Title

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Authors
Goshtasbi, Khodayar
Abouzari, Mehdi
Soltanzadeh-Zarandi, Sina
et al.

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# The Association of Age, Body Mass Index, and Frailty with Vestibular Schwannoma Surgical Morbidity

**Khodayar Goshtasbi, MS**[1,*], **Mehdi Abouzari, MD, PhD**[1,*], **Sina Soltanzadeh-Zarandi, BS**[1,*], **Brooke Sarna, BS**[1], **Ariel Lee, BS**[1], **Frank P. K. Hsu, MD, PhD**[2], **Hamid R. Djalilian, MD**[1,3]

[1]Department of Otolaryngology–Head and Neck Surgery, University of California, Irvine, USA

[2]Department of Neurological Surgery, University of California, Irvine, USA

[3]Department of Biomedical Engineering, University of California, Irvine, USA

## Abstract

**Objective:** To evaluate whether increased body mass index (BMI), age, or frailty influence vestibular schwannoma (VS) short-term surgical morbidity.

**Methods:** The 2005–2017 National Surgical Quality Improvement Program database was queried for patients with VS undergoing surgical resection. Age was stratified according to age <50, 50–64, and ≥65, while BMI was stratified based on a threshold of 30. Frailty score (0–5) was indicated based on functional status, diabetes, chronic obstructive pulmonary disease, congestive heart failure, and hypertension.

**Results:** A total of 1405 patients were included consisting of 56.7% females with a mean age of 50.7±13.8 years and mean BMI of 29.4±6.6. Patients <50 (n=604), 50–64 (n=578), and ≥65 (n=223), had different duration of surgery (428±173 *vs*. 392±149 *vs*. 387±154 minutes; $p<0.001$) and 30-day mortality rates (0.7% *vs*. 0% *vs*. 1.8%; $p=0.01$). However, post-operative length of stay (LOS) ($p=0.16$), readmission ($p=0.08$), reoperation ($p=0.54$), and complication rates were similar. Post-operative myocardial infarction ($p=0.03$) and wound infection ($p=0.02$) were more commonly observed in the obese cohort (BMI≥30) but readmission ($p=0.18$), reoperation ($p=0.44$), and complication rates were similar to those with BMI<30. Severely obese patients (BMI≥35) also had higher rates of deep vein thrombosis ($p=0.004$). Frailty score 0 (n=921), 1 (n=375), and 2–4

**Corresponding Author:** Hamid R. Djalilian, M.D., Division of Neurotology and Skull Base Surgery, Department of Otolaryngology–Head and Neck Surgery, University of California Irvine, 19182 Jamboree Road, Otolaryngology-5386, Irvine, CA 92697, Phone: (714) 456-5753, Fax: (714), 456-5747, hdjalili@hs.uci.edu.
CRediT authorship contribution statement
**Khodayar Goshtasbi:** Conceptualization, Methodology, Formal analysis, Writing - Original Draft, Review & Editing
**Mehdi Abouzari:** Conceptualization, Methodology, Formal analysis, Funding acquisition, Writing - Original Draft, Review & Editing
**Sina Soltanzadeh-Zarandi:** Methodology, Data Curation, Writing - Original Draft, Review & Editing
**Brooke Sarna:** Data Curation, Writing - Original Draft, Review & Editing
**Ariel Lee:** Data Curation, Writing - Original Draft, Review & Editing
**Frank P. K. Hsu:** Conceptualization, Writing – Review & Editing
**Hamid R. Djalilian:** Conceptualization, Supervision, Writing – Review & Editing
*Authors contributed equally to this work.



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(n=109) was associated with LOS (4.7±3.5 *vs.* 5.3±4.1 *vs.* 6.7±6.6 days, $p<0.001$) and prolonged intubation rates (1.0% *vs.* 2.4% *vs.* 3.7%; $p=0.03$).

**Conclusions:** Increased age, BMI, and frailty among VS patients were associated with different post-operative complication rates, operation time, or LOS. Knowledge of these can optimize care for at-risk patients.

