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Progressive disease in patients with cancer presenting to an emergency room with acute symptoms predicts short-term mortality

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Abstract *Goals:* Patients with symptomatic, advanced cancer continue to be referred late or not at all for hospice or palliative care. We conducted a retrospective cohort study to determine whether evidence of cancer progression is an independent predictor of short-term mortality in acutely symptomatic cancer patients. *Patients and methods:* We reviewed the records of 396 patients who visited the emergency center at a comprehensive cancer center in January 2000. Records were reviewed for clinical characteristics, including symptoms, type and extent of cancer, and whether the patient's cancer was stable or progressing (uncontrolled) at the time of the emergency center visit. Cox regression analysis was used to assess survival at 90 and 180 days, after controlling for patient characteristics. *Main results:* Patients who died within 14, 90, or 180 days were more likely to have disease progression than those who did not. Dyspnea on emergency center presentation and disease progression were independent predictors of death within 90 or 180 days, after controlling for patient age, symptoms, signs, and the presence of metastases. The odds ratios for death within 90 and 180 days were 3.97 and 4.34, respectively (95% confidence intervals: 1.44, 10.94 and 1.87, 10.09). *Conclusion:* Cancer disease progression is a clinical measure of increased risk of short-term mortality in acutely symptomatic cancer patients. Future studies should examine whether the use of this characteristic enhances identification of patients who could benefit from timely referral to hospice or palliative care. *Shortened abstract:* Symptomatic cancer patients presenting to a cancer center emergency room were more likely to die within 14, 90, or 180 days if they had evidence of recent progression of their cancer. Among patients with disease progression, 47% died within 90 days and 61% within 180 days.

Keywords Cancer progression · Mortality prediction · Survival

Introduction

Estimating life expectancies of patients with advanced cancer is difficult. Patients and their loved ones want an estimate of survival time, yet previous research suggests that clinicians, patients, and their families often overestimate this [3,12–14, 22, 23, 25]. Overestimating life expectancy may lead to delayed referrals to palliative care and hospice programs and to delayed discussions of end-of-life issues with patients and their families. Indeed, many experts believe that terminal cancer patients are not referred to hospice or palliative care services in a timely manner [4]. Among Medicare beneficiaries who died within 1 year of cancer diagnosis in 1996, 17% of those receiving hospice care did so only in the last 3 days of life, confirming a continuing problem of very late referral for this service [5].

Vigano and colleagues [24] reviewed the literature on survival prediction in terminal cancer patients and

observed that important independent predictors of shortened survival include performance status, the clinician's estimate of survival, cognitive failure, weight loss, dysphagia, anorexia, and dyspnea. Another recent review of the literature has also confirmed that these measures have prognostic value [17]. However, for virtually all of the patients in the studies reviewed by these experts, survival was measured from the time of admission to a palliative care or hospice program. This work does not address the problem of identifying patients who may benefit from earlier referral to hospice or palliative care programs.

An alternative approach would be to study a cohort of patients that has not yet been referred to such programs to determine whether earlier referral to hospice or palliative care is feasible. Previous studies indicate that patients dying of cancer frequently use acute-care hospitals [5, 10]; therefore, opportunities do exist for advance care planning (ACP). Earle and colleagues [5] recently demonstrated that emergency room (ER) visits and hospital admissions are quite common in the last month of life in older patients who died of cancer: According to the US Surveillance, Epidemiology and End Results Program/Medicare data from 1996, in the population over the age of 65, there were 0.46 ER visits and 0.62 hospital admissions per person in the last month of life. Thus, many dying cancer patients see acute-care providers, and opportunities for palliative care assessment and referral in such instances may be missed.

