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The importance of multidisciplinary team management of patients with non-small-cell lung cancer

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ABSTRACT

Historically, a simple approach to the treatment of non-small-cell lung cancer (NSCLC) was applicable to nearly all patients. Recently, a more complex treatment algorithm has emerged, driven by both pathologic and molecular phenotype. This increasing complexity underscores the importance of a multidisciplinary team approach to the diagnosis, treatment, and supportive care of patients with NSCLC. A team approach to management is important at all points: from diagnosis, through treatment, to end-of-life care. It also needs to be patient-centred and must involve the patient in decision-making concerning treatment. Multidisciplinary case conferencing is becoming an integral part of care. Early integration of palliative care into the team approach appears to contribute significantly to quality of life and potentially extends overall survival for these patients. Supportive approaches, including psychosocial and nutrition support, should be routinely incorporated into the team approach. Challenges to the implementation of multidisciplinary care require institutional commitment and support.

KEY WORDS

Non-small-cell lung cancer, multidisciplinary care

1. INTRODUCTION

Lung cancer is a major public health problem and the cause of the largest number of deaths from cancer in Canada, with approximately 25,500 new cases having been diagnosed and 20,600 deaths having occurred in 2011 [1]. Despite the magnitude of this health problem, significant stigmas are associated with a diagnosis of lung cancer [2,3]. Questions have even been raised about whether treatment should be offered for a smoking-related illness. Historically, much nihilism surrounds the effectiveness of systemic therapies, and only since the early 1990s has sufficient evidence been developed to support the routine use of chemotherapy for advanced non-small-cell lung cancer (NSCLC) [4].

Fortunately, significant advances in the management of NSCLC have been made since 2000. Data have emerged supporting not only first-, but also second- and third-line therapies [5–7]. Postoperative adjuvant therapy has become the standard of care for many patients with resected NSCLC [8,9]. Combined-modality treatment approaches—either chemoradiation [10] or trimodality treatments [11]—are widely adopted for well-functioning patients with locally advanced disease. Histologic differentiation of squamous from non-squamous disease has become a factor in treatment selection [12], and the discovery of molecular abnormalities in the *EGFR* (epidermal growth factor receptor) gene [13,14] and the *ALK* (anaplastic lymphoma kinase) gene [15] have led to treatment approaches driven by the molecular profile of tumours [16,17]. All of those changes have moved treatment from a simple approach applicable in most patients to a more complicated algorithm in which histology and molecular phenotype are important factors. This increasing complexity underscores the importance of taking a multidisciplinary approach to management that extends throughout the continuum of care from diagnosis to supportive and end-of-life care.

2. IMPORTANCE OF A MULTIDISCIPLINARY APPROACH TO LUNG CANCER

2.1 Diagnostic Assessment Clinics

Concerns have been raised about the potential for delays in the diagnosis of lung cancer and the high frequency of advanced disease at presentation. A prospective study of new lung cancer patients seen at the Juravinski Cancer Centre demonstrated that moving through the diagnostic process took patients approximately 4.5 months from onset of symptoms to commencement of treatment (Table I) [18]. Patients saw multiple specialists at separate appointments. Delays in completing diagnostic tests were often

TABLE I Summary of time delays experienced by lung cancer patients

	Period	*Delay (days)*	
		Median	*IQR*
T1	Time from initial symptoms to first presentation to a doctor	21	7–51
T2	Time from initial presentation to the last date of diagnostic testing ordered by the family physician	22	0–38
T3	Time from initial presentation to the first appointment with a specialist, either directly to the JCC or to a respirologist or thoracic surgeon	27	12–49
T4	Time between the initial appointment with the specialist and the last date of additional diagnostic testing	23.5	10–56
T5	Time from JCC referral to initial consultation	12	6–18
T6	Time from initial contact with a medical or radiation oncologist to the date of treatment start, defined as chemotherapy, radiation therapy, or the decision not to pursue treatment	10	2.5–28
T7	Global delay (overall time from onset of symptoms to commencement of definitive therapy)	138	79–175

IQR = interquartile range; JCC = Juravinski Cancer Centre.

compounded by the fact that tests were ordered sequentially by multiple physicians.

