

Correspondence

Sabri Soussi, Department of Anesthesia and Pain Management, Toronto Western Hospital, University Health Network, Room McL2-405, 399 Bathurst St., Toronto, ON M5T 2S8, Canada.
Email: sabri.soussi@uhn.ca

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Abstract

Background: Free flap reconstruction for head and neck cancer is associated with a high risk of perioperative complications. One of the modifiable risk factors associated with perioperative morbidity is intraoperative hypotension (IOH). The main aim of this pilot study is to determine if the intraoperative use of goal-directed hemodynamic therapy (GDHT) is associated with a reduction in the number of IOH events in this population.

Methods: A before-and-after study design. The patients who had intraoperative GDHT were compared to patients from a previous period before the implementation of GDHT. The primary outcome was the number of IOH episodes defined as five or more successive minutes with a mean arterial pressure <65 mmHg. The secondary outcomes included major postoperative morbidity and 30-day mortality.

Results: A total of 414 patients were included. These were divided into two groups. The control group ($n = 346$; January 1, 2018, to December 31, 2019), and the monitored group ($n = 68$; January 1, 2020, to May 1, 2021). The median intraoperative administered fluid volume was similar between the control and monitored groups (2250 interquartile range [IQR] [1607–3050] vs. 2210 IQR [1700–2807] mL). The monitored group was found to have an increased use of norepinephrine and dobutamine (respectively, 1.2% vs. 5.9% and 2.4% vs. 30.9%; $p < 0.05$). When adjusting for confounders (comorbidities, estimated blood loss, and duration of anesthesia) the incidence rate ratio (95% confidence interval) of number of IOH events was 0.94 (0.86–1.03), $p = 0.24$. The rate of postoperative flap and medical complications did not differ between the two groups.

Conclusions: Even though the use of vasopressors/inotropes was higher in the monitored group, the number of IOH episodes and postoperative morbidity and mortality were similar between the two groups. Further change in hemodynamic management will require the use of specific blood pressure targets in the GDHT fluid algorithm.

KEYWORDS

cardiac output, head and neck free flap surgery, hemodynamic monitoring, intraoperative hypotension, postoperative outcomes

1 | INTRODUCTION

The standard of care for large defects after head and neck cancer excision is free tissue transfer (FTT) reconstruction. These patients tend to be older with multiple comorbidities,[1] and thus are more prone to increased perioperative morbidity including delirium, pneumonia, cardiovascular events, acute kidney injury, and free flap failure.[2,3]

One of the modifiable risk factors associated with perioperative morbidity in this population is intraoperative hypotension (IOH).[4–6] The main challenge in perioperative fluid management is the balance of avoiding significant hypovolemia, which may induce IOH with end-organ hypoperfusion, without over-resuscitating the patient with the risk of not only organ edema but also free flap edema due to the absence of lymphatic drainage.[7] The avoidance of IOH due to vasodilation is even more challenging in free flap cases as the use of vasopressors to maintain blood pressure is still a matter of debate even if recent studies have reported that it does not increase the risk of flap complications.[8,9]

In these conditions, avoiding fluid administration or vasopressors may expose FTT patients to long periods of IOH, especially during times of minimal stimulation (e.g., microvascular anastomosis) leading to flap and organ hypoperfusion and dysfunction.[4,6] Several surgical specialties (e.g., major abdominal surgery) have made extensive use of goal-directed hemodynamic therapy (GDHT) based on relatively noninvasive cardiac output (CO) monitoring to optimize fluid balance during and after surgery, which has resulted in a decrease in postoperative morbidity.[10,11] Nonetheless, only scarce data exist on the impact of GDHT on the occurrence of IOH in major head and neck surgery patients, which may directly affect end organ and flap perfusion and postoperative outcomes.[12,13] GDHT may be a physiological approach in FTT patients to improve the prediction of treatment responsiveness (e.g., fluids, vasopressors, and inotropes) and the decreasing of IOH episodes and its associated morbidity. Therefore, we designed this before-and-after pilot study, which the primary aim is to assess if the intraoperative use of GDHT is associated with a reduction in the number of IOH events in this population. The secondary aims were to determine if there were differences in (i) intraoperative management with the addition of an advanced hemodynamic monitoring and (ii) the occurrence of postoperative complications.

2 | MATERIALS AND METHODS

2.1 | Study design and eligibility

This is a before-and-after study including all consecutive patients undergoing major head and neck surgery requiring free-flap reconstruction at the University Health Network (Toronto, Ontario, Canada).

