ORIGINAL ARTICLE

A time-to-treatment initiation analysis for treatment-naive early-stage resectable non-small cell lung cancer patients in the Malaysian private healthcare sector

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ABSTRACT

Introduction: Non-small cell lung cancer (NSCLC) remains a leading cause of cancer mortality in Malaysia, with 95% of cases diagnosed at advanced stages. Beyond screening for early detection, timely intervention is critical for optimal outcomes in early-stage, resectable NSCLC (e-NSCLC). Delays in the diagnostic, staging and referral pathway, measured as time-to-treatment initiation (TTI), are associated with poorer survival. This contemporary real-world study is the first to evaluate TTI in a cohort of Malaysian patients with e-NSCLC.

Materials and Methods: This is a retrospective study of 124 consecutive treatment-naive e-NSCLC patients who had a minimally invasive curative anatomical lung resection (lobectomy or segmentectomy) and systematic mediastinal nodal dissection between January 2021 and December 2024 at two tertiary private hospitals. Medical records were reviewed to capture key timepoints across three phases of care. The primary analysis (n=124) focused on demographics and assessed the timeline from initial general practitioner (GP) to specialist consultation, diagnosis, and definitive surgery. These patients were evaluated after surgical discharge to validation of histopathology and next-generation sequencing (NGS) reports, and oncology review. Patients who received adjuvant therapy were included in a secondary analysis to examine timelines from NGS report validation and oncology review to initiation of adjuvant therapy.

Results: The median time from the GP referral to surgery was 30.0 ± 24.5 days; GP consultation to specialist referral took 7.5 ± 17.0 days, specialist review to surgeon consultation took another 10.0 ± 16.3 days. Biopsy and staging PET-CT were completed within 3.0 ± 20.9 and 3.0 ± 20.5 days, respectively, from the initial specialist consultation. Definitive curative-intent surgery was performed 7.5 ± 13.1 days from the first cardiothoracic surgical consult and 18 ± 23.3 days following a confirmed histological diagnosis of NSCLC. The median interval from specialist review to definitive surgery was 20.0 ± 20.2 days. The median time from surgery to discharge and reporting of NGS results was 5.0 ± 2.6 days and 12.0 ± 7.7 days, respectively. Patients were seen at the first post-surgical review within 7.0 ± 3.7 days following discharge, while oncology review occurred at 19.0 ± 16.2 days post-surgery. For patients eligible for adjuvant therapy, treatment commenced 14.5 ± 11.4 days following the oncology review.

Conclusion: TTI is known to prognosticate recurrence-free and overall survival for e-NSCLC. This contemporary real-world experience from two leading tertiary cancer centres demonstrates the agility and efficiency of Malaysian private healthcare for prompt diagnosis, meticulous staging and timely, curative-intent definitive surgery for e-NSCLC, aligning with global benchmarks. Our study suggests, if prioritised, a swift TTI is highly achievable with appropriate expertise and coordinated resources, and should be incorporated as a deliverable national quality metric to drive improved outcomes for potentially curable e-NSCLC.

KEYWORDS:
Time-to-treatment initiation, non-small cell lung cancer, timely intervention, Malaysian healthcare

INTRODUCTION

Lung cancer remains a leading cause of cancer-related mortality globally, with non-small cell lung cancer (NSCLC) accounting for approximately 85% of cases.[1] In Malaysia, lung cancer ranks as the second and third most common malignancy in males and females respectively and remains the second leading cause of cancer-related mortality according to the Malaysian National Cancer Registry Report 2017–2021.[2] Notably, approximately 95% of lung cancer cases in Malaysia are diagnosed late at advanced stages III and IV, with adenocarcinoma NSCLC being the predominant histological subtype.[2]

NSCLC patients with early-stage, resectable (IA to IIIA) disease (e-NSCLC) have the highest long-term disease-free survival (DFS) and overall survival (OS), particularly when

