Heart, Lung and Circulation (2023) 32, 755–762
1443-9506/23/$36.00
https://doi.org/10.1016/j.hlc.2023.03.005

ORIGINAL ARTICLE

Thoracic Surgery and the Elderly; Is Lobectomy Safe in Octogenarians?

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Received 21 September 2022; received in revised form 5 January 2023; accepted 8 March 2023; online published-ahead-of-print 31 March 2023

Purpose Non-small cell lung cancer is the most common malignancy of the elderly, with 5-year survival estimates of 16.8%. The prognostic benefit of surgical resection for early lung cancer is irrefutable and maintained irrespective of age, even in patients over 75 years. Concerningly, despite the prognostic benefit of surgery there are deviations from standard treatment protocols with increasing age due to concerns of increased morbidity and mortality with surgery, without evidence to support this.

Method A state-wide retrospective registry study of Queensland's Cardiac Outcomes Registry's (QCOR) Thoracic Database examining the influence of age on the safety of Lung Resection (1 January 2016–20 April 2022).

Results This included 1,232 patients, mean age at surgery was 66 years (range 14–91 years), with 918 thoracotomies performed. Three deaths occurred within 30-days (0.24%). Octogenarians (n=60) had lower rates of smoking (26% vs 6%), respiratory, cardiovascular, and cerebrovascular disease suggesting this subset of patients is carefully selected. Octogenarian status was not associated with an increased all-cause morbidity (p=0.09) or 30-day mortality (p=0.06). Further to this it was not associated with re-operation (4.4% vs 8.3%, p=0.1), increased postoperative stay (6.66 vs 6.65 days, p=0.99) or myocardial infarction. An independent predictor of morbidity was male sex (OR 1.58, CI 1.2–2.1 p=0.001).

Conclusion Age ≥80 years did not increase surgical morbidity or mortality in the appropriately selected patient and should not be a barrier to referral for consideration of surgical resection.

Keywords Thoracic surgery • Frailty • Lung cancer • Octogenarian • Elderly • Morbidity • Mortality

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Introduction

Non-small cell lung cancer is the most common malignancy of the elderly, and most common cause of cancer death internationally [1]. The overall 5-year survival of lung cancer is poor, with estimates as low as 16.8% in 2004, across all stages of lung cancer [2]. The prognostic benefit of surgical resection for early lung cancer is irrefutable. With 10-year survival between 66%–94% for patients undergoing lobectomy for T1 N0 lung cancers, with a poorer prognosis noted with higher staged tumours [3]. Comparing lobectomy to stereotactic beam radiation therapy in patients over 75 years, consistently at 1, 3 and 5 years the overall survival was higher amongst surgical patients [3]. Consistently across all ages, survival was demonstrated to be superior amongst surgical patients compared to radiotherapy, immuno/chemotherapy or no intervention [1,4,5]. Concerningly, despite the clear survival benefit of surgical intervention, there is a trend of deviation from standard treatment protocols with increasing age [1].

The post-operative recovery, safety and quality of life in septuagenarians has been measured and examined against patients aged between 60–69 years and demonstrated to be comparable [6]. Septuagenarian mortality has been demonstrated to be approximately 3.8%, which is similar to the average quoted mortality of lobectomy independent of age [7].

The morbidity and mortality associated with increasing extremes of chronological age (>80 years), has scarcely been examined. In physiologically well octogenarians lobectomy offers superior survival benefit. The mortality of lung resection however is controversial, with one study demonstrating a mortality between 2.2%–4.2% in octogenarian's compared to 1.2%–2.2% in younger patients [5]. Whilst other data estimates a 1.7% mortality in octogenarians after lung surgery [8]. The morbidity rates reported in the literature are equally heterogenous (36%–60%) and are largely extracted from propensity-matched retrospective studies. However, morbidity has consistently been demonstrated to be lower in minimally invasive thoracic approaches (including video assisted thorascopic surgery and robotic lobectomy). Irrespective of these morbidity rates, however, quality of life was unaffected [6]. With clear survival benefit to surgical resection compared to other interventions, the current recommendation is for a physiological assessment of elderly individuals to determine suitability for resection [9]. This recommendation with the data proposed suggest that chronological age should not be a barrier to resection for early lung cancer.

