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ORIGINAL ARTICLE

Frailty assessment prior to thoracic surgery for lung or esophageal cancer: a feasibility study

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Abstract

Background Frailty assessment has not been thoroughly assessed in thoracic surgery. Our primary objective was to assess the feasibility of comprehensive frailty testing prior to lung and esophageal surgery for cancer. The secondary objective was to assess the utility of frailty indices in risk assessment prior to thoracic surgery.

Methods Prospectively recruited patients completed multiple physiotherapy tests (6-min walk, gait speed, hand-grip strength), risk stratification (Charlson Comorbidity Index, Revised Cardiac Risk Index, Modified Frailty Index), and quality of life questionnaires. Lean psoas area was also assessed by a radiologist using positron emission tomography/computed tomography scans. Data was analyzed using Fisher's exact, Mann-Whitney *U* and independent *t* tests.

Results The feasibility of comprehensive frailty assessment was assessed over a 4-month period among 40 patients (esophagus $n = 20$; lung $n = 20$). Risk stratification questionnaires administered in clinic had 100% completion rates. Physiotherapy testing required a trained physiotherapist and an additional visit to the pre-admission clinic; these tests proved difficult to coordinate and had lower completion rates (63–75%). Although most measures were not significantly associated with occurrence of complications, the Modified Frailty Index approached statistical significance ($p = 0.06$).

Conclusions Frailty assessment is feasible in the pre-operative outpatient setting and had a high degree of acceptance among surgeons and patients. Of the risk stratification questionnaires, the Modified Frailty Index may be useful in predicting outcomes as per this feasibility study. Pre-operative frailty assessment can identify vulnerable oncology patients to aid in treatment planning with the goal of optimizing clinical outcomes and resource allocation.

Keywords Frailty · Lung neoplasms · Esophageal neoplasms · Thoracic surgery

Introduction

Carcinomas of the lung and esophagus are among the top ten causes of cancer-related deaths in the world. Lung and esophageal cancers accounted for over 30 million years of life lost to premature mortality and nine million years of life lost to disability in 2015 [1]. With a mean age at diagnosis of 65–70 years, these malignancies continue to pose a major threat to the world's rapidly aging population [2, 3]. While lung and esophageal surgery are viable treatment options for many patients, they can be associated with significant morbidity, mortality, and adverse effects on post-treatment quality of life [4]. Despite standard preoperative testing to evaluate risk for surgery, some patients experience morbidity and never recover fully from surgery [5]. Subjective assessments can be poorly predictive of patient outcomes [6]. Surgeon impressions, although potentially accurate, are subjective and also suffer

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from a lack of reliability and reproducibility. Assessment of frailty, an age-related cumulative decline in multiple physiological systems, can identify vulnerable surgical patients who may benefit from preoperative rehabilitation or "prehab" or who may be more safely managed with nonsurgical therapy. A recent prospective cohort study of 125 patients found a high proportion (57%) of pre-frail patients (demonstrating one to two frailty traits) among those deemed candidates for thoracic surgery procedures [7]. This clearly highlights the need for pre-operative frailty testing in this patient population. The feasibility of prospective comprehensive frailty assessment has not been thoroughly explored in the thoracic surgery population [4, 8–10]. The primary objective of our study was to assess the feasibility of incorporating comprehensive frailty assessment into a standard pre-operative work-up within an academic thoracic surgery service. The secondary objective was to assess the utility of frailty testing for risk assessment prior to lung or esophageal cancer surgery by determining whether any of these frailty indices were associated with post-operative complications.

Materials and methods

Participants

Adult patients (≥ 18 years) with suspected or pathologically confirmed lung or esophageal cancer and consented for surgical resection at Toronto General Hospital (Toronto, Canada) were eligible to participate. We used convenience sampling, a form of non-probability sampling [11], to identify patients for prospective recruitment from seven surgeons' clinical practice. All eligible patients were approached in clinic over a 4-month period. All patients approached to take part in the study were aware of their diagnosis and were considered physically and psychologically able to cope with the consent and frailty testing process. The protocol was approved by the University Health Network Research Ethics Board and listed on a national clinical studies registry (NCT02803281).

Frailty testing

In addition to standard pre-operative testing, including staging positron emission tomography (PET)-computed tomography (CT) scans, each patient completed a series of previously validated frailty tests. Risk stratification and quality of life questionnaires were administered by a research assistant during a pre-operative clinic visit (Fig. 1).