One solution to reduce delays in diagnosis is the implementation of diagnostic assessment clinics. Such clinics provide a single point of access for the assessment of patients with suspected cancer, with access to diagnostic services and multidisciplinary consultation in a single location [19]. A systematic review of studies evaluating diagnostic assessment clinics found that they reduce the time to diagnosis, which decreases patient anxiety and increases patient satisfaction [19]. Most of the studies were conducted in breast cancer assessment units, and yet the lessons learned appear highly relevant to the lung cancer population. Diagnostic or rapid assessment clinics for patients with suspected lung cancer are becoming increasingly common across Canada.

Multiple team members are required for a successful lung diagnostic assessment clinic. Nurse navigators, respirologists, thoracic surgeons, interventional radiologists, and pathologists have important roles in this scenario. Nurse navigators play a key role in patient triage, coordination of diagnostic tests, and assessment of the informational and psychosocial needs of the patients [20]. Respirologists and thoracic surgeons both have a role in the initial assessment of patients and in the procurement of diagnostic material. An additional role for the respirologist lies in the preoperative assessment of patients who are potential candidates for surgical resection. A review of institutional data suggests that diagnostic material (core biopsy or fine-needle aspirate) is obtained by interventional radiology in 30%–40% of cases [21]. Lastly, the pathologist has a crucial role in establishing the diagnosis of lung cancer.

A key issue in the success of such a process is communication between the members of the diagnostic assessment team. Previously, the key role of the pathologist was to reliably distinguish between small-cell lung cancer and NSCLC. In older treatment algorithms, there was little evidence of histologic subtype influencing treatment selection [22]. However, treatment algorithms for NSCLC now depend heavily on histologic subtype. Agents such as bevacizumab and pemetrexed are appropriate treatments only for patients with non-squamous histology. Appropriate use of molecularly targeted treatments such as gefitinib, erlotinib, and crizotinib rely on the availability of tissue for molecular testing. The use of predictive biomarkers to guide treatment selection for NSCLC is now a part of standard care, and Canadian consensus recommendations to guide the appropriate use of biomarkers in NSCLC have been published (Table II) [23]. It is crucial that respirologists, thoracic surgeons, interventional radiologists, and pathologists function as a team to ensure that appropriate amounts of diagnostic material are obtained in all patients to permit complete pathology diagnosis and molecular testing.

A further role for specialized lung diagnostic clinics will emerge over the coming years as screening for lung cancer becomes more commonplace. Data from the recently published National Lung Screening Trial [24] demonstrated that, among individuals at high risk for developing lung cancer, 3 annual screens with low-dose computed tomography can reduce the relative risk of death from lung cancer by 20%. A greater proportion of early-stage (and presumably operable) lung cancers were observed. However, radiologic abnormalities were seen on computed tomography in 18%–27% of participants annually. Those abnormalities require either diagnostic evaluation or close surveillance, generating a significant workload.

2.2 Multidisciplinary Care and Case Conferencing

Multidisciplinary meetings or case conferences (MCCs) are assuming increasing importance in the delivery of cancer care. Organizations such as Cancer Care Ontario have required implementation of MCCs as part of quality improvement initiatives. The goal of MCCs is to review individual patients and to make

TABLE II Key Canadian consensus recommendations on the use of biomarkers in the treatment of non-small-cell lung cancer[23]

1	There is strong evidence that histologic subtype is predictive of treatment efficacy or toxicity, or both.
2	In cases with equivocal morphologic features, routine stains for mucin (such as alcian blue or periodic acid Schiff) and immunohistochemistry stains, including those for thyroid transcription factor 1, p63, and cytokeratins 5 and 6, should be performed and their interpretation stated in the pathology report. The staining pattern should be used to favour adenocarcinoma or squamous cell carcinoma or to report the tumour as NSCLC "not otherwise specified" in cases with equivocal staining patterns.
3	Assessment of biomarkers in patients with non-small-cell lung cancer is likely to become increasingly important. Therefore it is recommended that adequate diagnostic material be obtained so as to perform appropriate testing for both histologic subtyping and biomarker assessment.
4	It is recommended that diagnostic lung cancer samples from patients with non-small-cell lung cancer be routinely tested for activating mutations of *EGFR*. Given the available clinical data, this testing should be limited to patients with advanced NSCLC and non-squamous histology. Testing should be completed in a licensed clinical molecular genetics laboratory. Mutation testing is most relevant to treatment decisions in the first-line therapy setting.
5	Given that no specific therapy is approved for *ALK*-associated NSCLC, routine assessment for this biomarker cannot be recommended at the present time. [Note: Since publication of the recommendations, crizotinib has received approval from the U.S. Food and Drug Administration. Testing for *ALK* translocations needs to be in place once Health Canada approval of crizotinib is received.]

