

Brief Report: Medical Assistance in Dying in Patients With Lung Cancer



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ABSTRACT

Introduction: Medical assistance in dying (MAiD) was legalized in Canada in 2016. Cancer accounts for 60% to 65% of MAiD cases. Lung cancer, the most common cause of cancer death, is expected to make up a large number of MAiD cases. Lung cancer treatment has advanced in recent years; however, involvement of oncology specialists and use of systemic therapy in patients who receive MAiD are unknown.

Methods: All patients with lung cancer referred to the Champlain Regional MAiD Program from June 17, 2016, to November 30, 2020, were reviewed. Baseline demographics, diagnostic, referral, and treatment details were collected by retrospective review. Coprimary end points were the proportion of patients who met a medical oncologist or who received systemic therapy.

Results: During the study period, 255 patients with cancer underwent MAiD. Of these, 45 (17.6%) had lung cancer, comprising our final study population. Baseline characteristics: median age 72 years, 64% female, 85% former or current smoking history, 82% non-small cell, 4% small cell, and 13% clinical diagnosis without biopsy. Most patients (78%) were seen by a medical oncologist, though only 16 (36%) received systemic therapy for advanced disease. In subpopulations of interest, 45% of patients with programmed death-ligand 1 greater than or equal to 50% received immunotherapy and 75% with an oncogenic driver mutation received targeted therapy. There were 26 patients (58%) who had a documented discussion with their oncologist regarding the transition to best supportive care.

Conclusions: Most patients with lung cancer are assessed by an oncology specialist before MAiD, though less than half received systemic therapy. Among patients with more treatable forms of lung cancer, many patients still undergo MAiD without accessing, or in some cases being assessed for, these treatment options.

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Keywords: Lung cancer; End of life care; Assisted suicide; Canada

Introduction

On June 17, 2016, legislation was enacted in Canada legalizing medical assistance in dying (MAiD). Since that time, adults with a “grievous and irremediable” medical condition are able to access an assisted death provided by a medical or nurse practitioner.¹

Cancer accounts for most of the MAiD cases, both in Canada and in other jurisdictions where MAiD is legal.^{2,3} Lung cancer, as the most common cause of cancer death, is expected to make up a substantial proportion of MAiD cases.⁴

In the past decade, there have been significant advances in the treatment of lung cancer, with emphasis on

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targeted therapy and immunotherapy, making treatment both more effective and more tolerable.^{5,6} Previous studies on MAiD in patients with cancer suggest that most patients are engaged with palliative care services leading up to MAiD^{2,7}; however, the involvement of medical oncologists and use of systemic therapy are unknown. As part of the MAiD assessment process, patients must be informed of all “means that are available to relieve their suffering.”¹ For patients with lung cancer, a medical oncologist is in a key position to provide this information.

We performed a review of all patients with lung cancer who underwent MAiD in our region to identify the demographic and treatment factors in this population and to evaluate for any gaps in our current system of care delivery.

Materials and Methods

A retrospective review was completed of all patients with cancer who received MAiD through the Champlain Regional MAiD Network (CRMN) from June 17, 2016, to November 30, 2020. There was a gap from September 2018 to April 2019 owing to changeover in the recording system used by the CRMN. This program provides most of the MAiD services within the Champlain Local Health Integration Network, covering a population of 1.3 million people in eastern Ontario, Canada. This area largely overlaps with the catchment area for the tertiary care Ottawa Hospital Cancer Centre, the sole provider of oncology services in this population.

Cases were obtained from the CRMN database, which contains information on all MAiD provisions performed through the CRMN. Cases were filtered to identify those with lung cancer as the condition leading to MAiD request. Baseline demographic factors, diagnostic information, and treatment details were collected using retrospective review of the Ottawa Hospital electronic medical records.

The coprimary end points of this descriptive study were the proportion of patients seen by a medical oncologist within 90 days of death and the proportion of patients who received any systemic therapy for advanced disease.

This study was approved by the Institutional Research Ethics Board. As a retrospective review, no patient consent was required.

