Dyspnea in Terminally Ill Cancer Patients

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To determine the epidemiology of dyspnea in terminal cancer patients, we examined data from the National Hospice Study, which followed up patients during their last six weeks of life. The incidence of dyspnea in these patients was 70.2 percent, with prevalence rates generally exceeding 50 percent at any of three measurements. In addition to lung or pleural involvement by the tumor, the presence of underlying lung disease or cardiac and low performance on the Karnofsky scale were significantly associated with dyspnea. Lung, colorectal, and breast carcinomas were the most common tumor sites in our dyspneic patients and accounted for almost 60 percent of cancer diagnoses in these patients. In 23.9 percent of dyspneic terminal cancer patients, neither lung or pleural involvement nor underlying lung or heart disease could be identified as risk factors.

Although dyspnea is a well-known symptom of tumors involving the lung or pleura, shortness of breath is commonly present in terminal cancer patients who do not have lung or pleural involvement. Dyspnea in cancer patients may be caused by the tumor itself, treatment of the tumor, medical complications of the debilitated state, or underlying lung or cardiac disease. Dyspnea is the presenting complaint in 10 to 15 percent of patients with lung cancer and occurs in up to 65 percent of patients at some point during this illness. The epidemiology of dyspnea in terminally ill cancer patients, especially those without lung or pleural involvement, is less clear.

This study attempts to define the problem of dyspnea in terminally ill cancer patients, including identifying nonmalignant risk factors, using data obtained from the National Hospice Study. Although not specifically designed to evaluate dyspnea in terminally ill cancer patients, this prospective study of cancer patients in the last six weeks of life provides an excellent opportunity to examine this symptom.

**METHODS**

The National Hospice Study sampling frame and methodology have been described in detail elsewhere. Briefly, terminally ill cancer patients served by 40 hospices distributed nationally or by 14 conventional care settings (CC) who met eligibility criteria were asked to participate in a detailed prospective data collection effort. Patients were required to have confirmed malignant disease, be over 20 years of age, have a primary care person (PCP—usually a family member) to help care for them, and be medically certified as having a life expectancy of six months or less. A total of 1,754 patients and their PCPs were interviewed biweekly regarding the patient’s condition, symptoms experienced and services provided. Hospice and CC patients who gave their written informed consent were contacted and interviewed until the death of the patient. Since patient survival varied considerably, all data were converted to reflect the time prior to death. Thus, the last (T1) interview occurred on the average seven days prior to death, and questions asked of the patient or PCP refer to the biweekly period preceding the interview. The second to last interview (T2) occurred about 21 days before death, and the third and last (T3) occurred some 35 to 42 days prior to death. Patients’ experiences of symptoms were measured using a modified set of questions from Melzak. If the patient was unable to respond to an interview, the PCP was asked whether the symptom had occurred, although not about how severe it was. The proportion of patients able to respond to interviews decreased from 74.4 percent at T3 to 46.6 percent at T1.

Initial statistical analysis of data was performed using $\chi^2$ analysis, and subsequently multivariate loglinear analysis was performed to calculate the odds ratio of having dyspnea associated with selected patient characteristics.

**RESULTS**

**Incidence and Prevalence**

Dyspnea occurred in 70.2 percent of terminal cancer patients at some time during the last six weeks of life. Of all symptoms recorded in this study, only eating problems and pain exceeded the incidence of dyspnea. Prevalence rates at each measure generally exceeded 50 percent and increased as patients approached death (Table 1). Of patients who survived at least six weeks, 27.5 percent were reported to have dyspnea at all three times.

**Table 1—Prevalence of Dyspnea**

<table>
<thead>
<tr>
<th>Symptom Severity</th>
<th>T1</th>
<th>T2</th>
<th>T3</th>
</tr>
</thead>
<tbody>
<tr>
<td>“Self-report sample”</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>horrible</td>
<td>22</td>
<td>54</td>
<td>51</td>
</tr>
<tr>
<td>severe</td>
<td>69</td>
<td>83</td>
<td>92</td>
</tr>
<tr>
<td>moderate</td>
<td>75</td>
<td>90</td>
<td>69</td>
</tr>
<tr>
<td>mild</td>
<td>122</td>
<td>167</td>
<td>138</td>
</tr>
<tr>
<td>none</td>
<td>296</td>
<td>335</td>
<td>260</td>
</tr>
<tr>
<td>Overall</td>
<td>427</td>
<td>638</td>
<td>878</td>
</tr>
</tbody>
</table>

*No. of patients with dyspnea/no. of patients assessed at this measurement.
measures. The prevalence of “self report” patients who rated their symptom severity as “moderate” or worse exceeded 28 percent at every measurement.

Lung or Pleural Involvement and Other Risk Factors

In this study, 32.6 percent of terminally ill cancer patients had lung or pleural involvement (including primary and metastatic disease). Seventy-five percent of those patients with lung involvement reported dyspnea at some point. On the other hand, patients with lung or pleural involvement constituted only 39 percent of terminally ill patients reporting dyspnea.