Currently, there is very limited literature describing clinical predictors of short-term survival in cancer patients seeking care in emergency or other acute-care settings. Previously, Escalante and colleague [6, 7] investigated 122 ER patients at The University of Texas M.D. Anderson Cancer Center and found that a clinical picture characterized by extreme triage vital signs, a history of metastases, and presence of cancer progression were predictors of death within 2 weeks. However, their studies were limited to examining the outcomes of patients who presented with dyspnea, a subjective awareness of difficulty with breathing. The survival outcomes of ER cancer patients who present with other acute symptoms remain largely unknown. We hypothesized that in these ER patients, disease progression at the time of ER visit would be a clinical predictor of short-term survival. In this study, we identified the clinical characteristics associated with survival outcomes in a broad group of cancer patients presenting with a range of symptoms to the M.D. Anderson Cancer Center ER.

Patients and methods

Study setting

This study was a retrospective chart review of M.D. Anderson ER patients. The M.D. Anderson ER staff evaluates urgent and emergent medical problems for more than 15,000 cancer patients each year, and the M.D. Anderson ER also serves as a regional referral center. M.D. Anderson is a National Cancer Institute-designated comprehensive cancer center and cares for patients with the broadest possible spectrum of malignant disease. Our study protocol was approved by the M.D. Anderson Institutional Review Board.

Patient selection

There were approximately 925 patient visits to the ER in the month of January 2000. The records for 50% of these visits (462) were randomly selected for retrospective review. If the same patient made multiple visits to the ER in January 2000, the record for the earliest visit was reviewed, and those from subsequent visits were excluded. Sixty-six records were excluded from this study because they belonged to patients who visited the ER more than once during that time (36), were of M.D. Anderson employees (17), were of ER patients who did not have cancer (6), were incomplete clinical records (5), or were not from the month of January (2). Three hundred ninety-six patients (86%) were ultimately selected for this study.

Data collection

Most of the data collected were from the ER records. The information collected were patient demographics (age, gender, ethnicity, and geographic residence), up to four chief complaints (primary reasons for visiting the ER), and additional symptoms at presentation (dyspnea, constipation, abdominal distention, nausea and vomiting, dysphagia, and anorexia). Cancer diagnoses, presence of metastases, and disease progression were also examined. Pain was measured at triage using a pain scale with numerical values ranging from 0 to 10, with 10 corresponding to the most severe pain. Performance status at the time of the ER visit was measured using the Zubrod/Eastern Cooperative Oncology Groups/World Health Organization score: 0=normal activity; 1=symptoms but ambulatory; 2=some time in bed or chair, but <50% of the time; 3=bed- or chair-ridden >50% of the time; and 4=completely bed- or chair-bound. Vital signs at triage (heart rate, respiratory rate, systolic and diastolic blood pressure, and body temperature), along with ER disposition, were entered into the database as well.

Disease progression was assessed through chart review by one of two members of the investigative team (J.M.G. or R.L.V.) for each study patient. Disease progression was operationally defined as being present when the patient's primary treating oncologist or the oncologist who admitted the patient from the ER stated in progress notes that the patient's cancer was progressing despite treatment. If such statements were not available in the recent medical records

but the patient's most recent radiological studies indicated an increase in tumor burden, disease progression was also considered present. Finally, patients with leukemia or lymphoma were considered to have disease progression if they had relapsed disease. To evaluate interrater reliability, records of 24 lung cancer patients, 22 breast cancer patients, and 26 lymphoma patients were evaluated for progression by an oncologist who treats those patients, and this oncologist's results were compared with the study investigators' results. Percent agreement and kappa statistics for assessment of lung cancer, breast cancer, and lymphoma disease progression were 71% and 0.42, 64% and 0.28, and 73% and 0.47, respectively. The breast cancer cases for this assessment were then reviewed by a second member of the research team, a physician (J.M.G.) blinded to the gold standard assessment, with improved percent agreement and kappa of 86% and 0.63, respectively.

The M.D. Anderson online computer records were used to ascertain patient survival at 14, 90, and 180 days after first January 2000 ER visit. Social security records on the Internet were also accessed to identify as many dates of death as possible [9]. Patient names and identification numbers were eliminated from the study database to ensure confidentiality.

Statistical analyses

Chi-square statistical analyses were performed to look for associations between clinical characteristics and survival outcomes for all relevant categorical variables. Categorical variables were labeled as either "yes" or "no." Continuous variables such as blood pressure, body temperature, and Zubrod score were categorized into typical and extreme values according to the researchers' judgment, making chi-square analyses feasible for these variables. Age was retained as a continuous variable. *P* values of less than 0.05 were considered statistically significant in this study.