Results

During the study period, 255 patients with cancer underwent MAiD. Of these, 45 (17.6%) had lung cancer, comprising our final study population. Baseline characteristics are described in Table 1. There were a larger proportion of female compared with male patients (64%

Table 1. Baseline Characteristics of Study Population

Baseline Characteristic	No. Patients (N = 45)	%
Median age at diagnosis (y, range)	72 (55-91)	
Sex		
Male	16	36
Female	29	64
Marital status		
Common-law/married	12	27
Widowed	11	24
Separated	5	11
Single	10	22
Unknown	7	16
Smoking history		
Never	5	11
Former	22	49
Current	16	36
Unknown	2	4
Histologic type		
Adenocarcinoma	29	64
Squamous cell	6	13
NSCLC NOS	2	4
Small cell	2	4
No biopsy (clinical diagnosis)	6	13
Stage at death		
M0	3	7
M1	41	91
Unknown	1	2

NOS, not otherwise specified.

versus 36%). The most common histologic type was adenocarcinoma (n = 29, 64%), and there was a particularly small number of patients with SCLC (n = 2, 4%). A proportion of patients had a clinical diagnosis of lung cancer without a confirmatory biopsy (n = 6, 13%).

Of the 37 patients with biopsy-confirmed NSCLC, 33 (89%) had some biomarker testing performed (at least one of the following: programmed death-ligand 1 [PD-L1], EGFR, ALK, ROS1, KRAS, BRAF). PD-L1 status was negative (<1%), intermediate (1%–49%), high (≥50%), or unknown in two (5%), 10 (27%), 10 (27%), and 15 patients (40%), respectively. There were eight patients with confirmed oncogenic driver mutations (seven EGFR, one BRAF V600E).

Details regarding oncology specialist involvement are presented in Figure 1. Most patients (n = 40, 89%) had seen an oncology specialist at some point during their illness. Focusing on medical oncology, 29 (64%) had seen a medical oncologist within 90 days of death and 18 (40%) within 30 days of death. Just more than half of the patients (n = 26, 58%) had a documented discussion with an oncologist regarding the transition to best supportive care.

Treatment details are presented in Figure 2. Half of the patients had received radiation therapy for advanced disease (Fig. 2A). Only 16 (36%) received palliative

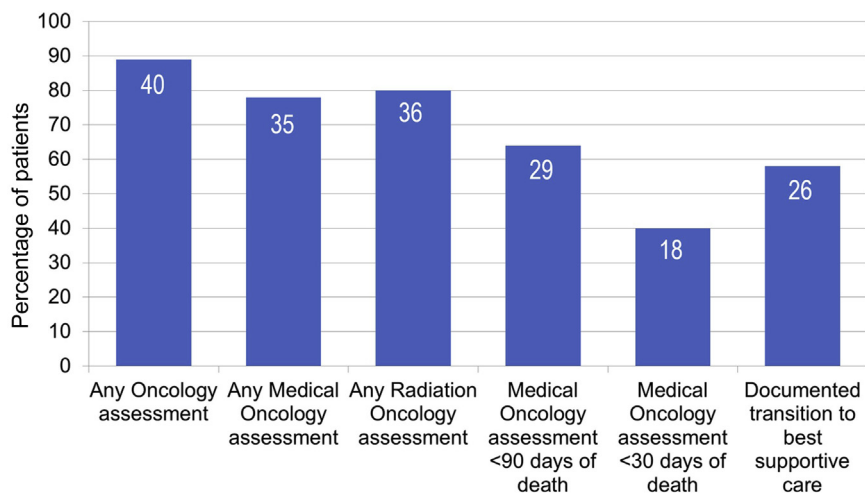


Figure 1. Involvement of oncology specialists before MAiD. MAiD, medical assistance in dying.

systemic therapy (Fig. 2B). In special populations of interest, four of nine patients (45%) with PD-L1 greater than or equal to 50% had received pembrolizumab immunotherapy (Fig. 2C) and six of eight patients (75%) with oncogenic driver mutations had received targeted therapy (Fig. 2D). Both patients with oncogenic driver mutations who did not receive targeted therapy had classical sensitizing EGFR mutations. Reasons for not receiving immunotherapy or targeted therapy included poor performance status, patient decision, and lack of medical oncologist.

