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The influence of the COVID-19 pandemic on lung cancer surgery in Queensland

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Abstract

Background: The coronavirus disease-19 (COVID-19) pandemic poses unprecedented challenges to global healthcare. The contemporary influence of COVID-19 on the delivery of lung cancer surgery has not been examined in Queensland.

Methods: We performed a retrospective registry analysis of the Queensland Cardiac Outcomes Registry (QCOR), thoracic database examining all adult lung cancer resections across Queensland from 1/1/2016 to 30/4/2022. We compared the data prior to, and after, the introduction of COVID-restrictions.

Results: There were 1207 patients. Mean age at surgery was 66 years and 1115 (92%) lobectomies were performed. We demonstrated a significant delay from time of diagnosis to surgery from 80 to 96 days ($P < 0.0005$), after introducing COVID-restrictions. The number of surgeries performed per month decreased after the pandemic and has not recovered ($P = 0.012$). 2022 saw a sharp reduction in cases with 49 surgeries, compared to 71 in 2019 for the same period.

Conclusion: Restrictions were associated with a significant increase in pathological upstaging, greatest immediately after the introduction of COVID-restrictions (IRR 1.71, CI 0.93–2.94, $P = 0.05$). COVID-19 delayed the access to surgery, reduced surgical capacity and consequently resulted in pathological upstaging throughout Queensland.

Introduction

Lung cancer (LC) is the most common cancer and cancer killer in the world, and the leading cause of cancer death.[1] Across all stages of LC, 5-year survival in 2004 was estimated at 16.8%, with a stepwise decline in survival with increasing stage.[2] Early-stage LC caries the best prognosis with Stage IA having 90%–80% survival, Stage IB 73%, Stage IIA 65% and IIB 56%, at 5-years, which declines steeply to 12%–41% for Stage III and 0%–10% for stage IV.[3] With evolving immunotherapies and the planned introduction of LC screening in Australia the overall survival will hopefully improve.

National Institute for Health and Care Excellence (NICE) guidelines for the diagnosis and management of lung cancer recommend intervention within 62 days from referral, and surgery within 31 days of decision to treat.[4] The British Thoracic Society (BTS) advocate from first consultation to intervention occur within 8 weeks.[5,6] Early surgical intervention improves survival.[7,8] Delays of 12 weeks decrease survival and increase risk of recurrence.[9] The influence of the COVID-19 pandemic on delivery of LC care has not been examined. With changes in the availability of hospital beds, operating list, and staff the pandemic could have lasting effects on LC survival across the globe, which may not be demonstrated for years. English National Health Service data demonstrated a reduction in national cancer screening during the pandemic and estimates a 5% increasing in LC mortality in the coming 5 years.[10] Clinically and statistically significant reduction in the number of LCs diagnosed has been correlated with prognostically significant upstaging of LC during the pandemic; with 44% being early stage (Ia–IIb) pre-pandemic, and only 39% during.[11] This unique healthcare crisis offers an opportunity to examine the existing infrastructure and how it can be improved.

The prognostic benefit of surgical resection for early LC is irrefutable. Comparing lobectomy to Stereotactic Beam Radiotherapy, at 1, 3 and 5 years survival was higher in surgical patients.[4,12,13] Across all ages, survival was demonstrated to be superior amongst surgical patients compared to alternate or no treatment.[14–17] Surgical excision can be considered at all stages of LC, however the prognostic benefit is most pronounced in Stage I and II. Surgery in Stage IIIA onward is usually preformed as part of a multi-modal treatment plan. Only 15% of LCs are diagnosed in early stages and consequently prognosis remains grim.[2,18,19] Trials introducing LC screening programs using Computed Tomography (CT) scanning in high-risk individuals has indicated promising results. CT screening detected a lung lesion in 24% of individuals compared to 7% with plain x-ray. Screening shifted stage at diagnosis, with 85% of LCs being identified in Stage I. Subsequent to this there is at least 20% reduction in cancer-specific mortality, and 40%–60% reduction in all-cause mortality.[19] With the planned introduction of LC Screening in Australia, increased detection of early stage LC, is expected. Contrary to the NICE and BTS Guidelines, and international practices the forefront of LC care in Australia is Physician lead. The Cardiothoracic/Thoracic Surgeon being the definitive point of referral rather than the primary, as part of a dedicated LC Clinic.[4,19] The impending paradigm shift in the epidemiology of LC in Australia, and international guidelines, suggest the infrastructure around LC needs review and redesign.

