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ORIGINAL ARTICLE

Factors associated with referral to medical oncology and subsequent use of adjuvant chemotherapy for non-small-cell lung cancer: a population-based study

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ABSTRACT

Background

Adjuvant chemotherapy (ACT) for non-small-cell lung cancer (NSCLC) is associated with improved survival in the general population, but may be underutilized. We explored the factors associated with referral to medical oncology and subsequent use of ACT among all patients with resected NSCLC in Ontario, Canada.

Methods

The Ontario Cancer Registry was used to identify all incident cases of NSCLC diagnosed in Ontario during 2004–2006. We linked electronic records of treatment and of physician billing to identify surgery, ACT, and medical oncology consultation. A multivariate logistic regression model was used to evaluate factors associated with referral to medical oncology and subsequent use of ACT.

Results

Among 3354 cases of NSCLC resected in Ontario during 2004–2006, 1830 (55%) were seen postoperatively by medical oncology, and 1032 (31%) were treated with ACT. Patients more than 70 years of age were less likely than younger patients to have a consultation [odds ratio (OR): 0.4; $p < 0.001$]. A higher proportion of cases with stage II or III NSCLC than with stage I disease were referred (ORs: 2.7, 2.0 respectively; $p < 0.005$). We observed substantial geographic variation in the proportion of surgical cases referred (range: 32%–88%) that was not explained by differences in case mix. Among cases referred to medical oncology, older patients (age 60–69 years, OR: 0.4; age 70+ years, OR: 0.1; $p < 0.001$) with greater comorbidity (Charlson comorbidity index: 3+; OR: 0.5; $p < 0.05$) and a longer postoperative stay (median length of stay: 7+ days; OR: 0.7; $p = 0.001$) were less likely to receive ACT. Use of ACT was greater in patients with stage II or III than with stage I disease (ORs: 3.0, 2.7 respectively; $p < 0.001$); use also varied with geographic location (range: 46%–63%).

Conclusions

The initial decision to refer to medical oncology is associated with age and stage of disease, and those factors have an even greater effect on the decision to offer ACT. Comorbidity and postoperative length of stay were not associated with initial referral, but were associated with use of ACT in patients seen by medical oncology.

KEY WORDS

Lung cancer, chemotherapy, health services research, outcomes, oncology

1. INTRODUCTION

Lung cancer remains the leading cause of cancer mortality in both men and women, being responsible for approximately 100,000 deaths annually in North America [1]. Despite advances in surgical technique, 5-year survival rates for stages I and II non-small-cell lung cancer (NSCLC) are only 60%–70% and 35%–40% respectively [2]. Since the year 2000, several clinical trials and a subsequent meta-analysis have demonstrated that cisplatin-based adjuvant chemotherapy (ACT) improves survival in patients with resected early-stage NSCLC [3–8].

In our previous study of the uptake of ACT during 2001–2006 in the Canadian province of Ontario, we found that toxicity and survival in a general population are what might be expected based on the results of the pivotal clinical trials [9]. In that previous work, we found that 22% of all incident cases underwent surgical resection and that 31% of surgical cases were treated with ACT [9]. Those rates of surgical resection and ACT suggest that ACT may be underutilized in patients with early-stage NSCLC. Underutilization

may relate to any combination of lack of referral from surgeon to medical oncology, oncologists not offering ACT, or patients declining ACT. Other reports have identified factors associated with utilization of surgery and chemotherapy for NSCLC [10–20], but many of those studies are limited by selection and referral biases, and only a handful described cancer treatment as a multi-step process that relies on upstream decisions made by referring physicians. Here, we explored factors associated with referral to medical oncology and the subsequent use of ACT among all patients with resected NSCLC in Ontario, Canada.

2. METHODS

2.1 Study Design and Population

This report constitutes a sub-study of a larger population-based retrospective cohort study that compared management and outcomes of early-stage NSCLC in the Canadian province of Ontario before and after 2004. Detailed methods and primary results were reported previously [9]. Ontario has a population of approximately 13.2 million people and a single-payer universal health insurance program [21]. The primary study population for the present report included all incident patients with NSCLC diagnosed in Ontario during 2004–2006 who underwent surgical resection within 24 weeks of diagnosis. The study was approved by the Research Ethics Board of Queen's University.