Patients were included if they were (i) adult patients (age ≥18 years), (ii) undergoing major head and neck free flap reconstructive surgery—defined as any head and neck ablative procedure or secondary reconstructive procedure involving FTT, (iii) had an arterial line placed at the time of surgery, and (iv) for the patients admitted after GDHT implementation, they had intraoperative advanced hemodynamic monitoring using a beat-by-beat minimally invasive CO estimation by pulse wave analysis (FloTrac; Edwards Lifesciences). Exclusion criteria was past medical history of cardiac arrythmia (e.g., atrial fibrillation) as CO estimation using pulse wave analysis is not accurate in this condition.[14]

Patients were divided into two groups based on the date of implementation of GDHT (i.e., before the implementation of GDHT (between January 1, 2017 and December 31, 2019) versus after the implementation of GDHT (between January 1, 2020 and May 1, 2021) with intraoperative CO monitoring). An arterial line was inserted in all patients.

The study protocol was approved by the University Health Network Ethics and Research Committee (August 30, 2021, ID 21-5664). Written informed consent from all enrolled patients was waived (retrospective noninterventional design with no risk to the participants). Reporting of this study was in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement and guidelines.[15]

2.2 | Data collection

The following data were collected retrospectively from patient records, either electronic or paper (anesthesia records and patient charts in the electronic patient record [EPR]) and compared between the two groups: patient demographics, body mass index (BMI), comorbidities, smoking status, alcohol consumption, antihypertensive treatments in the last 24 h before surgery and Charlson comorbidity index (CCI). Intraoperative data was extracted from the Drug Reconciliation Electronic Anesthesia Monitor (DREAM) database including invasive arterial pressures, pulse pressure variation (PPV), intravenous fluid volume and type administered (e.g., crystalloids, colloids), blood loss and blood product transfusion (i.e., packed red blood cells, fresh frozen plasma), vasopressors and inotropes administered (i.e., type, maximal dose, total dose, and duration), intraoperative urine output, lowest recorded hemoglobin level and highest plasma lactate level from serial arterial blood gases drawn during surgery, mechanical ventilation settings, depth of anesthesia monitoring (E-Entropy Monitor; GE Healthcare) and surgical duration. Furthermore, advanced hemodynamic parameters (e.g., CO, stoke volume [SV], and stroke volume variation [SVV]) were recorded for the monitored group. Invasive pressures were measured and recorded at 1-min intervals in the DREAM database. Artifactual data (e.g., pressures out of range or abrupt changes) were removed using previously published criteria.[16]

From the day of surgery to hospital discharge or death, we retrospectively collected from electronic records postoperative medical and surgical complications (i.e., infections, organ, and flap dysfunctions), postoperative hospital length of stay, and vital status.

After the implementation of GDHT, not all the patients had an intraoperative CO monitoring. These nonmonitored patients were not included in the study as the implementation of GDHT in the institution may have affected the way the anesthesiologists managed these patients intraoperatively.

2.3 | Perioperative care

All patients underwent general anesthesia during head and neck FTT surgery. Induction and the maintenance of anesthesia were performed at the discretion of the attending anesthesiologist with either sevoflurane (>0.7 minimum alveolar concentration [MAC]) and/or propofol continuous infusion targeting a state *entropy* (SE) index value *between 40 and 60*. Narcotics (e.g., remifentanil, fentanyl, hydromorphone) and rocuronium were titrated during the procedure as needed (train-of-four counts between 1 and 3 as a target for neuromuscular blockade). Protective ventilation was applied (tidal volume = 7 mL/kg of ideal body weight) while maintaining an inspiratory peak pressure <30 cmH_2O. Standard monitoring in both groups included electrocardiogram, pulse oximetry, central temperature, and inspiratory and expiratory gas concentrations as well as monitoring of depth of anesthesia (i.e., SE index). In all patients, invasive blood pressure was monitored via right or left radial artery. Arterial blood gases were performed intraoperatively in all patients as needed to monitor the adequacy of gas exchange and hemoglobin and lactate levels as per the institutional protocol. Hemodynamic optimization in both groups (i.e., fluids, vasopressors, inotropes) was left at the discretion of the attending anesthesiologist in both intervention and control groups based on the available hemodynamic parameters. In the intervention group, the anesthesiologists used an intraoperative GDHT algorithm based on CO optimization. The GDHT algorithm is presented in Supporting Information S1: Material 1.

