ANESTHESIOLOGY

Attributable Perioperative Cost of Frailty after Major, Elective Noncardiac Surgery: A Population-based Cohort Study

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EDITOR'S PERSPECTIVE

What We Already Know about This Topic

- Patients with frailty experience higher rates of perioperative mortality and morbidity
- The extent to which patients with frailty demonstrate higher costs in the year after surgery remains unclear

What This Article Tells Us That Is New

- In a linked administrative dataset of 171,576 patients age 66 yr or older undergoing elective, noncardiac surgery in Ontario between 2012 and 2018, 23,219 (13.5%) demonstrated frailty defined using a multidimensional frailty index
- After adjusting for confounders, patients with frailty demonstrated an absolute cost increase of $11,828 Canadian dollar (ratio of means 1.53; 95% CI, 1.51 to 1.56)
- Among the various components of total 1-yr costs, postacute care costs had the largest relative increase

ABSTRACT

Background: Patients with frailty consistently experience higher rates of perioperative morbidity and mortality; however, costs attributable to frailty remain poorly defined. This study sought to identify older patients with and without frailty using a validated, multidimensional frailty index and estimated the attributable costs in the year after major, elective noncardiac surgery.

Methods: The authors conducted a retrospective population-based cohort study of all patients 66 yr or older having major, elective noncardiac surgery between April 1, 2012, and March 31, 2018, using linked health data obtained from an independent research institute (ICES) in Ontario, Canada. All data were collected using standard methods from the date of surgery to the end of 1-yr follow-up. The presence or absence of preoperative frailty was determined using a multidimensional frailty index. The primary outcome was total health system costs in the year after surgery using a validated patient-level costing method capturing direct and indirect costs. Secondary outcomes included costs to postoperative days 30 and 90 along with sensitivity analyses and evaluation of effect modifiers.

Results: Of 171,576 patients, 23,219 (13.5%) were identified with preoperative frailty. Unadjusted costs were higher among patients with frailty (ratio of means 1.79, 95% CI 1.76 to 1.83). After adjusting for confounders, an absolute cost increase of $11,828 Canadian dollar (ratio of means 1.53; 95% CI, 1.51 to 1.56) was attributable to frailty. This association was attenuated with additional control for comorbidities (ratio of means 1.24, 95% CI, 1.22 to 1.26). Among contributors to total costs, frailty was most strongly associated with increased postacute care costs.

Conclusions: For patients with preoperative frailty having elective surgery, the authors estimate that attributable costs are increased 1.5-fold in the year after major, elective noncardiac surgery. These data inform resource allocation for patients with frailty.

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Frailty is a state of vulnerability to adverse health outcomes resulting from accumulation of multidimensional age- and disease-related deficits.[1,2] Individuals with frailty are vulnerable to stressors[1,3]; surgery is a substantive physiologic stress. As our population ages, the number of older patients with frailty presenting for surgery is increasing.[4,5] The presence of frailty more than doubles the risk of postoperative morbidity, mortality, and loss of independence.[1,6] People with frailty also consume significantly greater resources after surgery, including longer hospital stay (4 days

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on average), more nonhome discharges (6-fold higher), and more readmissions (50% greater).[7–9]

Although the association of frailty with adverse patient outcomes is well-established and summarized in systematic reviews,[10–14] leading healthcare quality frameworks, including the Institute for Healthcare Improvement's Triple Aim,[15] highlight the joint importance of understanding cost implications in conjunction with patient outcomes. A recent systematic review highlighted important knowledge gaps in understanding the impact of frailty on postoperative healthcare resource use.[16] Although associations between frailty and a 1.5- to 2-fold increase in costs are reported, available estimates are inadequately confounder-adjusted. Additionally, most cost data define frailty based on the Frailty Defining Diagnosis Indicator, which is a proprietary binary indicator that lacks the continuous and multidimensional characteristics that experts agree are required to meaningfully define frailty.[17]

To address our incomplete understanding of healthcare costs attributable to frailty after surgery, we conducted a retrospective population-based cohort study. Our primary objective was to use a validated, multidimensional frailty index combined with validated health system cost ascertainment methods to estimate the total perioperative costs attributable to frailty in the year after elective, major noncardiac surgery. Secondary objectives were to estimate the attributable cost of frailty at 30 and 90 days after surgery, as well as to evaluate postulated effect modifiers of the frailty–cost association.

