Parikh Anuraag (Orcid ID: 0000-0003-0968-1028)
Varvares Mark (Orcid ID: 0000-0002-6570-5672)
Lindeborg Michael (Orcid ID: 0000-0001-5860-6097)

Predicting Length of Stay in Head and Neck Patients Who Undergo Free Flap Reconstruction

Short Running Title: Length of Stay Risk Factors in Free Flaps

Authors: Michael M. Lindeborg[1,2]*, Rosh K.V. Sethi, MD, MPH[3]*, Sidharth V. Puram, MD PhD[4]*, Anuraag Parikh, MD[1,2], Bharat Yarlagadda, MD[1,2], Mark Varvares, MD[1,2], Kevin Emerick, MD[1,2], Derrick Lin, MD[1,2], Marlene L. Durand, MD[1,2,5], Daniel Deschler, MD[1,2]

*Equally contributing authors

Affiliations:
[1] Department of Otolaryngology, Massachusetts Eye and Ear Infirmary, Boston, Massachusetts, USA
[2] Department of Otolaryngology, Harvard Medical School, Boston, Massachusetts, USA
[3] Department of Otolaryngology, University of Michigan, Ann Arbor, Michigan, USA
[4] Department of Otolaryngology, Washington University School of Medicine in Saint Louis, Saint Louis, Missouri, USA
[5] Department of Medicine, Massachusetts General Hospital, Boston, MA, and Harvard Medical School, Boston, MA

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Corresponding Author:
Daniel G. Deschler, MD, FACS
Massachusetts Eye and Ear Infirmary
Harvard Medical School
243 Charles Street, Boston, MA 02114,
Email: daniel_deschler@meei.harvard.edu

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Abstract

Objective: Understanding factors that affect post-operative length of stay (LOS) may improve patient recovery, hasten post-operative discharge, and minimize institutional costs. This study sought to 1) describe length of stay (LOS) among head and neck patients undergoing free flap reconstruction and 2) identify factors that predict increased LOS.

Methods: A retrospective cohort was performed of 282 head and neck patients with free flap reconstruction for oncologic resection between 2011-2013 at a tertiary academic medical center. Patient demographics, tumor characteristics, surgical and infectious complications were characterized. Multivariable regression identified predictors of increased LOS.

Results: A total of 282 patients were included. Mean age was 64.7 years (standard deviation=12.2) and 40% were female. Most tumors were located in the oral cavity (53.9% of patients), and most patients underwent RFFF reconstruction (RFFF- 73.8%, ALT - 11.3% and FFF - 14.9%). Intraoperative complications were rare. The most common post-operative complications included non-wound infection (PNA or UTI) (15.6%) and wound breakdown/fistula (15.2%). Mean and median length of stay were 13 days (SD=7.7) and 10 days (IQR=7), respectively. Statistically significant predictors of increased LOS included flap take back (Beta Coefficient [C]=+4.26, $p<0.0001$), in-hospital pneumonia or urinary tract infection (C=+2.52, $p=0.037$), wound breakdown or

fistula (C=+5.0, P<0.0001), surgical site infection (C=+3.54, P=0.017) and prior radiation therapy (C=+2.59, P=0.004).

Conclusion: Several perioperative factors are associated with increased LOS. These findings may help with perioperative planning, including the need for vigilant wound care, optimization of antibiotics prophylaxis, and institution-level protocols for postoperative care and disposition of free flap patients.

Key Words: length of stay, free flap, head and neck cancer, radial forearm free flap, anterolateral thigh flap, fibula free flap, head and neck reconstruction

Level of Evidence: 2b; retrospective cohort.

Introduction

Head and neck cancer patients undergoing free flap reconstruction have variable inpatient lengths of stay (LOS), ranging from days to weeks to months.[1–3] Variation in LOS has important clinical implications for patient recovery, placement in rehabilitation and acute care facilities, and the initiation of adjuvant multimodality therapy.[4,5] Additionally, LOS is associated with significant hospital costs.[6,7] Prior studies across various surgical specialties have identified several risk factors associated with increased length of stay, including American Society of Anesthesiology (ASA) score, pre- and post-operative hemoglobin levels, age, co-morbidities, and need for blood transfusion, and have successfully targeted these to decrease length of stay, reduce cost and improve quality of care.[8–11]

Several factors have been associated with variability in LOS specifically among head and neck cancer patients. These include age, recent weight loss, excess alcohol use, malnutrition, history of diabetes, ASA score, Kaplan Feinstein comorbidity index (KFI) score, low preoperative hemoglobin, mucosal surgery, crystalloid replacement volume, and anesthesia or procedure duration.[1,2,12–15] While past head and neck studies have explored clinical risk factors associated with increased LOS, there is a lack of studies that stratify by flap type and include a wider range of risk factors.