Discussion

The option of a medically assisted death is becoming legal in an increasing number of jurisdictions around the world. In Canada, accessing an assisted death requires a formal assessment process with a number of safeguards. A request must be made in writing by the patient, and after this, two independent medical practitioners must agree that the patient meets all eligibility criteria, including the following: voluntary request, capable of giving informed consent, having a serious and incurable illness, irreversible decline in capability, and be experiencing enduring suffering. There is no requirement for practitioners who assess a patient for MAiD to have expertise in the condition causing the patient's suffering. During the study period, MAiD legislation required a patient's death be "reasonably foreseeable" to access MAiD; however, a specific timeline regarding prognosis was not required. A 10-day reflection period was required, unless the patient was at imminent risk of dying or losing capacity before that time.¹

To best of our knowledge, this study represents the first detailed report of patients with lung cancer who received MAiD. Lung cancer comprised 17.6% of all

MAiD deaths owing to cancer in our study, slightly lower than reported overall cancer death rates in which lung cancer makes up 25.5% of cancer deaths.⁸ We saw a higher proportion of female patients, which is a trend not found in other population-based lung cancer studies^{4,9-11} or studies of patients receiving MAiD.^{3,4} The difference in sex distribution may be due to small patient numbers; however, the trend is worth monitoring in future studies.

Similar to what is expected on the basis of the distribution of histologic subtypes of lung cancer in the general population, adenocarcinoma was the most common subtype. We noted a particularly small proportion of patients with SCLC at only 4%, compared with the expected rate of 12%.⁴ This could relate to the aggressive biology of SCLC, in which patients may deteriorate too quickly to undergo the formal assessment process for MAiD. The Canadian MAiD legislation was updated after the study period, now removing the 10-day reflection period for patients with a "reasonably foreseeable" death, and allowing final consent to be waived in specific circumstances.¹² It will be important to monitor if the trends regarding SCLC persist given this updated assessment process.

Among patients with NSCLC, most with pathologic confirmation of their malignancy had received at least one biomarker test. Although biomarker testing is recommended for all patients with NSCLC before embarking on systemic therapy,^{5,6} in real-world settings, this may not always be possible.⁹ Our biomarker testing results were affected by the time frame of the study, as EGFR was routinely tested in 2016, but PD-L1 was not universally added to our biomarker panel until 2018. We noted a proportion of patients who had a clinical diagnosis of lung cancer but declined a confirmatory biopsy and therefore did not have a detailed medical oncology