Materials and Methods

Design and Setting

This was a population-based cohort study conducted in Ontario, Canada (more than 14 million inhabitants), where universal physician and hospital health insurance (Ontario Health Insurance Plan) is provided to all residents. Healthcare data in Ontario are collected using standardized methods[18] and stored at ICES, an independent research institute in Ontario, Canada. Datasets used for the study included: the Discharge Abstract Database (all hospitalizations); the National Ambulatory Care Reporting System (emergency and outpatient care); the Continuing Care Reporting System (details of long-term and respite care); the Ontario Drug Benefits Database (prescription drug claims for residents 65 yr or older); the Registered Persons Database (all death dates), Home Care Database (receipt of home-based health services) and National Rehabilitation System (receipt of inpatient rehabilitation). The dataset was assembled and analyzed by a trained data analyst (R.T.) after protocol registration (https://osf.io/qy9h8/). Because all data were routinely collected and de-identified, the need for ethical review was legally waived. The article is reported according to appropriate guidelines.[19,20]

Cohort

We identified all Ontario residents aged 66 yr or older on the day of elective, major noncardiac surgery (an age range that reflects the older adult demographic and that allowed full capture of prescription medication data). Participants were identified using standardized methods to capture surgeries that occur during an elective hospital admission using established noncardiac surgical Canadian Classification of Interventions codes that represent surgeries of intermediate to high physiologic stress (see procedures in Supplemental Digital Content 1.0, https://links.lww.com/ALN/D152). These procedure codes have been used together extensively in previous studies.[21–25] To create a participant-level data set we identified the first eligible surgery for each participant from April 1, 2012, to March 31, 2018.

Exposure

Frailty was identified using a multidimensional frailty index[26] validly ascertained from health administrative data using the recommended methods of Searle *et al.*[27] This approach ensures that the required 30 multidimensional deficits are available for all participants to allow calculation of a frailty index value between 0 (no deficits present) and 1 (deficits present in all domains) based on the accumulating deficits model of frailty (Supplemental Digital Content 2.0, https://links.lww.com/ALN/D152).[26] The index includes dimensions assessing medications, comorbidities (cardiovascular, pulmonary, endocrinologic, neurologic, rheumatologic, liver and renal comorbidities), cancer, dementia, socioeconomic status, need for supported living, substance abuse, dental, skin, hearing and vision issues, and receipt of supportive medical devices. For primary analyses, frailty was coded as present or absent based on a frailty index value of less than 0.21 *versus* 0.21 or greater, respectively.[26,28] The calculated frailty index value was also captured as a continuous variable for sensitivity analyses.

Outcomes

Our primary outcome was total health system costs in 365 days from surgery (starting on the day of surgery, expressed in 2018 Canadian dollars) paid by the Ministry of Health, the public insurer for all Ontario residents. Standard and validated case costing algorithms were used to capture all publicly funded direct and indirect costs (*e.g.*, hospitalization, rehabilitation, nursing home care, medical diagnostics, pharmacy and provincially funded home-based health care),[29] accounting for each individual's resource intensity weight. We also calculated the component costs: hospitalization (inpatient, outpatient, or ambulatory surgical costs), postacute care (rehabilitation, complex continuing care, long-term [*i.e.*, skilled nursing facility] care, and home care services), physician billing (all physician service claims or capitated payments), and other (cancer care, dialysis, emergency department care, prescription medications).

Out-of-pocket costs for patients (*e.g.*, private physiotherapy or noninsured medical devices) were not captured. Secondary outcomes were costs accumulated at 30 and 90 days after surgery.