Methods

A retrospective multi-centre review of the Queensland Cardiac Outcomes Registry (QCOR) Thoracic Database was preformed, from 1/1/2016 to 2030/4/2022. All patients undergoing Thoracic Surgery >18 years of age for a primary lung cancer or pulmonary metastasis were included, across all contributing public centres.

COVID-19 was first recorded in Australia on 25/1/2020, however restrictions did not emerge until 26/3/2020. Patients diagnosed after 26/3/2020 or undergoing surgery after this date were therefore grouped as 'Post-COVID'. Those diagnosed or receiving surgery prior to 26/3/2020 were designated as 'Pre-COVID'.

Primary outcomes: Comparing pre-COVID and post-COVID

- Time to surgery (days)
  - Time from radiological diagnosis to surgery
  - Time from tissue diagnosis to surgery
  - Earliest recorded date of diagnosis to surgery
- Pathological upstaging
  - Progression from clinical to pathological staging, where the pathological stage increased a whole stage
    - That is, Clinical Stage I→ Pathological Stage II
    - Change of substage (i.e., Ia or Ib) was not considered significant
- Number of surgeries
  - Per month

Statistical method

All statistical analyses were conducted using Stata 17 Statistics software (College Station, TX, USA). Simple descriptive statistics were utilized 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. Log transformations were performed for non-normal distribution. For categorical and binary variable univariate analysis was preformed using a chi-squired or fisher's exact test. Those identified to have a $P < 0.1$ or clinically important were included in multi-variate logistic regression. Using the variables identified as significant in univariate and multi-variate logistic regression models and interrupted time series analysis (ITS) was performed to map dynamic influence of the evolving restrictions over-time.

Results

Table 1 shows that the groups before and during the pandemic were well matched. Pre-operatively five patients contracted COVID.

Mean testing (*t*-tests) is described in Table 2, and the ITS is described in Table 3. Logistic regression and ITS analysis of the time from tissue diagnosis to surgery, demonstrated that the delay to surgery was increasing throughout the pandemic as shown in Figure 1 (Incident Risk Ratio-IRR 1.0008, $P = 0.000$). Similarly, mean-time from the earliest diagnosis, pre and post-restrictions, varied from 66 to 71 days ($P = 0.0046$). Mean-time from earliest diagnosis to surgery was 1.19 times ($P = 0.00$) higher post-COVID and increasing (Fig. 2).

Multivariate ITS demonstrated that COVID-restrictions increased the average time from imaging to surgery from 62 to