**Keywords**

Vestibular schwannoma; Acoustic neuroma; NSQIP; Complications; Morbidity

## Introduction

Vestibular schwannomas (VS), also known as acoustic neuromas, are tumors of Schwann cell sheath comprising about 8% of all intracranial tumors.[1, 2] With an incidence of 1.09 per 100,000 in the United States, VS is considered the most common non-malignant nerve sheath tumor and the most frequent lesion in the cerebellopontine angle.[2–5] Patients with VS most commonly present with unilateral progressive hearing loss followed by tinnitus, ataxia, vertigo, and headache.[6] Treatment of VS consists of watchful waiting, radiation therapy, or surgery. Despite recent trends towards conservative management of VS, surgical resection is still the mainstay treatment for age- and health-appropriate patients who suffer from severe vertigo, persistent dizziness, or tumors larger than 3 cm.[7, 8] Surgical resection of VS can be performed via translabyrinthine, middle cranial fossa, or retrosigmoid approaches, all of which are associated with possible postoperative complications.[8, 9] Investigating potential predictors of morbidity in VS surgery can help improve pre- and post-operative management and optimize care for at-risk patients.

There has been emerging interest in investigating the influence of body mass index (BMI), age, or frailty on surgical complications. A recent review by Ri and colleagues demonstrated a positive association between obesity and morbidity in a wide variety of surgeries;[10] however, other investigators have failed to demonstrate an association in other cohorts including head and neck reconstruction.[11–13] Similarly, there have been mixed findings regarding the influence of advanced age on experiencing complications.[14–17] It is also possible that frailty, defined as the decline in physiological reserve and function across multiple organs, can influence mortality and morbidity following head and neck surgery.[14, 18] The influence of these factors as they relate to short-term morbidity following VS resection have not yet been investigated through a large national database. Herein, we summarize our findings on the influence of BMI, age, and frailty on VS surgical outcomes in the American College of Surgeons National Surgical Quality Improvement Program (NSQIP) database.

## Methods

This study did not require approval from UC Irvine institutional review board's biomedical research committee because of the use of publicly available data and lack of direct patient involvement or identifying information. The 2005–2017 NSQIP database was queried for patients with a diagnosis of VS undergoing resection. VS diagnosis was based on

International Classification of Disease (ICD) codes 225.1 (ICD-9) and D33.3 (ICD-10), and those undergoing surgical resection according to Current Procedural Terminology (CPT) codes 61520 (infratemporal or posterior fossa), 61526 (transtemporal [mastoid]), 61530 (transtemporal [mastoid] combined with middle/posterior fossa craniotomy/craniectomy), and 61616 (excision of base of posterior cranial fossa, jugular foramen, foramen magnum, or C1–C3, intradural including dural repair, with or without graft) were included. Cases without complete outcome reports or lost to follow-up were excluded. Extracted information consisted of patient demographics, pre-operative and perioperative clinical metrics, and 30-day post-operative outcomes. BMI, which was calculated from the reported weight and height, was binarized as obese (≥30 BMI) and non-obese (<30 BMI) patients. BMI was also separately binarized as severely obese (≥35 BMI) and non-severely obese (<35 BMI) patients to elucidate whether severe obesity specifically puts patients at higher risk of certain complications (e.g., thrombosis). Likewise, the American Society of Anesthesiologists (ASA) classification which is thought to estimate operational risk[19] was binarized as low (class 1–2) or high (class 3–4).