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timely surgical resection is performed.[3] However, delays in timepoints from diagnosis to definitive treatment known as *'time-to-treatment initiation'* (TTI), including curative surgery, can adversely impact outcomes for patients with potentially curable early-stage disease. Delays in TTI have been reported by even highly developed countries, including from the European Union, United Kingdom, and United States.[4]

The impact of TTI on survival for newly diagnosed NSCLC patients of all stages is significant. According to the Mayo Clinic Cancer Center (2000-2016) multi-site registry study, median OS was markedly better for patients with a TTI ≤20 days compared to those with a TTI > 20 days (39.1 vs 28.6 months, p<0.0001).[5] The survival benefit was most pronounced for patients with stage I and II disease; OS of 103.4 vs. 63.9 months (p<0.0001) and 72.3 vs. 46.8 months (p=0.0014), respectively.[5] A recent study involving more than 80,000 NSCLC patients (SEER, 2000-2019 database, USA) concluded that a prolonged TTI > 31 days had a negative impact on OS and cancer-specific cumulative mortality for stage I disease.[6] In another study, significantly better outcomes were observed for stage III patients with a shorter TTI, in patients who survived ≥ 5 years (p=0.029).[7]

These findings reiterate the importance of a prompt diagnosis and efficient staging work-up to ensure a brief TTI to improve outcomes particularly for e-NSCLC patients. The aim of our study was to evaluate the TTI across key timepoints in the patient journey such as initial presentations to the general practitioner (GP), lung or oncology specialist and cardiothoracic surgeon, first radiological finding or histological confirmation, and clinical diagnosis leading up to definitive curative-intent surgery. This study seeks to identify real-world barriers contributing to delays in TTI and propose strategies to enhance the care pathway for patients with e-NSCLC. Such insights will guide better healthcare resource allocation and improve service delivery for more timely intervention which should translate to superior patient outcomes.

MATERIALS AND METHODS

Study Population

A total of 124 consecutive treatment-naive patients with clinical stage IA to IIIB-N2 primary NSCLC who underwent definitive curative-intent anatomical surgical lung resection between January 2021 and December 2024 from two tertiary, urban private hospitals met the inclusion criteria and were included in the study (Figure 1). All patients were clinically staged pre-operatively with a PET-CT scan, and if indicated, a contrasted MRI brain scan. The standard operation in all patients was a lobectomy or segmentectomy, with concurrent systematic mediastinal lymph node dissection, performed with a minimally invasive uniportal approach under single lung ventilation general anaesthesia and conducted by a single cardiothoracic surgeon.

Data collection

Data was extracted retrospectively from medical records and reports, including progress notes, histopathology reports, laboratory findings, and imaging studies, in compliance with ethical standards. Demographic variables collected included age, sex, and ethnicity, while smoking status was recorded as current, former, or non-smoker. Presenting symptoms were categorised as either incidental (asymptomatic) findings or symptomatic presentations, which included cough, haemoptysis, dyspnoea, weight loss and chest pain. In addition to baseline characteristics, the study focused on capturing key clinical timepoints (in days) that reflected the time-to-treatment initiation, defined as the interval from the first GP consultation to the date of definitive surgery, and where applicable, to the initiation of adjuvant therapy.

Operational definition of key clinical timepoints

The following definitions were applied in the extraction and interpretation of key clinical timepoints from patients' medical records (Figure 2).