Overall, length of stay is an important outcome metric monitored by insurers and quality organizations, and a marker of hospital quality associated with cost of care and

patient outcomes. Therefore, this study aims to 1) describe LOS among head and neck patients undergoing free flap reconstruction and 2) identify factors that may predict increased LOS.

Materials and Methods

A retrospective review of all patients (N=282) who underwent free flap reconstruction, including anterolateral thigh flap (ALT), fibula free flap (FFF) or radial forearm free flap (RFFF) reconstruction after oncologic resection at a major tertiary care center between 2011 and 2013 was performed. Data for this study was derived, in part, from a previous retrospective cohort study investigating risk factors associated with increased operative time.[16] Institutional Review Board approval was obtained.

Length of stay data was collected for each patient, and was defined as the time between the day of surgery and the day of hospital discharge. Patient demographics, cancer staging, and clinical data such as previous cancer treatment, tumor site, and co-morbidities were collected. Inpatient events were characterized including flap take back (defined as flap failure or compromise requiring surgical intervention), post-operative transfusion, wound breakdown or fistula not related to infection, surgical site infection (SSI; both recipient and donor sites), and postoperative cardiac (myocardial infarction, arrhythmia, congestive heart failure), pulmonary (pulmonary embolism, respiratory distress or failure) and infectious complications (urinary tract infection, pneumonia).

Antibiotic prophylaxis protocol at study site was to stop antibiotic prophylaxis 24 hours after first peri-operative prophylactic dose.

Patient characteristics and inpatient events were characterized descriptively and stratified by flap type. Univariable comparisons were performed using student's T-test, chi-square test, and the Kruskal–Wallis test where appropriate. A linear multivariable regression analysis was performed to identify predictors of increased LOS. All data manipulation and statistical analysis was performed using STATA v13 (STATA Corp, NC).

Results

Patient Characteristics

A total of 282 patients underwent RFFF (N=208, 73.8%), FFF (N=42, 14.9%), or ALT (N=32, 11.3%) reconstruction after oncologic resection and were included in the study (**Table 1**).

Mean patient age was 64.7 years (standard deviation [SD]=12.2 years), 40% of patients were female, and 59.9% of patients had an American Society of Anesthesiologists (ASA) Physical Status Classification System status of 3 or 4. A high proportion of patients had advanced stage cancer, with 45.2% Stage IV and 54.8% Stage I-III. The most common tumor site was the oral cavity (53.9%). Forty-four percent of patients had received prior radiation therapy. Post-operatively, 48.9% of patients received packed red blood cell transfusion. The most common post-operative

complications were non-wound infection (PNA or UTI) (15.6%) and wound breakdown or fistula (15.2%).

Pre- and Peri-Operative Factors by Flap Type

Patient demographics, tumor characteristics, and pre- and peri-operative factors were stratified by flap type (**Table 2**). Pre-operative factors including patient age, gender and ASA status did not vary. There were significant differences, however, in tumor site and stage. Patients who underwent FFFs more commonly had stage IV tumors located in the oral cavity. History of prior radiation therapy was more common among patients who underwent RFFF as compared to those who had ALT or FFF patients. Though not significantly different, the data for in-hospital cardiac and pulmonary issues were variable across flap type.

Length of Stay

The mean length of stay was 13 days (SD=7.7, range 4-65). Duration of stay was similar when stratified by flap type (14.8 +/-9.4 days for ALT, 13.9 +/- 6.7 days for FFF, and 12.6 +/- 7.6 for RFFF). Median length of stay was 10 days (IQR=7), and was also not significantly different across flap types (**Table 2)**. In bivariable analysis, pre-operative radiation (XRT) was associated with a significant increase in LOS of approximately 2.5 days (**Figure 1A**). Wound complication (breakdown or fistula) was

also associated with a significant increase LOS of approximately 4 days (**Figure 1B**). Finally, patients who returned to the OR for flap take back had a significantly longer length of stay as compared to those who did not (**Figure 1C**).