recommendations about best management, but to keep in mind that individual physicians maintain ultimate responsibility for decision-making. Inherent in this process is the involvement of the patient in decision-making. The primary goal of MCCs is to improve patient outcomes, but improvements in a number of secondary outcomes could be attained as well (Table III)[25].

Implementation of MCCs has the potential to change treatment decisions. Baldwin *et al.*[26] reported an increase in the use of breast-conserving surgery for patients receiving a preoperative multidisciplinary assessment. Greer *et al.*[27] reported a change in management for 20% of cases reviewed in a multidisciplinary gyne-oncology tumour board. A systematic review of the literature identified multiple studies reporting an association between MCCs and improved survival[28]; however, methodologic limitations did not allow the authors to conclude that there was a causal association. Potential benefits for clinicians include increased evidence-based care, consideration of all treatment options, streamlined referrals, enhanced educational opportunities, collegial interaction, and improved access to clinical trials[29]. Patient benefits include improved survival, increased satisfaction, greater likelihood of receiving guideline-recommended treatment, increased access to information, and potentially more streamlined access to care[29].

Lung cancer MCCs bring together many health professionals, including thoracic surgeons, medical and radiation oncologists, radiologists, pathologists, and nurses, and may also include respirologists, nutritionists, social workers, and palliative care specialists. Little Canadian research on lung MCCs has been conducted, but data from a retrospective institutional review of a lung MCC in Australia showed that patients discussed in conference were more likely to receive chemoradiation and chemotherapy for advanced disease, and that they experienced longer survival than patients not presented at MCC[30]. It is hard to assess how selection bias may have influenced those conclusions.

TABLE III Functions of multidisciplinary case conferencing (MCC)[25]

- Discuss all appropriate investigations, treatment options, and recommendation for each patient presented at the MCC.
- Provide a forum for continuing education of health professionals
- Contribute to patient care, quality improvement activities, and practice audit.
- Contribute to the development of standardized patient management protocols.
- Contribute to innovation, research, and participation in clinical trials.
- Contribute to linkages between regions to ensure appropriate referrals and timely consultation to optimize patient care.

Despite the advantages of multidisciplinary care, uptake of MCCs is less than complete. An Australian survey suggests that only one third of hospitals have a multidisciplinary team[31]. An additional survey of lung cancer specialists in Australia reported that 91% of respondents indicated a need for moderate or significant improvement in at least one area of their MCC[32]. The challenge for the future is how to more fully integrate multidisciplinary care into the management of all patients with lung cancer.

2.3 Involving the Patient as Part of the Team

Poor communication can lead to adverse psychological outcomes for patients, including dissatisfaction with care, increased anxiety, and long-term maladjustment[33]. Promoting patient involvement in decision-making is an essential component of patient-centred care. Most patients expect to be fully informed about their disease[34,35], and most want to be actively or collaboratively involved in making treatment decisions[34,36]. Research demonstrates that, in practice, many patients fail to achieve their desired level of involvement in decision-making[37,38].

That failure may in part be explained by physicians not accurately assessing the preferences of their patients for involvement in the treatment decision-making process [39,40]. Patients whose perceived role in decision-making does not match their preferred role demonstrate more anxiety post-consultation than do patients who achieve a match [37]. Additionally, patients who perceive that they share decision-making responsibility with their physician express higher satisfaction with their encounter than do patients who report that they themselves or their doctor makes decisions. Data from a cohort of women with breast cancer indicate that women who are actively involved in decision-making at diagnosis demonstrate higher overall quality of life (QOL) 3 years after diagnosis [38].

A variety of strategies may be helpful in promoting information exchange for patients with lung cancer and in increasing their understanding of and level of involvement in treatment decision-making (Table IV).