Table 1 Demographics

Demographics	Pre-COVID $N = 782$	Post-COVID $N = 425$	P-value
Age	65.39	67.03	0.006
Gender			0.54
Male	399 (51.02%)	209 (49.18%)	
Smoking status			0.75
Never	92 (11.76%)	50 (11.76%)	1
Former	497 (61.25%)	248 (58.35%)	0.33
Current	195 (24.94%)	117 (27.53%)	
BMI	27.53 (5.57)	27.69 (5.86)	0.66
Coronary artery disease	107 (16.24%)	62 (17.71%)	0.55
Preoperative creatinine (μmol/L)	74.00 (63.00–88.00)	75.00 (66.50–89.00)	0.063
Diabetes mellitus	120 (15.44%)	73 (17.30%)	0.40
Cerebrovascular disease	32 (4.11%)	35 (8.27%)	0.003
Peripheral vascular disease	40 (5.13%)	24 (5.67%)	0.69
Respiratory disease	329 (42.56%)	156 (37.23%)	0.074
FEV1 (L)	2.63 (4.73)	2.58 (4.80)	0.88
Respiratory disease severity			
Mild	146 (47.25%)	59 (43.38%)	0.22
Moderate	159 (51.46%)	72 (52.49%)	
Severe	4 (1.29%)	5 (3.68%)	
Preoperative adjuvant therapy	30 (3.68%)	13 (3.07%)	0.48
Chemotherapy	11 (1.41%)	4 (0.94%)	0.78
Radiation	4 (0.51%)	3 (0.71%)	0.39
Chemoradiotherapy	14 (1.79%)	4 (0.94%)	0.70
Immunosuppressive therapy	38 (4.88%)	19 (4.50%)	0.77
Preoperative anticoagulation	30 (7.49%)	28 (6.65%)	0.59
Preoperative antiplatelet therapy	125 (16.19%)	76 (18.01%)	0.42
Previous cardiac surgery	48 (6.27%)	29 (6.97%)	0.64
Previous lung resection	60 (7.84%)	29 (6.97%)	0.58
Lesion side			0.66
Left	306 (39.53%)	159 (38.22%)	
Incision type			
Thoracotomy	595 (76.28%)	305 (71.76%)	0.085
VATS	180 (23.08%)	118 (27.76%)	0.072
Sternotomy	5 (0.64%)	2 (0.47%)	0.71
Resection type			
Lobectomy	710 (90.79%)	397 (93.41%)	0.11
Bi-lobectomy	31 (3.96%)	14 (3.29%)	0.56
Pneumonectomy	38 (4.86%)	13 (3.06%)	0.14
Nodal sampling/dissection			0.98
Sampling	576 (91.87%)	326 (91.83%)	
Dissection	51 (8.13%)	29 (8.17%)	
ICU admission	66 (8.49%)	29 (6.90%)	0.33
Clinical stage			0.81
I	342 (67.49%)	255 (70.53%)	
II	116 (22.88%)	63 (20.86%	
III	42 (8.28%)	23 (7.62%)	
IV	7 (1.38%)	3 (0.99%)	
Pathological stage			0.54
I	425 (67.46%)	213 (70.53%)	
II	171 (23.88%)	85 (21.14%)	
III	99 (13.83%)	49 (12.19%)	
IV	21 (2.93%)	13 (3.23%)	
Surgical histopathology			0.48
Adenocarcinoma	503 (65.67%)	283 (67.54%)	
Squamous cell carcinoma	164 (21.41%)	78 (18.62%)	
Small cell carcinoma	4 (0.52%)	2 (0.48%)	
Neuroendocrine tumours	54 (7.05%)	26 (6.21%)	
Metastasis	4 (0.52%)	3 (0.72%)	
Other/unspecified	16 (2.09%)	16 (3.82%)	
Large cell carcinoma	13 (1.70%)	4 (0.95%)	
Mixed type	8 (1.04%)	7 (1.67%)	
COVID pre-operatively	0 (0.00%)	5 (1.18%)	0.002

75 days ($P = 0.0000$). Figure 3 illustrates a persistent 1.2× increase in time from imaging to surgery, after COVID-restrictions ($P = 0.000$).

Logistic regression and ITS demonstrated that COVID-restrictions persistently reduced the number of surgeries performed per month, with an IRR of 0.98, (95% CI 0.95–0.99, $P = 0.012$).

Table 2 Mean time from diagnosis to surgery, pre & post restrictions (*t*-test)

	Pre-COVID	Post-COVID	*P*-value
Time from imaging to surgery (days)			
Day model	79 ± 71.17	96 ± 77.54	0.0005
Log transformation	62.08 ± 2.09	75 ± 2.15	0.0000
Time from tissue diagnosis to surgery (days)			
Day model	62 ± 75.53	64 ± 65.58	0.8
Log transformation	47.16 ± 1.98	50.49 ± 1.90	0.146
Earliest diagnosis to surgery (days)			
Day model	66 ± 81.32	71 ± 80.29	0.0043