Specific examination of morbidity and mortality following lung resection in octogenarians needs further investigation and has not been reviewed in the Australian population.

Method

We performed a retrospective multi-centre review of Queensland's Cardiac Outcomes Registry's (QCOR) Thoracic Database from 1 January 2016–20 April 2022. All patients undergoing lung resection for lung cancer or metastasis were included. Patients undergoing resection for non-cancerous lesions (i.e., infective/inflammatory pathology) were excluded. A waiver of consent was approved by the Gold Coast Hospital and Health Service's Human Research and Ethics Committee, in accordance with the National Health and Medical Research Council of Australia's regulations.

The primary outcomes examined were operative mortality defined as death within 30-days postoperatively, mortality at 90-days, and major morbidity. Major morbidity included composite and individual analysis of the following within 30-days of the primary operation: re-operation/return to theatre; prolonged air-leak (>72 hours); post-operative length of stay; pneumonia; pulmonary embolism; wound infection; new atrial fibrillation (AF); intensive care unit (ICU) admission (planned and unplanned); duration of ventilation in ICU; transfusion requirement and quantity of red blood cells; lung herniation; lung torsion; bronchial stump leak; peri-operative myocardial infarction (MI); and cerebrovascular accident (CVA).

Statistical Methodology

All statistical analyses were conducted using Stata Statistical Software Release 17 (StataCorp LLC, College Station, TX, USA). For this study patients were grouped into two groups; those 80 years or older (including nonagenarians) were collectively termed 'octogenarians' and those under the age of 80 years were 'non-octogenarians'. Simple descriptive statistics were utilised to assess the baseline characteristics of the participants. Mean and standard deviation (SD), or median and interquartile rage (IQR) were used to describe continuous variables. Categorical variables were analysed and displayed as proportions/frequencies. Continuous variables were compared with Student's t-test or Mann-Whitney U test, depending on their distribution. For categorical and binary variables univariate analysis was preformed using a chi-squared or Fisher's exact test. Those identified to have a $P<0.1$, were included in multi-variate logistic regression modelling.

Results

Preoperative Variables and Demographics

We examined 1,232 patients, 60 of whom were octogenarians, with one nonagenarian. Demographic and pre-morbid data are presented in Table 1. Age at surgery ranged from 14–91 years and the mean age at surgery was 66.18 years across the whole population. In the octogenarian group the mean age at surgery was 81.87 years. Gender distribution was equal in both octogenarians and non-octogenarians (51% verses 50% males, p=0.81). Octogenarians had lower rates of active cigarette use (6.66% vs 26.7%, $p<0.001$), but were more often a former smoker (70% vs 58%, $p<0.001$). Body mass index was slightly lower in the elderly group (25.68 vs

Table 1 Demographics.