We performed three primary analyses with BMI, age, and frailty as dependent variables to compare operation time, total length of stay (LOS), and short-term post-operative morbidities as reported by the NSQIP database. These morbidities, occurring up to 30 days post-operation, consisted of various surgical or medical complications, readmission, reoperation, or mortality. Since readmission and reoperation variables were added in 2012 and not available for 2007–2011 years, their percentages reflect a sub-cohort with available readmission/reoperation information instead of the entire population. Frailty was defined according to Subramaniam *et al.*'s modified frailty index (mFI) from 5 NSQIP variables: dependent functional status, diabetes, history of chronic obstructive pulmonary disease (COPD) or congestive heart failure (CHF), and hypertension requiring medication.[20] Statistical analysis was performed via PASW Statistics 18.0 software (SPSS Inc., Chicago, IL) and a $p<0.05$ was considered statistically significant. Categorical and continuous variables were compared using two-tailed unpaired *t*-test and chi-square test, respectively.

## Results

A total of 1405 patients were included consisting of 56.7% females. Surgical CPT's consisted of 772 (54.9%) 61520's, 362 (25.8%) 61526's, 117 (8.3%) 61530's, and 154 (11.0%) 61616's. The surgical approach (CPT code) did not associate with different rates of reoperation ($p$=0.11), readmission ($p$=0.97), or mortality ($p$=0.23). They did however correspond to statistically different LOS in days (61520: 5.3±4.5, 61526: 4.5±2.9, 61530: 5.0±3.5, 61616: 5.0±3.9; $p$=0.02) and operation time in minutes (61520: 390±160, 61526: 430±164, 61530: 408±151, 61616: 430±166; $p$<0.001).

### Obesity

In the cohort, 845 (60.1%) patients were non-obese and 560 (39.9%) were obese. The two cohorts' presentations and surgical outcomes and complications are compared in Table 1. Most surgical outcomes and complication rates were similar except myocardial infarction (MI) (N=0 *vs*. N=3, $p$=0.03) and wound infection (N=9 *vs*. N=15, $p$=0.02), which occurred more in obese patients. When patients were divided into severely obese (N=257) and non-severely obese (N=1144) cohorts, operation time (*p*=0.99) and LOS (*p*=0.13) remained similar. Though rates of post-operative MI remained significant when comparing severely obese to non-severely obese patients (0.8% *vs*. 0.1%; *p*=0.03), rates of wound infection became nonsignificant (3.1% *vs*. 1.4%; *p*=0.05). Also, deep vein thrombosis (DVT) rates were significantly higher in severely obese *vs*. non-severely obese patients (2.7% *vs*. 0.7%; *p*=0.004).

### Age

Patients were divided into three cohorts according to age: 1) age <50, N=604 (43.0%), 2) age 50–64, N=578 (41.1%), and 3) age ≥65, N=223 (15.9%). The three cohorts' surgical outcomes and complications are compared in Table 2, demonstrating similar LOS (*p*=0.33) and readmission (*p*=0.08) or reoperation (*p*=0.54) rates. It was observed that older patients had shorter operation time (*p*<0.001) with higher 30-day mortality rates (*p*=0.01). Of note, the 8 (0.57%) patients experiencing 30-day mortality had a mean age of 54.1±19.7 years and time from operation to death was 8.5±4.3 days.

### Frailty

mFI was assigned based on history of diabetes (N=115; 8.2%), chronic hypertension (N=449; 32.0%), COPD (N=11; 0.8%), CHF (N=0; 0%), and dependent functional status (N=29; 2.1%). While 921 (65.6%) of patients had none of the conditions, 375 (26.7%), 100 (7.1%), 8 (0.6%), and 1 (0.1%) had mFI scores of 1, 2, 3, and 4, respectively. Table 3 compares surgical outcomes and complications between patients with mFI 0, 1, and ≥2. It demonstrated that LOS and Intubation ≥ 48 hours were significantly highest among subjects with mFI 2–4. However, readmission (*p*=0.63), reoperation (*p*=0.42), and most complication rates remained similarly distributed.

## Discussion

The manuscript investigated a large VS cohort from the NSQIP database to demonstrate the influence of age, BMI, and frailty on short-term surgical outcomes following VS resection. It was observed that obesity was associated with a higher incidence of MI and wound infection, and severe obesity also led to a higher propensity for developing DVT. Patients of older age had higher mortality rates and shorter operation time, but medical and surgical complication rates were similar. Moreover, frailty was observed to be associated with higher LOS and days of intubation. Finally, we demonstrated that the three variables did not influence short-term reoperation or unplanned readmission rates.