- GP Consultation: The date of the patient's first visit to a GP for symptoms or concerns that ultimately led to the diagnosis of NSCLC.
- Specialist Consultation: The date the patient visits a relevant hospital-based specialist, e.g., respiratory physician or oncologist, for a consultation.
- Cardiothoracic Surgical Consultation: The date of the first consultation with a cardiothoracic surgeon regarding operative management for the NSCLC.
- PET-CT Scan: The date the first positron emission tomography-computer tomography (PET-CT) scan was performed for diagnostic and staging purposes.
- Brain MRI: The date the contrast-enhanced brain magnetic resonance imaging (MRI) procedure was performed to assess for potential occult brain metastases.
- Lung Biopsy Procedure: The procedural date of the first tissue biopsy which confirmed a histopathological diagnosis of NSCLC.
- Lung Biopsy Report Validation: The date the histopathology report confirming a NSCLC diagnosis was validated in the medical record by a certified pathologist.
- Surgery: The date of the definitive curative-intent surgical resection of the primary NSCLC.
- Discharge: The date the patient was formally discharged from the hospital following surgery.
- HPE Report Validation: The date the final histopathology examination (HPE) report of the resected tumour specimen was validated and made available in the medical record by a pathologist.
- NGS Report Validation: The date the next-generation sequencing (NGS) report for the surgical biopsy sample was validated by the molecular pathology laboratory and made available for clinical assessment by the oncologist.
- First Post-Surgical Review: The date of the first follow-up outpatient clinic visit with the cardiothoracic surgeon following surgery.
- Oncology Review: The date of the first formal oncology consultation for assessment, adjuvant treatment planning and follow-up.
- Adjuvant Therapy Initiation: Commencement of treatment (chemotherapy, immunotherapy and/or oral targeted therapy) within three months of the curative surgery.
- TKI Initiation: Commencement of tyrosine kinase inhibitors (TKI) as adjuvant therapy.

Data Analysis
The primary analysis (n=124) focused on demographics and assessed the timeline from the initial GP visit to specialist consultation, diagnosis and staging work-up, consultation with the cardiothoracic surgeon, to definitive surgery (Phase I). All patients were evaluated following surgical discharge to histopathology and NGS report validation, to the first post-surgical review and oncology review (Phase II) (Figure 2). A total of 66 patients eligible for adjuvant therapies were included in a secondary analysis to examine timelines from NGS report validation and oncology review to initiation of adjuvant therapy (Phase III). Further analysis was performed on the cohort of patients whose tumours harboured actionable mutations treated with a TKI, in particular oral targeted therapies, with or without chemotherapy, to evaluate the timeliness of TKI treatment initiation.

Statistical Methods
Descriptive analyses were performed to describe patients' demographics, including gender, age, ethnicity, risk factors, presenting symptoms, clinical stage at diagnosis and type of therapy received. Key clinical timepoints (from initial consultation with GPs to initiation of adjuvant therapy) were analysed using measurement of central tendency and dispersion, whereby the timeline data is presented as median ± standard deviation (SD) and range, i.e., minimum versus maximum. All statistical analyses were performed using R version 4.4.3 and Microsoft Excel 2019 (version 16).

RESULTS

Patient Demographics and Clinical Characteristics
In total, clinical data from 124 patients were retrieved in this study (Table I). The study cohort was predominantly female (52.42%), and the majority (54.84%) were aged between 40 and 64 years. Ethnic Malaysian Chinese (76.61%) were most represented in the study population, followed by foreign nationals (11.29%), Malaysian Indians (6.45%) and Malays (5.65%). In terms of risk factors, the majority were non-smokers (67.74%). A personal history of cancer and family history of cancer were reported in 14.52% and 29.84% of the population, respectively. Overall, 15.32% had a family history specifically for lung cancer.

Most cases (67.74%) were asymptomatic, discovered incidentally following opportunistic health screening. Among symptomatic patients, cough (21.77%) was the predominant symptom, followed by haemoptysis (8.87%), chest discomfort (4.03%), weight loss and shortness of breath (2.42% each). Based on the post-operative pathological TNM staging, the stages of disease were IA (33.87%), IB and IIB (20.16% each), followed by IIIA (15.32%), IIIB (5.65%) and IIA (4.84%). In total, 66 patients (53.23%) were eligible for post-surgical adjuvant therapy. Some patients with tumours that harboured targetable mutations received TKI-only therapy (18.55% of the overall study population) whilst a further 14.52% received a TKI in combination with chemotherapy. 19.35% of patients received adjuvant chemotherapy alone, and 1 patient received radiotherapy for local control for a positive R1 surgical margin.