	Non-Octogenarian	Octogenarian	P-value
	n=1,172	**n=60**	**<0.001**
Age	65.38 (9.45)	81.87 (1.97)	<0.001
Gender			
Female	585 (49.91%)	29 (48.33%)	0.81
Male	587 (50.09%)	31 (51.67%)	
Smoking Status			
Never	130 (11.36%)	10 (16.95%)	0.19
Former	686 (59.97%)	42 (71.19%)	0.086
Current	313 (27.36%)	4 (6.78%)	<0.001
BMI	27.67 (5.71)	25.86 (4.00)	0.018
Coronary Artery Disease	158 (13.95%)	13 (22.81%)	0.063
Preoperative Creatinine level (umol/L)	74.00 (63.00–88.00)	80.00 (69.00–104.00)	0.008
Diabetes Mellitus	184 (16.07%)	9 (15.25%)	0.87
Peripheral Vascular Disease	66 (5.75%)	6 (10.17%)	0.16
Coronary Artery Disease	158 (13.95%)	13 (22.81%)	0.063
Respiratory Disease Severity			
Mild	199 (46.28%)	8 (50.00%)	0.77
Moderate	222 (51.63%)	8 (50.00%)	0.9
Severe	9 (2.09%)	0 (0%)	0.56
Previous Lung Resection	46 (3.92%)	2 (3.33%)	0.82
Lesion Side			
Left	442 (38.37%)	27 (45.00%)	0.3
Right	710 (61.63%)	33 (55.00%)	
Surgical Approach			
Thoracotomy	875 (74.85%)	43 (71.67%)	0.58
VATS	289 (24.72%)	17 (28.33%)	0.53
Sternotomy	5 (0.04%)	0 (0.00%)	0.61
Resection Type			
Lobectomy	1125(95.99%)	58 (93.10%)	0.79
Bi-lobectomy	46 (3.92%)	2 (3.33%)	0.82
Pneumonectomy	1 (0.09%)	0	0.82
Nodal Sampling vs Dissection			
Sampling	868 (91.75%)	44 (97.78%)	0.14
Dissection	78 (8.25%)	1 (2.22%)	
ICU Admission	62 (5.43%)	4 (6.90%)	0.63
Clinical Stage			
I	545 (70.41%)	29 (72.50%)	0.67
II	167 (21.58%)	7 (17.50%)	
III	51 (6.59%)	4 (10.00%)	
IV	11 (1.42%)	0 (0.00%)	
Pathological Stage			
I	664 (62.82%)	34 (61.82%)	0.78
II	237 (22.42%)	15 (27.27%)	
III	127 (12.02%)	5 (9.09%)	
IV	29 (2.74%)	1 (1.82%)	
Histopathology			
Adenocarcinoma	750 (65.73%)	36 (60.00%)	0.21
Squamous cell carcinoma	217 (19.02%)	13 (21.67%)	
Small cell carcinoma	5 (0.44%)	1 (1.67%)	
Neuroendocrine tumours	79 (6.92%)	1 (1.67%)	
Metastasis	7 (0.61%)	1 (1.67%)	

Table 1. (continued).

	Non-Octogenarian	Octogenarian	P-value
	n=1,172	n=60	<0.001
Other/unspecified	22 (1.93%)	3 (5.00%)	
Large cell carcinoma	15 (1.31%)	1 (1.67%)	
Mixed type	22 (1.93%)	3 (5.00%)	
Benign	24 (2.10%)	1 (1.67%)	

Data are presented as mean (SD) or median (IQR) for continuous measures, and n (%) for categorical measures.

27.67, p=0.018). The rate of coronary artery disease (CAD) was higher in octogenarian's (22.81% vs 13.95%, p=0.063), and the baseline pre-operative serum creatinine level was higher (80 umol/L vs 74 umol/L, p=0.008). The distribution of staging and histopathological type of malignancy in the two groups was equivalent. Surgical approach and resection patterns did not differ between groups.

Morbidity

Simple descriptive morbidity outcomes are listed in Table 2. Multivariate logistic regression analysis of morbidity is presented in Table 3. Means testing for continuous variables of morbidity are described in Table 4. This analysis failed to demonstrate any clinically or statistically significant association with octogenarian status and increased morbidity, when analysed by individual outcome or composite morbidity. Multivariate regression analysis did reveal both risk factors and protective factors associated with morbidity, discussed below and listed in Table 5.

Octogenarians were not at elevated risk of unplanned ICU admission (OR=3.34, 95% CI 0.38–34.39, p=0.26). Male gender, however, was risk factor for unplanned ICU admission (OR 4.99, 95% CI 1.22–20.46, p=0.025), while lobectomy was protective, compared to pneumonectomy and Bi-lobectomy (OR 0.05, 95% CI 0.004–0.73, p=0.028).

All cause morbidity was not elevated in octogenarians, OR 1.66 (95% CI 0.65–2.95, p=0.09). Male sex however was an independent predictor of all cause morbidity (OR 1.58, CI 1.2–2.1 p=0.001).

Lower body mass index (BMI) demonstrated a protective effect (OR 0.005, 95% CI 0.81–0.96, p=0.006) against transfusion and reoperation (OR 0.9, 95% CI 0.84–0.96, p=0.001). Transfusion was linked to longer postoperative stays (OR 1.01, 95% CI 1.00–1.03, p=0.016).

The estimated prevalence of pulmonary embolism (PE) post thoracic surgery ranges from 1%–5% [10]. We observed a rate of 0.34% and 1.66% in non-octogenarians and octogenarians, respectively (p=0.092). Suggesting that the incidence of PE postoperatively was comparable to that observed internationally, although at the lower end of the expected rage.