2.2 Data Sources

The Ontario Cancer Registry (OCR) is a passive, population-based cancer registry that captures diagnostic and demographic information for at least 98% of all incident cases of cancer diagnosed in the province of Ontario [22,23]. The OCR provided the following information:

- International Classification of Diseases (version 9) code
- International Classification of Diseases for Oncology histology code
- Age
- Sex
- Place of residence

The OCR does not compile information about extent of disease or treatment. Community-based socioeconomic status (SES) at the time of diagnosis was linked to the OCR as previously described [24].

Records of hospitalization from the Canadian Institute for Health Information provided information about surgical interventions and hospital care [25]. Physician billing codes for chemotherapy from the Ontario Health Insurance Plan database were linked to the study database to identify the patients that received chemotherapy and their dates of treatment. The clinical databases of Ontario's regional cancer centres and Princess Margaret Hospital provided detailed additional records of chemotherapy delivered, including specific treatment regimens and dose information for approximately half the patients, as previously described [9]. Stage of disease at diagnosis is routinely captured only for patients seen at regional cancer centres.

2.3 Variable Definitions

Comorbidity was classified using the Charlson comorbidity index modified for administrative data, based on all non-cancer diagnoses recorded on any hospital admission for the study patients within 5 years before surgery [26,27].

Surgical resection was defined as pneumonectomy, lobectomy, or segmentectomy. To minimize error attributable to the miscoding of surgical procedures, a minimum length of stay was set at 3 days. Patients who died within that period remained in the study population to account for early postoperative deaths. Patients were classified as having surgery for NSCLC if they underwent surgery within 24 weeks of diagnosis. Patients receiving preoperative chemotherapy or radiotherapy (or both) were removed from the surgical population.

No single available administrative data source allows for the identification of medical oncologists in Ontario. Accordingly, as a proxy measure of medical oncologists, we identified 235 physicians who submitted billing records for NSCLC ACT during 2004–2006. Each surgical patient was considered to have been seen by a medical oncologist in the postoperative setting if any of the identified physicians submitted visit billing codes for that patient within 16 weeks after surgery. Adjuvant chemotherapy was defined as any chemotherapy delivered within 16 weeks after surgery.

2.4 Statistical Analysis

The primary objective of the study was to describe the factors associated with use of ACT among patients with resected NSCLC. To determine the extent to which referral practices influenced the odds of receiving ACT, we report factors associated with referral to medical oncology. Among patients seen by medical oncology, we report factors associated with the use of ACT. These distinct analyses evaluate the two fundamental steps required for a patient to be treated with ACT: an initial consultation with a medical oncologist, followed by a decision made between oncologist and patient about whether to proceed with ACT.

Factors associated with seeing a medical oncologist after surgery and receiving ACT were evaluated by univariate and multivariate logistic regression. Predictors were considered statistically significant at $p < 0.05$. All analyses were performed using the

SAS software application (version 9.1: SAS Institute, Cary, NC, U.S.A.).

3. RESULTS

During 2004–2006, 15,184 incident cases of NSCLC were diagnosed in Ontario, and 3354 patients had surgery. Table I shows the characteristics of the study population and the treatment groups. Among surgical cases, most patients (77%) were 60 years of age or older and had adenocarcinoma (55%) or squamous histology (30%). Patients with NSCLC were more likely to live in poorer neighborhoods (that is, SES quintiles 1 and 2) than in affluent communities (that is, SES quintiles 4 and 5).

As shown in Figure 1, 55% of surgical patients (1830 of 3354) were seen by a medical oncologist in the postoperative period, and 31% (1032 of 3354) were treated with ACT. Of patients not treated with ACT, 65% (1502 of 2322) were not referred to a medical oncologist. Of cases treated with ACT, 2% (22 of 1032) were not seen by a medical oncologist as determined under our study rules.

