Association of the Hospital Volume of Frail Surgical Patients Cared for with Outcomes after Elective, Major Noncardiac Surgery

A Retrospective Population-based Cohort Study

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ABSTRACT

Background: Frailty is a risk factor for adverse postoperative outcomes. Hospitals that perform higher volumes of surgery have better outcomes than low-volume providers. We hypothesized that frail patients undergoing elective surgery at hospitals that cared for a higher volume of similarly frail patients would have improved outcomes.

Methods: We conducted a retrospective, population-based cohort study using linked administrative data in Ontario, Canada. We identified all adult major, elective noncardiac surgery patients who were frail according to the validated Johns Hopkins Adjusted Clinical Groups (ACG®) frailty-defining diagnoses indicator. Hospitals were categorized into frailty volume quintiles based on volumes of frail surgical patients cared for. Multilevel, multivariable modeling measured the association of frailty volume with 30-day survival (primary outcome), complications, failure to rescue (secondary outcomes), and costs (tertiary outcome).

Results: Of 63,381 frail patients, 708 (1.1%) died after surgery. The thirty-day mortality rate in the lowest volume quintile was 1.1% compared to 0.9% in the highest. After adjustment for surgical risk, demographic characteristics, comorbidities, and clustering within hospitals, we found a significant association between frailty volume and improved survival (highest volume *vs.* lowest volume quintile: hazard ratio 0.51; 95% CI, 0.35 to 0.74; $P < 0.0001$). Although complication rates did not vary significantly between hospitals, failure-to-rescue rates were inversely related to volume.

Conclusions: Frail patients have reduced survival and increased failure to rescue when they undergo operations at hospitals having a lower volume of frail surgical patients. Concentration of perioperative care in centers that frequently treat high-risk frail patients could improve population outcomes. (ANESTHESIOLOGY 2017; 126:602-13)

THE populations of developed countries are aging rapidly; people aged 65 yr and older are the fastest growing demographic in Western countries.[1,2] Older patients undergo major surgery at a rate two to four times higher than younger age groups.[3] Older age is also associated with an approximately 2.5-fold increase in the risk of postoperative morbidity and mortality.[4,5] However, despite the well-established association between advanced age and adverse events, significant outcome variation exists between older patients that is not accounted for by differences in age and comorbidity burden alone.[6] Frailty, an aggregate expression of risk of adverse health outcomes due to age- and disease-related deficits that accumulate across multiple domains,[7,8] appears to be a key factor that explains this variation. Frailty

What We Know about This Topic

- Frailty increases risk for adverse postoperative outcomes
- Outcomes are generally better in hospitals that perform large numbers of complex surgery
- It remains unknown whether hospitals that care for large numbers of frail surgical patients also have better outcomes

What This Article Tells Us That Is New

- In a retrospective analysis of 63,381 frail patients, the authors evaluated the associations between hospital surgical volume of frail patients and 30-day survival
- Adjusted survival was significantly improved in the highest volume quintile compared to the lowest: hazard ratio 0.51 (95% CI, 0.35 to 0.74)
- Survival among frail patients was best in centers that care for large numbers of frail surgical patients

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is an independent risk factor for postoperative morbidity, increased resource use, and mortality.[9,10] Since the prevalence of frailty increases with age, more frail patients may be considered for elective surgery as the population ages.

Patients treated by hospitals and/or surgeons who perform a high volume of specific procedures tend to experience decreased rates of mortality, complications, and other adverse outcomes.[11,12] This volume–outcome relationship is often attributed to improved structures and processes of care at high-volume centers and the underlying experience and expertise of providers that volume may represent.[13] For example, while complication rates do not vary substantially between different hospitals based on procedural volume, patients cared for at high procedural volume hospitals experience lower rates of mortality following postoperative complications.[14] Frail and elderly patients require complex care due to the significant comorbidity burden, altered physiology, and cognitive issues that are common in this population. In nonoperative settings, specialized structures and processes of care are associated with improved outcomes for frail and elderly patients[15]; specialized geriatric care for hip fracture patients, many of whom are frail, results in improved postoperative outcomes.[16] While a significant body of knowledge exists describing the association between higher volumes of specific procedures and outcomes, limited data are available to describe the impact of the volume–outcome relationship in specific subgroups of complex patients, such as the frail elderly.[17,18] Given the aging of the population and the importance of improving the care and outcomes of frail surgical patients, further evidence is needed to examine the impact that structures of care may have on these high-risk patients.

Because existing evidence supports an association between improved postoperative outcomes and higher procedural volumes, we hypothesized that this association might generalize to the volume of frail patients cared for at a given hospital. Our specific objective was to measure the association of the hospital volume of frail elective surgery patients cared for with 30-day postoperative survival (primary outcome), in-hospital complications, and failure to rescue (FTR; secondary outcomes), independent of total surgical volume and other confounders. We further sought to determine the association between the volume of frail patients cared for and the costs of perioperative care (tertiary outcome).

Materials and Methods

We conducted a retrospective cohort study using linked health administrative data in Ontario, Canada, where hospital and physician services are provided to all residents through a publicly funded healthcare system and records of care are collected in health administrative data sets using standardized methods.[19,20] All data were linked deterministically using encrypted patient-specific identifiers. Ethical approval was provided by Sunnybrook Health Sciences Research Ethics Board (Toronto, Ontario, Canada), which waived the need for written or oral consent due to the anonymized nature of the utilized data.