Covariates

Variables that were postulated to be direct causal contributors to exposure, or present on the pathway between exposure and outcome, were not adjusted for in the primary analysis to avoid overadjustment bias.[30] Demographics (age, sex, neighborhood income quintile, rural *vs.* urban residence) were identified from the Discharge Abstract Database and from the Canadian Census. Standard methods were used to identify all Elixhauser comorbidities using International Classification of Diseases, Tenth Revision, codes from the Discharge Abstract Database in the 3 yr preceding surgery.[31] Prescription medications were captured from the drug database. Acute care hospitalizations, emergency department visits, and total health system costs in the year before surgery were captured from hospital and emergency department records and using costing algorithms. Preoperative residence in a long-term care facility was identified from the Continuing Care Reporting System. Specific inclusion and parametrization of confounders in adjusted models are specified in the Analysis section.

Sample Size

This was a population-based study; we included all eligible members of the Ontario population. With approximately 20,000 eligible surgeries per year in Ontario, we estimated that mean 1-yr healthcare costs of one older person having surgery would approximate $15,000 Canadian dollar ± 5,200.[32] Because our primary objective required estimation of a stable multivariable linear regression model for log-transformed costs (to account for skew), the methods of Riley *et al.*[33] suggested a minimum sample size of 488.

Missing Data

Our approach to missing data was prespecified in our registered protocol. Because no exposure or outcome data were missing, their imputation was not required. Because neighborhood income quintile was missing for 0.4% of participants, we centrally imputed the most common value (the median [*i.e.*, middle] income quintile).

Analysis

Description of the study cohort was stratified by frailty status, with differences in characteristics quantified using absolute standardized differences.[34] All analyses were performed using SAS v9.4 for Windows (SAS Institute, USA), and 95% CIs were estimated to reflect uncertainty in applying our findings outside of our study population because our approach to inference was not based on a null hypothesis testing framework.

We estimated the unadjusted and adjusted association of frailty with total health system costs in the year after surgery using linear regression with log-transformation of the cost-dependent variable to account for the expected skew.[35] The exponentiated coefficient from this model represents a ratio of means, reflecting the relative difference in mean costs between those with and without frailty. In addition to a binary term for frailty, adjusted models included terms for sex (binary), age (restricted cubic spline with three knots), year of surgery (restricted cubic spline with three knots), and procedure (categorical for each procedure code). Generalized Estimating Equations accounted for clustering in hospitals using an exchangeable correlation matrix. The absolute attributable difference in mean cost was estimated using predicted cost outputs from our log-transformed linear regression model, with uncertainty estimated *via* a nonparametric bootstrapped standard error across 200 resamples with replacement (computational limitations with our population-based sample precluded use of greater replicates).[36] The association of frailty with costs at 30 and 90 days after surgery were estimated as described for 1-yr costs.

Sensitivity Analyses

We conducted a series of prespecified sensitivity analyses. All sensitivity models included the same variables as the adjusted primary analysis, unless otherwise specified. First, to estimate the possible impact of comorbidity independent of frailty we additionally adjusted for each preexisting Elixhauser comorbidity as binary variables. Next, to explore the influence of each patient's preoperative cost accumulation trajectory independent of frailty, we additionally adjusted for costs accrued in the year before the index surgery (parameterized as a restricted cubic spline with three knots). We also estimated the association of the frailty index with 1-yr costs as a continuous, nonlinear term using a fractional polynomial.[37] Because individuals with shorter survival may have less time to accumulate costs, we re-ran our primary analysis with the log of time alive as an offset term to allow calculation of the rate of cost accumulation adjusted for survival time.

Effect Modification

We tested whether effect modification existed on the relative scale between frailty and prespecified potential effect modifiers. To do so, we included a multiplicative interaction term in the primary adjusted model between frailty and: (1) procedure category; (2) sex; and (3) age (accounting for potentially nonlinear effects using a three-knot restricted cubic spline). For categorical effect modifiers, we estimated the frailty–cost association at each level of the effect

modifier variable. For continuous effect modifiers, we created a plot to visualize the estimated association across the range of recorded values for the effect modifier.