2.3.1 *Audiotaping the Consultation*

A number of randomized trials have examined the effect of giving patients an audiotape of their consultation [41,42]. The results show that patients and their families often listen to these tapes on multiple occasions. Use of audiotapes improves recall of information and often improves patient satisfaction with the consultation. In general, anxiety about the information does not appear to increase.

2.3.2 *Providing Information Booklets*

Many educational materials are available for people diagnosed and living with cancer. Those materials include general information about cancer and its treatment and information about specific types of cancer. Information booklets from the Canadian Cancer Society are widely used as educational tools. A patient-focused booklet, *Understanding Lung Cancer,* is available (together with other lung cancer treatment guidelines) at the Cancer Care Ontario Web site: https://www.cancercare.on.ca/toolbox/qualityguidelines/diseasesite/lung-ebs/.

2.3.3 *Internet and Interactive CDs*

The Internet has become a widely used source of information about cancer treatments. Surveys demonstrate that at least 50% of patients use the Internet to look up health-related information. The problem with the Internet is that the quality of information varies enormously.

TABLE IV Elements of the palliative care consultation

- Illness understanding and education
- Symptom management (focus on pain, pulmonary symptoms, fatigue and sleep disturbance, mood, and gastrointestinal disturbance)
- Decision-making and advanced care planning
- Coping with illness; psychological and spiritual support
- Transition of care and referral to hospice
- Coordination of care between providers

Interactive CDs and DVDs are additional sources of electronic information available to cancer patients. Many cancer centres offer patient libraries or resource centres with computers and interactive learning material.

2.3.4 *Question Prompt Sheets*

Question prompt sheets are lists of questions that patients commonly ask. They include information about diagnostic tests, results, staging, treatment, and outcomes. Studies show that patients using question prompt sheets are more likely to ask questions of their doctor [43,44]. More questions may improve the exchange of information with the doctor and help patients to be more involved in the decision-making process.

2.3.5 *Decision Aids*

Decision aids are interventions designed to help patients become better informed about treatment options and outcomes relevant to their specific circumstances. These aids may be simple boards or brochures that compare the available treatment options, or they may be more elaborate computer-based programs, videotapes, and informal decision analysis tools. Patients using decision aids have greater knowledge and satisfaction, are more involved in decisions, and are less likely to feel regret in the future about their decisions [45].

Despite the wealth of information about strategies to improve information exchange with patients, little implementation of active strategies into routine clinical practice—such as audiotaping consultations, providing question prompt sheets, or incorporating decision aids—has occurred. Lung cancer patients are overrepresented in lower socioeconomic and less educated populations and may have less access to information. This lesser access increases the importance of implementing strategies to improve information exchange so as to better involve patients in the team.

2.4 Early Integration of Palliative Care in the Management of Patients with Advanced NSCLC

The traditional model of care introduced palliation late in the course of a lung cancer patient's illness. However, patients with advanced and metastatic lung cancer often have a high burden of symptoms. Data from the Cancer Quality Council of Ontario 2011 Cancer System Quality Index report demonstrate that up to 75% of lung cancer patients use hospital emergency departments in their last 3 months of life [46]. Analysis of utilization data for acute care hospitals suggest that many such visits might be prevented with improved community services directed to end-of-life care [47,48].

Given the high symptom burden experienced by NSCLC patients, introduction of palliative care earlier in the course of the illness has the potential to improve quality of care. Temel *et al.* [49] randomized newly diagnosed patients with advanced NSCLC to early palliative care integrated with standard oncologic care or to standard oncologic care alone. Patients in the experimental arm received palliative care visits at least monthly. The primary outcome was change in scores on the Trial Outcome Index from baseline to 12 weeks. Secondary outcomes examined measures of aggressive end-of-life care, defined as chemotherapy within 14 days of death; no hospice care; or admission to hospice within 3 days of death. Documentation of the resuscitation preferences of the patients was also assessed.

