HIGHER PERIOPERATIVE FLUID ADMINISTRATION IS ASSOCIATED WITH INCREASED RATES OF COMPLICATIONS FOLLOWING HEAD AND NECK MICROVASCULAR RECONSTRUCTION WITH FIBULAR FREE FLAPS

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Purpose: The purpose of this study is to evaluate the impact of perioperative fluid administration on the rates of postoperative complications following head and neck reconstruction with fibular free flaps (FFF). *Methods:* A retrospective cohort study of subjects undergoing head and neck reconstruction with FFF was completed. The primary predictor variable was the total volume of perioperative fluids administered on the day of surgery. The primary outcome variable was the presence of medical and surgical complications occurring within 30 days of surgery. Medical and surgical complications were stratified as major or minor based on severity level. Basic demographic information, comorbidity indices, and intraoperative parameters were abstracted as covariates. Univariable and multivariable models were developed to assess for associations between total fluid volume administered on the day of surgery and postoperative medical/surgical complications occurring within 30 days of surgery. *Results:* In 154 subjects, the partial flap failure rate was 3% and there were no complete flap failures. Total fluid volume was significantly associated with the presence of postoperative medical/surgical complications (OR = 1.21; 95% CI: 1.02–1.44; $p = 0.032$). A cutpoint for total fluid volume predicting any severity level of postoperative complication was identified at 5,500 mL. A cutpoint for total fluid volume predicting major postoperative complications was identified at 7,000 mL. *Conclusions:* The results of this study suggest that liberal fluid administration is associated with increased rates of medical/surgical complications following head and neck reconstruction with FFF. © 2016 Wiley Periodicals, Inc. Microsurgery 00:000–000, 2016.

Over the past two decades, there has been an increasing level of attention given to perioperative fluid management within the field of microvascular surgery. Liberal perioperative fluid administration has been previously shown to correlate with increased rates of postoperative medical and surgical complications following various types of free tissue transfer.[1–7] However, only a subset of these investigations has been conducted on populations of patients undergoing microvascular reconstruction of the head and neck.[3,4,7] Although the literature suggests that aggressive fluid regimens are associated with postoperative complications, restrictive fluid regimens in other types of surgery are known to contribute to postoperative hypovolemia, organ dysfunction, and in extreme cases, multiple organ failure and death.[8] Accordingly, intraoperative fluid administration in microvascular head and neck reconstruction remains a continued area of debate between anesthetic and surgical teams. At present, no definitive consensus has been reached regarding optimal fluid protocols for patients undergoing head and neck reconstruction with microvascular free tissue transfer.

Therefore, the purpose of this study was to further clarify the relationship between perioperative fluid administration and postoperative complications in microvascular head and neck reconstruction. The investigators hypothesized that patients receiving higher volumes of perioperative fluids would experience increased rates of both medical and surgical complications, as this relationship has been reported in other investigations.[3,4,7] The aim of this study was to characterize the various types of medical and surgical complications experienced by patients undergoing head and neck reconstruction with fibular free flaps (FFF) at a single institution and to correlate these outcomes with the volume of perioperative fluids administered on the day of surgery. A secondary aim of this study was to also identify additional demographic, clinical, and intraoperative features predicting subsequent postoperative complications within the same patient population.

PATIENTS AND METHODS

Study Design/Sample

To address the research purpose, the investigators designed and implemented a retrospective cohort study. A sample of subjects was derived from a consecutive population of patients undergoing head and neck reconstruction with FFF by a single surgeon (EJM) at Mayo

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Table 1. Recorded Postoperative Surgical Complications

Superficial surgical site infection[a]
Deep surgical site infection[b]
Hematoma formation
Hemorrhage
Flap dehiscence
Fistula formation
Partial flap failure[c]
Complete flap failure
Donor site complication[d]
Anastomotic complication
Venous complication
Arterial complication
Loss of Doppler signal
Mortality

[a]*Superficial abscess formation or local cellulitis involving the recipient site.*
[b]*Abscess formation of the recipient site involving deep or adjacent tissue planes and/or requiring extensive surgical debridement.*
[c]*Partial necrosis of free flap tissue.*
[d]*Less than 50% split-thickness skin graft take, tendon exposure, local donor site infection, etc.*
Adapted from Ettinger KS, Moore EJ, Lohse CM, Reiland MD, Yetzer JG, Arce K. Application of the Surgical Apgar Score to microvascular head and neck reconstruction. J Oral Maxillofac Surg 2016. doi: 10.1016/j.joms.2016.02.013; with permission.