It is fairly established that increased BMI can be a risk factor for developing various chronic medical comorbidities, such as diabetes, coronary artery disease, and hypertension.[21] The effects of increased BMI on surgical complications are more nuanced. For example, increased BMI has been associated with higher complication rates in gastric cancer surgery, esophageal cancer surgery, liver surgery, pancreatic surgery, and colorectal surgery.[10] On the contrary, studies on coronary artery bypass surgery as well as head and neck free flap and reconstruction surgeries have observed a lack of influence by BMI on complication rate.

[11–13] A recent institutional study by Lipschitz and colleagues demonstrated that obesity was not a risk factor for most post-operative complications.[22] Similar to that study, we found increased BMI to be associated with post-operative cardiovascular complications, which is in-line with previous studies acknowledging obesity as a risk factor for MI.[23] Though our observed association between obesity and wound infections or severe obesity and DVT are not in-line with Lipschitz *et al.*,[22] these finding resembles other similar findings in the surgical literature.[24–26] This manuscript further strengthens their conclusion by demonstrating similar rates of LOS, readmission, reoperation, pulmonary embolism, pneumonia, urinary tract infection, and septic shock rates, which were not evaluated by Lipschitz and colleagues. Slight discrepancies between the Lipschitz and our study and a lack of research on long-term readmission or reoperation rates warrant future studies to continue investigating the influence of BMI on VS surgical outcomes. Another recent study reported that elevated BMI was strongly associated with post-operative cerebrospinal fluid (CSF) leak within 6-months, which was observed in 7.7% of the 362 subjects.[27] This database was not well-suited for extrapolation of CSF leak or nerve injury complications, which were not available as dedicated variables and their specific entry by individual providers were not readily available/reliable. As such, future studies to investigate the effect of BMI, age, and frailty on short-term post-operative CSF leaks are warranted.

With the continuous increase in average life expectancy in the US and across the world,[28] a progressively aging population may be considered for VS surgery and the influence of this variable on surgical outcomes must thus be carefully evaluated. Advanced age has been shown to be associated with higher incidence of postoperative complications in pedicled flap reconstruction,[14] abdominal aortic aneurysm repair,[17] and open anterior skull base surgery.[29] Conversely, increased patient age may not cause adverse events in free-flap head and neck reconstruction[30] and digital revascularization and replantation.[15] In the presented VS cohort, we observed that older age was associated with increased 30-day mortality and a shorter operation time. It can be hypothesized that surgeons were likely to be more conservative with their time allocation (i.e., shorter duration) with older patients to reduce intra and post-operative risks. When dividing age into tertiles, the oldest and youngest cohort had higher mortality rates than the middle tertile. Although this is more easily justifiable for older patients, it can be hypothesized that the youngest cohort's mortality rate can be due to a less conservative time allocation (i.e., longer surgical duration) or baseline familial/genetic disorders leading to more extensive disease and operations. Through investigating the same national database, some studies have supported similar association between older age and short-term mortality in colectomy,[31] hepatectomy,[32]and orthopedic surgeries,[33] while others have reported a lack of association in bariatric,[34] and sleeve gastrectomy.[35] In a previous study of 6545 patients using the California Hospital Inpatient Discharge database, we found no significant association between older age and mortality following VS surgery.[36] Moreover, in a matched cohort study of VS surgical patients, Van Abel *et al.* claimed a trend toward a statistical association between older age and mortality despite it not reaching proper statistical difference ($p$=0.07).[37] The different findings between this report and the two aforementioned studies warrant researchers to continue investigating this topic and do not disregard age as a potential risk factor for major adverse events. Similar to our findings, a previous institutional study by Oghalai and colleagues reported mostly similar rates of VS post-operative complications between younger and older patients.[38] Lastly, the observed shorter operation among older patients may be attributed to a less aggressive treatment approach for this cohort and subtotal resection.