Wound infection in octogenarians was not significant (OR 4.35, 95% CI 0.49–38.52, p=0.187), however a sternotomy was associated with increased wound complications (OR 54.00, 95% CI 5.02–580.76, p=0.001) and this was associated with increased length of stay (OR 1.01, 95% CI 1.00–1.03, p=0.009).

Pneumonia was associated with a higher clinical staging, and longer admissions (OR 3.00 95% CI 1.19–7.55, p=0.020 and OR 1.15 95% CI 1.08–1.23, p=0.000, respectively) independent of and unaffected by octogenarian status (OR 4.06, 95% CI 0.19–88.88, p=0.374).

Lung herniation, lung torsion, bronchial stump complications, post-operative MI and CVA were exceedingly rare in the analysis and so no meaningful relationship could be discerned. Despite a slightly elevated rate of known ischaemic heart disease in the octogenarians, it was not associated with increased perioperative MI. The number of these events are detailed in Table 3.

Mean postoperative length of stay was 6.67 days and 6.65 days for non-octogenarians and octogenarians, respectively (95% CI 5.65–7.64, p=0.99).

Mortality

Only three deaths were recorded at 30-days, one of which was an octogenarian. Further to this, 12 deaths were recorded at 90-days, with still only one octogenarian. Octogenarian status was not associated with 30-day mortality (OR=9.915, 95% CI 0.88–110.9, p=0.06). Mortality at 90-days was equally not strongly associated with octogenarian status (OR 2.33, 95% CI 0.26–20.31, p=0.44).

Discussion

This analysis demonstrated that age ≥80 years was not associated with increased surgical morbidity and mortality in our cohort. Further to this, the observed rates of morbidity/mortality were equivalent to, or lower than, that observed in the literature.

Overall, the pre-morbid status of the octogenarians and non-octogenarians was comparable, with the only major differences noted between the groups in the smoking status, pre-operative creatinine level, and BMI. The most clinically pertinent of which was the active use of cigarettes. New AF was observed at a rate of 8.33% in octogenarians and 5.38% in non-octogenarians, without statistically significant difference. The expected incidence of new AF is 4%–60% depending on resection type and approach; independent of age we observed a combined incidence of 5.52% in our study

Table 2 Relative risk of morbidity, and mortality in octogenarians.

	<80 n=1,172	>80 n=60	RR	95% CI	P-value
Unplanned ICU Admission	19 (1.62%)	2 (3.33%)	1.61	0.56–4.58	0.43
Blood Transfusion	28 (2.39%)	2 (3.33%)	1.38	0.34–5.68	0.65
Return to Theatre	45 (3.84%)	5 (8.33%)	2.17	0.89–5.27	0.09
New AF	63 (5.38%)	5 (8.33%)	1.55	0.65–3.71	0.33
Wound Infection	7 (0.60%)	1 (1.67%)	2.79	0.35–22.32	0.31
Pneumonia	13 (1.11%)	2 (3.33%)	3.01	0.69–13.02	0.13
PE	4 (0.34%)	1 (1.67%)	4.88	0.55–43.02	0.12
Prolonged Air-Leak	126 (10.75%)	5 (8.33%)	0.78	0.33–1.82	0.5
MI	1 (0.09%)	0	0		0.82
30 Day Mortality	2 (0.17%)	1 (1.67%)	9.77	0.90–106.205	0.02
90-Day Mortality	11 (0.94%)	1 (1.67%)	2.18	0.31–15.11	0.43

Abbreviations: ICU, intensive care unit; AF, atrial fibrillation; PE, pulmonary embolism; MI, myocardial infarction; RR, relative risk; CI, confidence interval.

[11]. The combined incidence of re-operation in this cohort independent of age was 4.06%, which is comparable to existing literature [12].

Importantly, the rate of both planned and unplanned ICU admission for octogenarians was equivalent to non-octogenarians. Those that were admitted to ICU had comparable duration of intubation and ventilation. Transfusion patterns and re-operation between the two groups was equivalent. This suggests that, despite the increased age and presumed frailty of octogenarians, the burden of care and resources required for safe thoracic surgery does not change with age.