Table 2. Recorded Postoperative Medical Complications

Pulmonary complication
Unplanned mechanical ventilation[a]
Mechanical ventilation > 48 h
Pneumonia
Unplanned reintubation/unplanned tracheostomy
Cardiovascular complication
ST elevation myocardial infarction
Non-ST elevation myocardial infarction
Heart failure
Cardiac arrest
New cardiac arrhythmia[b]
Renal complication
Acute kidney injury[c]
Acute renal failure[d]
Genitourinary complication
Urinary tract infection
Neurologic complication
Ischemic or hemorrhagic cerebrovascular accident
Coma
Hematologic complication
Deep vein thrombosis
Pulmonary embolism
Infectious complication
Sepsis/septic shock
Postoperative blood transfusion
Unscheduled ICU admission

[a]*Any unplanned mechanical ventilation following normal postoperative extubation.*
[b]*New cardiac arrhythmia requiring treatment.*
[c]*Twofold increase in serum creatinine or urine output < 0.5 mL/kg/hour for 12 hours.*
[d]*Threefold increase in serum creatinine or urine output < 0.3 mL/kg/hour for 24 hours or anuria for 12 hours.*
Adapted from Ettinger KS, Moore EJ, Lohse CM, Reiland MD, Yetzer JG, Arce K. Application of the Surgical Apgar Score to microvascular head and neck reconstruction. J Oral Maxillofac Surg 2016. doi: 10.1016/j.joms.2016.02.013; with permission.

Clinic in Rochester, Minnesota between 2006 and 2014. Inclusion criteria for the study included age ≥18 years, adequate documentation of the perioperative fluid volume administered on the day of surgery, and a minimum follow-up time of at least 1 year. Exclusion criteria for the study included age ≤18 years, inadequate documentation of perioperative fluid administration, <1 year of postoperative follow-up, fibular free tissue transfer utilized for reconstruction of nonmaxillofacial structures (i.e., cervical spine reconstructions), and patients receiving microvascular reconstruction as a salvage procedure for a previously attempted microvascular free tissue transfer. Approval from the Mayo Clinic Institutional Review Board was obtained for completion of this study.

Study Variables

The primary predictor variable for the study was the total volume of perioperative fluids administered on the day of surgery. The primary outcome variable was the presence of medical and surgical complications occurring within 30 days of surgery. The types of surgical complications recorded are found in Table 1. All surgical complications necessitating a return to the operating room (OR) were classified as "major" complications. Any partial flap failures or complete flap failures were recorded as major complications regardless of whether a return to the OR was necessitated or not. Mortality was recorded as a major complication. Any surgical complication not necessitating a return to the OR (excluding partial/complete flap failures) was categorized as a "minor" complication. The types of medical complications recorded are found in Table 2. These medical complications were intentionally chosen (with minor additions and modifications) to mirror those set forth by the American College of Surgeons-National Surgical Quality Improvement Program (ACS-NSQIP), which is the most widely recognized quality measurement system for noncardiac surgery in the United States.[9] All medical complications were recorded as "major" complications with the exception of renal insufficiency, urinary tract infection (UTI), and postoperative blood transfusions.

Multiple covariates were also abstracted for the study and included patient age, gender, race, smoking status, Charlson Comorbidity Index[10] (Charlson score), American Society of Anesthesiologists Classification of Physical Status System (ASA score), preoperative diagnosis, duration of anesthesia, duration of surgery, types and volumes of colloidal solutions administered during surgery, types and volumes of blood products administered during surgery, types and dosages of vasopressors administered during surgery, preoperative hemoglobin, lowest intraoperative hemoglobin, history of preoperative head and neck radiation, and history of preoperative chemotherapy.

The Charlson comorbidity index[10] represents a validated scoring system that predicts the 10-year mortality for a patient based on the presence of 22 specific comorbid disease conditions. Each comorbid condition carries a specific score weighting based on the risk of mortality associated with the disease. The weighting system is as follows: 1 point (myocardial infarction, congestive heart failure, peripheral vascular disease, dementia, cerebrovascular disease, chronic lung disease, connective tissue disease, chronic liver disease, and diabetes); 2 points (hemiplegia, moderate or severe kidney disease, diabetes with end organ damage, any tumor, leukemia, and lymphoma); 3 points (moderate or severe liver disease); and 6 points (malignant tumor, metastatic disease, and AIDS). The summation of point values from each condition represents the overall comorbidity score.