Data Source

Data sets used for this analysis included the Discharge Abstract Database (DAD), which captures all hospitalizations; the Ontario Health Insurance Plan (OHIP) database, which captures physician service claims; the National Ambulatory Care Reporting System, which captures details of emergency and outpatient care; the Assistive Device Program Database, which records funding for medical devices; the Continuing Care Reporting System, which records details of long-term and respite care; the Ontario Drug Benefits Database, which records all outpatient prescription drug details for residents 65 yr of age and older; the Canadian Census to determine neighborhood income quintile; and the Registered Persons Database (RPDB), which captures all deaths for residents of Ontario. The analytic data set was generated from regularly collected data at the Institute for Clinical Evaluative Sciences (Toronto, Ontario, Canada), by a data analyst independent from the study team. Analysis was performed by the lead author. This article is reported per the STrengthening the Reporting of OBservational studies in Epidemiology and the REporting of studies Conducted using Observational Routinely-collected health Data guidelines.[21,22]

Study Population

We identified all episodes of surgical care for patients 18 yr and older having one of the following elective, intermediate- to high-risk noncardiac surgeries: peripheral arterial bypass, carotid endarterectomy, open abdominal aortic aneurysm repair, endovascular abdominal aortic aneurysm repair, total hip replacement, total knee replacement, large bowel surgery, partial liver resection, pancreaticoduodenectomy, gastrectomy, esophagectomy, pneumonectomy, lobectomy, nephrectomy, or cystectomy. These are all gender-neutral, intermediate- to high-risk operations and have been used together to study outcomes for surgical patients in Ontario (see Supplemental Digital Content section A, http://links.lww.com/ALN/B380, for a table of codes used).[23–28] Each episode of surgical care refers to the hospital admission that contained the record of the index surgery; no episodes of nonsurgical care were included in our analyses or calculations of volumes. All admissions were elective, and the validity and reliability of codes used to identify these elective procedures have been confirmed through reabstraction.[29,30] Episodes of care were identified between April 1, 2002 (to coincide with the introduction of International Classification of Diseases, Tenth Revision [to identify diagnoses] and Canadian Classification of Intervention [to identify procedures]) and March 31, 2014 (the latest time at which all data sets were complete when we conducted the study). We analyzed only the first episode of care for each patient to ensure a patient-level analysis. Patients cared for in a hospital that had treated fewer than 10 frail patients in the year before their surgery were excluded.

Exposure

Our exposure of interest was the number of frail patients cared for in the year before the index surgery at the index hospital. Frail patients were identified using the Johns Hopkins Adjusted Clinical Groups (ACG®) frailty-defining diagnoses indicator, a frailty instrument designed for use in health administrative data. The ACG® frailty-defining diagnoses indicator is a binary variable that uses 12 clusters of frailty-defining diagnoses (see Supplemental Digital Content section B, http://links.lww.com/ALN/B380, for a table of conceptual clusters)[31] and has been used to study frailty-related surgical outcomes[28,32,33] and healthcare resource use.[34,35] After elective surgery, patients identified as frail using the ACG® frailty-defining diagnoses indicator have significantly decreased short-term[33] and long-term[28] survival, as well as consume a high level of healthcare resources.[32] Because of the proprietary nature of the ACG® system, specific diagnostic codes used are not available for dissemination. Frailty-defining diagnoses were identified from all healthcare encounters in our health administrative data in the 3 yr *before* the index hospital admission. While there is no definitive-standard frailty instrument,[36] the concurrent validity of the ACG® frailty-defining diagnoses indicator has been previously compared against the Vulnerable Elderly Scale, which was collected as part of a comprehensive geriatric assessment.[37] Patients identified as frail using the ACG® indicator had higher Vulnerable Elderly Scale scores than those without frailty-defining diagnoses ($P < 0.005$). The ACG® indicator also showed construct validity in that the patients identified as frail using the indicator had characteristics consistent with multidimensional frailty, including a higher prevalence of falls, lower cognitive scores, and worse global functional scores than nonfrail patients.[37]

For our primary analysis, hospitals were divided into quintiles based on the number of elective frail surgical patients cared for in the year before the index surgery for each patient at each patient's hospital. This annual volume approach accounts for mergers or changes in hospital structure over time.[38] Although we conducted a patient-level analysis (*i.e.*, each individual patient was only entered into the cohort once, even if they had multiple surgeries during the study period), all episodes of care were used to calculate volume (*i.e.*, if one patient had multiple surgeries, each would count in the volume measure). The range of number of frail patients cared for at each hospital for each volume quintile was Q1 (10 to 62), Q2 (63 to 102), Q3 (103 to 143), Q4 (144 to 246), and Q5 (247 to 628). These cutoffs provided five groups with an equal number of patients per group as determined using the RANK procedure in SAS (USA).

Outcomes

The primary outcome was survival in the 30 days after surgery. We identified all deaths from any cause in the 30 days after surgery, including the date of death for each patient, from the RPDB. We identified whether a patient experienced any in-hospital complication using the DAD. Patients were classified as having a complication if they were assigned a type 2 diagnostic code (*i.e.*, the condition developed after admission) for any of the following conditions: cardiac arrest, myocardial infarction, atrial arrhythmia, ventricular arrhythmia, heart failure, stroke or transient ischemic attack, pneumonia, mechanical ventilation, pulmonary embolism, deep vein thrombosis, sepsis, septic shock, acute kidney injury, or unplanned return to the operating room (see Supplemental Digital Content section C, http://links.lww.com/ALN/B380, for a table of codes used). These events were identified while the patient was in hospital. FTR was defined as an in-hospital death that occurred in a patient having experienced a complication.[12] Total costs of care incurred by the provincially funded healthcare system were calculated at the patient level using standardized methods,[39] which combined all payments for hospital costs (source: DAD), physician and other clinician billings (source: OHIP), diagnostic procedures (source: OHIP), long-term and respite care (source: Continuing Care Reporting System), medical equipment (source: Assistive Device Program Database), and emergency and outpatient care (source: National Ambulatory Care Reporting System). We identified all costs accrued from the day of surgery to 30 days after surgery. Costs were standardized to 2014 Canadian dollars.

Covariates

Demographics were identified from the RPDB. Standard methods were used to identify all Elixhauser comorbidities based on International Classification of Diseases, Ninth Revision and International Classification of Diseases, Tenth Revision codes from the DAD in the 3 yr preceding surgery.[40] For patients aged 66 yr and older, we identified receipt of the following prescription medications in the year before surgery: angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, antiarrhythmics, anticoagulants, anticonvulsants, antidepressants, antipsychotics, insulin, oral antihyperglycemics, antiplatelet agents, benzodiazepines, beta blockers, oral corticosteroids, inhaled corticosteroids, inhaled bronchodilators, donepezil, rivastigmine, memantine, or galantamine. The Hospital-patient One-year Mortality Risk score was calculated for each patient. This score is an externally validated risk adjustment model with excellent discrimination (c-statistic, 0.89 to 0.92) and calibration for predicting mortality risk in hospitalized patients.[41] We also calculated the total number of intermediate- to high-risk elective surgeries performed at each hospital in the year before each patient's index surgery to account for the total volume of elective surgery at each institution.