The Modified Frailty Index (mFI) was developed by matching the Canadian Study of Health and Aging (CSHA) Frailty Index (CSHA-FI) to 11 variables (i.e., history of MI, diabetes, and cerebrovascular accident) collected by the American College of Surgeons NSQIP [12]. The Revised Cardiac Risk Index (RCRI), developed by Lee et al., uses six independent correlates of major cardiac complications with each risk factor assigned 1 point. Patients with 0, 1, 2, or more factors are assigned to classes I, II, III, or IV, respectively [13]. Similarly, the Charlson Comorbidity Index (CCI) is a weighted index that considers the number and the seriousness of comorbid disease to predict cumulative mortality and 10-year survival [14]. Finally, the Functional Assessment of Cancer Therapy questionnaire (FACT-G), was used as measure of health-related quality of life and includes physical well-being, functional well-being, social/family well-being, and emotional well-being [15]. Addition of esophageal-specific and lung-specific modules to the FACT-G results in the FACT-E and FACT-L, respectively [16, 17].

Further testing included the 6-minute walk test (6MWT), gait speed, and hand-grip test, all administered by a physiotherapist or research assistant during a pre-admission visit (Fig. 1). The 6MWT includes the total distance walked, which can range from 380 to 782 m as derived in healthy subjects from seven countries [18]. Secondary measures can include fatigue and dyspnea, measured with a modified Borg scale as well as arterial oxygen saturation measured via pulse oximetry [19]. Gait speed was measured by a trained physiotherapist in an unobstructed hallway with markings at 0 and 5 m. A standard digital stopwatch timed the travel. The sequence was repeated three times, allowing approximately 15 s between trials, with the average gait speed used for analysis [20]. A gait speed of < 1 m/s has been shown to identify those at high risk of health-related outcomes in well-functioning older people [21]. Grip strength, a sensitive marker of frailty in patients undergoing major abdominal surgery [22, 23], was measured on the dominant hand with a simple hand-grip dynamometer. Three values were taken and the average was used for analysis. Additionally, core muscle size, previously shown to be an effective risk

Fig. 1 Administration of frailty testing during clinic and pre-admission visits

stratification tool prior to esophagectomy, was assessed by a radiologist using pre-operative PET-CT scans. This was achieved by measuring the cross-sectional area and density of the left and right psoas muscles at the fourth lumbar (L4) vertebrae [24–26].

Data collection and analysis

Patient demographics, tumor characteristics, outcomes of length of stay, post-operative complications, and 90-day mortality were collected using the electronic patient record. At our center, complications are prospectively collected then discussed at a monthly meeting where final adjudication of Clavien-Dindo classification [27] is performed by a group of thoracic surgeons.

Descriptive statistics were used to describe the distribution of baseline characteristics. Univariate statistics were used to describe the relationship between each individual risk assessment modality and post-operative complications. The Fisher's exact test was used for categorical variables. Continuous variables were analyzed using the parametric independent *T* test or the non-parametric Mann-Whitney *U* test, based on data normality.

Results

Feasibility of comprehensive frailty assessment

To assess feasibility, a total of 48 eligible patients were approached to participate over a 4-month period. Patient recruitment was stopped upon achieving a pre-determined number of subjects in each cohort. Due to limited personnel (i.e., two research assistants), patients were only recruited from a maximum of two clinics on any given day. A total of 40 patients (83%; esophagus $n = 20$; lung $N = 20$) consented to participate. Reasons for withholding consent included an inability to speak English fluently, competing appointments, and unwillingness to commit to additional hospital visits for further testing.

Table 1 lists the baseline characteristics of the participants, including the procedures and interventions experienced by patients. Minimally invasive esophagectomy and VATS lobectomy were the two most common operations performed for esophageal and lung cancer, respectively (Table 1).

One hundred percent of participants completed the risk stratification questionnaires including the mFI, RCRI, and CCI. Approximately 78% of patients completed the QOL FACT-L/E questionnaires. Patients required approximately 10–15 min of clinic time to complete the abovementioned questionnaires. Physiotherapy testing, including the 6MWT, gait speed, and hand grip testing proved difficult to coordinate with completion rates of 75%, 63%, and 65% respectively. All but one patient (98%) had a pre-operative PET-CT scan for calculation of LSA by a staff radiologist (Table 2).