The institutional postoperative flap protocol includes flap checks every hour for the first 24 h followed by every 2–4 h for the remainder of the inpatient stay.

2.4 | Study endpoints

The primary outcome is the number of IOH episodes defined as the minimum of five successive minutes with a mean arterial pressure (MAP) below 65 mmHg with a subsequent return to a MAP greater than these cutoff values for an additional 5 min between induction and patient extubation. We considered a cumulative hypotensive duration of 5 min or greater during surgery to avoid capturing durations that may not significantly influence organs/flap hypoperfusion (e.g., 1–2 min).[6,17,18] The duration of IOH was defined as a MAP < 65 mmHg. The durations below different MAP targets were also reported (i.e., <55, <60, <70, or <75 mmHg). We also reported the ratio of total intraoperative time spent in IOH to the total duration of anesthesia and the time-weighted average MAP less than 65 derived by dividing the area under the curve (AUC-MAP) by the time interval between the first and the last MAP measurements.[19]

Other secondary outcomes included postoperative complications within 30 days after the procedure and total length of hospital stay. Complications were classified as medical or surgical and included acute kidney injury as defined in the Kidney Disease Improving Global Outcomes (*KDIGO*) guidelines,[20] cardiovascular complications (e.g., myocardial injury or ischemia), severe respiratory complications (e.g., intubation, pneumonia, pulmonary edema), infectious complications (e.g., pneumonia, urinary tract infection, wound infection) and flap complications (e.g., partial or total flap failure, reoperation during the same admission) as per the International Classification of Diseases, Tenth Revision (ICD-10) codes. Intensive care unit (ICU) admission rate within the 30 days after surgery, duration of hospital stay after surgery, and in-hospital and 30-day mortality were also collected as secondary outcomes.

2.5 | Sample size

Due to a lack of data regarding the primary outcome (i.e., IOH episodes) in the studied population, we did not perform an a priori sample size calculation. Nonetheless, a post hoc power calculation was conducted to estimate the power to detect the observed differences in IOH between the two groups. Given the two groups sample sizes of respectively $n = 346$ and $n = 68$, an effect size of 0.33 (i.e., Cohen's standardized effect size, d, based on the means (standard deviations) of the two groups), and an $\alpha = 0.05$ (two-sided), the estimated power is 70% (function *pwr.t2n.test* from *pwr* R package).[21] The present pilot study is not powered enough to detect changes in the incidence of IOH and serves as preliminary evidence.

2.6 | Statistical analysis

Patients with intraoperative hemodynamic monitoring and historical controls were compared regarding demographic data, comorbidities, surgical and flap data, intraoperative fluid volume, vasopressors use and transfusion, and outcomes (i.e., IOH and postoperative complications). Continuous variables were compared using the Mann–Whitney test and presented as medians and interquartile ranges. Categorical variables were compared using the χ^2 or Fisher's exact test as appropriate and presented as counts (%). Missing values were handled by multiple imputations by chained equations (MICE).[22] Poisson and logistic regression models were used to assess the association between group assignment and outcomes and adjust for confounders.[23–25] Incidence rate ratios (IRRs) or odds ratios (ORs) were presented with 95% confidence interval (95% CI) as appropriate. Considering the rule of a minimum of 5–10 events for each predictor variable considered in the regression model, only the most clinically relevant variables were included in the multivariate model with the intervention (i.e., intraoperative hemodynamic monitoring). Variables with collinearity were excluded from the regression models

(variance inflation factor >5 indicating the presence of multicollinearity). Two-sided tests were applied with $p \leq 0.05$ considered statistically significant. All the analyses were performed using SPSS 24.0 software (SPSS) and the R statistical software (https://www.r-project.org/).

3 | RESULTS

From a total of 574 successive head and neck free flap reconstructive surgery patients admitted during the period of the study, 414 patients were included ($n = 346$, before the implementation of GDHT (before group) and $n = 68$, after the implementation of GDHT with intraoperative CO monitoring (monitored group). The study flowchart in represented in Supporting Information S1: Material 2.

A total of 160 patients were admitted after the implementation of GDHT (January 1, 2020) but were not monitored intraoperatively (i.e., CO monitoring) and therefore, were not included in the study. A sensitivity analysis regarding the characteristics of this group of patients is presented in Supporting Information S1: Materials 3 and 4.