Sample Size and Prespecified Analytic Approach

Because we could not estimate an anticipated effect size due to a lack of similar studies, we could not provide a formal power analysis. Therefore, we used a population sample where all available individuals were included in our study. Our primary outcomes were determined *a priori*, as was our analytic plan and approach. This data set was specifically generated for this analysis.

Statistical Analysis

SAS Enterprise Guide 6.1 (SAS) was used for all analyses. Patient characteristics were compared between frailty volume quintiles using chi-square tests for binary and categorical variables, ANOVA for normally distributed continuous variables, and the Kruskal-Wallis test for nonnormally distributed continuous variables. The distributions of continuous variables were visually inspected to determine whether they followed a normal or nonnormal distribution.

Because our outcome measures feature a variety of data types, appropriate regression techniques were chosen for each outcome as dictated by the data form used to measure the outcome of interest. Survival (*i.e.*, time to death from any cause) was analyzed using proportional hazards regression (the proportional hazards assumption was verified with the log-negative-log plot). Binary outcomes (complications and FTR) were analyzed using logistic regression. Cost data were right-skewed. We used a generalized linear model with a log link and gamma-distributed errors. This model accounts for skewed data and provides a relative measure of association (*i.e.*, percentage increase in cost). Studies of surgical costs have shown this regression approach to decrease error relative to other regression techniques.[42–44]

Although frailty is considered to be primarily an issue for older patients, frailty may have a more pronounced impact on the postoperative outcomes of younger patients[28]; we therefore did not restrict our study population by age. All models used generalized estimating equation methods using a robust sandwich covariance matrix estimate to account for patients clustered within hospitals. For our primary analysis, we performed unadjusted and multivariable adjusted proportional hazards regression. Frailty volume quintile (with the lowest volume quintile as the reference category) was the predictor variable of interest. For our adjusted model, we included all variables available to us that we hypothesized could confound the exposure–outcome association. These variables included patient gender, age (as a restricted cubic spline with five knots), neighborhood income quintile (as a five-level categorical variable), rural residence, year of surgery (as a restricted cubic spline with three knots), and each Elixhauser comorbidity (as binary variables). The Hospital-patient One-year Mortality Risk score was included as a linear predictor. Because frailty volume could simply be a proxy for the overall annual elective surgical volume at the index hospital, we accounted for total surgical volume as a five-level categorical variable based on total elective surgical volume quintiles. We also calculated the variance inflation factor between frailty volume and total volume to estimate the possibility of collinearity between these two variables.

We also performed an *a priori* specified analysis to determine the continuous association between frailty volume and survival. To account for the possibility of a continuous relationship between volume and outcome, we evaluated several transformations using fractional polynomials.[45] A logarithmic transformation of volume was identified as the best continuous fit using fractional polynomial analysis (based on the Akaike information criterion). The natural logarithm of frailty volume was entered into the multivariable proportional hazards model described above in place of frailty volume quintile. We then used the parameter estimate generated from the model to calculate the hazard ratio (HR) for volume across the range of frailty volumes identified in our study.

Further *post hoc* sensitivity analyses were performed to assess the robustness of our primary findings. First, we restricted analysis to patients 65 yr old or older. This analysis included the same covariates as those in the primary analysis plus binary variables to represent each of the prescription medications listed in the *Covariates*. Next, to estimate whether total surgical volume exhibited a similar association with outcome as frailty volume (*i.e.*, was the effect of frailty volume simply a reflection of total surgical volume despite control for the latter in our primary analysis), we analyzed the association between total surgical volume and survival in frail patients. For this analysis, we removed frailty volume quintile from the primary model and used total surgical volume quintile as our predictor variable of interest.

For our secondary outcomes, the associations between frailty volume quintile and complications, FTR, and costs were evaluated first on an unadjusted basis, with frailty volume quintile entered into each model as the sole predictor. Multivariable models were then constructed and accounted for the same covariates as in the primary adjusted analysis.

After completion of our analyses, it was recognized that within our data, increasing frailty volume was independently associated with improved survival, while increasing total surgical volume was independently associated with decreased survival. Therefore, we calculated the joint HRs between each quintile of frailty volume and total surgical volume (by multiplying the respective regression parameter estimates). These estimated joint HRs were used to construct a heat map to represent the association of the interaction between these different volume measures and survival.

Missing Data

Main outcome and exposure variables were complete for all participants. Neighborhood income quintile was imputed for with the group median for 0.4% of patients; rurality was imputed with the most common value (not rural) for 0.1% of patients. Follow-up was complete for all patients. No other data were missing, and all linkages were complete.

Results

We identified 74,981 episodes of care at 81 distinct hospitals for patients with a preoperative frailty-defining diagnosis who had undergone an elective, intermediate- to high-risk noncardiac surgery; this represented 13% of all such surgeries in adults (fig. 1). Our analysis was limited to 63,381 frail patients having their first episode of care in a hospital that had cared for at least 10 frail surgical patients in the previous year. Patients were older and primarily female, with the majority of patients having an American Society of Anesthesiologists score of III or worse. Low, middle, and high frailty volume hospitals differed significantly by most patient characteristics (table 1).

Of the 63,381 patients included, 708 (1.1%) patients died within 30 days of surgery. Before risk adjustment, there was a dose–response relationship between frailty volume quintile and mortality (table 2), which persisted after multivariable adjustment ($P = 0.001$). Model specifications are provided in table 3. Compared to the lowest frailty volume quintile, frail patients in all but the second lowest volume quintile had a statistically significantly reduced risk of 30-day death (fig. 2). No difference in death risk was found between the three highest frailty volume quintiles (quintile 4 *vs.* 3 adjusted HR, 1.08; 95% CI, 0.92 to 1.27; quintile 5 *vs.* 3 adjusted HR, 1.11; 95% CI, 0.91 to 1.36; quintile 5 *vs.* 4 adjusted HR, 1.03; 95% CI, 0.84 to 1.27).