Table II shows results of the multivariate analysis to evaluate factors associated with referral to medical oncology. Patients more than 70 years of age were less likely than younger patients to have a consultation [odds ratio (OR): 0.4; $p < 0.001$]. A higher proportion of patients with stage II or III NSCLC than with stage I disease were seen by oncologists (OR: 2.7 and 2.0 respectively; $p < 0.005$). Patients who underwent pneumonectomy were more likely to be referred than were patients who underwent lobectomy (OR: 1.4; $p < 0.05$). We observed substantial geographic variation in the proportion of surgical cases referred to medical oncology (range: 32%–88%) that was not explained by differences in patient demographics or comorbidity.

Among referred cases, older patients (age 60–69 years, OR: 0.4; age 70+ years, OR: 0.1; $p < 0.001$) with

TABLE I Characteristics of patients with non-small-cell lung cancer who were diagnosed in Ontario during 2004–2006 and who underwent surgical resection, with the proportions referred to medical oncology and treated with adjuvant chemotherapy (ACT)

Characteristic	*Case group*[a] *[*n *(%)]*		
	Surgical	*Referred to medical oncology*[b]	*Treated with ACT*[c]
Patient-related			
Patients	3354	1830	1032
Sex			
Male	1718	913 (53)	502 (55)
Female	1636	917 (56)	508 (55)
Age			
20–49 Years	180	125 (69)	96 (77)
50–59 Years	601	407 (68)	290 (71)
60–69 Years	1078	628 (58)	388 (62)
70+ Years	1495	670 (45)	236 (35)
SES quintile[d]			
1	717	361 (50)	201 (56)
2	783	437 (56)	269 (62)
3	718	391 (54)	203 (52)
4	603	329 (55)	172 (52)
5	529	309 (58)	163 (53)
Unavailable	4	—	—
CCI score			
0	2460	1392 (57)	802 (58)
1–2	764	384 (50)	189 (49)
3+	130	54 (42)	19 (35)
Disease-related			
Histology			
Adenocarcinoma	1830	1005 (55)	547 (54)
Squamous carcinoma	1018	531 (52)	293 (55)
Large-cell carcinoma	72	37 (51)	21 (57)
Mixed	102	64 (63)	36 (56)
Carcinoma NOS	332	193 (58)	113 (59)
Pathologic stage			
I	581	437 (75)	208 (48)
II	281	250 (89)	180 (72)
III	215	186 (87)	126 (68)
IV	128	105 (82)	45 (43)
Unknown	2149	852 (40)	451 (53)
System-related			
Geographic region of Ontario			
A	1386	763 (55)	412 (54)
B	502	160 (32)	101 (63)
C	291	173 (59)	108 (62)
D	335	203 (61)	93 (46)
E	73	64 (88)	32 (50)
F	106	81 (76)	37 (46)
G	207	120 (58)	76 (63)
H	452	264 (58)	151 (57)
Unavailable	2	—	—

[a] "Surgical" include patients who underwent surgical resection; "referral to medical oncology" includes surgical patients who were seen by a medical oncologist within 16 weeks after surgery; "treatment with ACT" includes surgical patients who started adjuvant chemotherapy within 16 weeks after surgery.

[b] Percentages reflect the proportion of all surgical patients seen by medical oncology. Proportions may not add to 100% because of rounding.

[c] Percentages reflect the proportion of all patients seen by medical oncology who were treated with ACT. Proportions may not add to 100% because of rounding.

[d] SES quintile 1 represents patients from the poorest communities in Ontario. Proportions may not add to 100% because of rounding.

SES = socioeconomic status; CCI = Charlson comorbidity index; NOS = not otherwise specified.