Multivariable Analysis of Pre- and Peri-operative Factors Associated with Greater Length of Stay (LOS)

A multivariable regression model was performed to identify factors associated with greater LOS **(Table 3)**. Significant predictors of increased length of stay included flap take back (Beta Coefficient [C]=+4.26, p<0.0001), in-hospital pneumonia or urinary tract infection (C=+2.52, p=0.037), wound breakdown or fistula (C=+5.0, P<0.0001), SSI (C=+3.54, P=0.017), and history of prior radiation therapy (C=+2.59, P=0.004) (**Table 3**). Of note, there was no significant difference in LOS between patients who had either pneumonia, a UTI, or both pneumonia and a UTI.

Discussion

In this study, we investigated the factors that may affect LOS for head and neck cancer free flap reconstructive surgeries in 282 patients at a tertiary medical center. Flap take back, post-operative pneumonia or urinary tract infection (UTI), wound breakdown or fistula, SSIs, and history of prior radiation therapy were associated with increased length of stay. Notably, flap type was not associated.

Head and neck cancer free flap patients are often at increased risk for postoperative infection due to multiple wound areas, clean-contaminated operation sites, underlying comorbidities, and prolonged operation time.[17] SSIs and wound complications (breakdown or fistula) were associated with substantially increased LOS. The literature reports that SSIs can occur in up to 22-39% of head and neck cases, even with the use of antibiotic prophylaxis.[13] Other head and neck studies not only corroborate that SSI is an independent risk factor for LOS, but also show that SSI increases the risk for thirty-day readmission.[14,18–20] Past studies have explored the use of postoperative antibiotic prophylaxis; however, no randomized controlled study has demonstrated a significant reduction in SSIs with postoperative prophylaxis.[17] Of note, programs implementing infection-control protocols such as the Center for Medicare and Medicaid's National Surgical Care Improvement Project have demonstrated a lower than expected rate of SSIs.[17,21] Type and duration of perioperative antibiotic prophylaxis, degree of wound surveillance post-operatively, and rehabilitative support are interventions that have the potential to successfully diminish infection rate.[22–24]

Post-operative non-wound infections, such as pneumonia and UTI, represent common yet avoidable post-operative complications that prolong discharge in head and neck cancer patients. Past studies have found that hospital acquired pneumonia occurs in as many as 4.7-9.7% of head and neck patients post-operatively, but few have examined its impact on LOS.[25–27] Penel et. al showed that post-operative pneumonia

was correlated with an increased length of stay; however, prolonged antibiotic use after free flap construction may not decrease pneumonia risk.[13] Khariwala et. al demonstrated that a prolonged course of antibiotics was actually associated with a higher risk of pneumonia in free flap patients.[28] Additionally, other respiratory complications such as prolonged ventilator dependence are associated with increased length of stay.[20] To date, there has been limited data surrounding antibiotic type and duration to minimize non-wound infections in complicated free flap surgical patients.[17] Head and neck surgical teams should explore both pharmacological measures, such as optimizing perioperative antibiotics, and non-pharmacological measures, such as early ambulation, local antiseptic care, and greater care with intubation and urinary catheter placement.[29]

History of radiation therapy was associated with increased length of stay. It is notable that the majority of head and neck free flap studies demonstrate a positive association between pre-operative radiation therapy and post-operative infectious complications or flap survival.[30–35] Robust infection prevention protocols may prove especially beneficial for patients with a history of radiation therapy.

Past studies have found that increased operative time may be associated with increased length of stay in free flap patients.[20] In our cohort, operative time was not significantly associated with increased length of stay. With improvements in free flap surgical techniques and down trending operative times, operative time may not be a

strong predictor of post-operative complications.[16] Operative time may also be a proxy for surgical complexity and increase the risk for complications and length of stay.

Non-modifiable pre-operative patient-specific factors (e.g. history of chemotherapy and or radiation) are associated with increased LOS, and should be taken into account when planning for patient disposition. The factors can also be used to identify patients who may be at higher risk for perioperative complications. Institution-specific practices may also play a role, and merit further exploration. For example, we previously found that LOS and hospital mortality are comparable to non-academic centers, even though academic center patients are often more complicated, and have higher rates of chemotherapy and radiation.[36] Careful attention to history of radiation and other clinical factors associated with complications and increased LOS may optimize the quality of patient care and minimize related healthcare expenditures.

This study is limited by its retrospective design, potential for absence of other confounding variables not ascertainable in the patient's medical record. Other variables worth investigating in future studies include post-operative delirium, substance use or withdrawal, need for post-acute care, and need for tracheostomy or feeding tube at discharge. The sample size of this study is relatively small, includes more males than females, and samples patients from only a single institution. To control for institution-specific factors that could influence length of stay, future studies with a broader, more diverse study population can help to confirm these findings.