While there was no statistical difference between the octogenarian and non-octogenarian groups with respect to prolonged air-leak, across the entire population 10.6% had a prolonged leak. Meta-analysis predicts an approximate

Table 3 Multivariate logistic regression analysis for morbidity and mortality.

	Non-Octogenarian n=1,172	Octogenarian n=60	OR	95% CI	P-value
All Cause Morbidity	224 (20.82%)	18 (30%)	1.66	0.93–2.95	0.09
Return to Theatre	45 (3.84%)	5 (8.33%)	1.52	0.4–4.70	0.471
ICU Admission					
Total	62 (5.30%)	4 (6.67%)			
Unplanned	19 (30.65%)	2 (50%)	3.34	0.38–34.39	0.26
Transfusion					
Red blood products	28 (2.39%)	2 (3.33%)	1.46	0.33–6.41	0.617
Units transfused	4.22 (+/-5.94)	3 (+/-2.83)	1.66	0.38–7.26	0.49
New AF	63 (5.38%)	5 (8.33%)	1.25	0.23–6.81	0.796
Pneumonia	13 (1.11%)	2 (3.33%)	4.06	0.19–88.88	0.374
PE	4 (0.34%)	1 (1.67%)	7.51	0.72–78.30	0.092
Prolonged Air-Leak	126 (10.75%)	5 (8.33%)	0.57	0.20–1.62	0.294
Lung Torsion	2 (0.17%)	0			
Lung Herniation	1 (0.09%)	0			
Bronchial Stump Complication	0	0			
Wound Infection	7 (0.60%)	1 (1.67%)	4.35	0.49–38.52	0.187
MI	1 (0.09%)	0			
CVA	2 (0.17%)	0			
30-Day Mortality	2 (0.17%)	1 (1.67%)	9.915	0.88–110.9	0.06
90-Day Mortality	11 (0.94%)	1 (1.67%)	2.33	0.26–20.31	0.44

Abbreviations: ICU, intensive care unit; AF, atrial fibrillation; PE, pulmonary embolism; MI, myocardial infarction; CVA, cerebrovascular accident; CI, confidence interval; OR, odds ratio.

Table 4 Means testing for continuous variables.

	Non-Octogenarian		Octogenarian		P-value
	Mean (+/-SD)	95% CI	Mean(+/-SD)	95% CI	
Postoperative Length of Stay	6.67 (+/-12.31)	5.95–7.40	6.65 (+/-3.75)	5.65–7.64	0.99
Hours Ventilated	26.18 (+/-86.07)	-1.72 to 54.07	22		
RBC Units Transfused	4.22 (+/-5.94)	1.87–6.57	3 (+/-2.83)	-22.41 to 28.41	0.78

Abbreviations: CI, confidence interval; SD, standard deviation.

incidence rate of 15% for prolonged air-leak, indicating a lower-than-expected rate in our cohort, irrespective of age [13].

Male gender was associated with increased risk of all cause morbidity; the reason for this is not apparent in this study, however this has been observed in other thoracic literature [13].

Duration of hospitalisation postoperatively for both groups was comparable. Unfortunately, the rates of hospital readmissions were not captured in this data set. This information would be complementary to the results provided here and would offer a more holistic view of the morbidity of lung resection.

The mortality rate in this population at 30-days was 0.24%, with only three deaths being recorded in 1,232 patients. One of these deaths was an octogenarian, however this analysis failed to demonstrate a statistically significant relationship between being an octogenarian and mortality at 30- or 90-days (OR=9.915, 95% CI 0.88–110.9, p=0.06 and OR 2.33, 95% CI 0.26–20.31, p=0.44, respectively). Compared to the expected mortality of lobectomy/lung resection, across the whole study population the observed mortality at 30-days was drastically lower (0.24% vs 2%–3%) [14,15]. The literature would estimate between 43–73 deaths at 90-days (3.5%–5.9%) in a population this size; whereas we observed only 12 deaths (0.98%) [15,16]. The equivalent mortality between

Table 5 Important covariables identified and utilised in multi-variate analysis.