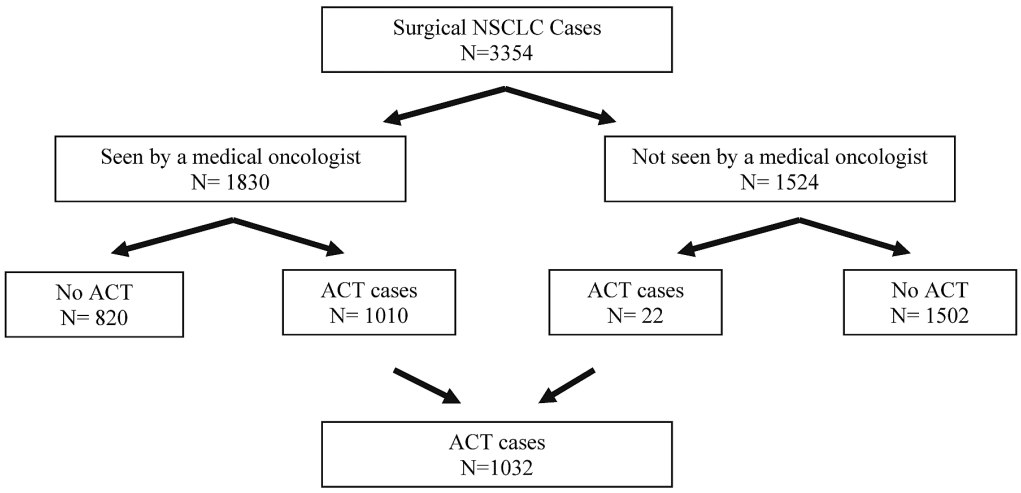

FIGURE 1 Care pathway for all patients with non-small-cell lung cancer (NSCLC) who were diagnosed in Ontario during 2004–2006 and who underwent surgical resection. ACT = adjuvant chemotherapy.

greater comorbidity (Charlson comorbidity index 3+, OR: 0.5; $p < 0.05$) and a longer postoperative stay (median length of stay 7+ days, OR: 0.7; $p = 0.001$) were less likely to receive ACT. Use of ACT was greater in patients with stage II or III than with stage I disease (OR: 3.0 and 2.7 respectively; $p < 0.001$). Patients who underwent pneumonectomy were more likely than patients who underwent lobectomy to receive ACT (OR: 1.5; $p < 0.05$). Among patients seen by medical oncology, some geographic variation was evident in rates of ACT utilization (range: 46%–63%).

As shown in Table II, there was a consistent association of younger age, less comorbidity, extent of surgery, and earlier stage of disease for each of the two steps in the care pathway. Age and comorbidity had a greater association with use of ACT among patients seen by medical oncology and a lesser effect on referral patterns. Furthermore, postoperative length of stay was associated with use of ACT, but not with pattern of referral to medical oncology. Conversely, although there was substantial regional variation in referral patterns to medical oncology among all surgical cases (range: 32%–88% referral rates), regional variation in the use of ACT was of a lesser magnitude among patients actually seen by medical oncology (range: 46%–63% use of ACT).

4. DISCUSSION

Clinical trials and evidence-based guidelines have demonstrated that curative-intent therapy for early-stage NSCLC includes surgical resection of the primary tumour and consideration of cisplatin-based ACT [4]. Beyond the evidence and treatment guidelines, a multitude of complex patient-, disease-, and system-related factors determine the care of patients with cancer.

In this large population-based study, we explored the factors associated with two steps in the care pathway after surgical resection: namely, referral to medical oncology and administration of ACT. Several important findings emerged. First, 22% of incident patients undergo surgical resection. After surgery, only 55% of those surgical patients see a medical oncologist and only 31% receive ACT. Those observations mean that, in Ontario, only 7% of all incident cases of NSCLC received curative-intent surgery and adjuvant chemotherapy. Furthermore, among surgical patients not treated with ACT, 65% never saw a medical oncologist in consultation. Age, stage of disease, comorbidity, and extent of surgery are associated with each step of care, but age, comorbidity, and postoperative length of stay appear to have more influence over the decision at the medical oncology and patient levels to use ACT than over the decision by surgeons to refer to oncology. Finally, large regional differences in practice, evident at both steps in the care pathway, are not explained by differences in patient demographics or comorbidity. Our data suggest that the regional differences are driven to a greater extent by upstream differences in referral rates to medical oncology than by treatment decisions at the consultant–patient level. It is possible that the discordant referral patterns and treatment rates across geographic regions reflect the fact that physicians and centres may interpret the evidence and magnitude of benefit associated with ACT quite differently.