There has been emerging interest to utilize frailty as a qualitative measure for predicting disease survival or treatment outcomes. Frail patients have been shown to be at an increased risk of experiencing major adverse events following cardiac[39] and hip surgeries.[40] In a comprehensive study, frailty was also shown to increase rates of morbidity and mortality following general, gynecologic, neurosurgical, otolaryngologic, plastic, thoracic, urologic, and vascular operations.[41] Similar to findings in this study, prolonged ventilation and LOS have been associated with increased frailty in cardiopulmonary,[42] spine,[43] or geriatric surgeries.[44] Utilizing an abbreviated mFI from the NSQIP variables,[20] we were able to establish a direct link between increased frailty and increased LOS and intubation duration. However, contrary to some reports,[43, 45] this VS cohort did not have an association between mFI and rates of readmission, reoperation, or other surgical or medical complications. Given the potential utility of a frailty measure in determining operative outcomes and potential complications, it is necessary to continue investigating its utility as a valuable clinical tool in VS peri- and post-operative planning.

This study contains several limitations. The data analyzes a de-identified retrospective national database, leaving room for reporting error or inclusion bias. The collected variables are standardized across all surgeries, thus certain VS-specific surgical complications such as tumor size, degree of resection completeness, CSF leak, or nerve injury were not included for assessment. For instance, it has been suggested that tumor size may directly influence surgical and functional outcomes,[46, 47] but we were unable to account for it as a confounder. Certain VS surgical complications including CSF leak and nerve injury/palsy can potentially extend LOS and cause readmission/reoperation, but this was not investigated due to database limitations. Different surgical approaches may also have dissimilar propensities for intra- and post-operative morbidities, though this was not investigated in this patient cohort. Despite these limitations, the presented study provides valuable information regarding the influence of BMI, age, or frailty on short-term morbidities following VS surgery, which can be utilized for optimizing care for at-risk patients.

## Conclusions

Obese patients undergoing VS surgery had a higher risk of developing short-term MI, wound infection, and DVT. VS resection in older patients was associated with shorter operation time and higher mortality rates, while frailty index correlated with prolonged intubation or LOS. Further investigation of the influence of these important clinical parameters on short-term morbidity and outcomes following VS surgery can help optimize pre-operative planning and post-operative care for patients with risk factors.

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## Highlights

- The NSQIP database was explored to evaluate whether increased age, BMI, and frailty influence vestibular schwannoma surgical morbidity.
- Post-operative adverse events such as myocardial infarction, wound infection, and deep vein thrombosis were more common among obese patients.
- Modified frailty score was associated with different length of stay and intubation rates among patients underwent VS surgical resection.
- These findings may help optimize pre-operative planning and post-operative care for at-risk surgical patients.

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**Table 1.**

Patient presentations and surgical outcomes and complications following vestibular schwannoma resection in obese and non-obese patients. All values in parentheses are percentages.