Phase I (pre-operative care): GP consultation to Diagnosis
The median time from the first timepoint of GP consultation to treatment initiation by surgery was 30.0 ± 24.5 days (n= 58), whereby it took 7.5 ± 17.0 days from GP referral to specialist consultation (Table II). Given that many patients self-presented directly to the specialist, the median time from specialist consultation to surgery was 20.0 ± 20.2 days. During the specialist consultation, diagnostic and staging procedures including PET-CT, contrast-enhanced brain MRI, and tissue biopsy were planned and performed. The median time from the specialist consultation to the completion of the procedures, i.e., PET-CT, brain MRI, and biopsy, was 3.0 ± 20.5, 11.0 ± 19.0, and 3.0 ± 20.9 days, respectively. In particular, pathologist validation of the lung biopsy report occurred at 2.0 ± 2.2 days following the biopsy procedure, allowing for timely diagnosis and appropriate treatment planning.

Phase II (operative care): Surgical consultation to surgery and oncology care
In this analysis (n= 124), the overall median time from GP and specialist consultation to treatment initiation by surgery was 30.0 ± 24.5 and 20.0 ± 20.2 days, respectively (Table II). The specialist referral to the cardiothoracic surgeon took a median of 10.0 ± 16.3 days, and the time interval from validation of the diagnostic HPE biopsy report to surgery was 18.0 ± 23.3 days. Definitive curative surgery was performed at a median of 7.5 ± 13.1 days from the first surgical consultation, with most patients operated on within two weeks or less, of that initial surgical consultation. The majority of the patients were discharged within 5.0 ± 2.6 days with no reported in-hospital or 30-day mortality. Post-resection morbidity was minimal. The most common complications were small, self-limiting parenchymal air leaks. No patient required airway re-intubation or mechanical ventilatory support, or surgical re-exploration for bleeding or repair of air leaks or bronchopleural fistulas. Three patients (2.4%) developed a post-operative chylothorax, presumably from nodal dissection that required a prolonged hospital stay but settled fully with conservative therapy which included institution of total parenteral nutrition. Analysis and validation of HPE reports for the resected lobe/segment and mediastinal lymph nodes were available at a median of 4.0 ± 2.5 days, within the hospitalisation period for most patients. Surgical specimens were also sent for NGS testing, and genomic reports were validated at 8.0 ± 7.2 days following the resected tumour HPE validation and within 12.0 ± 7.7 days from surgery. Following hospital discharge, all patients returned for a post-surgical review within 7.0 ± 3.7 days, and all were offered an oncology referral for an independent evaluation on the need for adjuvant therapy. In total, 104 patients visited the oncologist, within 19.0 ± 16.2 days of surgery.

Phase III (post-operative care): Oncology care to adjuvant therapy initiation
66 patients were prescribed adjuvant therapy and included in the sub-analysis of adjuvant therapy initiation (Table III). Following oncology review, patients who required adjuvant therapy had their treatment initiated within 14.5 ± 11.4 days. Among patients whose tumours harboured targetable mutations and were eligible for TKI treatment, the time taken