Results

We identified 171,576 older patients having elective, major noncardiac surgery; 23,219 (13.5%) were identified with preoperative frailty. Patient characteristics by the presence of frailty are provided in table 1. Patients with frailty tended to have higher costs accumulated in the year preceding surgery and were more likely to be diagnosed with comorbidities. Patients without frailty presented more often for joint replacement surgery, whereas patients with frailty more often had major vascular or cancer-related surgeries. No required data were missing.

Cost of Frailty

Total and component perioperative costs in the year starting on the day of surgery for patients with and without frailty are presented in table 2. The unadjusted ratio of means for costs at 1 yr in patients with frailty compared with those without frailty was 1.79 (95% CI, 1.76 to 1.83) and 1.53 (95% CI, 1.51 to 1.56) after adjustment for confounders. This was equivalent to an absolute mean-adjusted cost difference of $11,828 (95% CI, 11,805 to 11,850) attributable to the presence of preoperative frailty. Costs were higher for those with frailty within each component; postacute care costs had the largest relative increase (3.2-fold increase; table 2). Unadjusted and adjusted costs were also higher for those with frailty at 30 days (unadjusted ratio of means 1.42; 95% CI, 1.39 to 1.45; adjusted ratio of means 1.26; 95% CI, 1.25 to 1.27) and 90 days (unadjusted ratio of means 1.57; 95% CI, 1.54 to 1.61; adjusted ratio of means 1.37; 95% CI, 1.35 to 1.38) after surgery.

Sensitivity Analyses

When preoperative frailty status was parameterized as a continuous variable, there continued to be a significant association with postoperative costs. As a continuous linear term, each 0.1 unit increase in the frailty index was associated with a relative increase in mean costs of 1.39 (95% CI, 1.37 to 1.41; fig. 1). As a nonlinear fractional polynomial, increasing frailty index score was associated with increasing costs across the recorded range of frailty index values, with an inflection point at a frailty score of 0.4 (fig. 1).

After additional adjustment for comorbidity, the adjusted frailty–cost association was attenuated (ratio of means 1.24; 95% CI, 1.22 to 1.26). A similarly attenuated association was found when we additionally adjusted for 1-yr preoperative costs (ratio of means 1.27; 95% CI, 1.26 to 1.29). Finally, 2,816 (12.1%) patients with frailty died within 365 days after surgery compared with 4,046 (2.7%) patients without frailty. Accounting for the rate of cost accumulation per time alive, the adjusted association between frailty and costs was larger than for the primary analysis (ratio of means 1.71; 95% CI, 1.68 to 1.73).

Effect Modification

The association between frailty and perioperative costs was slightly greater for women with frailty (ratio of means 1.56; 95% CI, 1.54 to 1.59) compared with men with frailty (ratio of means 1.51; 95% CI, 1.49 to 1.53). The association between frailty and costs varied by surgical procedure and was most pronounced after total hip replacement (ratio of means 1.68; 95% CI, 1.64 to 1.72). The smallest association was estimated after pancreaticoduodenectomy (ratio of means 1.20; 95% CI, 1.13 to 1.29; fig. 2). Frailty was associated with the greatest relative increase in costs at younger ages. The association continuously decreased in a curvilinear fashion up to age 95 (fig. 3). For example, compared with those without frailty, patients aged 65 yr with frailty had a 1.69-fold (95% CI, 1.63 to 1.75) increase in costs, whereas patients aged 95 yr had a 1.41-fold (95% CI, 1.35 to 1.48) increase. To provide context for these differences based on postulated effect modifiers, the beta coefficient for each interaction term tested excluded the null value (0) from its 95% CI.