| Variable | Non-obese cohort (N=845) | Obese cohort (N=560) | *P* value |
|---|---|---|---|
| Age | 50.2±14.4 | 51.5±12.7 | 0.09 |
| Gender: Female | 494 (58.8) | 303 (54.1) | 0.11 |
| Smoking status | 82 (9.7) | 52 (9.3) | 0.79 |
| **Diabetes** | **40 (4.7)** | **75 (13.4)** | **<0.001** |
| **Chronic hypertension** | **207 (24.5)** | **242 (3.2)** | **<0.001** |
| Time of surgery (minutes) | 401.4 ± 157.0 | 413.4 ± 168.0 | 0.17 |
| Length of stay (days) | 4.9 ± 3.9 | 5.2 ± 4.2 | 0.11 |
| 30-day readmission* | 71 (9.5) | 60 (11.9) | 0.18 |
| 30-day reoperation* | 59 (7.9) | 46 (9.1) | 0.44 |
| 30-day mortality | 3 (0.4) | 5 (0.9) | 0.19 |
| Deep vein thrombosis | 7 (0.8) | 8 (1.4) | 0.28 |
| Pulmonary embolism | 3 (0.3) | 3 (0.5) | 0.61 |
| Pneumonia | 11 (1.3) | 4 (0.7) | 0.29 |
| Reintubation | 10 (1.1) | 6 (1.1) | 0.84 |
| Intubation ≥ 48 hours | 14 (1.7) | 8 (1.4) | 0.73 |
| **Superficial/deep wound infection** | **9 (1.1)** | **15 (2.7)** | **0.02** |
| Organ/deep space infection | 11 (1.3) | 4 (0.7) | 0.29 |
| Urinary tract infection | 9 (1.7) | 6 (1.1) | 0.99 |
| Blood transfusion | 23 (2.7) | 9 (1.6) | 0.17 |
| Stroke | 3 (0.4) | 4 (0.7) | 0.34 |
| Cardiac arrest | 0 (0) | 2 (0.4) | 0.08 |
| **Myocardial infarction** | **0 (0)** | **3 (0.5)** | **0.03** |
| Sepsis | 15 (1.8) | 13 (2.3) | 0.47 |
| Septic shock | 1 (0.1) | 1 (0.2) | 0.76 |

Independent sample *t*-tests and chi-square tests were utilized for continuous and categorical variables, respectively. Asterisk indicates percentages depending on the total patients with available reported variable, since readmission and reoperation data are not available for all patients.

**Table 2.**

Surgical outcomes and complications following vestibular schwannoma resection according to patients' age. All values in parenthesis are percentages.

| **Variable** | **Age <50 (N=604)** | **Age 50–64 (N=578)** | **Age ≥65 (N=223)** | ***P* value** |
|---|---|---|---|---|
| Age | 29.2±7.1 | 29.9±6.5 | 28.9±5.6 | 0.13 |
| Gender: Female | 336 (55.6) | 339 (58.7) | 122 (54.7) | 0.46 |
| **Smoking status** | **75 (12.4)** | **52 (9.0)** | **7 (3.1)** | **<0.001** |
| **Diabetes** | **24 (4.0)** | **55 (9.5)** | **36 (16,.)** | **<0.001** |
| **Chronic hypertension** | **89 (14.7)** | **214 (37.7)** | **142 (63.7)** | **<0.001** |
| **Time of surgery (minutes)** | **427.7±173.0** | **391.5±149.2** | **386.9±154.1** | **<0.001** |
| Length of stay (days) | 5.0±3.8 | 4.9±4.0 | 5.4±4.4 | 0.33 |
| 30-day readmission* | 51 (9.5) | 50 (9.8) | 0/203 (14.8) | 0.08 |
| 30-day reoperation* | 42 (7.8) | 42 (8.2) | 21 (10.2) | 0.54 |
| **30-day mortality** | **4 (0.7)** | **0 (0)** | **4 (1.8)** | **0.01** |
| Deep vein thrombosis | 4 (0.7) | 7 (1.2) | 4 (1.8) | 0.33 |
| Pulmonary embolism | 4 (0.7) | 1 (0.2) | 1 (0.4) | 0.43 |
| Pneumonia | 5 (0.8) | 5 (0.9) | 5 (2.2) | 0.17 |
| Reintubation | 6 (1.0) | 8 (1.4) | 2 (0.9) | 0.76 |
| Intubation ≥ 48 hours | 9 (1.5) | 7 (1.2) | 6 (2.7) | 0.31 |
| Superficial/deep wound infection | 13 (2.2) | 8 (1.4) | 3 (1.3) | 0.53 |
| Organ/deep space infection | 7 (1.2) | 7 (1.2) | 1 (0.4) | 0.61 |
| Urinary tract infection | 8 (1.3) | 4 (0.7) | 3 (1.3) | 0.51 |
| Blood transfusion | 12 (2.0) | 11 (19) | 9 (4.0) | 0.15 |
| Stroke | 3 (0.5) | 1 (0.2) | 3 (1.3) | 0.10 |
| Cardiac arrest | 1 (0.2) | 0 (0) | 1 (0.4) | 0.31 |
| Myocardial infarction | 1 (0.2) | 1 (0.2) | 1 (0.4) | 0.70 |
| Sepsis | 10 (1.7) | 10 (1.7) | 8 (3.6) | 0.17 |
| Septic shock | 2 (0.3) | 0 (0) | 0 (0) | 0.26 |