Table 3 Interrupted time series analysis; COVID-restrictions on time to surgery

	IRR	95% CI	*P*-value
Time from imaging diagnosis	1.21	1.11–1.34	0.000
Tissue diagnosis to surgery			
Immediate effect	0.9146	0.7659–1.0921	0.0086
Sustained effect	1.0008	1.0005–1.0012	0.000
Time from earliest diagnosis to surgery	1.19	1.09–1.30	0.00

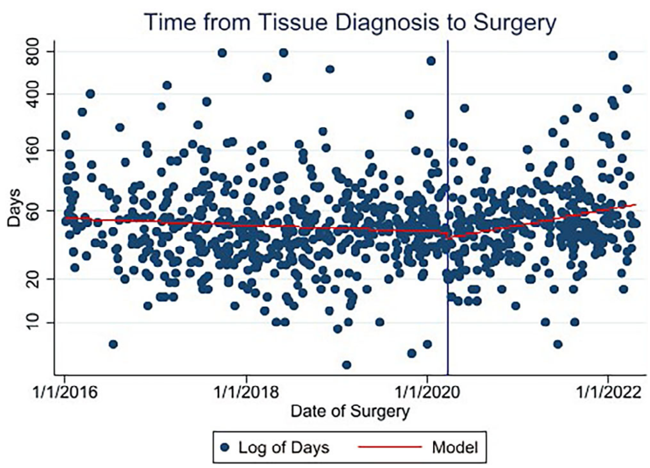

Fig. 1. Time from tissue diagnosis to surgery.

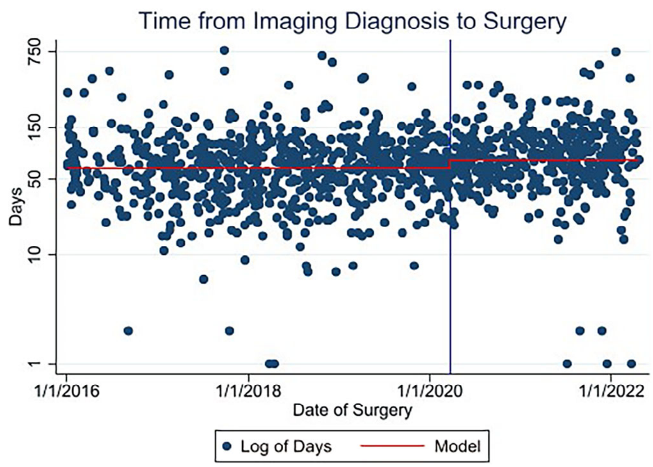

Fig. 3. Time from imaging diagnosis to surgery.

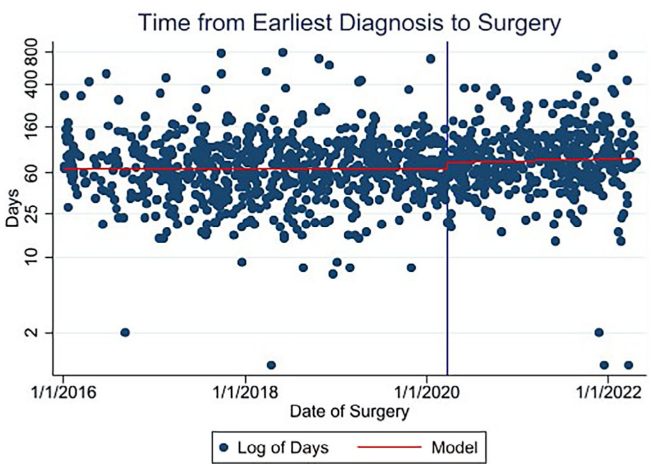

Fig. 2. Earliest diagnosis to surgery.

Surgery after the introduction of restrictions was associated with an increased risk of pathological upstaging. The immediate effect on upstaging was more pronounced (IRR 1.71, $P = 0.05$) however this reduced with time (IRR 0.96, $P = 0.022$). Figure 5 demonstrates the proportion of upstaging, over time and relative to case load.