Early palliative care resulted in improved QOL. Patients randomized to early palliative care experienced significant improvements in scores on the Functional Assessment of Cancer Therapy (Lung module and Lung Cancer subscale) and the Trial Outcome Index. Fewer patients randomized to early palliative care received aggressive end-of-life care (33% vs. 54%), and more patients had their resuscitation preferences documented in the medical record (53% vs. 28%). Duration of hospice care appeared longer in the palliative care group (median: 11 days vs. 4 days), and patients appeared to have a better understanding of changes in their prognosis over time [50]. A surprising observation was that patients randomized to early palliative care survived longer than did patients with usual oncologic care (11.6 months vs. 8.9 months, $p = 0.02$). The foregoing findings have some limitations, given that the study was relatively small, conducted in a single institution, and not preplanned with respect to the survival observations. In addition, because of differences in the delivery of health care and, in particular, of palliative care in the United States, it is not clear how generalizable the findings are to the Canadian health care system.

Within a palliative care consultation, multiple domains have to be assessed (Table IV). The initial consultation in the foregoing trial took a median of 55 minutes. Most of the time was spent addressing symptom management, patient and family coping, and illness understanding [51]. Implementation of early palliative care for Canadian lung cancer patients has significant resource implications and will require expansion of services for many institutions.

2.5 Other Supportive Care Strategies to Support the Multidisciplinary Team

2.5.1 Bone Directed Therapy

Complications such as hypercalcemia, pain, pathologic fractures, and the need for radiation or surgical intervention are common problems for patients with metastatic NSCLC. In other diseases (for example, myeloma and metastatic breast and prostate cancer), guidelines routinely recommend the use of bisphosphonates such as pamidronate or zoledronic acid to reduce the risk of skeletal related events (SREs) [52–54], and yet bisphosphonates are not commonly used in NSCLC patients with bone metastases.

There are differences between metastatic NSCLC and metastatic breast cancer or myeloma. Median survival in metastatic NSCLC is considerably shorter. Bone metastases are common, but bone-dominant metastatic NSCLC is less common. The symptom burden is often driven by visceral sites of metastatic disease rather than by bone metastases. Lastly, bisphosphonates for NSCLC are not routinely reimbursed by many provincial funding agencies in Canada. Nevertheless, there are data demonstrating that bisphosphonates reduce the risk of SREs in patients with lung cancer. A randomized trial of zoledronic acid versus placebo in 773 patients with lung cancer and other solid malignancies failed to show a significant reduction in SREs (38% vs. 44%, $p = 0.127$) [55]; however, in a multiple-event analysis, the trial demonstrated a reduction in the cumulative risk of SREs (hazard ratio: 0.73; $p = 0.017$). In an exploratory analysis of the lung cancer subgroup of patients, those with elevated N-telopeptide had an increased risk of SREs and also an increased risk of death [56,57]. The association was less apparent in the zoledronic acid group, suggesting a treatment-related interaction. In a multivariate analysis, treatment with zoledronic acid predicted improved overall survival. This provocative subgroup observation requires validation.

More recently, denosumab, a monoclonal antibody against the receptor activator of nuclear factor KB ligand was shown to be noninferior to zoledronic acid in patients with myeloma and solid tumours other than breast or prostate cancer (hazard ratio: 0.84; 95% confidence interval: 0.71 to 0.98) [58]. No difference in overall survival was observed between the groups. However, a *post hoc* subgroup analysis examining overall survival according to tumour type demonstrated improved overall survival for NSCLC patients randomized to denosumab (hazard ratio: 0.79; 95% confidence interval: 0.65 to 0.95). Greater suppression of N-telopeptide levels was observed for patients randomized to denosumab.

The role of bone-directed therapy for patients with bone metastases from NSCLC needs rethinking. Data support some benefit from anti-bone-resorptive therapy with either zoledronic acid or denosumab. The mode of administration and side-effect profile of these agents show some differences. Future work should focus on identifying the particular NSCLC patients that will benefit most from such therapy.

In considering supportive approaches to bone metastases, it is important not to forget the role of palliative radiation in the management of NSCLC patients with symptomatic bone metastases [59,60]. Radiation can improve pain symptoms in 50%–60% of patients and should routinely be considered. For most patients, data support the use of short-course radiation (that is, a single faction) rather than longer courses [61,62]. To support patient-centred care, many institutions have set up specific radiation clinics for the management of symptomatic bone metastases. Patients can be triaged and seen in a short period of time. Where feasible, patients can be seen, simulated, and be given a single radiation treatment on the same day.