Discussion

In this population-based cohort study of older patients undergoing elective, major noncardiac surgery, we estimate that a 1.5-fold increase in adjusted costs in the year after surgery is attributable to the presence of preoperative frailty. This association appears to be present across the first postoperative year with effect estimates being larger the farther from surgery costs were accrued. In sensitivity analyses adjusting for comorbidities or preoperative costs, the association of frailty with increased postoperative costs was maintained, although the effect size was attenuated to a 1.24-fold increase and a 1.27-fold increase, respectively. Further modifications of the frailty–cost association were also notable in younger patients and after certain procedures, especially total joint replacement. As the number of older people with frailty requiring surgery continues to increase, the additional costs required to care for such patients will need to be allocated in health system planning. Future research should aim to develop and evaluate approaches to help improve outcomes and reduce healthcare resource utilization for older adults with frailty.

Frailty is consistently associated with at least 2-fold adjusted increases in adverse clinical and patient-reported outcomes after surgery.[12,16,38,39] Therefore, it is not surprising that health system costs are also strongly associated with the presence of preoperative frailty. However, quantifying the relative and absolute increases in costs attributable to frailty using multidimensional and clinically relevant frailty exposure and robust health system costing methods is key to inform health systems as they

Table 1. Baseline Characteristics by Frailty Status

Characteristics	Frailty		Absolute Standard Difference
	No (n = 148,357)	Yes (n = 23,219)	
Demographics			
Age, yr, mean ± SD	74 ± 6	76 ± 7	0.33
Female, %	55	46	0.19
Preoperative Frailty Index, mean ± SD	0.13 ± 0.04	0.26 ± 0.05	2.79
1-yr costs before surgery, mean ± SD	8,215 ± 11,774	24,405 ± 29,678	0.72
Comorbidities, %			
Alcohol abuse	0.4	3.3	0.21
Atrial fibrillation	2.2	15.9	0.49
Blood loss	4.2	16.4	0.41
Cancer	18.9	44.2	0.56
Cardiac valvular disease	1.4	5.6	0.23
Cerebrovascular disease	1.1	7.6	0.32
Chronic obstructive pulmonary disease	4.2	19.2	0.48
Chronic renal disease	0.6	5.5	0.29
Coagulopathy	0.7	2.9	0.17
Congestive heart failure	1.4	15.2	0.52
Deficiency anemia	0.2	0.8	0.08
Dementia	0.1	3.1	0.24
Depression	0.5	5.4	0.29
Diabetes mellitus, uncomplicated	13.5	30.7	0.42
Diabetes mellitus, complicated	6.2	35.9	0.78
Dialysis	0.2	1.5	0.15
Disease of pulmonary circulation	1.0	3.3	0.16
Drug abuse	0.1	0.6	0.09
Hemiplegia	0.1	1.0	0.13
Hypertension, uncomplicated	31.6	60.6	0.61
Hypertension, complicated	0.1	1.3	0.14
Liver disease	0.3	1.5	0.12
Metastases	3.0	15.4	0.44
Obesity	3.6	5.9	0.11
Peptic ulcer disease	1.2	3.3	0.15
Peripheral vascular disease	1.2	10.1	0.39
Psychoses	0.0	0.6	0.10
Rheumatic disease	0.3	2.1	0.16
Venous thromboembolism	0.2	1.1	0.11
Weight loss	0.5	3.6	0.22
Procedure, %			
Carotid endarterectomy	1.9	2.7	0.06
Endovascular abdominal aortic aneurysm repair	1.9	3.4	0.09
Gastrectomy or esophagectomy	1.4	3.2	0.12
Large bowel and rectal surgery	11.6	20.5	0.25
Open abdominal aortic aneurysm repair	1.3	1.9	0.05
Pancreaticoduodenectomy	0.5	1.5	0.10
Partial or total nephrectomy	2.9	5.2	0.12
Partial liver resection	0.7	2.1	0.11
Peripheral vascular surgery	2.4	8.3	0.27
Pneumonectomy or lobectomy	2.4	6.4	0.19
Total or radical cystectomy	0.9	2.3	0.11
Total hip replacement	25.4	17.9	0.18
Total knee replacement	46.8	24.7	0.47