Table I: Study population demographics and clinical characteristics

Characteristic		Total (n)	Percentage
Sex	Female	65	52.42%
	Male	59	47.58%
Age	Median (IQR)	63 (53.75-68.00)	
	Mean ± SD	60.76 ± 10.26	
	18-39	3	2.42%
	40-64	68	54.84%
	>65	53	42.74%
Ethnicity	Chinese	95	76.61%
	Foreigner	14	11.29%
	Indian	8	6.45%
	Malay	7	5.65%
Risk factors	Smoking history		
	Never	84	67.74%
	Former	26	20.97%
	Current	14	11.29%
	Cancer history		
	Personal history of cancer	18	14.52%
	Family history of cancer	37	29.84%
	Family history of lung cancer	19	15.32%
	No history of cancer	74	59.68%
Symptoms	Incidental (Asymptomatic)	84	67.74%
	Symptomatic	40	32.26%
	Cough	27	21.77%
	Haemoptysis	11	8.87%
	Loss of weight	3	2.42%
	Chest discomfort	5	4.03%
	Shortness of breath	3	2.42%
	Others*	5	4.03%
Pathological Stage	IA	42	33.87%
	IB	25	20.16%
	IIA	6	4.84%
	IIB	25	20.16%
	IIIA	19	15.32%
	IIIB	7	5.65%
Adjuvant Therapy	Tyrosine kinase inhibitor only	23	18.55%
	Osimertinib	19	15.32%
	Gefitinib	2	1.61%
	Afatinib	1	0.81%
	Alectinib	1	0.81%
	Chemotherapy only	24	19.35%
	Radiotherapy	1	0.81%
	Combination therapy	18	14.52%
	Osimertinib + chemotherapy	14	11.29%
	Alectinib + chemotherapy	3	2.42%
	Dacomitinib + chemotherapy	1	0.81%
	No adjuvant therapy	58	46.77%

*Includes symptoms like dizziness, palpitation, body aches and post-nasal drip. IQR: Interquartile range, SD: Standard deviation

from oncology review to TKI therapy initiation was 17.0 ± 37.9 days and within 26.5 ± 36.7 days from validation of the NGS report by the molecular pathologist.

DISCUSSION

This study is a comprehensive and contemporary analysis of time-to-treatment initiation among a cohort of treatment-naïve patients with resectable e-NSCLC managed in the Malaysian private healthcare sector. The median time from the initial GP visit to definitive surgery was 30.0 days, indicating timely diagnosis and relatively prompt access to pre-operative care. Our work is the first study in Malaysia to evaluate TTI exclusively for early-stage disease. It is comparable to the only prior local TTI study which reported a median interval of 1.1 months from first hospital visit to treatment initiation although > 95% of patients in this 2006 study had inoperable disease.[8] Two studies conducted in the United States reported median intervals of 27 days and 28 days from diagnosis to treatment initiation.[9-10] Similarly, a study in Singapore found a median interval of 28 days from multidisciplinary clinic visit to treatment, with a range of 4 to 111 days.[11] These comparable timelines underscore the efficiency and agility of the Malaysian private healthcare system, which aligns with regional and international standards and falls within the clinically significant window of 45 days for improved patient outcomes.[12]

The median interval from GP to specialist consultation was 8.0 days, suggesting most patients were referred promptly.

Table II: Overall timeline and key intervals from GP or specialist consultation to surgery and oncology review

Start Timepoint	End Timepoint	n	Median ± SD (days)	Min (days)	Max (days)
Overall: General practitioner	Surgery	58	30.0 ± 24.5	8	125
Overall: Specialist consultation	Surgery	123	20.0 ± 20.2	1	117
Lung biopsy report validation	Surgery	101	18.0 ± 23.3	1	174
General practitioner	Specialist consultation	58	7.5 ± 17.0	1	97
Specialist consultation	Diagnostics (Brain MRI)	73	11.0 ± 19.0	1	78
Specialist consultation	Diagnostics (PET-CT)	121	3.0 ± 20.5	1	95
Specialist consultation	Diagnostics (Biopsy)	102	3.0 ± 20.9	1	79
Lung biopsy procedure	Lung biopsy report validation	101	2.0 ± 2.2	1	13
Specialist consultation	Cardiothoracic Surgeon consultation	123	10.0 ± 16.3	1	82
Cardiothoracic Surgeon consultation	Surgery	124	7.5 ± 13.1	1	104
Surgery	Discharge	124	5.0 ± 2.6	3	24
Surgery	HPE report validation	124	4.0 ± 2.5	1	15
Surgery	NGS report validation	76	12.0 ± 7.7	2	48
HPE report validation	NGS report validation	76	8.0 ± 7.2	1	45
Discharge	First post-surgical review	124	7.0 ± 3.7	1	35
Surgery	Oncology review	104	19.0 ± 16.2	3	94