2.5.2 *Psychosocial Support*

The National Comprehensive Cancer Network defines distress as "a multifactorial unpleasant emotional experience of a psychological (cognitive, behavioural, emotional) social, and/or spiritual nature that might interfere with the ability to cope effectively with cancer, its physical symptoms and its treatment." Distress extends along a continuum ranging from common, normal feelings of vulnerability, sadness, and fear, to problems that can become disabling, such as depression, anxiety, panic, social isolation, and existential and spiritual crisis [63]. Screening for, and dealing with, psychosocial distress is an integral part of the multidisciplinary care of lung cancer patients. However, a national survey of U.S. oncologists found that fewer than one third of respondents were familiar with National Comprehensive Cancer Network guidelines, and only two thirds reported routinely screening for psychosocial distress [64]. Despite significant levels of psychosocial distress among patients, only half the responding oncologists indicated that mental health services were affiliated with their practice [65]. Psychosocial care of oncology patients is clearly an undermet need.

According to Cancer Care Ontario, the domain of psychosocial oncology includes the formal study, understanding, and treatment of the social, psychological, emotional, spiritual, QOL, and functional aspects of cancer as applied across the cancer trajectory from prevention through bereavement. It seeks to develop and integrate new knowledge and techniques of the psychosocial and biomedical sciences as they relate to cancer care [66]. Table V summarizes the key domains of the Cancer Care Ontario psychosocial oncology framework. Implementation of appropriate psychosocial care has the potential to improve the QOL for patients. A randomized trial of a social-worker-led intervention addressing the social domain of QOL (support, community resources, financial and legal issues, and advanced directives) resulted in clinical meaningful improvements for patients undergoing active treatment [67]. Integration of psychosocial support into the routine care of patients with advanced NSCLC should be a key component of the multidisciplinary team.

TABLE V Key domains that define the Cancer Care Ontario psychosocial framework [66]

A	Raising awareness: understanding and defining psychosocial health care
B	Standard of care: • Facilitating effective communication • Identifying psychosocial health needs • Designing and implementing a plan • Systematically monitoring, evaluating, and readjusting plans
C	Health care providers
D	Patient and family education
E	Quality oversight and monitoring progress
F	Workforce competencies
G	Standardized nomenclature
H	Psychosocial research

2.5.3 *Nutritional Support*

Weight loss is a common problem for patients with NSCLC [68]. As many as 20% of patients with advanced NSCLC present with weight loss in excess of 5% in the preceding 3 months [69]. In addition to weight loss, malnourishment (low serum albumin) is prognostic of worse survival for patients. Weight loss is also a common experience for patients undergoing concurrent chemoradiation. Experience during the 6 months immediately after implementation of concurrent chemoradiation at the Juravinski Cancer Centre showed that patients lost a median of 5 kg while on treatment.

Given the prevalence of weight loss among patients with advanced NSCLC, nutrition support should be considered part of the multidisciplinary management of this patient population. Dietary assessment and supplementation has the potential to reduce the impact of weight loss. Pharmacologic interventions have a role as well. A systematic review by the Cochrane Collaboration demonstrated that megestrol acetate can improve appetite and weight gain [70]. Less clear is whether those benefits translate into QOL improvements. Further research into cachexia and weight loss in patients with metastatic NSCLC is clearly needed. Such research requires close collaboration between dieticians or nutritionists and the primary oncology teams.

3. SUMMARY

The management of patients with advanced NSCLC has clearly become quite complex. New treatment algorithms, dependent on the histologic and molecular profile of the tumour, are emerging. Multidisciplinary care offers not only significant benefits to patients, but also many advantages to the team, including promotion of evidence-based care and opportunities for both continuing educational and quality assurance. Still, challenges with the implementation of multidisciplinary care remain, and regional centres must take responsibility to extend the implementation process. It is important to consider the use of technology such as videoconferencing facilities to broaden MCC coverage. However, this kind of extension will happen only with the ongoing support of institutions and provincial cancer agencies.

4. CONFLICT OF INTEREST DISCLOSURES

PME has received honoraria from AstraZeneca, Roche, Eli Lilly, and Amgen for speaking or participating on advisory boards.

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