Frailty was determined using a multidimensional frailty index ranging from 0 to 1 (0.21 or greater reflects the presence of frailty). Costs are expressed in 2018 Canadian dollars. No missing values were present for any measures in this table.

increasingly face the rapid aging of our population and the growing number of older people with frailty presenting for surgery.[40,41] Based on our data, during 5 yr in a province with a population of 14 million, each of more than 23,000 elective surgeries for people with frailty cost more than $25,000 extra per case; this equates to an additional $600 million in health system spending. Although adjustment for confounders attenuated this cost difference, adjusted attributable costs still amounted to almost $275 million in additional health spending attributable to preoperative frailty. This means that, without adequate resourcing, surgical care for older people with

Table 2. Total Perioperative and Component Costs at 1 yr by Frailty Status

Costs	Frailty		Absolute Standard Difference
	No	Yes	
Total costs	26,559 ± 26,151	52,434 ± 50,448	0.64
Hospital costs	15,928 ± 17,281	29,371 ± 36,688	0.47
Postacute care costs	2,502 ± 7,790	7,945 ± 16,452	0.42
Physician billing	5,037 ± 3,450	8,228 ± 5,490	0.70
Other costs	3,092 ± 7,182	6,889 ± 12,238	0.38

Hospital costs include inpatient surgeries and hospital admissions, as well as same-day surgeries after the index procedure). Postacute care costs include rehabilitation, complex and continuing care, long-term care, and home care services. Physician billing includes any insured physician service, as well as capitated costs for non–fee-for-service primary care provision. Other costs include prescription medications, cancer care, dialysis, and emergency department visits.[28] All costs are expressed in 2018 Canadian dollars, presented as mean ± SD.

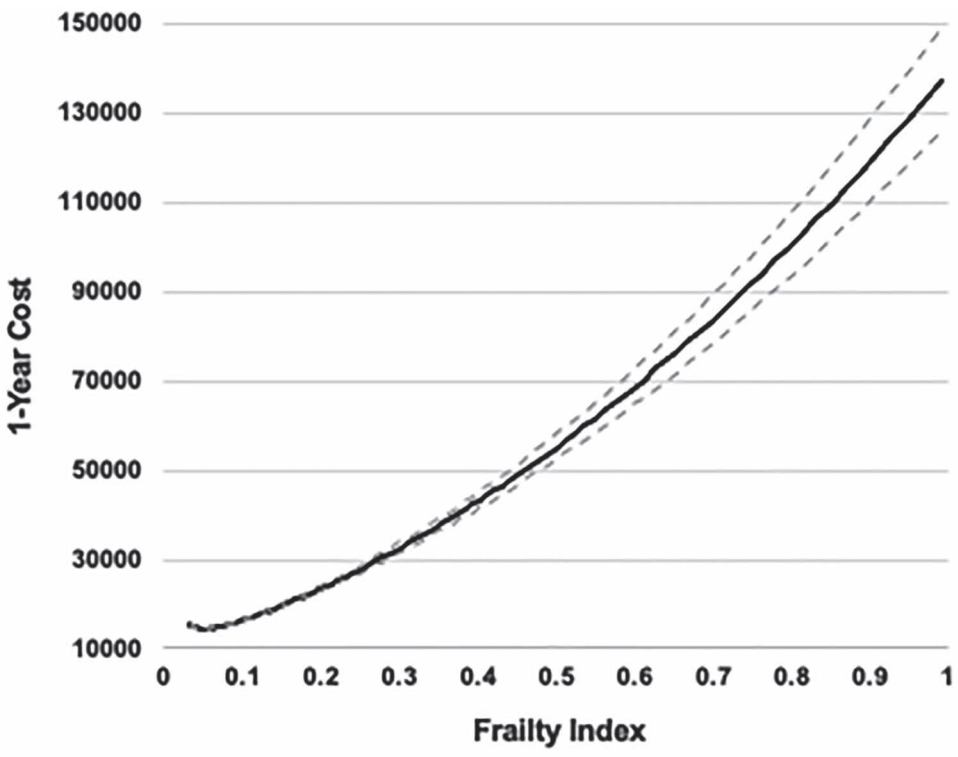

Fig. 1. Adjusted association of frailty and 1-yr postoperative costs with frailty parameterized as a continuous, non-linear second-degree fractional polynomial. *Dark line* represents the mean, with shaded areas representing 95% CI.