The two groups before ($n = 346$) versus monitored (GDHT) ($n = 68$) had no statistically significant differences in terms of age, comorbidities (Charlson score), past medical history of hypertension, and duration of anesthesia (Table 1). When comparing the two groups before versus monitored, the number of episodes of IOH and the total duration of IOH did not significantly change with the use of hemodynamic monitoring (respectively, 6 [2–12] vs. 8 [3–14] $p = 0.15$; and 93 [33–173] vs. 109 [47–180] min, $p = 0.21$). Advanced monitoring was not associated with the number of IOH events and a postoperative composite outcome (i.e., AKI, myocardial injury/ischemia, and infections within 30 days after surgery) when adjusting for confounders (i.e., age, comorbidities, estimated blood loss, duration of anesthesia) with respectively an adjusted IRR 0.94 (0.86–1.03), $p = 0.24$ (Poisson regression) and an adjusted odds ratio 1.28 (0.67–2.43), $p = 0.44$ (logistic regression) (Supporting Information S1: Materials 5 and 6). Intraoperative hemodynamic parameters between the groups did not statistically differ (Table 2). Intraoperative administered fluid volume (2250 [1607–3050] mL vs. 2210 [1700–2807] mL, $p = 0.99$) was comparable in both groups. The use of norepinephrine and dobutamine increased from 1.2% to 5.9% ($p = 0.01$) and 2.4% to 30.9% ($p < 0.001$) respectively and the total dose of phenylephrine increased from 480 (160–1344) µg to 640 (240–2156) µg ($p = 0.05$) in the monitored group.

TABLE 1 Demographic data in the included population and in the before GDHT period group and the monitored group during the GDHT period.

	Included patients ($n = 414$)	Before GDHT period group ($n = 346$)	Monitored patients during the GDHT period ($n = 68$)
Age, years	63 (55–72)	62 (54–72)	64 (59–71)
Male gender	257 (62.1%)	211 (57.9%)	46 (67.6%)
BMI, kg/m^2	25 (21–28)	25 (21–29)	24 (22–29)
Medical history			
Age-adjusted Charlson comorbidity index	6 (4–10)	6 (4–10)	6 (4–10)
Diabetes mellitus, *n* (%) ($n = 401$)	77 (19.2%)	65 (19.5%)	12 (17.9%)
Chronic heart failure, *n* (%) ($n = 116$)	1 (0.9%)	0 (0.0%)	1 (1.5%)
Coronary artery disease, *n* (%) ($n = 399$)	24 (6.0%)	20 (6.0%)	4 (6.1%)
Stroke, *n* (%) ($n = 398$)	11 (2.8%)	9 (2.7%)	2 (3%)
Hypertension, *n* (%) ($n = 397$)	179 (45.1%)	150 (45.3%)	29 (43.9%)
Chronic renal disease, *n* (%) ($n = 399$)	16 (4.0%)	13 (3.9%)	3 (4.5%)
COPD, *n* (%) ($n = 396$)	43 (10.9%)	35 (10.6%)	8 (11.9%)
Chronic liver disease, *n* (%) ($n = 401$)	6 (1.5%)	5 (1.5%)	1 (1.5%)
Medication history			
Antihypertensive medications, *n* (%) ($n = 166$)[a]	147 (88.6%)	122 (89.7%)	25 (83.3%)
Surgery type			
Mucosal defect, *n* (%)	271 (65.4%)	228 (65.9%)	43 (63.2%)

Note: No significant difference was seen between the two groups regarding the listed baseline variables in Table 1.

Abbreviations: BMI, body mass index; COPD, chronic obstructive pulmonary disease; GDHT, goal-directed hemodynamic therapy.

[a]Among patients with a past medical history of hypertension.

TABLE 2 Intraoperative data in the included population and in the before GDHT period group and the monitored group during the GDHT period.