SD: Standard deviation, MRI: Magnetic resonance imaging, PET-CT: Positron emission tomography-computed tomography, HPE: Histopathology examination, NGS: Next generation sequencing

Table III: Time-to-treatment initiation for study population eligible for adjuvant therapy

Start Timepoint	End Timepoint	n	Median ± SD (days)	Min (days)	Max (days)
Overall: General practitioner	Adjuvant treatment initiation	30	62.5 ± 22.6	29	122
Overall: Specialist consultation	Adjuvant treatment initiation	54	51.0 ± 19.4	17	106
Oncology review	Adjuvant treatment initiation	54	14.5 ± 11.4	4	51
Oncology review	TKI initiation	36	17.0 ± 37.9	5	143
NGS report validation	TKI initiation	22	26.5 ± 36.7	8	154

SD: Standard deviation, NGS: Next generation sequencing, TKI: Tyrosine kinase inhibitor

However, data for the GP timepoint was only available in 58 out of 124 patients in the primary analysis. In reality, many patients either sought second opinions, were referred from other institutions, or self-presented directly to specialists or the surgeon. This latter practice is not uncommon here as the GP is not the clinical gatekeeper in Malaysian healthcare. Direct patient access or self referral to a relevant specialist especially in the private setting is allowed, and a frequent occurrence.

Detection of early-stage lung cancer remains a significant challenge. In the present study, 67.74% of cases were detected incidentally, highlighting the paucity of noticeable red-flag symptoms in early-stage disease, with asymptomatic NSCLC an incidental chance finding either from health screening or through imaging performed for other purposes. By the time symptoms such as a persistent cough, haemoptysis, or chest pain appears, the disease has often progressed to an advanced stage. Nevertheless, GPs could improve early detection by maintaining a high clinical suspicion and low threshold to investigate patients who present with a persistent cough (the predominant symptom in this series). Broadening screening criteria to include the high-risk non-smoker especially those with a family history of cancer, a personal history of cancer or most pertinently, a family history of lung cancer, either with an artificial intelligence-enhanced chest radiograph or the gold standard low-dose computed tomography (LDCT) scan will also be helpful. Our findings highlight the need to sustain and reinforce public awareness campaigns for earlier symptom recognition and encourage timely presentation to healthcare services.

The current study demonstrated upon specialist referral, essential diagnostic and staging investigations such as PET-CT scan, MRI, tissue biopsy and histopathological examination, could be conducted promptly, if prioritised, facilitating swift and appropriate treatment planning. The high efficiency in diagnosing and staging our patients is a reflection of the highly experienced and dedicated multidisciplinary teams (MDT) within the two comprehensive tertiary healthcare institutions, comprising respiratory physicians, oncologists, cardiothoracic surgeons, pathologists, nuclear medicine physicians and radiologists, all working together seamlessly, in delivering high-quality clinical care. Notably, both hospitals have regular MDT tumour board meetings. Implementing an MDT approach improved 5-year overall survival rates among patients with stage III lung cancer, for both those who underwent surgical resection and those who did not.[13] The shorter patient journey we report can be partly attributed to quicker turnaround times and shorter waiting times for various tests and services. As tertiary-level regional one-stop private cancer centres equipped with the latest state-of-the-art radiological imaging and laboratory equipment, the need to send patients or tissue samples elsewhere is mitigated.

In this study, all patients underwent PET-CT scan procedures. A contrast-enhanced brain MRI scan to exclude occult cerebral metastases was only performed for clinical stage II/III disease or if clinically indicated, in accordance with current national and international guidelines.[14-15] The data gap in the tissue biopsy procedure is attributed to patients whose tumours were not amenable to biopsy, patients who refused a pre-operative biopsy or sought care elsewhere, wherein the exact biopsy procedural dates were not traceable. In cases without histological confirmation of NSCLC pre-surgery, an intra-operative frozen section biopsy was performed prior to the curative resection.