Ultimately, this study demonstrates that multiple factors may be associated with significantly increased LOS, many of which may be modifiable. Though high-volume free flap programs often have established peri-operative protocols, efforts to optimize care pathways and minimize length of stay continue to be essential. Further studies that prospectively investigate the impact of programs targeting these factors would be valuable in better understanding their merit and potential for intervention.

Conclusion

This study identifies several pre- and perioperative factors during head and neck free flap reconstructive surgery that are associated with increased length of stay. Initiatives to address these factors could decrease LOS, leading to hospital savings and improved patient outcomes. These initiatives may include optimizing perioperative antibiotic use, as well as the institution of specific protocols to minimize risk for surgical site infection and medical complications such as pneumonia and urinary tract infection.

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Tables and Figures

Table 1: Patient Demographics.

TABLE 1:
PATIENT DEMOGRAPHICS

Variable	Number (%)
Age, Mean (STD)	64.7 (12.2)
Female Gender	112 (39.7)
ASA 3 or 4	169 (59.9)
Stage I-III	137 (54.8)
Stage IV	113 (45.2)
Flap Type	
ALT	32 (11.3)
FFF	42 (14.9)
RFFF	208 (73.8)
Tumor Site	
Cutaneous/Temporal	29 (10.3)
Hypopharynx	15 (5.3)
Larynx	37 (13.1)
Oral Cavity	152 (53.9)
Oropharynx	24 (8.5)
Sinus/Maxilla	25 (8.9)
ORN (yes)	20 (7.1)
Preoperative XRT	126 (44.7)
Packed RBC Transfusion	138 (48.9)
Flap takeback (yes)	37 (13.1)
In-hospital cardiac issue	21 (7.5)
In-hospital pulmonary issue	22 (7.8)
In-hospital non-wound infection (PNA or UTI)	44 (15.6)
In-hospital wound breakdown or fistula	43 (15.2)
In-hospital surgical site infection	25 (8.9)
LOS (days), Mean (STD)	13.0 (7.7)
LOS (days), Median (IQR)	10.0 (7.0)

Abbreviations: ASA, American Society of Anesthesiology Physical Classification; LOS, Length of Stay; ORN, Osteoradionecrosis; XRT, radiation; PNA, pneumonia; UTI, urinary tract infection; STD, standard deviation; IQR, interquartile range. Surgical site infection includes both donor and recipient sites. Table adapted from Lindeborg et al., 2020.[16]

Table 2: Pre- and Peri-Operative Factors by Flap Type.[a]

TABLE 2:
PRE- AND PERI-OPERATIVE FACTORS BY FLAP TYPE

Variable	ALT (32)	FFF (42)	RFFF (208)	P-value
Age (years)	65.8 (10.6)	63.3 (11.8)	64.9 (12.5)	0.487
Female, No. (%)	14 (43.8)	14 (33.3)	84 (40.4)	0.615
ASA 3 or 4, No. (%)	23 (71.9)	18 (42.9)	128 (61.5)	0.074
Tumor Site				<0.0001
Cutaneous/Temporal	3 (9.4)	1 (2.4)	25 (12.0)	
Hypopharynx	1 (3.1)	0 (0)	14 (6.7)	
Larynx	1 (3.1)	0 (0)	36 (17.3)	
Oral Cavity	7 (21.9)	41 (97.6)	104 (50)	
Oropharynx	7 (21.9)	0 (0)	17 (8.2)	
Sinus/Maxilla	13 (40.6)	0 (0)	12 (5.8)	
Stage				<0.0001
I-III	8 (25.8)	1 (3.2)	128 (68.1)	
IV	23 (74.2)	30 (96.8)	60 (31.9)	
ORN (yes)	0 (0)	7 (16.7)	13 (6.3)	0.068
Preoperative XRT	17 (53.1)	12 (28.6)	97 (46.6)	0.059
Packed RBC Transfusion	21 (65.6)	19 (45.2)	98 (47.1)	0.131
Flap takeback (yes)	4 (12.5)	5 (11.9)	27 (13.0)	0.981
In-hospital cardiac issue	0 (0)	6 (14.3)	15 (7.2)	0.072
In-hospital pulmonary issue	5 (15.6)	5 (11.9)	12 (5.8)	0.067
In-hospital non-wound infection (PNA or UTI)	6 (18.8)	7 (16.7)	31 (14.9)	0.797
In-hospital wound breakdown or fistula	7 (21.9)	4 (9.5)	32 (15.4)	0.377
In-hospital surgical site infection	4 (12.5)	4 (9.5)	17 (8.2)	0.614