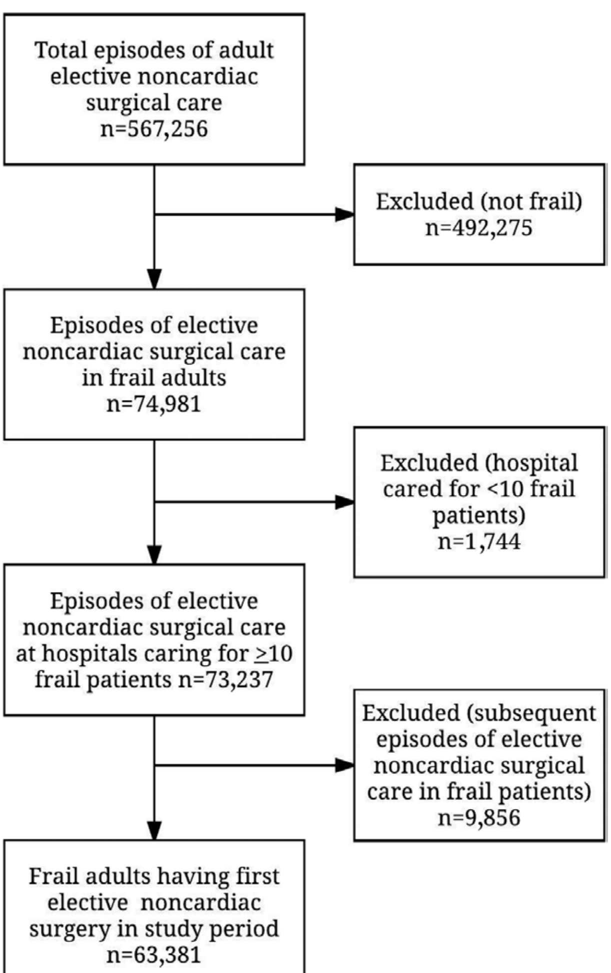

Fig. 1. Study flow diagram.

The variance inflation factor between frailty volume and total volume was 4.35, suggesting that there was moderate correlation between these volume measures (see Supplemental Digital Content section D, http://links.lww.com/ALN/B380, for scatter plot of total surgical volume *vs.* frail surgical volume). When modeled without frailty volume quintile, we found no dose–response relationship between total hospital volume quintile and mortality risk (quintile 1, reference; quintile 2 adjusted HR, 1.03; 95% CI, 0.88 to 1.21; quintile 3 adjusted HR, 1.02; 95% CI, 0.87 to 1.20; quintile 4 adjusted HR, 0.83; 95% CI, 0.70 to 0.99; quintile 5 adjusted HR, 0.88; 95% CI, 0.74 to 1.05).

In our sensitivity analyses, frailty volume was also significantly associated with mortality when modeled as continuous variable (fig. 3) with a $P < 0.001$ for the natural logarithm of frailty volume. When analysis was limited to patients 65 yr old or older, the same pattern of association was found (quintile 1, reference; quintile 2 adjusted HR, 0.89; 95% CI, 0.74 to 1.08; quintile 3 adjusted HR, 0.70; 95% CI, 0.56 to 0.88; quintile 4 adjusted HR, 0.62; 95% CI, 0.48 to 0.79; quintile 5 adjusted HR, 0.58; 95% CI, 0.42 to 0.79).

The results of secondary analyses are described in table 2; model specifications are provided in Supplemental Digital Content section E (http://links.lww.com/ALN/B380). Patients operated upon in higher frailty volume hospitals had lower rates of complications; however, no statistically significant association between frailty volume and complication risk was found in either the unadjusted or adjusted analyses ($P = 0.5$). Higher frailty volumes were associated with a lower odds of FTR ($P = 0.021$), an association that was significant for all but the second lowest frailty volume quintile (table 2). Total healthcare costs increased significantly from lowest to highest frailty volume quintile (see mean costs in table 2).

The joint HRs for frailty volume and total surgical volumes are represented as a heat map (fig. 4), where darker red represents decreased survival and darker blue represents improved survival. Frail individuals cared for in hospitals with high total surgical volumes but low frailty volumes had decreased survival, while frail individuals cared for at mid to high frailty volume hospitals tended to have improved survival regardless of total surgical volume, although this effect was more pronounced at lower levels of total surgical volume.

Discussion

Frail patients who undergo major, elective noncardiac surgery in hospitals that operate on a low volume of frail patients have decreased survival and increased risk of FTR compared to