Duration of anesthesia was recorded as the time elapsed in hours between the anesthesiology team assuming care of the patient upon entrance into the OR to the exact time of the postanesthesia care unit (PACU) assuming care of the patient upon completion of the procedure. Duration of surgery was recorded as the elapsed time in hours between the documented time of incision and the documented time of closure. Distinguishing between duration of anesthesia and duration of surgery was intentionally performed in order to stratify differences in outcomes resulting from anesthesia delays (i.e., delays in obtaining vascular access, delays in induction of general anesthesia, delays in postoperative extubation, and so on) versus intraoperative surgical delays resulting from challenges within the procedure itself.

Data Collection and Management

The electronic medical records of the subjects in the study pool were retrospectively reviewed for abstraction of all necessary study variables and demographic data. The collected data was securely stored in a Mayo Clinic sponsored Research Electronic Data Capture[11] (REDCap) database designed specifically for the research project by the primary author (KSE). All authors participating in data abstraction were calibrated on the appropriate use and population of the REDCap database prior to initiating chart review. Access to the REDCap database was limited to the primary author, the authors involved with data abstraction, and the project biostatistician. Any missing data following initial abstraction attempts was subsequently identified and incorporated into the database by the primary author.

Data Analysis

Total fluid volume was calculated as the sum of all crystalloid and colloid fluid volumes administered on the day of surgery. Preoperative diagnoses were categorized into six broad categories for the purposes of statistical analysis: malignant neoplasm, benign neoplasm, infection or osteomyelitis, osteoradionecrosis (ORN), medication-related osteonecrosis of the jaws (MRONJ), and trauma. ASA score was dichotomized by combining subjects with ASA classification 1 with 2 and ASA classification 3 with 4. Continuous features were summarized with medians, interquartile ranges (IQRs), and ranges; categorical features were summarized with frequency counts and percentages.

Associations with the presence of any medical or surgical complication were evaluated using logistic regression models and summarized with odds ratios and 95% confidence intervals (CIs). Identical analysis was also performed to assess for associations with the presence of major complications. An optimal cutpoint for total fluid to predict complications was chosen by maximizing χ^2 statistics from univariable comparisons between subjects with and without complications. Multivariable models were developed using stepwise selection, with the P values for a feature to enter or leave the model set to 0.05, and best subsets selection. Model discrimination (how well the features in the model separate subjects with and without the event of interest) was summarized using the area under a receiver operating characteristics curve, or AUC. The AUC can range from 0.5 to 1.0, with higher values indicating improved predictive ability or improved discrimination. Model calibration (how well the predicted probabilities of the event estimated by the model agree with the observed event) was summarized using the Hosmer and Lemeshow goodness-of-fit test. A statistically significant P values from this test would reject the null hypothesis that the features in the model fit the data well. Statistical analyses were performed using version 9.3 of the SAS software package (SAS Institute, Cary, NC). P values <0.05 were considered statistically significant.

RESULTS

The study cohort was composed of 161 subjects undergoing microvascular head and neck reconstruction with FFF by a single surgeon (EJM) between 2006 and 2014. Three subjects were excluded due to age being <18 years at the time of microvascular reconstruction. Four subjects were excluded on the basis of FFF reconstruction being completed for cervical spine reconstruction. The final study sample was composed of 154 subjects. All 154 subjects met the appropriate inclusion criteria and their electronic medical records were retrospectively reviewed for abstraction of all variables and covariates.