Other factors significantly associated (p<.05) with dyspnea included underlying lung disease (risk ratio of 2), low level on Karnofsky Performance Scale (risk ratio 1.7) and underlying cardiac disease. Neither patient age nor sex were associated with dyspnea when controlling for lung disease and performance status. Of note, 23.9 percent of terminal patients who reported dyspnea had neither underlying lung or cardiac disease nor lung or pleural involvement. Clinical features of dyspneic and nondyspneic patient subsets, as well as of the entire population of our terminally ill cancer patients, are presented in Table 2.

Although the ten most common cancer sites were the same among our dyspneic patients, our nondyspneic patients, and the entire population (Table 2), some important differences were apparent. As expected, a much larger proportion of our dyspneic patients had lung cancer (p<.0001). In contrast, colorectal cancer was less common (although still second in importance) in dyspneic patients compared with nondyspneic patients (p<.001). Lung, colorectal, and breast carcinomas accounted for 59.5 percent of the cancer sites in our dyspneic subset.

Discussion

Our data indicate that dyspnea is much more common in terminally ill cancer patients than previously recognized. Its incidence in terminally ill cancer patients in the National Hospice Study (70.2 percent) is more than double that reported by Twycross and Lack (30 percent). Furthermore, the severity of this symptom was at least moderate in more than 28 percent of terminally ill cancer patients who were able to grade their shortness of breath.

Not surprisingly, the most important predictor of dyspnea was the presence of lung or pleural involvement, which occurred in 32.6 percent of our patients. Considering that lung cancer is the leading cause of cancer death in both men and women and that up to 65 percent of these patients experience dyspnea, the contribution of lung cancer to dyspnea in terminal cancer patients is substantial. Furthermore, Minna et al estimated that 30 percent of patients with malignant disease will develop pulmonary metastasis at some time during the clinical course of their disease. Mechanisms for dyspnea in patients with bronchogenic carcinoma include: (1) replacement of lung tissue to the extent that a restrictive ventilatory defect is produced; (2) pneumonia, atelectasis, or whole lung collapse occurring behind an occluded primary or segmental bronchus; (3) entrapment of the phrenic nerve by tumor-filled mediastinal nodes, and resulting diaphragmatic paralysis; and (4) lymphatic spread or interstitial edema, reducing lung compliance. Either primary lung tumors or metastatic pleural disease may cause pleuritic chest pain with resulting splinting or...
Dyspnea in cancer patients with pulmonary or pleural involvement may be related to treatment of the carcinoma, eg, postradiation fibrosis or postpneumonectomy.

Alternatively, dyspnea in terminally ill cancer patients, including lung cancer patients, may be unrelated to the tumor itself. Cigarette smoking, the most important cause of lung cancer, also causes chronic obstructive pulmonary disease, an additional risk factor for the development of dyspnea in this study. Last, dyspnea in terminally ill cancer patients may be a manifestation of the debility of terminal cancer. Reported causes include anemia, pulmonary embolism and congestive heart failure.

The National Hospice Study data confirm the importance of these pathophysiologic mechanisms. Although age and sex of patients were not associated with dyspnea in terminally ill cancer patients, this symptom was significantly related to underlying respiratory and cardiac diseases. Of note, 23.9 percent of dyspneic terminally ill cancer patients had none of these risk factors (lung or pleural involvement or underlying cardiac or respiratory disease). Dyspnea in these patients most likely represented the "debility of terminal cancer," which includes general muscle weakness and medical complications. The association of poor performance status and dyspnea in our patients further supports this concept. Dyspnea was a reported symptom in terminally ill cancer patients of all sites, and the distribution of cancer sites in dyspneic patients generally reflected the distribution of cancer sites for the entire population of the National Hospice Study. Notable exceptions include lung cancer that was overrepresented in dyspneic patients and colorectal cancer that was underrepresented in our dyspneic subset. Nearly two thirds of our dyspneic patients had cancer of one of the three leading sites (lung, colorectal, or breast).

Our study did not assess the response of physicians to dyspnea in terminally ill cancer patients, but several treatments have been recommended. The best of these options will depend on the specific clinical needs of the individual cancer patient. The first step in the treatment of dyspnea in terminally ill cancer patients, however, is for clinicians to recognize its high prevalence and to look for it in their cancer patients.

REFERENCES

Annual Meeting, National Association of Medical Directors of Respiratory Care (NAMDRC)

The ninth annual meeting of NAMDRC will be held at the Del Coronado Hotel, San Diego, March 21-22. Sessions will include discussion of home care; results of multicenter study of prolonged mechanical ventilation; mechanical ventilation in the home and at alternate community sites; use of hyperbaric oxygen; transtracheal oxygen therapy. Dr. Kenneth M. Moser will deliver the keynote address. For information, contact Mr. Michael Stafford, Executive Director, NAMDRC, PO Box 7011, Arlington, VA 22207 (703:527-1032).