Table 1 Baseline characteristics of patient cohort

Sample size	40
Age, mean (SD)	64.3 (10.1)
Sex, *n* (%)	
Male	25 (63%)
Female	15 (37%)
ECOG, *n* (%)	
0	14 (35%)
1	21 (53%)
2	2 (5%)
3	2 (5%)
Missing	1 (2.5%)
Smoking status, *n* (%)	
Never	15 (38%)
Former	19 (48%)
Current	6 (15%)
Pack-years smoked, median (IQR)	26 (10, 40)
Esophageal cancer, *n* (%)	
Adenocarcinoma	17 (43%)
Squamous cell carcinoma	3 (8%)
Stage, *n* (%)	
0	1 (3%)
I	3 (8%)
II	3 (8%)
III	12 (30%)
IV	1 (3%)
Lung cancer, *n* (%)	
Adenocarcinoma	14 (35%)
Squamous cell carcinoma	4 (10%)
Large cell carcinoma	1 (3%)
Non-small cell carcinoma	1 (3%)
Stage, *n* (%)	
IA	8 (20%)
IB	8 (20%)
IIB	2 (5%)
IIIA	2 (5%)
Procedure type, *n*	
Open esophagectomy	2
Minimally invasive esophagectomy	8
Hybrid esophagectomy (laparotomy + VATS)	6
Open esophagogastrectomy	3
VATS lobectomy	14
Segmentectomy	3
Wedge resection	3
Received chemotherapy, *n* (%)	
Neo-adjuvant	
Esophagus	13 (33%)
Lung	0
Adjuvant	
Esophagus	1 (3%)
Lung	3 (8%)
Received radiation, *n* (%)	
Neo-adjuvant	
Esophagus	10 (25%)
Lung	0
Adjuvant	
Esophagus	1 (3%)
Lung	2 (5%)

Table 2 Frailty test completion rates

Frailty test	Completion rate, *n* (%)
6-min walk test	30 (75)
Gait speed	25 (63)
Hand-grip test	26 (65)
Psoas area	39 (98)
Modified Frailty Index (11-item score)	48 (100)
Revised Cardiac Risk Index	48 (100)
Charlson Comorbidity Index	48 (100)
Health-related quality of life surveys	31 (78)

Clinical utility of frailty testing

A total of 14 (35%) patients experienced post-operative complications, of which five (36%) were Clavien-Dindo class III or IV (Suppl. Table 1). The median length of hospital stay was 9 days (interquartile range, 3 to 14.5). One patient, with stage III (T3N1M0) esophageal adenocarcinoma, died secondary to pneumonia and septic shock prior to surgery (Suppl. Table 1). Notably, this patient had a mFI score of 2, and a CCI equating to a 10-year survival of 0.001%. They went on to receive pre-operative chemoradiation and decompensated significantly prior to surgery. Supplementary Table 2 enumerates the various post-operative complications for each patient and their respective mFI score. The sole class III complication was pleural effusion, requiring drainage. Class IV complications consisted of respiratory failure ($n = 3$) and cardiogenic shock ($n = 1$; Suppl. Table 2).

Higher mFI scores appeared to be associated with occurrence of post-operative complications and this approached statistical significance ($p = 0.06$). It is important to note that nearly 80% (20/26) of patients that did not suffer post-operative complications had low mFI scores (0–1) (Table 3). Other risk stratification questionnaires including RCRI, CCI, FACT, and physiotherapy tests (i.e., 6MWT, gait speed, hand grip, and LSA) remained comparable between the two groups in this patient population (Table 3).

Discussion

The value of pre-operative frailty testing has yet to be thoroughly examined in the thoracic surgery population. Our feasibility study examined the practicality of comprehensive frailty testing in patients undergoing thoracic surgery for lung and esophageal cancer. Comprehensive pre-operative frailty testing is feasible, especially using risk stratification questionnaires. The mFI was easy to administer resulting in 100% completion rates. Physiotherapy tests, including the 6MWT, gait speed, and hand grip test, were challenging to coordinate with patients and trained personnel. A larger study is required to assess whether they might provide a clinically meaningful assessment of risk prior to thoracic surgery.

Table 3 Measures of frailty and post-operative outcomes

Frailty test	No complications ($n = 26$)	Complications ($n = 14$)	*p*
Modified Frailty Index (/11), % (*n*)			0.06
0	14 (54%)	4 (29%)	
1	6 (23%)	3 (21%)	
2	3 (12%)	5 (35%)	
3	3 (12%)	0	
4	0	2 (14%)	
Revised Cardiac Risk Index, % (*n*)			0.75
I	3 (12%)	0	
II	18 (69%)	10 (71%)	
III	5 (15%)	3 (21%)	
IV	1 (4%)	1 (7%)	
Charlson Comorbidity Index, % (*n*)			1.00
0–5	17 (65%)	9 (64%)	
6–11	9 (35%)	5 (36%)	
FACT-E, median (IQR)	133.5 (125–134)	134 (93–146)	1.00[a]
FACT-L, median (IQR)	114 (104–118)	106.2 (93–127)	0.18[a]
6-min walk distance (m), median (IQR)	465 (369–576)	456 (338–548)	0.49[a]
Gait speed in meters/s, median (IQR)	1.2 (1.1–1.4)	1.4 (1.1–1.5)	0.36[a]
Hand-grip test in kg, median (IQR)	27.4 (23–36)	34 (26.7–47.7)	0.14[a]
Psoas area in cm^2, median (IQR)	10.0 (7.2–13.6)	10.9 (7.2–12.5)	0.99[a]