Table 1. Baseline Characteristics of Study Population by Frailty Volume Quintile

Demographic	Lowest Volume Quintile, n = 12,549	Quintile 2, n = 12,798	Quintile 3, n = 12,769	Quintile 4, n = 12,585	Highest Volume Quintile, n = 12,680	*P* Value
Age, yr, mean (SD)	70 (12)	69 (12)	69 (12)	69 (12)	68 (12)	< 0.001
Female, %	64.4	63.7	61.6	62.8	64.0	< 0.001
Rural, %	17.9	16.7	15.5	14.7	13.3	< 0.001
Neighborhood income quintile, median (IQR)	3 (4,2)	3 (4,2)	3 (4,2)	3 (4,2)	3 (4,2)	< 0.001
Comorbidities						
ASA score < 2	45.3	41.8	40.9	40.8	44.4	< 0.001
Alcohol abuse, %	1.8	1.8	2.2	2.0	2.0	0.09
Atrial arrhythmia, %	5.3	5.8	6.0	5.8	5.2	0.028
Blood loss anemia, %	9.9	10.4	10.1	9.5	8.5	< 0.001
Cardiac valve disease, %	2.0	2.4	2.4	2.8	2.7	< 0.001
Coagulopathy, %	2.7	2.6	2.4	1.9	2.1	< 0.001
Chronic obstructive pulmonary disease	10.0	10.7	11.1	11.9	12.0	< 0.001
Cerebrovascular disease, %	3.9	0.9	5.2	0.7	3.6	< 0.001
Disease of pulmonary circulation, %	1.7	1.9	2.0	2.3	2.3	0.004
Dementia, %	2.2	2.0	2.0	1.4	1.2	< 0.001
Depression, %	3.7	3.7	4.3	3.7	5.0	< 0.001
Deficiency anemia, %	0.8	0.8	0.8	0.8	0.5	0.004
Diabetes mellitus without complications, %	16.5	16.2	16.5	16.2	16.8	0.683
Diabetes mellitus with complications, %	8.1	10.2	11.6	11.2	9.4	< 0.001
Dialysis, %	0.6	1.0	1.1	1.0	0.9	0.001
Drug abuse, %	0.5	0.6	0.9	0.7	0.7	0.016
Heart failure, %	6.7	6.7	6.2	6.1	5.2	< 0.001
Hemiplegia, %	0.8	0.8	0.9	0.8	0.7	0.78
HIV or AIDS, %	NA	NA	NA	NA	NA	NA
Hypertension with complications, %	1.4	2.0	2.0	1.9	1.7	0.001
Hypertension without complications, %	35.9	38.8	39.9	47.5	48.4	0.001
Liver disease, %	0.7	0.8	0.9	0.9	1.0	0.119
Malignancy, %	7.1	7.3	7.5	7.7	8.3	0.002
Metastases, %	0.8	1.2	1.2	1.3	1.7	< 0.001
Obesity	22.8	26.6	25.6	30.7	25.4	< 0.001
Peptic ulcer disease, %	1.2	1.1	1.1	1.0	1.2	0.572
Peripheral vascular disease, %	3.4	3.6	4.8	3.4	3.3	< 0.001
Psychoses, %	1.1	0.8	0.7	0.5	0.6	< 0.001
Renal disease, %	2.4	3.0	2.9	2.9	2.3	< 0.001
Rheumatic disease, %	1.4	1.5	1.4	1.5	1.4	0.71
Venous thromboembolism, %	1.0	0.8	0.8	1.1	0.9	0.181
Weight loss, %	2.0	1.7	1.7	1.9	1.5	0.038
One-year mortality risk						
HOMR score, mean (SD)	25 (9)	24 (9)	25 (9)	25 (10)	24 (9)	< 0.001
Healthcare resource use						
Acute hospitalization in year before index admission	71.4	71.7	71.3	72.7	74.3	< 0.001
Emergency department visit in year before index admission, %	42.4	42.3	42.4	45.9	49.6	< 0.001
Procedure						
Total hip replacement, %	24.4	24.9	25.6	27.1	28.0	< 0.001
Total knee replacement, %	44.9	45.2	39.8	44	46.3	
Carotid endarterectomy, %	1.2	2.2	3	1.7	1.6	
Endovascular AAA repair, %	1.2	0.6	1.2	0.8	1	
Open AAA repair, %	0.4	1.7	2.4	1	1.4	
Peripheral arterial bypass, %	1.4	4.5	5.8	2.9	3.2	
Nephrectomy, %	2.9	2.5	2.9	3.4	2.5	
Cystectomy, %	0.9	0.8	1	1.1	1.8	
Large bowel surgery, %	18	13.4	13.4	11.6	9.1	
Liver resection, %	0.3	0.3	0.5	1	1.2	
Pancreaticoduodenectomy, %	0.3	0.3	0.4	0.6	0.9	
Gastrectomy or esophagectomy, %	1.7	1.8	1.9	2.2	1.4	
Lobectomy or pneumonectomy, %	1.2	2	2.3	2.7	1.6	
Hospital characteristics						
No. of frail surgical patients per year, range	10–62	63–102	103–143	144–246	247–628	
No. of total surgical patients per year, mean (SD)	402 (188)	728 (235)	956 (268)	1,152 (424)	2,106 (656)	

NA (not applicable) indicates that cell sizes were suppressed due to counts under 7.

AAA = abdominal aortic aneurysm; AIDS = acquired immunodeficiency syndrome; ASA = American Society of Anesthesiologists; HIV = human immunodeficiency virus; HOMR = Hospital-patient Once-year Mortality Risk; IQR = interquartile range.

Table 2. Study Outcomes

Outcome		Frailty Volume Quintile				
		1 (Lowest)	2	3	4	5 (Highest)
30-day survival*	n (%)	168 (1.3)	173 (1.4)	139 (1.1)	114 (0.9)	114 (0.9)
	Unadjusted HR	Reference	1.03	0.84	0.70	0.68
	95% CI	Reference	0.83–1.28	0.67–1.05	0.55–0.89	0.53–0.86
	Adjusted HR	Reference	0.83	0.6	0.58	0.54
	95% CI	Reference	0.64–1.08	0.45–0.81	0.42–0.79	0.37–0.77
Complications	n (%)	798 (6.4)	815 (6.4)	824 (6.5)	797 (6.3)	769 (6.1)
	Adjusted OR	Reference	0.92	0.90	0.90	0.87
	95% CI	Reference	0.81–1.05	0.78–1.05	0.77–1.06	0.72–1.05
Failure to rescue	n (%)	78 (9.8)	96 (11.8)	73 (8.9)	70 (8.8)	58 (7.5)
	Adjusted OR	Reference	0.95	0.62	0.60	0.41
	95% CI	Reference	0.64–1.40	0.39–0.99	0.36–0.99	0.21–0.77
Cost	Mean ($CAD, 2014)	$20,576	$20,970	$21,939	$21,440	$21,776
	Adjusted IRR	Reference	1	1.03	1.03	1.03
	95% CI	Reference	0.99–1.01	1.01–1.04	1.01–1.04	1.02–1.05

* Primary study outcomes.
$CAD = Canadian dollars; HR = hazard ratio; IRR = incidence rate ratio; OR = odds ratio.

frail patients who undergo surgery at hospitals that operate on higher volumes of frail patients. This finding compliments existing research demonstrating that higher volumes of specific surgical procedures are associated with lower mortality and lower complication rates,[12,14] while highlighting that elective surgical outcomes may presumably be improved by focusing on care of this specific high-risk patient population.