	Included patients (n = 414)	Before GDHT period group (n = 346)	Monitored patients during the GDHT period (n = 68)
Intraoperative data			
Anesthesia duration, min	537 (463–633)	531 (457–640)	558 (493–647)
Crystalloids, mL	3500 (2500–4500)	3500 (2500–4500)	3500 (3000–4200)
Use of albumin, n (%) (n = 408)	69 (16.9%)	53 (15.6%)	16 (23.5%)
Received transfusion, n (%) (n = 408)	41 (10.0%)	33 (9.7%)	8 (11.8%)
Urine volume, mL	775 (500–1282)	740 (471–1247)	1010 (580–1365)*
Estimated blood loss, mL	225 (100–400)	200 (50–400)	300 (200–600)*
Fluid balance, mL	2180 (1547–3000)	2250 (1607–3050)	2210 (1700–2807)
Mean SE index values	51 (43–58)	50 (42–58)	54 (48–61)*
Total dose of phenylephrine, µg	550 (160–1520)	480 (160–1344)	640 (240–2156)*
Total dose of ephedrine, mg	20 (10–40)	20 (10–35)	25 (5–40)
Use of norepinephrine, n (%) (n = 398)	8 (2.0%)	4 (1.2%)	4 (5.9%)*
Use of dobutamine, n (%) (n = 398)	29 (7.3%)	8 (2.4%)	21 (30.9%)*
Highest lactate during the procedure, mmol/L	1.3 (1.0–1.7)	1.2 (0.9–1.6)	1.3 (1.0–1.8)
Highest BD during the procedure, mmol/L	−2.6 (−4.0 to −1.0)	−3.0 (−4.1 to −1.7)	−2.0 (−3.5 to −0.6)*
Lowest Hb within 48 h after surgery, g/L	90 (78–103)	91 (78–105)	85 (76–96)
Hemodynamic parameters			
Mean heart rate, bpm	76 (68–82)	75 (67–83)	79 (71–82)
Mean MAP, mmHg	74 (70–79)	73 (69–78)	73 (70–77)
Mean PPV, %	8 (6–10)	8 (6–10)	8 (6–10)
Mean stroke volume, mL	—	—	71 (62–85)
Mean SVV, %	—	—	9 (7–11)
Mean cardiac output, L/min	—	—	5.6 (4.7–6.4)
Mean cardiac index, L/min/m^2	—	—	3.0 (2.6–3.4)
Outcomes			
Primary outcome			
Number of IOH events (MAP < 65 during 5 min), n[a]	6 (2–12)	6 (2–12)	8 (3–14)
Secondary outcomes			
MAP < 75			
Duration of MAP, min	304 (202–396)	307 (194–411)	330 (219–403)
Time-weighted average MAP, mmHg	0.57 (0.39–0.72)	0.58 (0.39–0.73)	0.6 (0.48–0.72)
Number of IOH events, n[a]	14 (10–19)	14 (10–19)	16 (12–19)
MAP < 70			
Duration of MAP, min	204 (105–301)	211 (94–304)	224 (140–310)
Time-weighted average MAP, mmHg	0.37 (0.20–0.55)	0.38 (0.19–0.55)	0.41 (0.25–0.55)
Number of IOH events, n[a]	12 (7–18)	12 (6–18)	14 (9–19)

(Continues)

TABLE 2 (Continued)

	Included patients ($n = 414$)	Before GDHT period group ($n = 346$)	Monitored patients during the GDHT period ($n = 68$)
MAP < 65			
Duration of MAP, min	92 (38–171)	93 (33–173)	109 (47–180)
Time-weighted average MAP, mmHg	0.18 (0.07–0.32)	0.18 (0.06–0.31)	0.20 (0.08–0.33)
MAP < 60			
Duration of MAP, min	26 (9–69)	26 (10–68)	33 (15–73)
Time-weighted average MAP, mmHg	0.05 (0.00–0.13)	0.05 (0.01–0.12)	0.06 (0.02–0.15)
Number of IOH events, n[a]	1 (0–4)	1 (0–4)	2 (0–5)
MAP < 55			
Duration of MAP, min	6 (1–17)	6 (1–20)	7 (3–21)
Time-weighted average MAP, mmHg	0.01 (0.00–0.03)	0.01 (0.00–0.03)	0.01 (0.00–0.03)
Number of IOH events, n[a]	0 (0–1)	0 (0–1)	0 (0–1)
MAP < 50			
Duration of MAP, min	2 (0–4)	2 (0–5)	2 (1–4)
Time-weighted average MAP, mmHg	0.00 (0.00–0.00)	0.00 (0.00–0.00)	0.00 (0.00–0.00)
Number of IOH events, n[a]	0 (0–0)	0 (0–0)	0 (0–0)

Note: Continuous variables were expressed as median (interquartile range) and were compared with the Mann–Whitney *U* test. Categorical variables were expressed as numbers (%) and were compared with the Fisher's exact test or the χ^2 test as appropriate.