The summary of baseline features and outcomes for all 154 subjects under study are summarized in Table 3. There were no complete flap failures within the study cohort and the partial flap failure rate was 3%. A total of 110 (71%) subjects experienced a medical and/or surgical

Table 3. Summary of Baseline Features and Outcomes for All Subjects, $N = 154$

Feature[a]	Median (IQR; range)
Age at surgery (years)	60 (51–67; 18–86)
Charlson score	2 (2–3; 0–12)
Preoperative hemoglobin (g/dL)	13.4 (12.2–14.6; 8.5–17.3)
Lowest intraoperative hemoglobin (g/dL)	9.7 (8.7–11.1; 5.5–14.5)
Duration of anesthesia (hours)	10.5 (9.0–11.9; 6.7–16.7)
Duration of surgery (hours)	8.7 (7.4–10.1; 3.9–14.1)
Length of stay (days)	7 (6–9; 5–67)
Total fluid (mL)	6532 (5410–8327; 2825–17070)
Days of tracheostomy dependence (*N = 142*)	6 (5–8; 3–457)
Days of feeding tube dependence (*N = 120*)	17 (11.5–24; 3–738)
Sex	*N* (%)
Female	51 (33)
Male	103 (67)
Race (*N = 148*)	
White	141 (95)
Black	2 (1)
Asian	2 (1)
American Indian/Alaska Native	1 (1)
Other	2 (1)
Race (*N = 148*)	
White	141 (95)
All others	7 (5)
Smoking status (*N = 145*)	
Never smoked	72 (50)
Actively smoking	20 (14)
Previous smoking history	53 (37)
Preoperative diagnosis	
Malignant	111 (72)
Benign	12 (8)
Infection or osteomyelitis	7 (5)
ORN	20 (13)
MRONJ	1 (1)
Trauma	3 (2)
Preoperative diagnosis	
Malignant	111 (72)
All others	43 (28)
ASA classification	
1	4 (3)
2	78 (51)
3	70 (45)
4	2 (1)
ASA classification	
1–2	82 (53)
3–4	72 (47)
Preoperative head and neck radiation	46 (30)
Preoperative chemotherapy	25 (16)
Use of colloid	126 (82)
Use of albumin	75 (49)
Use of dextran	1 (1)
Use of gelatin	0
Use of hydroxyethyl starches	60 (39)
Use of packed red blood cells	70 (45)
Use of platelets	0
Use of cryoprecipitate	0
Use of fresh frozen plasma	1 (1)
Use of epinephrine	2 (1)
Use of norepinephrine	0
Use of ephedrine	120 (78)
Use of phenylephrine	96 (62)
Use of vasopressin	0
Use of any vasopressor	139 (90)
Surgical complications	
Superficial surgical site infection	13 (8)
Deep surgical site infection	7 (5)
Hematoma formation	14 (9)
Hemorrhage	2 (1)
Flap dehiscence	38 (25)
Fistula formation	17 (11)
Partial flap failure	5 (3)
Complete flap failure	0
Donor site complication	30 (19)
Anastomotic complication	3 (2)
Any return to OR	20 (13)
Medical complications	
Pulmonary	12 (8)
Renal (acute renal failure)	1 (1)
UTI	1 (1)
Thromboembolic	3 (2)
CNS/PNS	1 (1)
Cardiovascular	14 (9)
Sepsis/septic shock	3 (2)
Postoperative transfusion	65 (42)
ICU admission	23 (15)
Death	1 (1)
Any surgical or medical complication	110 (71)
Any major surgical or medical complication	51 (33)

[a]*Sample sizes for features with missing data or for subgroups of interest are indicated in italics in parenthesis.*

Adapted from Ettinger KS, Moore EJ, Lohse CM, Reiland MD, Yetzer JG, Arce K. Application of the Surgical Apgar Score to microvascular head and neck reconstruction, J Oral Maxillofac Surg 2016. doi: 10.1016/j.joms.2016.02.013; with permission.

complication. Univariable comparisons of features for subjects with and without postoperative complications are depicted in Table 4. The optimal cutpoint for total fluid to separate subjects with and without complications occurred at 5,500 mL. A total of 111 (72%) subjects received total fluid volumes $\geq$5,500 mL and 43 (28%) subjects received total fluid volumes $<$5,500 mL.

The multivariable model to predict medical/surgical complications is summarized in Table 5. The AUC of this model was 0.74 and the *P* values from the Hosmer and Lemeshow goodness-of-fit test was 0.47, indicating that the features in the model fit the data well. Total fluid volume (OR = 1.21; 95% CI: 1.02–1.44; $p = 0.032$) remained a significant independent predictor of medical/surgical complications within this model, as did Charlson

Table 4. Univariable Comparisons Between Subjects With and Without Complications; $N = 154$