The volume–outcome relationship in surgical care has been recognized for more than 30 yr.[46] The fact that hospitals that perform a higher volume of complex surgical procedures achieve lower rates of morbidity and mortality likely reflects an underlying set of structures and processes of care that promote these improved outcomes, while also accounting for the experience and expertise gained through routine performance of each procedure. Similar factors may underlie the improved outcomes that we have identified regarding the care of frail surgical patients. Frail patients are known to be sensitive to processes of care and may benefit from perioperative care pathways that address their unique risk profile. Based on our primary analysis, which represented volume as a quintile, as well as our sensitivity analysis that evaluated the continuous impact of frailty volume on mortality risk, the association of frailty volume appears to be most relevant in low-volume settings, which are those that operate on approximately 100 frail patients or less per year. The incremental increase in survival between the highest (greater than 246 frail patients per year; adjusted HR, 0.51) and second highest (144 to 246 frail patients per year; adjusted HR, 0.56) frailty volume quintiles was much smaller than the increase from the lowest frailty volume quintile (10 to 62 frail patients per year; adjusted HR, 1.0) to the middle quintile (103 to 143 frail patients per year; adjusted HR, 0.60). This is further supported by the lack of statistical difference in survival between the highest three quintiles in pairwise comparisons. Similarly, there is notable flattening of the continuous relationship between volume and survival beyond the 100-patient mark (fig. 2). Therefore, our findings support a minimum volume approach to the care of frail elderly patients, as opposed to a volume-maximizing strategy.

This minimum volume approach is further supported by the joint HRs expressed in figure 4. In the third, fourth, and highest frailty volume quintiles, 14 of 15 joint HRs calculated with total surgical volume support improved postoperative survival. Meanwhile, for patients in the lowest frailty volume quintile, being cared for in higher total surgical volume hospital was associated with decreasing survival as total volume increased. While our data do not contain measures that can delineate a causal mechanism for this association, we hypothesize that being a frail patient in a busy, high-throughput hospital that is not accustomed to the complex care required by frail patients may lead to an inappropriate match between the care needs of a frail patient and the care routinely provided in such hospitals. Prospective health services research is needed to identify the specific structures and processes that underlie these associations to inform optimization of the perioperative healthcare system for our aging surgical population. In the interim, we must conclude that the frailty volume–outcome association should be considered independent of total surgical volume.

Frailty is a robust risk factor for mortality in surgical and nonsurgical populations, a risk that is manifested through vulnerability to stressors. Major surgery induces substantial physiologic stress even in healthy patients, and recent studies suggest that the early postoperative period is a time of particularly elevated risk for frail surgical patients.[28,47] The daily risk of death in the early postoperative period is significantly elevated in frail patients; compared to nonfrail patients, frail patients have a

Table 3. Adjusted Multivariable Regression Model for the Primary Outcome of 30-day Survival

Covariate	HR	95% CI
Frailty volume quintile		
1 (lowest reference)	1.00	1.00–1.00
2	0.84	0.64–1.10
3	0.60	0.45–0.80
4	0.56	0.41–0.77
5 (highest)	0.51	0.35–0.74
Total volume quintile		
1 (lowest reference)	1.00	1.00–1.00
2	1.36	1.04–1.78
3	1.65	1.20–2.27
4	1.51	1.03–2.20
5 (highest)	1.75	1.15–2.66
Year of surgery (three-knot restricted cubic spline)	0.97	0.94–1.00
Age (five-knot restricted spline)	1.14	1.06–1.23
	0.50	0.29–0.88
	3.20	0.98–10.42
Female (*vs.* male)	1.46	1.25–1.71
Rural (*vs.* not or none)	0.92	0.75–1.14
Neighborhood income quintile		
1 (lowest reference)	1.00	1.00–1.00
2	1.09	0.87–1.37
3	1.06	0.84–1.34
4	0.93	0.73–1.19
5 (highest)	1.16	0.92–1.47
Comorbidities		
ASA score		
≤ 2 (reference)	1.00	1.00–1.00
3	0.64	0.54–0.75
4	3.12	2.13–4.02
5	6.78	4.35–10.53
Alcohol abuse (*vs.* not or none)	1.66	1.15–2.40
Atrial arrhythmia (*vs.* not or none)	1.03	0.81–1.32
Blood loss anemia (*vs.* not or none)	1.69	1.38–2.06
Cardiac valve disease (*vs.* not or none)	1.73	0.82–1.69
Coagulopathy (*vs.* not or none)	0.98	0.72–1.34
Chronic obstructive pulmonary disease	1.38	1.14–1.66
Cerebrovascular disease (*vs.* not or none)	1.45	1.17–1.79
Disease of pulmonary circulation (*vs.* not or none)	1.09	0.76–1.56
Dementia (*vs.* not or none)	1.85	1.43–2.38
Depression (*vs.* not or none)	0.88	0.62–1.26
Deficiency anemia (*vs.* not or none)	1.20	0.71–2.04
Diabetes mellitus without complications (*vs.* not or none)	0.92	0.77–1.09
Diabetes mellitus with complications (*vs.* not or none)	1.34	1.11–1.63
Dialysis (*vs.* not or none)	1.70	1.13–2.54
Drug abuse (*vs.* not or none)	1.13	0.53–2.38
Heart failure (*vs.* not or none)	1.80	1.41–2.33
Hemiplegia (*vs.* not or none)	1.19	0.77–1.84
Hypertension with complications (*vs.* not or none)	1.12	0.70–1.77
Hypertension without complications (*vs.* not or none)	0.81	0.67–0.97
Liver disease (*vs.* not or none)	1.35	0.76–2.41
Malignancy (*vs.* not or none)	1.02	0.83–1.24
Metastases (*vs.* not or none)	1.34	0.94–1.92
Obesity (*vs.* not or none)	1.28	1.02–1.60
Peptic ulcer disease (*vs.* not or none)	1.00	0.66–1.53
Peripheral vascular disease (*vs.* not or none)	0.90	0.68–1.19
Psychoses (*vs.* not or none)	1.24	0.57–2.69
Renal disease (*vs.* not or none)	1.02	1.75–1.39
Rheumatic disease (*vs.* not or none)	1.00	0.54–1.87
Venous thromboembolism (*vs.* not or none)	1.63	1.05–2.54
Weight loss (*vs.* not or none)	1.00	0.73–1.37
One-year mortality risk		
HOMR score (per 1 unit increase)	1.06	1.04–1.07
Healthcare resource use		
Acute hospitalization in year before index admission (*vs.* not or none)	0.93	0.76–1.13
Emergency department visit in year before index admission (*vs.* not or none)	0.88	0.72–1.07
Procedure		
Total hip replacement (reference)	1.00	1.00–1.00
Total knee replacement	0.79	0.56–1.09
Carotid endarterectomy	1.28	0.73–2.26
Endovascular AAA repair	2.01	1.21–3.34
Open AAA repair	2.64	1.84–3.78
Peripheral arterial bypass	2.45	1.75–3.42
Nephrectomy	2.76	1.87–4.09
Cystectomy	3.19	1.75–5.80
Large bowel surgery	2.82	2.17–3.67
Liver resection	3.64	1.84–7.21
Pancreaticoduodenectomy	1.36	0.54–3.45
Gastrectomy or esophagectomy	3.16	2.17–4.61
Lobectomy or pneumonectomy	2.49	1.55–3.98