frailty is likely to consume a growing portion of perioperative budgets over time.

In addition to adequate budgeting by payors and system administrators, ours and related data further help to inform considerations around the higher costs attributable to frailty. First, although limited by use of different frailty instruments and control for confounding, the relative increase estimated in our study is consistent with previous studies using the proprietary Adjusted Clinical Groups frailty defining diagnoses indicator, which have also demonstrated an approximately 1.5-fold increase.[16] This suggests that the degree of relative cost increase attributable to frailty may be generalizable. Next, although we found increases in all aspects of postoperative health spending, postacute care costs were more than three times higher for people with frailty. Because postacute care appears to be a major driver of increased costs and nonhome discharge is identified by older surgical patients as a primary adverse outcome to avoid,[42,43] research and program development are urgently needed to help older people with frailty maintain

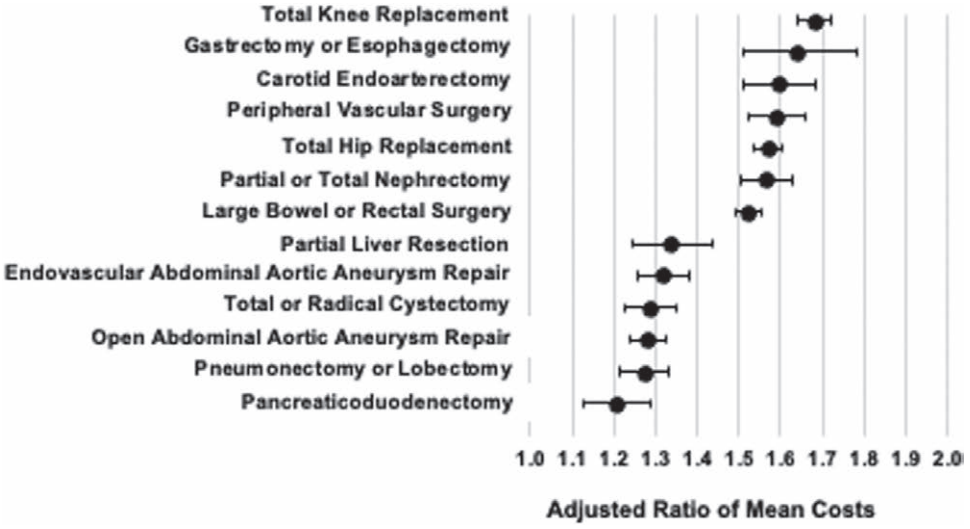

Fig. 2. Cost attributable to frailty based on major, elective noncardiac surgical procedure. Costs presented as a ratio of means with 95% CI compared with patients without frailty undergoing the same procedures.