Mean LOS in days (SD)	14.8 (9.4)	13.9 (6.7)	12.6 (7.6)	0.125
Median LOS in days (IQR)	12 (9)	11 (7)	10 (6)	0.094

Abbreviations: ALT, anterolateral thigh; ASA, American Society of Anesthesiology Physical Classification; FFF, fibular free flap; LOS, Length of Stay; ORN, Osteoradionecrosis; RFFF. Radial forearm free flap; XRT, radiation; PNA, pneumonia; UTI, urinary tract infection; STD, standard deviation; IQR, interquartile range. Surgical site infection includes about donor and recipient sites.
[a] There were no statistically significant differences in patient demographics and preoperative characteristics across flap type except for tumor site and tumor stage. Student's t-test and the Kruskal–Wallis test was used for quantitative data, while chi-square test was used to analyze proportional data.

Table 3: Multivariable Linear Regression of Pre- and Perioperative Factors Associated with Greater Length of Stay.

TABLE 3:
MULTIVARIABLE LINEAR REGRESSION OF PRE- AND PERIOPERATIVE FACTORS ASSOCIATED WITH GREATER LENGTH OF STAY

Variable	Beta Coefficient	95% Confidence Interval	P-Value
Pre-operative and Demographic factors			
Female gender (vs. Male)	- 1.11	-2.87 - 0.66	0.217
Age (per 1 additional year)	+ 0.05	-0.02 - 0.13	0.162
Stage IV (vs. Stage I-III)	+ 0.02	-1.91 - 1.96	0.982
History of ORN	+ 1.45	-6.36 – 9.27	0.715
Preoperative XRT	+ 2.59	0.84 – 4.35	0.004
ASA 3 or 4 (vs. 1-2)	+ 1.09	-0.65 – 2.82	0.219
Flap type			
ALT	REF		
FFF	+ 2.31	-1.15 – 5.78	0.189
RFFF	- 0.01	-2.73 – 2.72	0.999
Perioperative complications (yes vs. no)			
Transfusion	+ 0.89	-0.86 – 2.63	0.317
Flap takeback	+ 4.26	1.68 – 6.84	0.004

Cardiac complication	+ 2.60	-0.69 – 5.88	0.120
Pulmonary complication	+1.80	-1.47 – 5.08	0.280
Non-wound infection (PNA or UTI)	+ 2.52	0.15 – 4.89	0.037
Wound breakdown or fistula	+ 4.98	2.60 – 7.35	<0.0001
Surgical site infection	+ 3.54	0.63 – 6.45	0.017

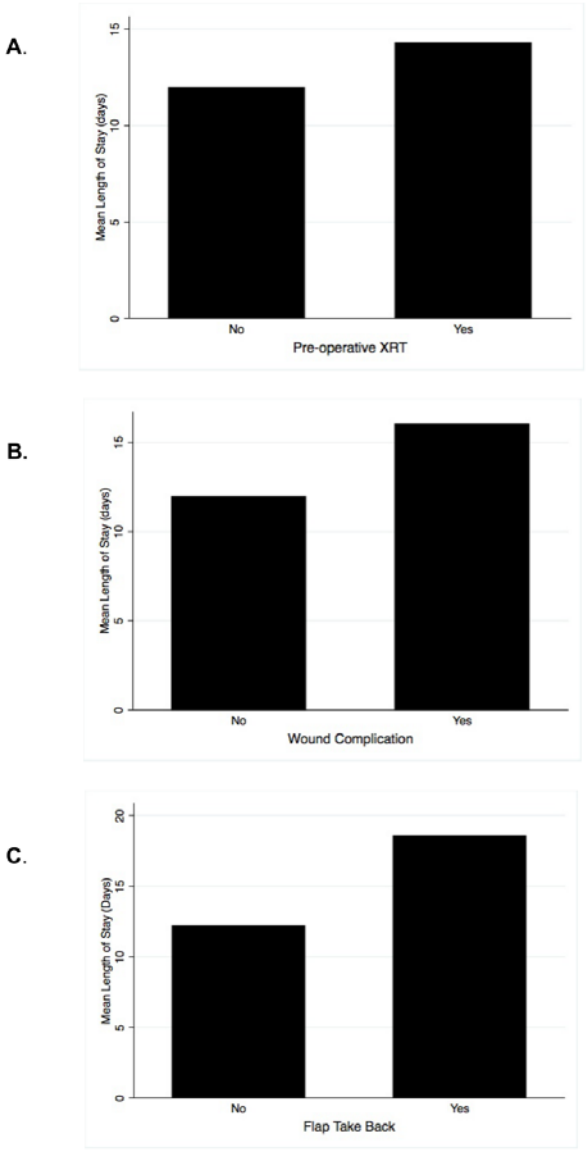
Abbreviations: ASA, American Society of Anesthesiology Physical Classification; LOS, Length of Stay; ORN, Osteoradionecrosis; XRT, radiation; PNA, pneumonia; UTI, urinary tract infection. Surgical site infection includes both donor and recipient sites.