Time-weighted average MAP was documented as the ratio of total intraoperative time spent in IOH to the total duration of anesthesia.

Abbreviations: BD, base deficit; GDHT, goal-directed hemodynamic therapy; Hb, hemoglobin; HD, hemodynamic; IOH, intraoperative hypotension; MAP, mean arterial pressure; PACU, postanesthesia care unit; PPV, Pulse pressure variation; SE, state entropy; SVV, Stroke volume variation.

[a]An episode of IOH is defined as at least five successive minutes with a MAP below the defined target with a subsequent return to a MAP greater than these cutoff values for an additional 5 min.

*$p < 0.05$, comparisons to the before hemodynamic monitoring period group.

The rate of postoperative medical and surgical complications did not differ between the two groups. Duration of hospital stay and 30-day mortality were comparable between the two groups (Table 3).

4 | DISCUSSION

In this study, the implementation of intraoperative advanced hemodynamic monitoring was not associated with a reduction in the number of episodes of IOH or the composite outcome of postoperative AKI, myocardial injury/ischemia, and infectious complications within 30 days after surgery. However, the administration of vasopressors and inotropic agents increased, illustrating changes in management that took place with the introduction of GDHT.

In free flap reconstruction for head and neck cancer, achieving a hemodynamic target using excessive fluid infusion is associated with decreased flap survival rates and extended hospital stays. In previous retrospective studies of free flap reconstruction, total intraoperative fluid volume was associated with increased rates of postoperative surgical or medical complications and longer hospitalization.[2,7,26,27] Along this line, it is highly likely that the administration of intravascular fluids in free flap surgeries requires a targeted and personalized approach based on physiological parameters (i.e., CO).

Advanced hemodynamic monitoring has been proposed to preserve organ perfusion during high-risk surgery, and to decrease postoperative morbidity.[28,29] GDHT using intraoperative CO monitoring can decrease the intraoperative crystalloid volume replacement and avoid intraoperative overload and its associated organs and flap edema.[7,26,27,30,31] GDHT utilizes physiologic parameters to provide accurate estimates of multiple hemodynamic variables and predictions of responsiveness to potential therapeutic interventions including intravascular fluid repletion and vasoactive/inotropic agents. This approach is relevant to free flap microvascular surgery, as it could facilitate a better decision-making by the anesthesiologist regarding whether a hypotensive patient would best respond to fluids, vasopressors, or inotropes.[32,33]

Goal-directed fluid (GDHT) administration is different from fluid restriction. As seen in prior works assessing intraoperative GDHT protocols in major noncardiac surgery, there was not a significant decrease in average volume of administered fluid.[34,35] This was further evidenced in the current study, as both the monitored group and standard group received not significantly different intravenous

TABLE 3 Postoperative complications in the included population and in the before GDHT period group and the monitored group during the GDHT period.

	Included patients (n = 414) (%)	Before GDHT period group (n = 346) (%)	Monitored patients during the GDHT period (n = 68) (%)
Acute kidney injury, n (%)[a] (n = 406)	34 (8.4)	26 (7.7)	8 (11.8)
Myocardial injury or ischemia, n (%)[a] (n = 406)	20 (4.9)	18 (5.3)	2 (2.9)
Severe respiratory complications, n (%)[a,b] (n = 394)	8 (2.0)	7 (2.1)	1 (1.6)
Infectious complications, n (%)[a] (n = 409)	28 (6.8)	20 (5.9)	8 (11.8)
Postoperative composite outcome, n (%)[a,c] (n = 406)	77 (19.0)	61 (18.0)	16 (23.5)
Flap complications, n (%)[a,d]	16 (4.1)	11 (3.3)	5 (7.9)
Hospital length of stay, days	10 (7–13)	9 (7–13)	10 (7–15)
Thirty-day mortality, n (%) (n = 414)	1 (0.2)	1 (0.3)	0 (0.0)

Note: Continuous variables were expressed as median (interquartile range) and were compared with the Mann–Whitney U test. Categorical variables were expressed as numbers (%) and were compared with the Fisher exact test or the χ^2 test as appropriate. No significant difference was seen between the two groups regarding the listed outcomes in Table 3.

Abbreviations: BMI, body mass index; COPD, chronic obstructive pulmonary disease; GDHT, goal-directed hemodynamic therapy; ICU, intensive care unit.

[a]Within 30 days after surgery.

[b]Mechanical ventilation, pneumonia, and pulmonary edema.

