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ORIGINAL ARTICLE



Improving referral of patients for consideration of adjuvant chemotherapy after surgical resection of lung cancer

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ABSTRACT

Background

Clinical trials demonstrate improved survival for patients with completely resected non-small-cell lung cancer (NSCLC) who receive adjuvant chemotherapy. Concerns have been raised about the implementation of those data. The present study measured rates of referral for adjuvant chemotherapy and barriers to referral, and it also evaluated a knowledge translation strategy to change practice.

Methods

An audit and feedback approach was used. Using a retrospective cohort of patients undergoing thoracotomy at St. Joseph's Hospital in Hamilton, Ontario, during January–December 2008, anonymized data were presented to a group of thoracic surgeons for evaluation and feedback.

Results

Among 150 thoracotomies performed, 55 patients with NSCLC were potentially eligible for adjuvant chemotherapy, but only 27 (49%) were referred for it. Significant variability in referral between surgeons (19%–100%) was observed. Reasons for non-referral were poorly documented in the medical record, but appeared to be primarily the surgeon's decision. The feedback session with surgeons produced a number of constructive suggestions to implement change in practice.

Conclusions

Our findings suggest that surgeon choice was the most significant barrier to implementation of adjuvant chemotherapy for NSCLC. Audit and feedback was a useful knowledge translation strategy. However, longer follow-up is needed to document change in practice.

KEY WORDS

Non-small-cell lung cancer, adjuvant chemotherapy, health outcomes research, knowledge transfer, quality improvement

1. INTRODUCTION

Lung cancer is the most common cause of cancer-related death in Canada, and about 85% of lung cancer cases are non-small-cell lung cancer (NSCLC)[1,2]. Only a small proportion of cases are amenable to surgical resection. Historically, adjuvant chemotherapy has not routinely been recommended after surgical resection, because available data failed to demonstrate statistically significant improvements in survival[3].

In recent years, more appropriately powered trials using newer chemotherapeutic agents have demonstrated that adjuvant chemotherapy improves the 5-year survival of patients undergoing complete surgical resection[4–7]. Initial data from the International Adjuvant Lung Trial presented in 2003[4] showed a modest 3.9% improvement in 5-year survival for patients with resected stages I–III NSCLC. Three additional trials—JBR.10[6], CALGB 9633[7], and ANITA[5]—confirmed that adjuvant chemotherapy resulted in significant improvements in survival for patients with resected NSCLC. The absolute gains in 5-year survival were 12% for stage II and 15% for stage III disease[8]. Those data were rapidly incorporated into clinical algorithms. Accordingly, Cancer Care Ontario (CCO) guidelines from 2006 were updated to recommend the routine use of postoperative chemotherapy in resected stages II–IIIA NSCLC patients[9]. After publication of those guidelines, subset analyses from CALGB 9633 and JBR.10 expanded the role of adjuvant chemotherapy to include patients with resected stage IB tumours 4 cm or larger in size[7,10].

Despite publication of the foregoing data, it is apparent that there are barriers to the uptake of adjuvant chemotherapy for NSCLC. Retrospective data from several Canadian centres report referral rates

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in the 44%–50% range for adjuvant chemotherapy in resected stages IA–III lung cancer[11–13]. A review of provincial administrative databases in Ontario between 2004 and 2006 found that only 31% of patients undergoing resection for NSCLC (n = 1032) received any postoperative adjuvant chemotherapy[14]. That figure is likely an underestimate of the uptake of adjuvant chemotherapy because the databases did not allow for the exclusion of stages IA and IB tumours less than 4 cm in size.

Outcomes data for individual Local Health Integration Networks (LHINs) across Ontario are available from CCO. Data for the Hamilton–Niagara–Haldimand–Brant LHIN, which is the primary catchment area for the Juravinski Cancer Centre, show that the proportion of patients receiving adjuvant chemotherapy (44.3%) was below the provincial average in 2007–2008[15]. The goal of the present multicomponent quality assurance study was to improve the quality of cancer care by determining the rate of referral of patients potentially eligible for adjuvant chemotherapy, by identifying barriers to referral, and by implementing a knowledge translation strategy to improve referral of patients for consideration of adjuvant chemotherapy.

2. METHODS

Our retrospective cohort study looked at all patients who underwent a thoracotomy at St. Joseph's Hospital, Hamilton, Ontario, and who were discharged between January and December 2008. Only patients having a thoracotomy for primary lung cancer were included in the review. The patients considered eligible for adjuvant chemotherapy consideration were those with stages IB (tumours ≥ 4 cm), II, and III NSCLC. Three additional cases of resected small-cell lung cancer (SCLC) were also included.