AAA = abdominal aortic aneurysm; ASA = American Society of Anesthesiologists; HOMR = Hospital-patient One-year Mortality Risk; HR = hazard ratio.

30-fold increase in mortality risk on postoperative day 3.[28] There is also evidence that frailty may be a risk factor for FTR. In patients undergoing elective aortic aneurysm repair, frailty was associated with a 1.7-fold increase in the odds of FTR.[47] Although our FTR analysis had a relatively small number of events and was a secondary analysis, the fact that higher frailty volume hospitals in our study had lower mortality rates and lower FTR rates suggests that these hospitals may have mechanisms in place to mitigate some of the specific risks presented by frail patients. This finding supports future efforts to study and optimize structures and processes of perioperative care to improve the care and outcomes of frail elderly surgical patients.

Finally, the improvements in outcomes at high frailty volume hospitals do not appear to substantially increase the costs of care. Previous studies relating mortality, complications, and FTR with processes of care found that higher care intensity (and higher cost care) was associated with higher mortality and complication rates but lower FTR risk.[48] In our study, we found that as volume increased, mortality and FTR risk decreased substantially, while cost increased by only 3% (although this was statistically significant). This

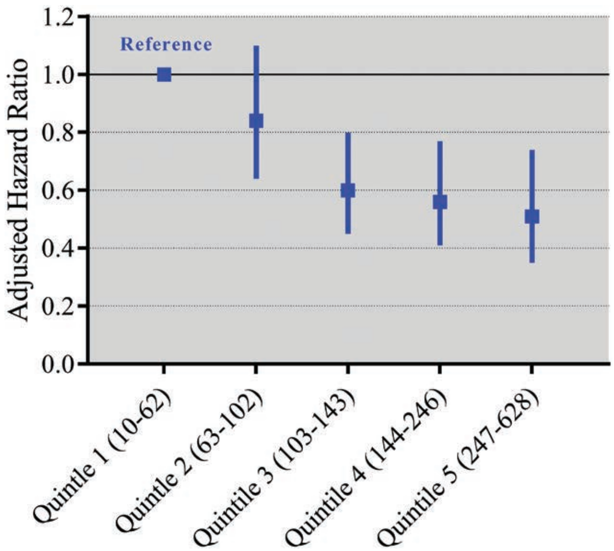

Fig. 2. Adjusted association of hospital frailty volume quintile with mortality risk. The adjusted hazard ratio for 30-day mortality (*vertical axis*) is presented for each frailty volume quintile (*horizontal axis*) with the lowest quintile as the reference category. Estimates with 95% CIs less than 1 indicate a significant decrease in the risk of postoperative death. Numbers in parentheses on the horizontal axis indicate volume of frail surgical patients treated annually.

suggests that the processes of care that may be in place at higher volume hospitals do not require substantial additional monetary resources to achieve improved outcomes.

Strengths and Limitations

Our study features several important strengths. Our use of population-based data allowed us to investigate the impact of volume across an entire province in a universal payer healthcare system, and our results may be generalizable to similar healthcare systems. Furthermore, we utilized administrative data definitions with known accuracy and reliability to define our cohort, exposures, and outcomes. We were also able to control for important patient-level confounders such as demographics, comorbidities, and preoperative health systems use. By accounting for clustering by individual hospital when estimating our exposure–outcome associations, we were able to generate unbiased estimates of standard error for our exposure of interest; analyses lacking this approach are likely to overestimate the statistical significance of volume.

This study also has limitations. Health administrative data are not primarily collected for research purposes and sources of bias; in particular, misclassification bias can confound associations in unpredictable ways. While our frailty instrument is the only frailty measure currently validated for use in health administrative data, it is a binary definition that does not measure different severities of frailty. Furthermore, different frailty instruments typically have limited agreement; therefore, the generalizability of our findings to frail populations defined using different tools may be limited. Finally, our costs analysis is based on cost incurred in a single-payer universal health insurance system and may not generalize to all healthcare systems.