Discussion

Time to surgery

The Pandemic created significant delays to surgery. The time from earliest diagnosis to surgery increased by 5 days ($P = 0.0043$), although it must be acknowledged this groups imaging and biopsy together. Time from biopsy to surgery increased by 2 days ($P = 0.8$) after restrictions were introduced (Table 2). Figures 1 and 2 demonstrate that these delays were increasing, despite decreasing cases.

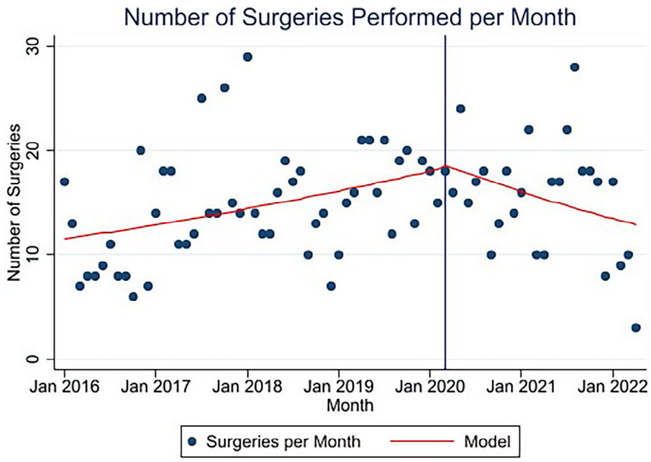

Fig. 4. Surgeries/month.

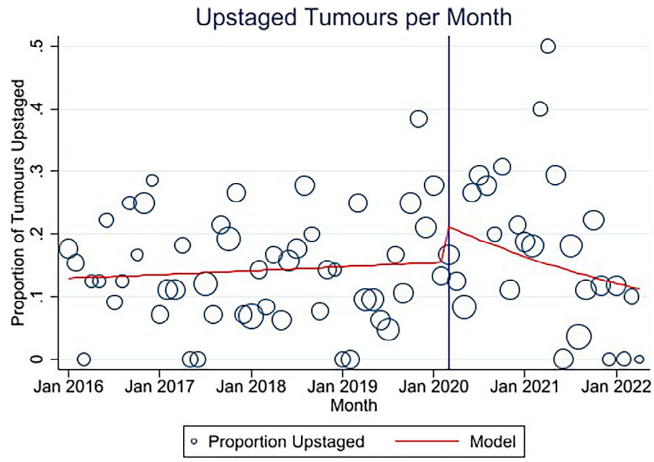

Fig. 5. Proportion of upstaged tumours/month.

The greatest delay to patient care was from imaging to intervention, increasing by 17 days ($P = 0.0005$). This delay was persistent throughout the pandemic, (Fig. 3; IRR 1.21, 95% CI 1.11–1.34), despite declining case load (Fig. 4).

Concerningly, these delays to surgery during the Pandemic, fall atop of already lengthy delays. Meta-analysis demonstrates survival reduces when surgery is delayed by 42 days from staging.[4,6,20] Imaging or biopsy are sufficient to clinically stage and our cohort had delays to intervention of 79 and 62 days, respectively pre-COVID. This analysis does not include time that precedes imaging/biopsy. Therefore, the real-world experience of time from diagnosis to surgery, exceeds the data presented here. NICE Guidelines for diagnosis and treatment of LC suggest a target of 62 days from referral to treatment, and 31 days from the decision to treat to surgery.[4] Contemporary studies in other Australian states estimate that two-thirds of patients receive surgery within 14-days of diagnosis.[21]

Pathological upstaging

Delays to intervention, allow for disease progression and can result in clinical/pathological upstaging of disease that may exclude patients from primary resection. The QCOR database only records surgical patients, those patients denied surgery due to these delays and upstaging will not be captured.