Independent sample *t*-tests and chi-square tests were utilized for continuous and categorical variables, respectively. Asterisk indicates percentages depending on the total patients with available reported variable, since readmission and reoperation data are not available for all patients.

### Table 3.

Surgical outcomes and complications following vestibular schwannoma resection according to patients' age. All values in parenthesis are percentages.

| Variable | mFI 0 (N=921) | mFI 1 (N=375) | mFI 2–4 (N=109) | *P* value |
|---|---|---|---|---|
| **Age** | **46.8 ± 13.2** | **57.6 ± 11.9** | **60.0 ± 10.1** | **<0.001** |
| **Gender: Female** | **549 (59.6)** | **187 (49.9)** | **61 (56.0)** | **0.01** |
| Smoking status | 99 (10.7) | 24 (6.4) | 11 (10.1) | 0.05 |
| **Diabetes** | **0 (0)** | **24 (6.4)** | **91 (83.5)** | **<0.001** |
| **Chronic hypertension** | **0 (0)** | **341 (90.9)** | **108 (99.1)** | **<0.001** |
| Time of surgery (minutes) | 409.2±162.0 | 401.1±155.9 | 399.6±176.5 | 0.64 |
| **Length of stay (days)** | **4.7±3.5** | **5.3±4.1** | **6.7±6.6** | **<0.001** |
| 30-day readmission* | 81 (9.9) | 39 (11.6) | 11 (11.6) | 0.63 |
| 30-day reoperation* | 63 (7.6) | 32 (9.5) | 10 (10.5) | 0.42 |
| 30-day mortality | 5 (0.5) | 2 (0.5) | 1 (0.9) | 0.88 |
| Deep vein thrombosis | 9 (1.0) | 3 (0.8) | 3 (2.8) | 0.19 |
| Pulmonary embolism | 2 (0.2) | 3 (0.8) | 1 (0.9) | 0.24 |
| Pneumonia | 7 (0.8) | 7 (1.9) | 1 (0.9) | 0.21 |
| Reintubation | 6 (0.7) | 8 (2.1) | 2 (1.8) | 0.05 |
| **Intubation ≥ 48 hours** | **9 (1.0)** | **9 (2.4)** | **4 (3.7)** | **0.03** |
| Superficial/deep wound infection | 13 (1.4) | 9 (2.4) | 2 (1.8) | 0.45 |
| Organ/deep space infection | 9 (1.0) | 4 (1.1) | 2 (1.8) | 0.71 |
| Urinary tract infection | 9 (1.0) | 3 (0.8) | 3 (2.8) | 0.19 |
| Blood transfusion | 18 (2.0) | 8 (2.1) | 6 (5.5) | 0.06 |
| Stroke | 4 (0.4) | 1 (0.3) | 2 (1.8) | 0.11 |
| Cardiac arrest | 1 (0.1) | 1 (0.3) | 0 (0) | 0.72 |
| **Myocardial infarction** | **1 (0.1)** | **0 (0)** | **2 (1.8)** | **0.001** |
| Sepsis | 17 (1.8) | 8 (2.1) | 3 (2.8) | 0.79 |
| Septic shock | 1 (0.1) | 1 (0.3) | 0 (0) | 0.72 |

mFI: modified frailty index. Independent sample *t*-tests and chi-square tests were utilized for continuous and categorical variables, respectively. Asterisk indicates percentages depending on the total patients with available reported variable, since readmission and reoperation data are not available for all patients.