[c]Postoperative acute kidney injury and/or myocardial injury or ischemia and/or infectious complications (including wound infection).

[d]Flap partial or total flap failure, reoperation during the same admission.

fluid volumes throughout their procedure. The advantage of GDHT is the appropriate timing of fluid intervention, thereby optimizing CO and oxygen delivery, beyond either empiric fluid administration or simply reducing the total amount of administered fluid.[32] In GDHT, intravascular fluid is administered to patients only when it is indicated, as opposed to empiric administration.[33,34,36] This personalized approach is thought to avoid the complications associated with excessive or restrictive fluid administration.[37,38]

The effectiveness of GDHT algorithms has been previously demonstrated for intermediate to high-risk non-cardiac surgery.[35,39–41] Kim et al. and Hand et al. reported that GDHT is associated with a decrease in ICU stay durations in a head and neck free flap surgery population.[12,13] Nonetheless, only the first study showed an association of GDHT with flap survival rate and a decrease in reoperations,[12] and none of these two studies showed a significant decrease in the postoperative medical complications (e.g., pneumonia/pulmonary edema, atrial fibrillation, stroke). The current study did not find any reduction in hospital length of stay by implementing GDHT algorithms. The postoperative morbidity was also similar between the GDHT or empiric fluid administration groups. It is difficult to compare our results to the previous studies including the same population for two reasons: (i) the goal-directed hemodynamic management algorithms and the primary outcomes were different when compared to the previous studies and (ii) the current study was not powered enough to allow a definitive conclusion regarding potential benefits of GDHT.

The current pilot study has several limitations. First, we did not check if strict adherence to the GDHT algorithms were followed. It is possible that in some cases the anesthesiologists may have used a more pragmatic approach as opposed to the algorithm-recommended interventions. The results may have been different if a more strict and standardized strategy was used to optimize compliance. Second, GDHT was limited to the intraoperative period only and postoperative management may have impacted clinical outcomes. Unfortunately, because of the retrospective design of the study, we were not able to collect in detail the postoperative hemodynamic management of these patients. Last but not least, the main limitation of this study is that it was not powered enough to show an association between intraoperative GDHT and perioperative outcomes. Nonetheless, this study provides an accurate estimate of the incidence of the perioperative outcomes (especially IOH episodes) in major head and neck surgery patients. This will help to design well-powered multicenter randomized controlled trials on the potential benefits of GDHT in this population.

5 | CONCLUSION

The implementation of intraoperative GDHT was not associated with reduction in the number or duration of IOH episodes during major head and neck free flap reconstructive surgery. However, the use of vasopressors and inotropic agents was higher in the GDHT group illustrating changes in management that took place with advanced hemodynamic monitoring. Further higher-powered studies are required with specific blood pressure targets in the GDHT fluid algorithm to study the effects of GDHT in free flap surgery, especially on postoperative outcomes.

AUTHOR CONTRIBUTIONS

Justine Philteos: Data curation; formal analysis; methodology; project administration; visualization; writing—original draft; writing—review and editing. **Stuart A. McCluskey**: Conceptualization; data curation; methodology; project administration; resources; supervision; validation; visualization; writing—original draft; writing—review and editing. **Sophia Emerson**: Conceptualization; data curation; formal analysis; investigation; methodology; validation; visualization; writing—original draft; writing—review and editing. **George Djaiani**: Conceptualization; methodology; project administration; resources; validation; visualization; writing—review and editing. **David Goldstein**: Conceptualization; investigation; methodology; project administration; resources; supervision; validation; visualization; writing—review and editing. **Sabri Soussi**: Conceptualization; data curation; formal analysis; investigation; methodology; project administration; supervision; validation; visualization; writing—original draft; writing—review and editing.

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CONFLICT OF INTEREST STATEMENT

Dr. McCluskey has received honoraria from Edwards Lifesciences for advisory work and speaker's support. The remaining authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

Requests for access to study data should be directed to the corresponding author for consideration and can be provided pending appropriate institutional review board approvals.

ETHICS STATEMENT

The study protocol was approved by the University Health Network Ethics and Research Committee (August 30, 2021, ID 21-5664). Written informed consent from all enrolled patients was waived (retrospective non-interventional design with no risk to the participants).

TRANSPARENCY STATEMENT

The lead author Sabri Soussi affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

ORCID

Sabri Soussi https://orcid.org/0000-0002-1489-4768

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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