List of Figure Legends/Titles

Figure 1: Univariate Analysis of Factors Associated with Increased Length of Stay

Figure 1 Legend: Univariable Analysis of Factors Associated with Increased Length of Stay. (**A**) Pre-operative radiation (XRT). (**B**) Wound Complication. (**C**) Flap Take Back.

Figure 1: Univariate Analysis of Factors Associated with Increased Length of Stay



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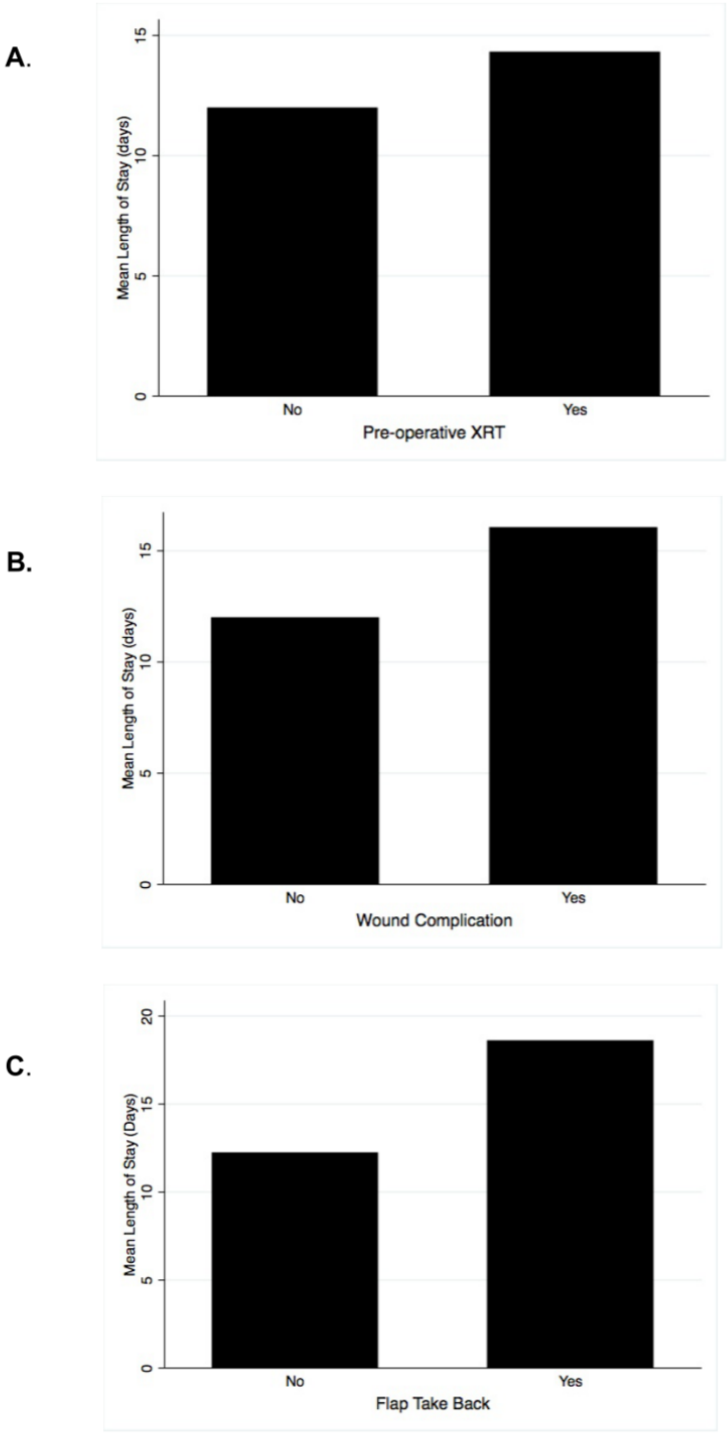

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