	None, $N = 44$	Any complication, $N = 110$		
Feature[a]	Median (IQR)		Odds ratio (95% CI)	*P* values
Age at surgery (years)	55.5 (50–64)	61 (52–70)	1.33 (1.03–1.71)[b]	0.028
Charlson score	2 (2–2)	2 (2–3)	1.57 (1.07–2.29)[c]	0.020
Lowest intraoperative hemoglobin (g/dL)	10.2 (9.0–11.6)	9.5 (8.6–10.6)	0.77 (0.63–0.95)[c]	0.015
Duration of anesthesia (hours)	10.2 (8.8–12.2)	10.5 (9.0–11.6)	1.03 (0.87–1.23)[c]	0.72
Duration of surgery (hours)	8.7 (7.2–10.3)	8.8 (7.5–10.1)	1.02 (0.85–1.23)[c]	0.81
Total fluid (mL)	5994 (4648–7466)	6771 (5597–8467)	1.22 (1.03–1.45)[d]	0.025
Sex		*N (%)*		
Female	14 (32)	37 (34)	1.0 (reference)	
Male	30 (68)	73 (66)	0.92 (0.44–1.94)	0.83
Race (*N = 148*)				
White	39 (95)	102 (95)	1.0 (reference)	
All others	2 (5)	5 (5)	0.96 (0.18–5.13)	0.96
Smoking status (*N = 145*)				
Never smoked	21 (54)	51 (48)	1.0 (reference)	
Actively smoking	6 (15)	14 (13)	0.96 (0.33–2.84)	0.94
Previous smoking history	12 (31)	41 (39)	1.41 (0.62–3.19)	0.41
Preoperative diagnosis				
Malignant neoplasm	28 (64)	83 (75)	1.0 (reference)	
All others	16 (36)	27 (25)	0.57 (0.27–1.21)	0.14
ASA score				
1–2	26 (59)	56 (51)	1.0 (reference)	
3–4	18 (41)	54 (49)	1.39 (0.69–2.83)	0.36
Preoperative head and neck radiation	9 (20)	37 (34)	1.97 (0.86–4.53)	0.11
Preoperative chemotherapy	2 (5)	23 (21)	5.55 (1.25–24.66)	0.024
Preoperative hemoglobin (g/dL)				
<12.2	12 (27)	26 (24)	1.0 (reference)	
12.2 to <13.4	10 (23)	25 (23)	1.15 (0.42–3.15)	0.78
13.4 to <14.6	11 (25)	30 (27)	1.26 (0.48–3.33)	0.64
≥14.6	11 (25)	29 (26)	1.22 (0.46–3.22)	0.69
Total fluid (mL)				
<5500	20 (45)	23 (21)	1.0 (reference)	
≥5500	24 (55)	87 (79)	3.15 (1.49–6.68)	0.003
Use of colloid	32 (73)	94 (85)	2.20 (0.94–5.15)	0.068
Use of albumin	20 (45)	55 (50)	1.20 (0.60–2.42)	0.61
Use of hydroxyethyl starches	13 (30)	47 (43)	1.78 (0.84–3.76)	0.13
Use of packed red blood cells	13 (30)	57 (52)	2.57 (1.21–5.42)	0.014
Use of ephedrine	29 (66)	91 (83)	2.48 (1.12–5.49)	0.025
Use of phenylephrine	28 (64)	68 (62)	0.93 (0.45–1.91)	0.83
Use of any vasopressor	38 (86)	101 (92)	1.77 (0.59–5.32)	0.31

[a]*Sample sizes for features with missing data or for subgroups of interest are indicated in italics in parenthesis. Features present in fewer than 5 subjects are not listed.*
[b]*Odds ratio represents a 10-unit increase.*
[c]*Odds ratio represents a 1-unit increase.*
[d]*Odds ratio represents a 1000-unit increase.*
Adapted from Ettinger KS, Moore EJ, Lohse CM, Reiland MD, Yetzer JG, Arce K. Application of the Surgical Apgar Score to microvascular head and neck reconstruction. J Oral Maxillofac Surg 2016. doi: 10.1016/j.joms.2016.02.013; with permission.

score (OR = 1.49; 95% CI: 1.03–2.16; $p = 0.036$) and history of preoperative chemotherapy (OR = 4.90; 95% CI: 1.07–22.39; $p = 0.040$). A second multivariable model using the same features but also incorporating the total fluid cutpoint of 5,500 mL is shown in Table 6. The AUC of this model was 0.72 and the *P* values from the Hosmer and Lemeshow goodness-of-fit test was 0.094, again indicating that the features in the model fit the data well. Total fluid volume of ≥5,500 mL remained a significant independent predictor of postoperative complications within this second multivariable model (OR = 2.87; 95% CI: 1.32–6.25; $p = 0.008$).