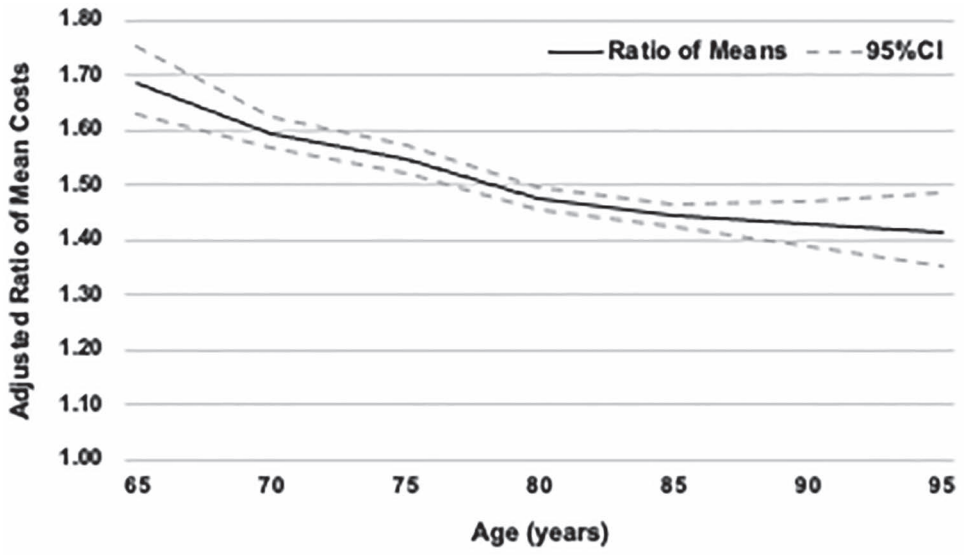

Fig. 3. Adjusted cost increase attributable to frailty as a function of increasing age. Cost presented as a ratio of means with 95% CI compared with patients the same age without frailty.

independence after surgery and transition home effectively.[42] Although prehabilitation appears to be promising in this regard,[44] available high-quality trials specific to frailty fail to demonstrate efficacy without high levels of program adherence.[45,46]

Although we found significant associations between frailty and costs across all primary, secondary and sensitivity analyses, we also identified substantial modifiers of this association. Likely reflecting the increased demands for postacute care, the relative association of frailty and costs was greatest at a year after surgery and attenuated at postoperative days 30 and 90. Additionally, due to a higher mortality rate among people with frailty, our primary analysis may have underestimated the association of frailty with costs among those who survived the full postoperative year. When we accounted for time alive, the adjusted association of frailty with costs rose from a 1.5- to a 1.7-fold increase. This suggests that, if interventions are developed to improve clinical outcomes for surgical patients with frailty, they may not directly decrease costs.

However, they could increase the value of perioperative care if added resources result in improved long-term patient outcomes.[47] Effect modification by age and surgical procedure largely reflected directional effects seen in the frailty–mortality association, with larger effect estimates identified at younger ages and after relatively physiologically less intense surgery like joint replacement.[48] Reasons for attenuated associations after more intensive surgeries like pancreaticoduodenectomy remain to be elucidated but could be related to factors present in patient selection that are not captured in routinely collected data, or the impact of frailty being diluted after procedures with higher baseline rates of morbidity. Ultimately, these data suggest that more granular approaches may be required to address health system costs across surgery types and the full perioperative journey.

Strengths and Limitations

Use of population-based data support generalizability to similar jurisdictions and health systems; however, more contemporary data would improve generalizability to current practice. Generalizability to substantively different systems also cannot be directly inferred. We used validated and reliable methods to identify our cohort, our exposure, and our outcome, and followed a pre-registered protocol. This should reduce misclassification and reporting bias. Although we were able to identify different component inputs to increased total costs, future research will be required to understand how adverse events and interventions may mediate cost accumulation. Future research will also be required to understand the out-of-pocket and informal caregiving costs incurred by patients and their families after surgery.

Conclusions

Frailty is associated with a significant increase in health system costs across the first postoperative year, resulting hundreds of millions in extra health system spending. However, the attributable costs vary based on patient and procedural characteristics. Future efforts to deliver perioperative care for the aging population will require health system planning, program development, and implementation strategies that consider the unique resource needs and trajectories of older patients with frailty.

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Competing Interests

Dr. Hallet has received speaking honoraria from Ipsen (Mississauga, Ontario, Canada), Advanced Accelerator Applications (Millburn, New Jersey), Medtronic (Vancouver, British Columbia, Canada), and Bristol Myers Squibb (New York, New York). The other authors declare no competing interests.

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