[a] Mann-Whitney *U* test

As society ages, an increasing number of elderly patients are undergoing surgery for lung and esophageal cancer. Accurately predicting surgical risk is beneficial to patients, surgeons, and the healthcare system. It allows judicious allocation of resources and can empower patients to make informed decisions prior to surgery. Frailty assessment can also enable surgeons to plan pre- and post-operative care with the aim of decreasing patient morbidity, mortality, and the associated costs to the hospital and healthcare community at large.

Standardized frailty assessment may offer a more sensitive and objective measure of a patient's physiologic reserve, enabling identification of patients who are poor candidates for surgery. Our study indicates that patients and health care providers can be receptive to the concept of pre-operative frailty testing. With the support and enthusiasm of all seven thoracic surgeons at our hospital, research assistants and allied health staff, our study achieved a high rate of acceptance among patients, with 83% of all screened patients agreeing to participate in pre-operative frailty testing.

Virtually all patients were willing to completing risk stratification and QOL questionnaires. As they were administered in clinic immediately after consent was obtained for surgery, patients did not have to make additional visits to the hospital. Physiotherapy testing on the other hand, had poorer uptake among patients and proved difficult to coordinate. Coordinating these additional assessments with other required appointments may improve participation.

With limited resources, it may be more practical to implement interventions that minimize cost and time commitment, while offering a clinically meaningful contribution to risk assessment. Risk stratification and QOL questionnaires, are easy to administer with minimal to no additional cost. The mFI was shown to approach significance in providing a reasonably accurate assessment of surgical risk, despite the fact that this feasibility study was not powered for this outcome and that our patient population was highly variable with a range of interventions. Nonetheless, this preliminary data suggests that the mFI may have a value in predicting outcomes. This correlates with the pathophysiologic basis of frailty as a predictor of peri-operative outcomes. Normal physiologic function involves a continuous interplay of body systems—a dynamic process that allows one to respond adequately to internal and external stressors including critical illness and surgery [28]. By capturing data on several comorbidities (including cardiovascular disease, respiratory disease, and functional status), the mFI score reflects alterations in the dynamics of multiple organ systems, which ultimately lead to functional decline that is characteristic of the frailty phenotype. Although of proven benefit in cardiac and orthopedic surgical patients, frailty has not been widely studied in general thoracic surgery patients reported only in three retrospective studies. A retrospective analysis by Velanovich et al. of 4648 patients undergoing general thoracic surgery found a statistically significant relationship between higher mFI scores and increased risk of post-operative morbidity and mortality in mid- to high-complexity thoracic operations ($p < 0.0001$) [9]. Moreover, Tsiouris et al.'s review of 1940 patients demonstrated that an mFI of > 3/11 ($P = 0.027$), contaminated wounds ($p = 0.028$), ASA grade 4 ($p = 0.009$), and dependent functional status ($p = 0.03$) were the main predictors of major complications after lobectomy for lung cancer [10]. Similarly, Hodari et al.'s study also found a strong correlation between mFI and morbidity and mortality after esophagectomy ($p = 0.015$) [4]. These studies however, are limited by their retrospective study design and the use of a large administrative dataset [29]. Our study provides prospective data on the feasibility of comprehensive frailty testing to identify high risk patients *before* surgery.

Completing frailty testing in the context of a larger prehabilitation program may facilitate individualized pre-operative assessments, including medical optimization, functional, and nutritional assessments, as well as counseling for mood-related issues and smoking cessation prior to surgery [30]. This holistic, multidisciplinary approach would further empower patients and their families prior to consenting for major surgery.

The limitations of our study include our small convenience sample size, with a short follow-up period and limited statistical power to assess non-feasibility outcomes. Additionally, the variability in diagnoses and operative procedures and the small numbers in our study cohort may have dampened the signal to noise ratio, thereby drowning out potential significance of the various frailty indices being studied. Future studies may stratify their assessment by diagnosis and operation to gain a deeper understanding of the clinical utility of frailty testing in thoracic surgery.

Our findings indicate that preoperative, comprehensive frailty testing is feasible for a thoracic surgical population. The mFI appears promising as an isolated measure of pre-operative risk. Physiotherapy tests carry a logistical burden that may jeopardize their uptake into clinical practice. Larger studies are needed to validate our findings and investigate whether comprehensive frailty testing provides a clinically meaningful contribution to risk assessment prior to thoracic surgery for cancer.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflicts of interest.

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