A total of 51 (33%) of subjects experienced major medical (17%) and/or surgical (16%) complications. Univariable comparisons of features for subjects with and without major postoperative complications are depicted in Table 7. The optimal cutpoint for total fluid volume to separate subjects with and without major complications occurred at 7,000 mL. A total of 65 (42%) subjects received total fluid volumes of ≥7,000 mL and 89 (58%)

Table 5. Multivariable Model to Predict Any Complication; $N = 154$

Feature	Odds ratio (95% CI)	*P* values
Charlson score	1.49 (1.03–2.16)[a]	0.036
Preoperative chemotherapy	4.90 (1.07–22.39)	0.040
Total fluid (mL)	1.21 (1.02–1.44)[b]	0.032

[a]*Odds ratio represents a 1-unit increase.*
[b]*Odds ratio represents a 1000-unit increase.*
Adapted from Ettinger KS, Moore EJ, Lohse CM, Reiland MD, Yetzer JG, Arce K. Application of the Surgical Apgar Score to microvascular head and neck reconstruction. J Oral Maxillofac Surg 2016. doi: 10.1016/j.joms.2016.02.013; with permission.

Table 6. Multivariable Model With Fluid Cutpoint to Predict Any Complication; $N = 154$

Feature	Odds ratio (95% CI)	*P* values
Charlson score	1.50 (1.02–2.20)[a]	0.040
Preoperative chemotherapy	4.43 (0.96–20.38)	0.056
Total fluid (mL)		
<5500	1.0 (reference)	
≥5500	2.87 (1.32–6.25)	0.008

[a]*Odds ratio represents a 1-unit increase.*

subjects received total fluid volumes of <7,000 mL. After adjusting for total fluid, no other variable remained statistically significantly associated with the presence of major complications. The AUC of the univariable model for total fluid analyzed as linear variable was 0.61 and the AUC of the univariable model for total fluid analyzed as ≥7,000 mL versus <7,000 mL was 0.62.

Subgroup analysis was performed on subjects receiving microvascular FFF reconstruction for a preoperative diagnosis of a malignant neoplasm. This subgroup comprised the largest percentage of the study population and also represented the most common diagnosis group receiving head and neck reconstruction with free tissue transfer at the investigators institution. Among the subset of 111 (72%) subjects with malignant neoplasms, the only feature that was statistically significantly associated with the presence of major complications in a univariable setting was total fluid ≥7,000 mL (odds ratio 2.28; 95% CI 1.03–5.04; $p = 0.042$; AUC = 0.60). After adjusting for total fluid, no other feature studied was statistically significantly associated with the presence of major complications.

DISCUSSION

The primary objective of this study was to further clarify the relationship between perioperative fluid administration and the presence of postoperative complications for patients undergoing microvascular head and neck reconstruction. The a priori hypothesis was that liberal perioperative fluid administration would correlate with increased rates of both medical and surgical complications, as this relationship has also been reported in a limited number of other investigations.[3,4,7] The study also aimed to identify additional demographic, clinical, and intraoperative features predicting subsequent postoperative complications within the same patient population.

Higher perioperative fluid administration was ultimately found to be a significant independent predictor of postoperative medical and surgical complications for patients undergoing head and neck reconstruction with FFF. A cutpoint for total fluid volume that predicted the presence of any postoperative complications was identified at ≥5,500 mL. Patients receiving ≥5,500 mL of fluid were nearly three times as likely to experience postoperative medical and surgical complications when compared to individuals receiving a lesser volume. Additionally, total fluid volume was also identified as the only statistically significant predictor of "major" postoperative complications within the same population. A higher cutpoint for total fluid volume to predict major complications was identified at ≥7,000 mL. Fluid administration in excess of 7,000 mL was also identified as the only statistically significant predictor of major postoperative complications within the subgroup individuals undergoing FFF for malignant neoplasms.