The proportion of tumours pathologically upstaged across the whole database prior to the pandemic averaged around 20% of the population (Table 4), comparable to contemporary literature.[20,22] COVID-Restrictions resulted in an immediate increase in clinically significant upstaging. Surgeries after restrictions were 1.7 times more likely to be upstaged ($P = 0.05$). This occurred when restrictions were at their highest and all elective operating was suspended and hospital beds were reserved in anticipation for a COVID-19 surge, irrespective of the hospital, geographic proximity to a 'Hot-spot' and the endemic effects of COVID-19.

Figure 5 demonstrates the proportion of upstaged tumours declined later in the pandemic (IRR 0.96, $P = 0.022$). This effect aligned with slight relaxation of restrictions and resumption of selected services. The restrictions and influence of COVID-19 on the states thoracic centres was not uniform, with some centres resumed full operative capacity, while others were restricted to emergency services.

Operative capacity

Prior to the pandemic the number of cases preformed across Queensland was steadily increasing. Upon the introduction of COVID-restrictions, the number of cases being performed per months started to decline sharply and has not recovered. This relationship is demonstrated in Figure 4 and was statistically significant (IRR 0.98, $P = 0.012$). Comparing 2022, in a four-month period, 49 resections were performed, while in 2019, 71 resections would have been performed in the same time. The sharp reduction in 2022 coincided with inter-state boarders opening, and rising COVID-19 number in Queensland.

Cumulative effect of restrictions

Acknowledging the individual influence that restrictions had on time to surgery, pathological upstaging and operative capacity described above, the cumulative effects of COVID-Restrictions on LC care becomes more pronounced (Fig. 5). In the face of prolonging time to intervention, there will be an increased rate of pathological progression amongst these patients, combining this with a drastic decrease in the operative capacity of the thoracic service and there will be an increasing number of patients that did not receive thoracic surgery due to disease progression. Unfortunately, this analysis does not capture this, but the pre-pandemic thoracic surgery growth and now declining caseloads implies this.

The pre-pandemic rate of pathological upstaging was comparable to contemporary literature, however the sharp increase noted with the introduction in restrictions, will have prognostic implications in the future. Increasing pathological stage is directly linked to a reduction in 5-year survival, independent of intervention.[23] Similarly those patients not receiving surgery, will have reduced

Table 4 Significant clinical to pathological upstaging an interrupted time series analysis

	Pre-COVID $n = 782$	Post-COVID $n = 425$	P-value
Clinically significant upstaging	106 (21.41%)	70 (23.41%)	0.45
Upstaging/month interrupted time series analysis	IRR	95% CI	P-value
Immediate effect	1.71	0.93–2.94	0.05
Sustained effect	0.96	0.93–0.99	0.022

survival surgical resection consistently carries survival benefit compared to other treaments.[12,14–16]

Unfortunately, the long-term survival and recurrence data is not captured in QCOR, and further prospective monitoring of this group is needed to understand the lasting effects of the pandemic.

Limitations

This is a retrospective study of a state-wide database. Limitations relate recording surgical cases only, without data on non-surgical patients. Further to this, the pathological upstaging that occurs due to lengthy delays to treatment in patients that are then declined surgery is not capture and cannot fully be appreciated by this study. There may be unaccounted for variables not included in the database that might influence the outcomes.

The time series analysis can only be performed on the data available, the real-life time from first diagnosis is likely longer than what is presented here, as the date of referral/respiratory review is not recorded in the database.

During the pandemic, the QLD government outsourced patients to private hospitals to facilitate resection. This data is not recorded in QCOR and so the influence of the private sectors is unclear. Further to this, QLD hospitals catchments extend into NSW. Diversion of patients from NSW to local thoracic centres is not captured in this database.