The documented time interval from specialist visit to cardiothoracic surgeon consultation was a median of 10.0 days, during which much of the diagnostic and staging work-up was done. Following surgical consultation, the transition to surgery was prompt, with a median of 7.5 days, highlighting efficient operative scheduling practices and appropriate resource allocation in the private healthcare setting. However, ultimately this surgical urgency is driven by the singular focus and priority of the operating surgeon whose practice is largely dedicated to thoracic oncology. In this series, definitive surgery was performed at a median of 18.0 days following histological confirmation of a NSCLC.

All patients experienced an uneventful surgery with no in-hospital or 30-day mortality recorded, and median hospitalisation stay was 5.0 ± 2.6 days. Post-resection morbidity was minimal and no patient required airway re-intubation or mechanical ventilatory support, or surgical re-exploration for bleeding or repair of air leaks. The three patients who developed a post-operative chylothorax, all had prolonged hospital stays requiring total parenteral nutrition with full resolution of the chylous leak in each case. Only one patient experienced a prolonged hospital stay up to 24 days, due to a surgical wound infection requiring corrective treatment. A previous study demonstrated that for patients who received surgery-only for early-stage disease, those who had surgery between 4 and 6 weeks were associated with a 6% increased risk of death whilst a greater mortality risk (17%) was recorded for those who received surgery more than 6 weeks after diagnosis compared to patients treated immediately.[9] Presently, evaluation for cancer recurrence and survival outcomes for most patients in this study remains premature, however, we intend to continue meticulous follow-ups and correlate their DFS and OS with TTI in a future analysis.

Post-operatively, the validation of the final HPE report took a median of 4.0 days, reflecting rapid turnaround time from laboratory processing to report validation by the pathologist. This facilitates vital clinical decision-making before patient discharge, including ordering relevant genomic and biomarker tests during the index hospitalisation to guide adjuvant therapy planning. This has significantly aided the post-surgical oncology review, as shown in this study, as it took only 19.0 days from surgery to the oncologist review, and another 14.5 days for adjuvant treatment initiation.

Our study aligns with the recent shift in adjuvant therapy for early-stage, resectable NSCLC from conventional platinum-based chemotherapy and radiation therapy, either together or separately, to oral targeted therapies and immune checkpoint inhibitors. In this cohort, 31 out of 47 (65.9%) eligible EGFR-mutated NSCLC patients (data not shown) were offered standard of care osimertinib either alone or in combination with platinum-based chemotherapy, based on the significant DFS and OS benefit demonstrated in the phase III randomised ADAURA trial.[16-17] The relatively low uptake in our study suggests financial barriers to access osimertinib remain, even in an urban private setting. Notably, a few patients were prescribed an earlier generation TKI due to limited affordability. Future strategies must address such financial toxicity to ensure more equitable care.

In this study, we excluded patients exposed to neoadjuvant therapies. However, the treatment paradigm for e-NSCLC is rapidly evolving. Systemic immune checkpoint inhibitor therapy, i.e., nivolumab (CheckMate 816)[18-19], pembrolizumab (KEYNOTE-671)[20], durvalumab (AEGEAN)[21], nivolumab (CheckMate 77T)[22] for non-oncogene driven NSCLC, given as a neoadjuvant-only therapy or as part of a peri-operative 'sandwich' protocol has resulted in significant improvements in not only event-free survival (EFS), but even OS, particularly for stage III disease. Immunotherapy is fast becoming the standard of care ,and naturally this will alter the patient journey considerably, including TTI for early-stage resectable disease. Similarly, the awaited findings of neoadjuvant osimertinib use (NeoADAURA)[19] may further shift the treatment paradigm. With such advances, the timeliness of diagnosis including genomic molecular profiling and coordination between the multidisciplinary care team will become paramount to ensure patients receive optimal biomarker driven care within the appropriate timeline.