A number of additional features were also identified as being predictive of postoperative complications. Charlson Comorbidity index remained significantly associated with the presence of postoperative complications when all severity levels of complications were considered. Similar findings have also been reported by other authors utilizing various comorbidity indices to stratify patients undergoing microvascular head and neck reconstruction relative to the presence of postoperative complications.[3,5,12–14] In each of these previous investigations, a patient comorbidity index was identified as a significant predictor of postoperative complications; however, the various comorbidity indices found to be associated with complications varied in each of the studies (ASA score,[3,13,14] Kaplan Feinstein Index (KFI),[5] Adult Comorbidity Evaluation 27[12]). The single study that specifically evaluated the Charlson Comorbidity index in addition to other comorbidity indices (ASA score and KFI), ultimately found that only ASA score was predictive of postoperative complications.[3]

It is interesting to note that perioperative fluid volume remained significantly associated with the presence of complications across multiple analyses, yet duration of surgery and duration of anesthesia were never identified as significant predictors of complications in either univariable or multivariable analyses. Covariance between fluid volume and duration of surgery or anesthesia might be expected on the basis of their interrelationship; however, this was not borne out within the findings of the study. Analogous results have also been reported by other

Table 7. Univariable Comparisons Between Subjects With and Without Major Complications; $N = 154$

	None or minor, $N = 103$	Any major, $N = 51$		
Feature[a]	*Median (IQR)*		Odds ratio (95% CI)	*P* values
Charlson score	2 (2–3)	2 (2–3)	1.13 (0.93–1.38)[b]	0.21
Lowest intraoperative hemoglobin (g/dL)	9.9 (8.9–11.3)	9.1 (8.3–10.2)	0.77 (0.63–0.96)[b]	0.017
Duration of anesthesia (hours)	10.3 (8.7–12.0)	10.7 (9.5–11.6)	1.11 (0.94–1.31)[b]	0.23
Duration of surgery (hours)	8.6 (7.2–10.0)	9.0 (8.1–10.5)	1.14 (0.95–1.35)[b]	0.15
Total fluid (mL)	6213 (5313–7800)	7273 (5569–8821)	1.20 (1.04–1.39)[c]	0.014
Age at surgery (years)	*N (%)*			
18–50	25 (24)	13 (25)	1.0 (reference)	
51–60	30 (29)	11 (22)	0.71 (0.27–1.85)	0.48
61–67	29 (28)	10 (20)	0.66 (0.25–1.77)	0.41
68+	19 (18)	17 (33)	1.72 (0.67–4.39)	0.26
Sex				
Female	34 (33)	17 (33)	1.0 (reference)	
Male	69 (67)	34 (67)	0.99 (0.48–2.01)	0.97
Race (*N = 148*)				
White	93 (94)	48 (98)	1.0 (reference)	
All others	6 (6)	1 (2)	0.32 (0.04–2.76)	0.30
Smoking status (*N = 145*)				
Never smoked	48 (50)	24 (49)	1.0 (reference)	
Actively smoking	17 (18)	3 (6)	0.35 (0.09–1.32)	0.12
Previous smoking history	31 (32)	22 (45)	1.42 (0.68–2.96)	0.35
Preoperative diagnosis				
Malignant neoplasm	71 (69)	40 (78)	1.0 (reference)	
All others	32 (31)	11 (22)	0.61 (0.28–1.34)	0.22
ASA classification				
1–2	55 (53)	27 (53)	1.0 (reference)	
3–4	48 (47)	24 (47)	1.02 (0.52–2.00)	0.96
Preoperative head and neck radiation	29 (28)	17 (33)	1.28 (0.62–2.63)	0.51
Preoperative chemotherapy	15 (15)	10 (20)	1.43 (0.59–3.46)	0.43
Preoperative hemoglobin (g/dL)				
<12.2	25 (24)	13 (25)	1.0 (reference)	
12.2 to <13.4	22 (21)	13 (25)	1.14 (0.44–2.96)	0.79
13.4 to <14.6	29 (28)	12 (24)	0.80 (0.31–2.06)	0.64
≥14.6	27 (26)	13 (25)	0.93 (0.36–2.38)	0.87
Total fluid (mL)				
<7000	68 (66)	21 (41)	1.0 (reference)	
≥7000	35 (34)	30 (59)	2.78 (1.39–5.54)	0.004
Use of colloid	81 (79)	45 (88)	2.04 (0.77–5.39)	0.15
Use of albumin	46 (45)	29 (57)	1.63 (0.83–3.21)	0.16
Use of hydroxyethyl starches	40 (39)	20 (39)	1.02 (0.51–2.02)	0.96
Use of packed red blood cells	41 (40)	29 (57)	1.99 (1.01–3.94)	0.047
Use of ephedrine	81 (79)	39 (76)	0.88 (0.40–1.97)	0.76
Use of phenylephrine	61 (59)	35 (69)	1.51 (0.74–3.06)	0.26
Use of any vasopressor	93 (90)	46 (90)	0.99 (0.32–3.06)	0.99

