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Chemotherapy Use, Performance Status, and Quality of Life at the End of Life

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ABSTRACT

Importance Although many patients with end-stage cancer are offered chemotherapy to improve quality of life (QOL), the association between chemotherapy and QOL amid progressive metastatic disease has not been well-studied. American Society for Clinical Oncology guidelines recommend palliative chemotherapy only for solid tumor patients with good performance status.

Objective To evaluate the association between chemotherapy use and QOL near death (QOD) as a function of patients' performance status.

Design, Setting, and Participants A multi-institutional, longitudinal cohort study of patients with end-stage cancer recruited between September 2002 and February 2008. Chemotherapy use (n = 158 [50.6%]) and Eastern Cooperative Oncology Group (ECOG) performance status were assessed at baseline (median = 3.8 months before death) and patients with progressive metastatic cancer (N = 312) following at least 1 chemotherapy regimen were followed prospectively until death at 6 outpatient oncology clinics in the United States.

Main Outcomes and Measures Patient QOD was determined using validated caregiver ratings of patients' physical and mental distress in their final week.

Results Chemotherapy use was not associated with patient survival controlling for clinical setting and patients' performance status. Among patients with good (ECOG score = 1) baseline performance status, chemotherapy use compared with nonuse was associated with worse QOD (odds ratio [OR], 0.35; 95% CI, 0.17-0.75; *P* = .01). Baseline chemotherapy use was not associated with QOD among patients with moderate (ECOG score = 2) baseline performance status (OR, 1.06; 95% CI, 0.51-2.21; *P* = .87) or poor (ECOG score = 3) baseline performance status (OR, 1.34; 95% CI, 0.46-3.89; *P* = .59).

Conclusions and Relevance Although palliative chemotherapy is used to improve QOL for patients with end-stage cancer, its use did not improve QOD for patients with moderate or poor performance status and worsened QOD for patients with good performance status. The

QOD in patients with end-stage cancer is not improved, and can be harmed, by chemotherapy use near death, even in patients with good performance status.

INTRODUCTION

Physicians have voiced concerns about the benefits of chemotherapy for patients with cancer nearing death.[1]– [5] In 2012, an American Society of Clinical Oncology (ASCO) expert panel identified chemotherapy use among patients for whom there was no evidence of clinical value[6] as the most widespread, wasteful, and unnecessary practice in oncology. Adequate patient performance status is often used as an indicator of whether the patient will be able to tolerate chemotherapy and respond to treatment. For this reason, performance status is used to gauge whether chemotherapy will offer clinical value.

Specifically, ASCO guidelines recommend against the use of chemotherapy in solid tumor patients who have not benefited from prior treatment and who have an Eastern Cooperative Oncology Group (ECOG)[7]performance status score of 3 or more (ie, bad or more debilitated than "capable of only limited self-care, confined to bed or chair more than 50% of waking hours").[6] This recommendation is supported by studies from the 1980s, which found that chemotherapy administered to patients with poor performance status resulted in low response rates, high rates of toxic effects, and short survival.[8,9] Because patients with good performance status are expected to benefit most from chemotherapy, trials have targeted those patients and have largely excluded cancer patients with poor performance status. As a result, evidence for treatment benefit or harm has rarely been quantified in patients with poor performance status. Research is needed to evaluate the benefits and harms of chemotherapy use among metastatic cancer patients stratified by performance status.

Despite the lack of evidence to support the practice, chemotherapy is widely used in cancer patients with poor performance status and progression following an initial course of palliative chemotherapy.[1,4,10,11] A study of patients with non–small-cell lung cancer (NSCLC) found that 28% of patients had performance status scores of 3 or 4 at presentation and that nearly 40% of these patients were receiving chemotherapy.[12]Available data for patients with NSCLC show a response rate of 2% for third-line and 0% for fourth-line chemotherapy.[13] This situation is not unique to NSCLC. A Norwegian study characterizing patients receiving palliative chemotherapy at a regional cancer center revealed that 53% had a performance status score of 2 and 16%, performance status scores of 3 and 4 at the start of last cancer therapy.[14] Overall, 10% received chemotherapy in the last 30 days of life. Among those patients, 21% had lung cancer; 15%, colorectal; 13%, prostate; and 9%, breast cancer. Of the breast cancer patients, 12% were receiving second-line therapy (associated with 3- to 6-month duration of response)[15] 19%, third-line therapy (2- to 4-month duration of response)[16,17]; and 21%, third-line therapy or higher. Hormone receptor status was not noted in the Norwegian study,[14] but in triple-negative breast cancer patients, duration of response was even shorter: 9 weeks after second-line therapy and 4 weeks after third-line therapy.[18]

The goal of palliative chemotherapy for patients with incurable cancer is to prolong survival and promote QOL. We have shown that chemotherapy use among patients with metastatic cancer whose cancer has progressed while receiving prior chemotherapy was not

significantly related to longer survival but was associated with more aggressive medical care in the patient's final week and heightened risk of dying in an intensive care unit.10 The aim of the current study is to examine the association between patients' performance status and the effect of chemotherapy on QOL in the last week of life. We hypothesize that patients with good performance status who receive additional palliative chemotherapy will have significantly worse QOL at the end of life than those who do not receive chemotherapy, and that patients with poor performance status will not experience QOL improvements with chemotherapy.

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