Our study demonstrates that if prioritised, a swift TTI for eNSCLC is highly feasible especially in the private healthcare setting where the necessary expertise and facilities are abundantly available and easily accessible. Although survival outcome was not the focus of this study, numerous studies confirm the association between TTI and clinical outcomes. In general, longer diagnostic intervals and treatment delays are associated with higher mortality and worse prognosis.[9,24-25] Interestingly, Loh et al.[8] found no significant association between treatment delays and long-term survival (in the only other Malaysian TTI lung cancer study to date), however, it is important to note only 5% of their patient cohort had resectable disease. Similarly, Skaug reported no significant correlation between treatment delays and long-term survival but only a minority (11%) underwent surgery.[26] In such cases, prognosis is more often driven by disease biology and stage of disease rather than timing of intervention, unlike in our study, which specifically evaluates early-stage, resectable NSCLC, where timely surgical management plays a pivotal role in achieving good outcomes. When lung cancer is diagnosed at an early, localised stage, the opportunity for a cure with surgical resection is real and possible. Hence, timely intervention is an imperative to prevent disease progression to an unresectable and incurable stage.

The small sample size of only 124 patients in the first analysis, followed by 66 patients in the second analysis, results in a low statistical power, and a greater risk of Type I and Type II errors, and reduced reliability in accurately determining the TTI for NSCLC patients in Malaysia. Ideally, TTI should encompass the interval from symptom onset to the initial GP visit, however this was precluded by the lack of reliable data on symptom onset due to challenges such as the subjective nature of symptoms, patient forgetfulness, variability in awareness and willingness to seek care, the GP's referral practices and access to tertiary medical care. Additionally, the generalisability of our findings is limited as the sample was drawn from only two private, urban tertiary hospitals, which may not represent the wider population and thus introduce selection bias. Finally, this study did not evaluate long-term cancer recurrence rates or survival following surgery or adjuvant therapy hence, we are unable to assess treatment durability and effectiveness. Future research will incorporate recurrence monitoring and survival outcomes to enable a more comprehensive understanding of how TTI impacts long-term prognosis for Malaysian patients with e-NSCLC.

CONCLUSION

This contemporary real-world study underscores the efficiency and agility of the private healthcare sector in Malaysia, in delivering timely diagnostic and high quality multi-disciplinary and multi-modal driven curative-intent surgical care for early-stage, resectable NSCLC, whilst highlighting critical gaps in the post-operative transition to adjuvant therapy. Strategies to mitigate financial toxicity are urgently required to ensure better access and more equitable adjuvant oncology care. Adopting TTI as a national performance metric (clinical key performance indictor) will help improve timeliness, equity, and long-term outcomes across lung cancer care pathways. It is unlikely such timely care can be achieved in the public sector (Ministry of Health and University) hospitals in the foreseeable future due to overwhelming clinical caseload, lengthy waiting times, limited resources and funding, and shortage of specialist staff and equipment. Leveraging on the vast expertise and resources readily available in high volume private centres of excellence through an impactful public-private collaboration seems most sensible and can quickly help close this unacceptable care gap in the provision of a timely and quality service for any Malaysian diagnosed with lung cancer.

Authors' Contributions

Anand Sachithanandan: Conceptualization, Methodology, Project administration, Supervision, Writing – review & editing. Hoh Hong Huat: Investigation, Formal analysis, Project administration, Validation, Writing – review & editing. Lee Joyin: Data curation, Formal analysis, Visualisation, Writing – original draft. Lim Yi Shwen: Data curation, Formal analysis, Visualisation, Writing – original draft. Naim Che Kamaruddin: Investigation, Data curation, Visualisation. Fatin Najihah Muhammad Lutfi: Data curation, Visualisation. Yong Wong Wai Shieh: Data curation, Visualisation. Siti Ayuni Hassanudin: Data curation. Ten Yi Yang: Data curation. Lam Mynn Dee: Data curation. Janelle Wee Chia Ern: Writing – original draft. Deva Rani Raja Sakar: Writing – review & editing. Shobana Satchithananthan: Writing – review & editing.

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