The literature exploring factors associated with referral to medical oncology and use of ACT among patients with resected NSCLC is limited. A study by Winget *et al.* [28] that included 561 patients with stage IB and II NSCLC diagnosed in Alberta during 2004–2006 found that advanced age and rural residence were inversely associated with the likelihood of attendance at a consultation with a medical oncologist. Among the 226 patients who saw a medical oncologist, ACT was not recommended in 25% of cases, and it was refused by

TABLE II Factors associated with referral to medical oncology (MO) and with use of adjuvant chemotherapy (ACT) after MO referral in patients with non-small-cell lung cancer who were diagnosed in Ontario during 2004–2006 and who underwent surgical resection (n = 3354)

Factor	*Referred to MO*				*Treated with ACT*			
	Proportion referred after surgery (%)[a]	*Multivariate analysis*			*Proportion treated after referral (%)*	*Multivariate analysis*		
		OR	*95% CI*	p *Value*		*OR*	*95% CI*	p *Value*
Patient-related								
Sex								
Male	53	Ref			55	Ref		
Female	56	1.1	1.0 to 1.3	0.175	55	0.9	0.8 to 1.2	0.518
Age								
20–49 Years	69	Ref			77	Ref		
50–59 Years	68	1.1	0.7 to 1.6	0.766	71	0.7	0.4 to 1.1	0.158
60–69 Years	58	0.7	0.5 to 1.0	0.078	62	0.4	0.3 to 0.7	<0.001
70+ Years	45	0.4	0.3 to 0.7	<0.001	35	0.1	0.1 to 0.2	<0.001
SES quintile[b]								
1	50	Ref			56	Ref		
2	56	1.3	1.0 to 1.6	0.034	62	1.4	1.0 to 1.9	0.045
3	54	1.2	0.9 to 1.5	0.139	52	0.8	0.6 to 1.1	0.114
4	55	1.2	1.0 to 1.6	0.085	52	0.8	0.6 to 1.1	0.171
5	58	1.3	1.0 to 1.7	0.069	53	0.8	0.6 to 1.1	0.173
CCI score								
0	57	Ref			58	Ref		
1–2	50	0.9	0.7 to 1.1	0.260	49	0.9	0.7 to 1.2	0.557
3+	42	0.7	0.5 to 1.0	0.077	35	0.5	0.2 to 0.9	0.015
Disease-related								
Histology								
Adenocarcinoma	55	Ref			54	Ref		
Squamous carcinoma	52	1.0	0.8 to 1.2	0.937	55	1.1	0.9 to 1.4	0.483
Large-cell carcinoma	51	0.9	0.6 to 1.6	0.826	57	1.1	0.5 to 2.3	0.749
Mixed	63	1.3	0.8 to 2.1	0.253	56	1.1	0.6 to 1.9	0.796
Carcinoma NOS	58	1.5	1.1 to 1.9	0.007	59	1.1	0.8 to 1.6	0.466
Pathologic stage								
I	75	Ref			48	Ref		
II	89	2.7	1.8 to 4.2	<0.001	72	3.0	2.1 to 4.3	<0.001
III	87	2.0	1.2 to 3.1	0.004	68	2.7	1.8 to 4.0	<0.001
IV	82	1.4	0.8 to 2.3	0.248	43	0.7	0.4 to 1.1	0.114
Unknown	40	0.2	0.2 to 0.2	<0.001	53	1.3	1.0 to 1.8	0.048
Treatment-related								
Surgery								
Lobectomy	54	Ref			54	Ref		
Segmentectomy	51	0.9	0.7 to 1.0	0.091	49	0.8	0.6 to 1.0	0.050
Pneumonectomy	65	1.4	1.1 to 1.8	0.011	70	1.5	1.1 to 2.1	0.016
Median LOS following surgery								
0–6 Days	55	Ref			61	Ref		
7+ Days	54	1.1	0.9 to 1.2	0.528	49	0.7	0.6 to 0.9	0.001
System-related								
Geographic region of Ontario								
A	55	Ref			54	Ref		
B	32	0.2	0.2 to 0.3	<0.001	63	1.2	0.8 to 1.8	0.386
C	59	0.5	0.4 to 0.7	<0.001	62	1.3	0.9 to 2.0	0.171
D	61	0.7	0.5 to 1.0	0.038	46	0.5	0.3 to 0.7	<0.001
E	88	2.4	1.1 to 5.0	0.024	50	0.9	0.5 to 1.6	0.759
F	76	1.1	0.6 to 1.8	0.773	46	0.7	0.4 to 1.3	0.266
G	58	0.8	0.6 to 1.1	0.208	63	1.2	0.8 to 1.8	0.473
H	58	0.7	0.6 to 0.9	0.014	57	1.1	0.8 to 1.5	0.748