Conclusion

Patients with frailty-defining diagnoses who undergo elective surgery at hospitals that care for a low volume of frail elective surgical patients have decreased 30-day survival and are more likely to die after experiencing a postoperative complication. These findings suggest that improving the outcomes of patients undergoing major surgery may be accomplished not only through a focus on centers performing higher volumes of specific surgeries but also through a focus on avoiding low-volume centers in regard to the number of frail patients cared for. Further study is required to confirm these findings in other jurisdictions

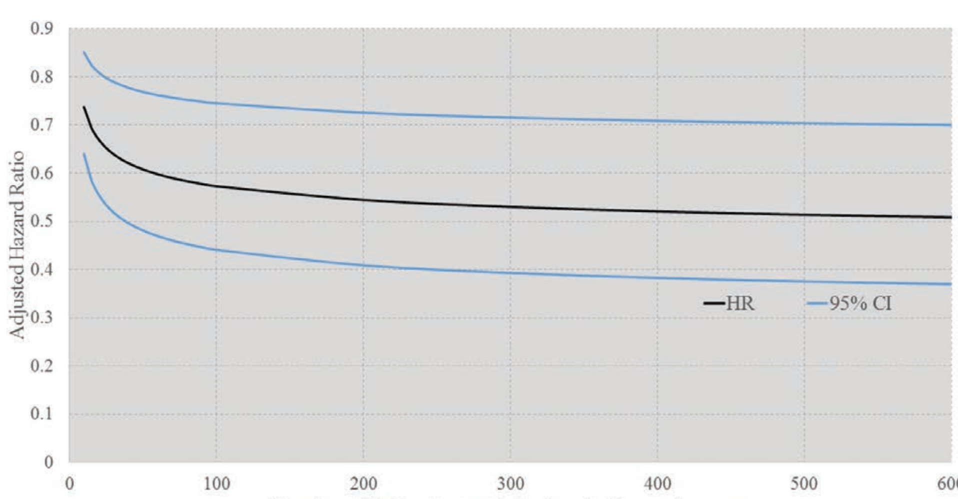

Fig. 3. Adjusted association of hospital frailty volume quintile with mortality risk. This figure demonstrates the continuous relationship between frailty volume and mortality risk. Frailty volume was transformed using the natural logarithm function, and using the parameter estimate from the multivariable survival model, we calculated the hazard ratio (HR) for mortality across the range of volumes identified in our study. Any segment where the 95% CIs are less than 1 represents a significantly decreased risk of death.

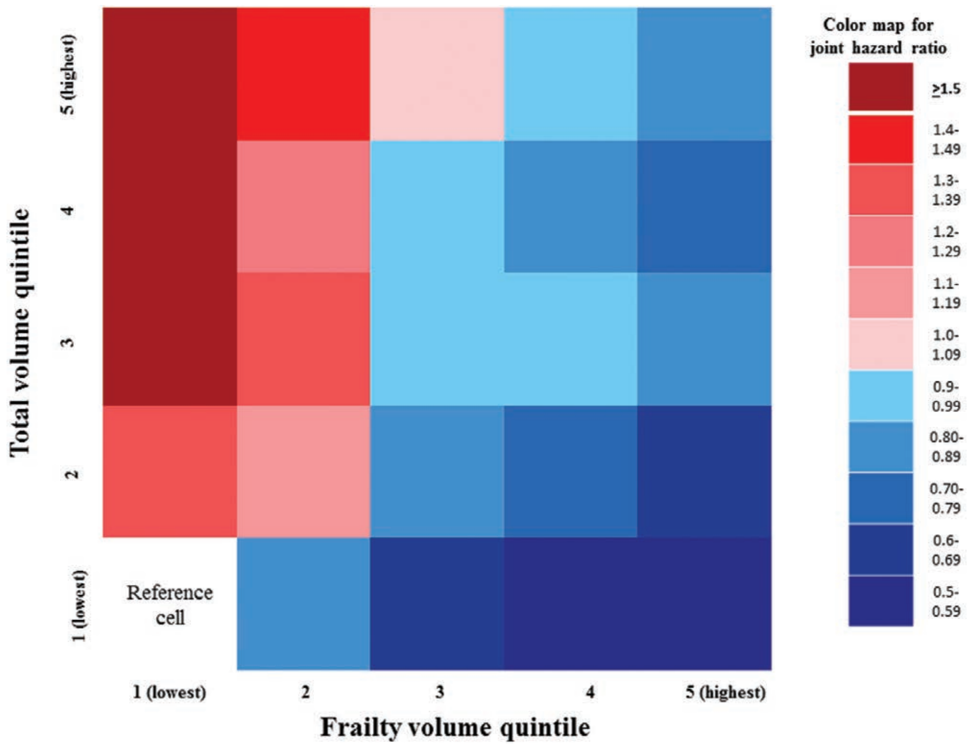

Fig. 4. Joint hazard ratios between frail surgical volume quintile and total surgical volume quintile. This figure demonstrates the joint hazard ratios between frailty volume quintile and total surgical volume quintile. Joint hazard ratios were generated by multiplying the multilevel, multivariable adjusted regression parameters for each frailty volume quintile with those from each total surgical volume quintile. *Red colors* represent decreased survival (*darker shades* = worse survival), while *blue colors* represent improved survival (*darker shades* = improved survival).

and to identify which improved structures and processes of care underlie this frailty volume–outcome relationship.

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Competing Interests

No authors declare any relevant conflicts of interest within the past 36 months.

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ANESTHESIOLOGY REFLECTIONS FROM THE WOOD LIBRARY-MUSEUM

"Fresh" Laughing Gas or "Wonderful" Odontunder from Dr. Ira W. Stoughton

As he advertised from the corner of 10th and Greene Streets (*left*) in Philadelphia, Pennsylvania, Dr. Ira W. Stoughton (1854 to 1920) offered his dental patients a choice of general or local anesthesia. According to this trade card from the Wood Library-Museum's Ben Z. Swanson Collection, Dr. Stoughton offered his patients "Pure, fresh [Laughing] Gas daily." Although he advertised it as "Dr. Stoughton's Wonderful Pain Obtunder," his local anesthetic was branded "Odontunder" and advertised with a cherub winging around with a banner (*right*). Analysis of Odontunder revealed a 1.35% concentration of cocaine in its proprietary mixture. Conveniently for Dr. Stoughton, his supplier of local anesthetics had, by 1910, become geographically local—the Odontunder Manufacturing Company had moved from Ohio to Stoughton's Philadelphia. (Copyright © the American Society of Anesthesiologists' Wood Library-Museum of Anesthesiology.)

George S. Bause, M.D., M.P.H., Honorary Curator and Laureate of the History of Anesthesia, Wood Library-Museum of Anesthesiology, Schaumburg, Illinois, and Clinical Associate Professor, Case Western Reserve University, Cleveland, Ohio. UJYC@aol.com.