The influence of the social paradigms shifts in health seeking behaviour during COVID has not been measured in this analysis. With lockdowns and encouragement to isolate, it is unclear how many patients delayed seeking treatment during the pandemic. Fear of contracting COVID-19, distrust in the health-care system, vaccination controversy, spreading of miss-information and encouragement to isolate when experiencing respiratory symptoms could all feasibly influence the diagnosis of LC. Equally, the influence of COVID on hospital presentations, access to medical care and chest imaging is unclear. In a period of fierce resource conservation patients may have had investigations omit that would have led to their diagnosis. Conversely with increasing respiratory presentations the rate of incidental diagnosis of LCs during the pandemic may have increased; a trend the surgical performance did not accommodate. There may have also been variability in access to medical care throughout the state that is not accounted for in this database. While the influence on LC surgery in QLD is partially demonstrated by this review, the influence of COVID-19 on LC as a larger entity is unclear.

Future directions

Lung cancer referrals are primarily directed to respiratory physicians in Australia. This inherently delays the contact of a surgical candidate and a thoracic surgeon. The existing care model leads to unnecessary delays, such as the time awaiting respiratory review, respiratory function testing, imaging, biopsy, MDT discussion and thereafter time to surgical review and intervention. The involvement of a surgeon at the primary point of referral could expedite care. Dedicated multidisciplinary LC clinics could streamline patients to a surgical or non-surgical streams. Following the completion of respiratory function testing and imaging surgeons could then be more proactively involved in biopsy and excision, utilizing navigational bronchoscopy, image guided biopsy (in hybrid theatres), mediastinoscopy or endobronchial ultrasound biopsy. Immediate histological examination suggestive of malignancy at the time of biopsy could then result in immediate completion resection. This would reduce the delay from tissue sampling to resection from 60 days, to 0.

Queensland had less COVID-19 burden compared to NSW and Victoria. The delays and upstaging noted in the Queensland data is likely less than what is expected in Victoria and NSW. Examination of the pandemic's impact on these health-systems is required to better understand the influence of COVID-19 on LC surgery in Australia. Further to this, cross analysis with the Queensland/Australian oncology registries to understand the influence of the pandemic on non-surgical LC is recommended.

The introduction of LC Screening in Australia poses a challenge to the existing infrastructure, with a predicted increase in the detection of surgical disease. These already lengthy delays to treatment need be reviewed. The introduction of surgical lead LC clinics may help to improve the access to care and LC outcomes.[4]

Conclusion

The COVID-19 pandemic undoubtedly negatively affected the care of patients with lung cancer in Queensland. Restrictions introduced by the pandemic lead to a statistically and clinically significant increase in the time from diagnosis to surgery. Further it markedly reduced the operative capacity of the state's Thoracic Surgical Service. While this did not result in a sustained pathological upstaging of disease, the number of surgeries performed reduced over time despite the static incidence of LC in the Australian population. The full implications of the changes that the pandemic made to LC surgery in Queensland and consequently survival and recurrence is not completely captured by this analysis. In preparation for the introduction of LC screening in Australia, the pre-pandemic performance of the Thoracic Oncological Service needs review and restructuring, with the development of Rapid Lung Cancer Clinics and early involvement of Thoracic Surgeons.

Author contributions

Frazer Kirk: Conceptualization; data curation; formal analysis; investigation; methodology; project administration; resources; writing – original draft; writing – review and editing. **Kelsie Crathern:** Investigation; writing – review and editing. **Shantel Chang:** Formal analysis; investigation. **Matthew S. Yong:** Conceptualization; methodology; writing – review and editing. **Cheng He:** Project administration; resources; supervision; writing – review and editing. **Ian Hughes:** Formal analysis; investigation; methodology; software; validation. **Sumit Yadav:** Resources; writing – review and editing. **Wing Lo:** Resources; writing – review and editing. **Christopher Cole:** Resources; supervision; writing – review and editing. **Morgan Windsor:** Investigation; resources; writing – review and editing. **Rishendran Naidoo:** Investigation; resources; writing – review and editing. **Andrie Stroebel:** Conceptualization; project administration; resources; supervision; writing – review and editing.

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Conflict of interest statement

None declared.

Ethical approval

Ethical Approval by Gold Coast University Hospital and Health Service Human Research Ethics Committee. HREC Reference: EX/2022/QGC/84819.

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