[a]*Sample sizes for features with missing data or for subgroups of interest are indicated in italics in parenthesis. Features present in fewer than 5 subjects are not listed.*

Adapted from Ettinger KS, Moore EJ, Lohse CM, Reiland MD, Yetzer JG, Arce K. Application of the Surgical Apgar Score to microvascular head and neck reconstruction. J Oral Maxillofac Surg 2016. doi: 10.1016/j.joms.2016.02.013; with permission.

[b]*Odds ratio represents a 1-unit increase.*

[c]*Odds ratio represents a 1000-unit increase.*

authors who identified liberal fluid administration as an independent risk factor for postoperative medical and flap complications, yet found no association between complications and the duration of anesthesia in microvascular head and neck reconstruction.[4]

It was also notable that the use of vasopressors was not significantly associated with the presence of postoperative complications, particularly flap-specific complications. The contraindication against intraoperative vasopressors has long been a fervently maintained belief within the field of microvascular surgery, as these medications hypothetically reduce flap perfusion and theoretically lead to an increased likelihood of flap complications. Within this study, administration of ephedrine did reach statistical

significance for predicting complications in univariate analysis; however, this association did not remain significant in subsequent multivariable modeling. Similar findings were also seen with the intraoperative administration of phenylephrine, which was not found to be significantly associated with complications in any level of univariable or multivariable analysis. When the administration of phenylephrine and ephedrine were considered together (the use of any vasopressor), no univariable or multivariable associations were identified. These findings suggest that the use of intraoperative vasopressors in microvascular head and neck reconstruction does not predispose patients to postoperative complications—a finding that has also been substantiated by numerous other investigations within the literature.[15–19]

Based on the results of this study, the judicious administration of fluids to patients undergoing microvascular free tissue transfer to the head and neck is warranted to prevent potentially serious untoward postoperative complications. Efforts should be made to limit perioperative fluid volumes to <5,500 mL to prevent all degrees of postoperative complications and fluid restriction of <7,000 mL should be heavily considered to reduce the incidence of serious postoperative complications. These findings are echoed in the results of other investigators who have also previously identified liberal fluid administration as a risk factor for complications following various types of free tissue transfer.[1–7] When specifically considering head and neck reconstruction, a smaller number of studies have also provided similar fluid parameters to predict postoperative complications.[3,4,7] In a retrospective analysis of 241 cases of head and neck free flaps, Haughey et al.[4] identified fluid administration above 7 L of crystalloid to be associated with major medical complications between 1999 and 2001. Clark et al.[3] identified crystalloid replacement exceeding 130 mL/kg/day as an independent predictor of postoperative medical complications in a retrospective cohort study of 185 head and neck free flap patients between 1999 and 2007. Finally, Farwell et al.[7] identified higher numbers of postoperative surgical complications occurring in individuals receiving an average of 6.6 L of fluid in a retrospective cohort study of individuals undergoing major head and neck surgical procedures (including free flaps) between 1995 and 1997.

CONCLUSIONS

The results of this study further corroborate the findings of previous investigations in that excessive perioperative fluid administration has the potential to negatively influence outcomes in microvascular head and neck reconstruction. While this study is limited by its retrospective design and relatively small sample size, it nevertheless provides additional support to the growing body of evidence implicating liberal fluid replacement as a risk factor for postoperative complications. While some perioperative risk factors (i.e., patient comorbidity) are relatively immutable prior to surgery, perioperative fluid administration remains a relatively modifiable aspect of surgical care with the potential to positively influence outcomes. As head and neck reconstructive surgeons continue to endeavor to find ways to reduce the frequency and severity of postoperative complications, it is likely that perioperative fluid administration will remain at the forefront of this discussion. Accordingly, it will be of paramount importance for future prospective studies to be conducted to further evaluate the impact of fluid administration on outcomes in microvascular head and neck reconstruction.

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