[a] Seen by a medical oncologist within 16 weeks after surgery.
[b] SES quintile 1 represents patients from the poorest communities in Ontario.
OR = odds ratio; CI = confidence interval; Ref = reference group; SES = socioeconomic status; CCI = Charlson comorbidity index; NOS = not otherwise specified; LOS = length of stay.

patients in 13% of cases [15]. Kassam *et al.* [29] described patterns of referral and use of ACT at the University Health Network or Princess Margaret Hospital in Toronto during 2003–2005. Among the 204 patients with resected early-stage NSCLC, referral to oncology increased to 63% in 2004–2005 after presentation of the JBR.10 and Cancer and Leukemia Group B results at the 2004 annual meeting of the American Society of Clinical Oncology. Among patients seen by medical oncology after presentation of those results, 54% were treated with ACT—a proportion that is remarkably similar to the result of 55% in the present study. A third Canadian study led by Younis [30] reported referral rates and use of ACT among patients with resected NSCLC in Nova Scotia during 2005. Of the 108 patients with resected early-stage disease, 44% were referred to medical oncology (73% of patients with stage II or III disease), and ACT was delivered to 62% of those referred (73% of patients with stage II or III disease. Consistent with the results from Winget *et al.* and from the present study, age, stage, and centre or regional variation were found to have an effect on referral patterns and treatment practices. Data from a single-centre report in Paris are consistent with the Canadian studies: among 219 patients with resected NSCLC in 2004–2005, ACT was delivered to 40% [31]. Age, stage, and comorbidity were found to influence patterns of treatment.

Consistent across the present and the foregoing studies is the observation that older age is associated with lower rates of referral to medical oncology and lower rates of ACT use. Although part of the differential might relate to greater comorbidity and patient preference, it is also possible that surgeons and medical oncologists might believe the survival benefit to be less and the toxicities greater in elderly patients treated with ACT. However, recent data from clinical trials and population-based studies suggest that ACT for NSCLC is well tolerated and associated with a survival benefit in elderly patients [32–34]. However, patients who meet the eligibility criteria for clinical trials might not be representative of the overall lung cancer population.

Our study is the largest reported to date to evaluate factors influencing referral to medical oncology and use of ACT in a contemporary population, but several methodologic limitations merit comment. Although the data sources used describe the general aspects of disease, treatment, and outcome for all patients in Ontario, detailed information related to chemotherapy administration, treatment toxicity, performance status, and stage of disease is not available for all patients. That lack of detail limits our ability to evaluate the appropriateness of case selection for ACT. Furthermore, our data do not allow us to understand which patients may have refused referral or ACT after referral, and why those patients elected not to pursue aggressive cancer care despite the potential for an increased cure rate. Furthermore, because medical oncologists are not explicitly identified in the current health administrative databases used in our study, we had to use surrogate measures to identify those physicians, which might have led to some misclassification error. However, the data suggest that our approach has good face validity, because 98% of cases receiving ACT were classified as having seen medical oncology.