Data collected for analysis included patient demographics, surgical information, pathology, referral to medical oncology, and current patient status. Demographic data consisted of sex, birth date, and smoking history. The method of cancer diagnosis, the date of surgery, the type of surgery, the attending surgeon (anonymized), and the date of discharge were abstracted from the medical record. Staging information, using the 6th edition of the TNM staging guidelines[16], was captured from pathology reports and clinical information. For patients referred to medical oncology, any offer and subsequent administration of adjuvant chemotherapy was noted. For patients not referred, the reason for lack of referral was extracted when available. Health outcomes collected were lung cancer recurrence and death.

The sample size was chosen to reflect a year of practice and not *a priori* statistical calculations. The analysis is primarily descriptive. The primary outcome is the rate of referral of patients eligible for adjuvant chemotherapy. Barriers to patient referral are secondary outcomes. Variability in the referral rate by surgeon, disease stage, and length of hospital stay (<10 vs. ≥10 days) are assessed. Ten days was chosen arbitrarily to reflect patients who had prolonged stays in hospital. The study was approved by the St. Josephs Hospital Research Ethics Board.

Upon completion of data collection and analysis, a knowledge translation strategy of audit and feedback, plus educational outreach, was applied[17–19]. A summary of the evidence, together with the findings of the audit were presented at a thoracic surgery departmental meeting attended by all members. Data were presented anonymously. A semi-structured discussion took place to identify ways to improve the referral rates of patients undergoing resection of primary lung cancers. Thoracic surgeons were asked for their impressions of the data and of its strengths and limitations, and for suggestions on how to improve the uptake of adjuvant chemotherapy.

3. RESULTS

During the selected period, 150 patients underwent a thoracotomy, with 123 having the procedure because of a primary lung neoplasm. The remaining 27 patients were not included in the review because they had surgery for benign masses (n = 4), pulmonary metastases from non-lung primaries (n = 13), carcinoid or sarcomatoid tumours (n = 6), or metastatic disease (n = 4). Table I summarizes the demographic data for the 123 included patients. Of those 123 patients, 55 had stage IB (≥4 cm), II, or III NSCLC or resected SCLC and were considered potentially eligible for adjuvant therapy. Their baseline characteristics were similar to those of the overall population of patients undergoing surgical resection.

Multiple preoperative diagnostic tests were performed in this patient population (Table II). The most commonly performed tests were bronchoscopies (60%) and needle biopsies (46%). Notably, a diagnosis was made by bronchoscopy in only 12% of patients. Needle biopsy was the most definitive preoperative diagnostic test in 40% of patients. Diagnosis was established at the time of thoracotomy in 57 patients (46%).

Nearly three quarters of the thoracotomies were performed by 2 surgeons (Table III). The most frequent surgical procedure was a lobectomy (67%). Half the cancers were adenocarcinomas (53%), and approximately one third were squamous cell carcinomas (35%). Most patients had stage I NSCLC (77%), but 13% had stage II NSCLC, and 6%, stage III. In 3 patients (2%), the surgical resection was for limited-stage SCLC.

Of these 55 patients eligible for consideration of adjuvant chemotherapy, 27 (49%) were referred to medical oncology for a postoperative consultation (Table IV). The referral rate varied significantly between surgeons, ranging from 19% to 100%. The

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TABLE I Demographic data for all patients undergoing a thoracotomy for primary lung cancer and for those deemed potentially eligible for adjuvant chemotherapy

Variable	*Thoracotomy patients*					
	Overall			*Adjuvant-eligible*		
	*(*n*)*	*(%)*	*Mean*	*(*n*)*	*(%)*	*Mean*
Patients	123			55		
Sex						
Male	50	41		23	42	
Female	73	59		32	58	
Age at diagnosis (years)			68.7±8.4			68.7±8.5
Smoking						
Never smoked	7	6		4	7	
Formerly smoked	58	47		25	45	
Currently smokes	54	44		24	44	
Unknown	3	2		1	2	
Cigar smoker	1	1		1	2	
Overall pack–years			43.3±25.8			42.3±26.5

TABLE II Summary of diagnostic tests performed on all included patients

Variable	*Value*
Patients (*n*)	123
Preoperative tests [*n* (%)]	
Bronchoscopy with biopsy	19 (15)
Bronchoscopy with wash/brush	74 (60)
Needle biopsy	56 (46)
Mediastinoscopy	34 (28)
Test establishing lung cancer diagnosis [*n* (%)]	
Bronchoscopy with biopsy	8 (6)
Bronchoscopy with wash/brush	7 (6)
Needle biopsy	49 (40)
Mediastinoscopy	2 (2)
Thoracotomy	57 (46)

rate of referral of patients with stage IB disease 4 cm or larger (33%) was substantially lower than that for patients with stage II and III disease (64%). An exploratory analysis evaluated the impact of length of hospital stay on referral. The median length of stay was 5 days (standard deviation: 20.1 days). Patients hospitalized for 10 days or more were referred at a lower rate than patients hospitalized for less than 10 days (40% vs. 51%).