Morbidity	Variable	OR	95% CI	P-value
All Cause Morbidity		1.66	0.93–2.95	0.09
	Male gender	1.58	1.2–2.1	0.001
Unplanned ICU Admission		1.66	0.56–4.58	0.43
	Male gender	4.99	1.22–20.46	0.025
	Lobectomy	0.05	0.004–0.73	0.028
Transfusion		1.46	0.33–6.41	0.617
	Post-op length of stay	1.01	1.00–1.03	0.016
	BMI	0.005	0.81–0.96	0.006
	Pre-operative creatinine (umol/L)	1.01	0.00–1.01	0.014
Pneumonia		4.06	0.19–88.88	0.374
	cTNM	3	1.19–7.55	0.020
	Post-op length of stay	1.15	108–1.23	0.000
Return to Theatre		1.52	0.4–4.70	0.471
	BMI	0.9	0.84–0.96	0.001
Wound Infection		4.35	0.49–38.52	0.187
	Sternotomy	54	5.02–580.76	0.001
	Post-op length of stay	1.01	1.00–1.03	0.009
Number of Transfusions		1.66	0.38–7.26	0.49
	Sternotomy	15.43	1.54–154.61	0.02
	Post-op length of stay	1.01	1.00–1.03	0.019
	Pre-operative creatinine (umol/L)	1.01	0.99–1.01	0.054

Abbreviations: OR, odds ratio; CI, confidence interval; ICU, intensive care unit; cTNM, clinical TNM stage; BMI, body mass index.

non-octogenarians and octogenarians is consistent with the existing literature [6,7].

Limitations

Retrospective review of registry data has inherent limitations. No frailty metrics are recorded in the QCOR database, and there is no standardised frailty metric utilised across thoracic surgery. There is a lack of information regarding the selection process for surgery at each centre, which may have varied. Additionally, there is an absence of data on those patients that were declined surgery. Consequently, the total number of octogenarians examined was low (n=60/1,232), and, with low expected rates of adverse outcome/mortality, small changes in the absolute number of events can influence statistical significance. Therefore, the relationships represented here may not be maintained in larger groups, and equally there may be relationships present that the study did not demonstrate. A broader understanding of the selection bias of this registry data will only be achieved prospectively or with data linkage to oncology databases.

The exceptionally low rates of mortality noted across the whole populations and octogenarians maybe be explained in by an innate selection bias within the population, whereby careful selection of surgical candidates has led to lower rates of mortality. Review of the pre-morbid status of octogenarians in this group does not suggest any major differences compared to the younger patients. Equally, the improved outcomes may be the consequence of larger socio-economic, geographic and/or demographic factors unique to Queensland, Australia, thereby limiting the generalisability of the mortality data noted in international literature to this population. Although not explained by this study, the lower mortality rates observed in our population are reassuring that elderly patients will not come to any increased adverse harm through referral for consideration of surgery, and those selected for surgery have comparable survival to younger patients. The aversion to refer patients of advanced age for a surgical opinion due to presumed frailty is not founded in evidence. The data presented here suggest that surgery can be safely preformed in advanced age. Given the well-established survival and quality-of-life benefits surgery confers, all patients with surgically resectable disease should at least be assessed for surgical candidacy by a thoracic surgeon.

Future Directions

To strengthen the analysis presented here, data-linkage with the Australian Institute of Health and Welfare's National Death Index to assess longer term survival is needed. Additionally, to fully understand the disease burden and influence of agism in lung cancer care in our population, combining the Queensland Oncology Database and QCOR data, both retrospectively and prospectively, is essential. Expansion of the QCOR Thoracic Database to a national surgical database should be considered, with a view to record longer term survival (1, 3 and 5 years). With the planned introduction of lung cancer screening and voluntary assisted dying in Australia, the direction of thoracic surgery in the elderly is unclear. Understanding the safety, survival benefit and quality-of-life implications for various treatment is vital to guide patients through societal paradigms shifts ahead.

Conclusion

Independent of age, the morbidity and mortality observed in our population was significantly lower than that recorded in the literature. Age $\geq$80 years did not increase surgical morbidity or mortality in the appropriately selected patient and should not be a barrier to referral for consideration of surgical resection.

Declarations

Ethical Approval for this study was granted by the Gold Coast University Hospital and Health Service Human Research Ethics Committee. HREC Reference: EX/2022/QGC/84771.

In line with QCOR's data access policy approval for individual site data was obtained from the respective site's Director of Cardiothoracic Surgery.

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