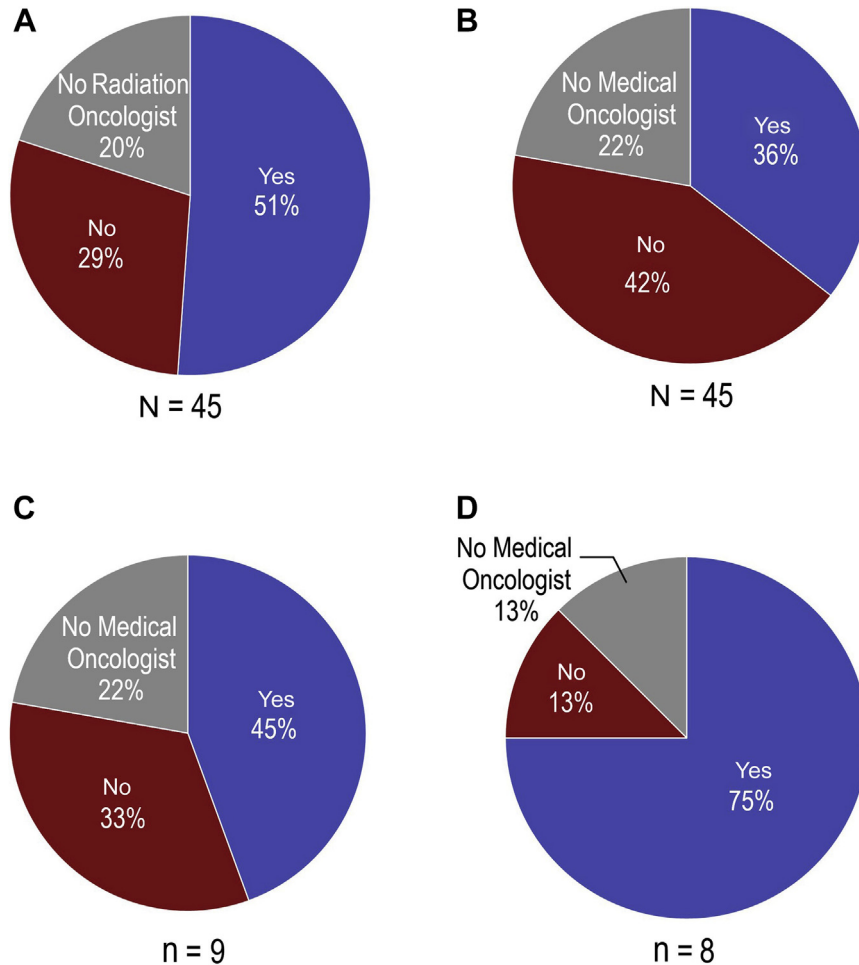


Figure 2. Treatment details. (A) Radiation therapy for advanced disease. (B) Systemic therapy for advanced disease. (C) Immunotherapy use for patients with PD-L1 greater than or equal to 50% (excludes one patient with PD-L1 high and a sensitizing *EGFR* mutation). (D) Targeted therapy for patients with targetable oncogenic driver mutations. PD-L1, programmed death-ligand 1.

assessment. This is a population wherein the role of circulating tumor DNA could be considered for driver mutation testing as a less invasive option to a traditional biopsy. This may help ensure that patients with a highly treatable oncogenic driver mutation are not missed before pursuing MAiD.

Most patients were assessed by an oncology specialist at some point during their disease course; however, approximately one in five patients did not have a medical oncology assessment at the time of diagnosis of advanced disease. Systemic therapy uptake was low in the overall population but did increase within the subgroup of patients with PD-L1 high disease or targetable oncogenic driver mutations. True population-based systemic therapy rates in lung cancer are difficult to estimate, as most published studies focus on the population of patients referred to an oncologist or cancer center with an uptake of 40% to 76% in these selected populations.^{10,11,13} With this in mind, the low systemic

therapy uptake in our population is not surprising, given our broad inclusion criteria that allowed, for example, patients without a biopsy diagnosis to be included. As well, patients who pursue MAiD may be philosophically more accepting of death and perhaps less likely to accept life-prolonging anticancer therapy.

The lack of medical oncologist involvement in more than 20% of patients is of some concern, especially for patients with more treatable forms of lung cancer. Within Canada, only 1.3% of MAiD provisions are performed by oncologists, despite the high proportion of MAiD cases being owing to cancer.² Although not a required element of reporting for MAiD deaths, a few of the providers indicated that consultation with the patient's oncologist was done before MAiD provision.² Requiring a formal consultation with a medical oncologist before MAiD for all patients with cancer is not supported by the current MAiD legislation.¹⁴ It is presumed that

medical practitioners performing assessments for MAiD will consult with other specialists as they see fit. Nevertheless, treatments for lung cancer are changing rapidly, and patients who in recent past would have been too unwell for or unwilling to receive cytotoxic chemotherapy may now be eligible for targeted therapy or other forms of systemic therapy. Therefore, we suggest that centers providing cancer care collaborate with MAiD providers to ensure a streamlined assessment process for patients, with consideration to expediting oncology consultations for patients expressing an imminent request for MAiD.

Our study is limited by its small sample size and retrospective nature. Its strengths lie in the detailed demographic and treatment information available for patients who receive MAiD, which has not been described before in the literature.

In conclusion, patients with lung cancer makeup a smaller proportion of cancer-associated MAiD cases compared with the population who died from lung cancer. An especially low rate of SCLC was found. Most patients were assessed by an oncology specialist, though less than half received systemic therapy. Given the growing complexity of treatment options in lung cancer, close collaboration between oncologists and MAiD providers is required to ensure that patients retain appropriate access to MAiD, while being fully informed of all their treatment options.

CRediT Authorship Contribution Statement

Sara Moore: Conceptualization, Methodology, Data curation, Formal analysis, Writing - original draft.

Chloé Thabet: Data curation, Writing - review & editing.

Paul Wheatley-Price: Conceptualization, Methodology, Writing - review & editing, Supervision.

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