No mention of adjuvant chemotherapy discussions appeared in the medical records for 27 of the 28 eligible patients not referred to a medical oncologist. The remaining 1 patient was offered a referral, but decided against it. Of the 27 patients referred, 26 were seen in consultation at the Juravinski Cancer Centre for a discussion of adjuvant chemotherapy (1 patient received care at another facility). For 5 of those patients, chemotherapy was not offered because of their poor health status. Of the 21 (67%) offered chemotherapy, 14 elected to proceed with treatment. The remaining patients chose not to receive chemotherapy.

Accurate follow-up information within 6 months of the present review was available for 50 of the 55 eligible patients. For 1 patient, no active physician was noted; 1 patient was in a long-term care facility; and 3 patients had died with unknown recurrence status. Lung cancer recurrence was documented in 23 patients (46%). A higher rate of recurrence was observed among eligible patients not referred for consideration of chemotherapy (64% vs. 28%).

All 4 current thoracic surgeons were present for the feedback session. Evidence supporting the use of adjuvant chemotherapy was summarized. There was agreement by all the surgeons that the criteria were appropriate. The data presented in this paper were generally received positively, although the surgeons suggested that referral patterns may have changed since 2008. Additionally, the sample size for the study may have been too small to make meaningful conclusions about risk of recurrence. Still, the data were felt to be valid, and there was agreement that referral rates could be improved. A variety of strategies were suggested to improve patient referral:

- Discussing all cases in multidisciplinary cases conferences
- Creating a prospective surgical database that would allow for monitoring of referral for adjuvant therapy
- Ensuring that patients with a complicated postoperative course would be considered for referral
- Implementing a nurse navigator role to identify all patients potentially eligible for postoperative adjuvant chemotherapy—a role that would serve

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TABLE III Surgical data for all patients with non-small-cell lung cancer (NSCLC) stages I–III and small-cell lung cancer (SCLC)

Variable	*Value*
Patients (*n*)	123
Surgeon [*n* (%)]	
J	17 (14)
K	44 (36)
L	47 (38)
M	3 (2)
N	12 (10)
Surgery type [*n* (%)]	
Wedge resection	27 (22)
Lobectomy	82 (67)
Pneumonectomy	14 (11)
Histologic diagnosis [*n* (%)]	
Adenocarcinoma	65 (53)
Squamous	43 (35)
Large-cell	6 (5)
Bronchoalveolar	1 (1)
Mixed	4 (3)
Small-cell	3 (2)
Pathologic stage [*n* (%)]	
NSCLC IA	37 (30)
NSCLC IB	
<4 cm	31 (25)
≥4 cm	27 (22)
NSCLC IIA	3 (2)
NSCLC IIB	14 (11)
NSCLC IIIA	4 (3)
NSCLC IIIB	4 (3)
Limited SCLC	3 (2)

TABLE IV Referral rate, by surgeon and by stage, of patients potentially eligible for adjuvant chemotherapy: non-small-cell lung cancer (NSCLC) stage IB/II/III and limited small-cell lung cancer (SCLC)

Variable	*Patients referred (n/N)*	*Referral rate (%)*
Surgeon		
J	8/9	89
K	4/21	19
L	7/17	41
N	8/8	100
Pathologic stage		
NSCLC IB (≥4 cm)	9/27	33
NSCLC IIA	3/3	100
NSCLC IIB	8/14	57
NSCLC IIIA	3/4	75
NSCLC IIIB	2/4	50
Limited SCLC	2/3	67
TOTAL	27/55	49

as a prompt for referral in patients who might otherwise be overlooked
- Repeating the assessment in another year as part of a continuous quality improvement cycle

4. DISCUSSION AND CONCLUSIONS

The present study provides important information about the uptake and implementation of evidence supporting the use of adjuvant chemotherapy after complete surgical resection of lung cancer. Practice-changing data emerged between 2003 and 2005[4–7], supporting a potentially large improvement in survival with the use of adjuvant chemotherapy. Health outcomes data from that time period demonstrated an improvement in the survival of lung cancer patients corresponding to the implementation of treatment[14]. Nevertheless, data from a number of sources showed variability in the implementation of adjuvant chemotherapy. Within our own LHIN, the rate of uptake was below the provincial average, suggesting a need to understand the nature of the problem and to implement strategies that would bring about a change in practice.