The lack of information about pathologic stage makes it difficult to understand the degree to which low referral rates and underutilization of ACT is a problem in Ontario. The published literature contains very few population-based studies that describe stage distribution among unselected patients with NSCLC who undergo surgical resection. In one of the only such studies, Strand *et al.* [35] used a population-based national cancer registry to describe stage distribution for 2411 NSCLC patients who underwent surgical resection in Norway during 1993–1999. Stage IB, II, and IIIA disease was identified in 38%, 25%, and 6% of patients respectively. Extending those estimates to the Ontario NSCLC surgical population in 2004–2006 would yield approximately 2314 patients with stage IB, II, or IIIA disease, all of whom would potentially be considered eligible for ACT. Yet our study demonstrates that only 1830 patients were referred to medical oncology and only 1032 received ACT, suggesting that a substantial proportion of patients potentially eligible for ACT based on stage were not being referred or treated. Although it is likely that the distribution of disease stage among resected patients in Norway during 1993–1999 is different from the distribution in Ontario during 2004–2006, the projected figures provide a starting point for estimating the unknown denominator of potential ACT-eligible cases in the province. Stage of disease is now routinely captured in Ontario for all cases of NSCLC (https://www.cancercare.on.ca/cms/One.aspx?portalId=1377&pageId=48174). Accordingly, future work will be able to identify the number of stage IB, II, and IIIA cases more accurately in Ontario and will generate benchmark estimated utilization figures for the province.

Not all patients who undergo potentially curative surgical resection will be eligible for ACT. No survival benefit has been demonstrated for small stage I cancers [6], and so it may be totally appropriate for surgeons to make a decision not to refer that subgroup of patients. Similarly, given that NSCLC is a disease of the elderly, not all patients might be able to tolerate ACT because of greater comorbidity. However, it is worth noting that pooled data from clinical trials [34] and a population-based study [32] have both demonstrated improved outcomes in elderly patients treated with ACT. In the present population-based study, age and comorbidity index both had a significant influence on referral and treatment patterns. But what cannot be gleaned from our study is whether the decision not to refer to oncology and not to offer ACT to the entire eligible elderly population or to those with comorbidities was indeed the correct one. Only a more

intensive chart review would be able to determine whether patients who are fit enough for treatment are truly being denied ACT by lack of referral. Similarly, our population-based study could not identify the subset of patients who were offered referral and ACT, but who declined treatment.

In addition to its very large sample size and resulting statistical power, a major strength of the current study is the fact that, by virtue of the OCR, our study population included all cases of NSCLC within Ontario. Being unselected, it therefore represents the largest such study of ACT for NSCLC in the contemporary era. By including the entire population of interest, it is possible to minimize the referral and selection biases that plague traditional institution-based observational studies [36].

5. CONCLUSIONS

We observed important differences in the rates of referral to medical oncology and use of ACT across age groups and across regions of Ontario that are not explained by differences in patient characteristics. Among all surgical cases, a substantial proportion are not being referred to medical oncology and are therefore not being given full consideration for ACT. Differences across geographic regions appear to be greatest upstream, at the decision about whether to refer to medical oncology. Further work is necessary to understand referral patterns and treatment rates in a more current era and to better understand how patient preference and physician recommendation influence those differences in care. Strategies to mitigate potentially modifiable differences in care and their impact on outcomes at the population level are needed.

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7. CONFLICT OF INTEREST DISCLOSURES

CMB is supported as a Cancer Care Ontario Research Chair in Health Services. FAS holds the Scott Taylor Chair in Lung Cancer Research at Princess Margaret Hospital. GD holds the Kress Family Chair in Esophageal Cancer at the Princess Margaret and Toronto General hospitals. The present study was supported by the Institute for Clinical Evaluative Sciences, which is funded by an annual grant from the Ontario Ministry of Health and Long-Term Care. The opinions, results, and conclusions reported here are those of the authors and are independent from the funding sources. No endorsement by Institute for Clinical Evaluative Sciences or the Ontario Ministry of Health and Long-Term Care is intended or should be inferred.

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