Previous studies reported rates of referral for adjuvant chemotherapy ranging from 44% to 50%[11–13,20]; however, differences in study methodology made direct comparisons of those results with our data somewhat inaccurate. Neither the CCO review nor the single-institution data separated stage IB based on tumour size, and they therefore include patients who would not be offered adjuvant therapy. Our data represent a more accurate estimate of eligible patient referral.

The data make it clear that uptake for patients with larger stage IB (≥4 cm) NSCLC is lower than that for patients with stages II or III disease. Lower rates of referral for the former group of patients have also been observed by other centres[13,20]. Subset analyses of the CALGB and JBR.10 trials were published after the major publications, and those analyses are discordant with a meta-analysis concluding lack of survival benefit for all patients with stage IB NSCLC[21]. It is unclear whether the observations reported here and by others about referral of stage IB patients represents a lack of knowledge of the subset analyses or questions about the validity of the data.

A further disease-related parameter relates to patients with complicated postoperative care. Our data suggest that patients hospitalized beyond 10 days (a surrogate for postoperative complications) are less likely to be referred for adjuvant therapy. Although some of those decisions may well be appropriate, it is still reasonable for this group of patients to meet with a medical oncologist to discuss available treatment options.

Our data suggest that surgeon decision was the major barrier to referral of patients for consideration of adjuvant therapy. The medical records for most of

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the study patients not referred contained no mention of the issue of adjuvant therapy. The rate of referral for consideration of adjuvant chemotherapy varied considerably between surgeons (range: 19%–100%). Explanations for that variability can be found in the knowledge-transfer literature. Rogers[22] describes stages of new knowledge adoption, in which a small proportion of early adopters are followed by most individuals. However, a proportion of late adopters show significant delays in taking up new knowledge. Our data suggest that 2 of the thoracic surgeons are late adopters of the adjuvant chemotherapy evidence. Recognition of that reality becomes important in considering strategies to implement physician change. Compare with other physicians, late adopters may well require different approaches to prompt a change in behavior.

Our knowledge-translation strategy was based on literature, including a Cochrane review, identifying audit-and-feedback interventions combined with educational outreach meetings as an effective means of changing physician practice[17–19,23]. The feedback session provided important insight into solutions to changing practice. There was clear acceptance of the evidence for adjuvant chemotherapy—and for the validity of our study's principal finding. Our session was therefore able to focus on developing strategies to bring about change. First, a belief was expressed that the situation may already have changed, although that belief is not strongly supported by provincial data. Greater discussion of cases in the setting of a multidisciplinary case conference may help to achieve more appropriate patient selection. Creation of a surgical database should allow for periodic monitoring of referral rates. Lastly, expansion of an existing nurse navigator role provides real-time monitoring of patient referrals and provides a safety net to ensure appropriate and timely referral.

Our study does have limitations. First, the number of patients was relatively small, and so formal statistical comparisons were not possible. The retrospective nature of the study makes it difficult to accurately classify reasons for non-referral for adjuvant therapy. Extraction of data from the medical record did not allow for a detailed assessment of patient factors such as distance from the cancer clinic and availability of transportation, for which prospective data collection would be required. A high proportion of the study patients received a wedge resection rather than a lobectomy. It is possible that those patients were less fit and were not referred for chemotherapy for that reason. However, variability in preoperative assessment and staging, including invasive staging of the mediastinum might also reflect quality-of-care concerns. Our study did not allow for a formal assessment of logistics issues such as differences in support staff, residents, or research staff. However, no obvious differences in those factors were observed. Finally, as the surgeons indicated during the feedback session, the data represent patient care in 2008 and may not be generalizable to the current patient population. The 7th edition of the TNM staging classification has been implemented, reclassifying many of the larger stage IB tumours into stage II[24,25]. That change might potentially influence referral rates. However, the earlier time period allowed us to collect follow-up information, which suggested that rates of recurrence were higher among patients not referred for consideration of adjuvant therapy.

Our research has provided important insights into local patterns of practice for patients with resected lung cancers, but it is important to appreciate the need to close the loop in the quality improvement cycle[26,27]. An integral part in our audit-and-feedback strategy is to reassess referral rates as a follow-up to our intervention. Although a clear intention to change practice was expressed, it is essential to document an actual change in practice in response to our knowledge translation initiative.

5. ACKNOWLEDGMENTS

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6. CONFLICT OF INTEREST DISCLOSURES

PME and JAZ have no relevant financial disclosures to make.

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