All variables that exhibited a statistically significant association with survival outcomes on bivariate analysis were then entered into a Cox regression model to determine potential predictors of death at 90 and 180 days. The frequency of death within 14 days was too low (N=21) to permit stable multivariate modeling. In the regression analyses, variables with *P* values of less than 0.05 were considered independent predictors, whereas variables with *P* values between 0.05 and 0.10 were considered potential predictors of death. Vital status could not be confirmed for 17 patients (4%) at 90 days and for 24 patients (6%) at 180 days. These patients were excluded in the analyses of death within 90 and within 180 days. Analyses were performed using SPSS (Chicago, IL) version 11.5 and SAS (Cary, IL).

Results

Demographic and clinical characteristics of the study population are shown in Table 1. The median age was 56 years (range: 15–96); 51% of patients were female, and 74% resided in Texas. Approximately one third of the patients had hematologic cancers. Other common cancers included breast (14%), gastrointestinal (13%), and lung (small and non-small cell, 11%). Sixty-eight patients (17%) presented with dyspnea, and 97 (24%) showed evidence of disease progression at the time of their ER visit. Eleven percent of the study patients had Zubrod scores of 3 or 4 at the time of the ER visit, indicating that they were confined to the bed or chair more than 50% of waking hours. Twenty-one patients (5%) died within 14 days, 86 (22%) died within 90 days, and 120 (30%) died within 180 days.

Bivariate associations between clinical characteristics and patients with or without disease progression are presented in Table 2. Among patients who had cancer progression, more than half had a history of metastatic disease, compared with 11% without disease progression (P<0.001). Other characteristics that were more frequent among patients with disease progression included extreme ER temperatures and heart rates at triage. Poor functional status, as indicated by a Zubrod score of 3 or 4, was more frequent among patients with disease progression than among those without (21% vs 3%, P<0.01). Common acute cancer-related symptoms such as dyspnea, nausea and vomiting, and fatigue were not significantly associated with disease progression. Mean and median survival were significantly less for patients with disease progression, at 92.4 and 77.0 days, respectively, compared with 153.6 and 180 days for those whose disease was stable (P<0.001). All three mortality outcomes were significantly more common in patients with disease progression than in patients without. In particular, at 90 and 180 days, 48 and 61% of patients presenting to the ER with disease progression had died, compared with 13 and 20% of those without disease progression, respectively (P<0.001). The survival of the study cases stratified by disease progression is presented in Fig. 1.

Table 3 summarizes the characteristics of patients who died within 14, 90, and 180 days. For all three of these outcomes, the patients who died tended to be older than those who survived. Twenty-one patients died within 14 days, and a majority of them (76%) showed evidence of disease progression. Forty-three percent of patients who died within 14 days complained of dyspnea, compared with just 16% of the survivors at 14 days (P<0.01). Poor performance status and extreme elevation or depression of systolic blood pressure were also more common among the 14-day deaths. In all three groups, patients who died were more likely to have metastases or complaints of abdominal distention on presentation to the ER.

Table 4 displays the independent predictors of death within 90 or 180 days, after controlling for age, presence of

Table 1 Patient characteristics (*N*=396)

Characteristic	Number (%)
Age (years)[a]	
≥65	104 (26)
≤45	105 (26)
Gender	
Female	202 (51)
Geographic location	
Texas	293 (74)
USA, non-Texan	78 (20)
Other countries	23 (6)
Unknown	2 (.5)
Ethnicity	
White	284 (72)
Black	49 (12)
Hispanic	47 (12)
Asian	16 (4)
Primary cancer type (missing 1)	
Hematologic	137 (35)
Breast	56 (14)
Gastrointestinal	50 (13)
Lung	42 (11)
Genitourinary	35 (9)
Gynecologic	25 (6)
Other	51 (13)
Disease status	
History of metastases	152 (38)
Disease progression at time of ER visit	97 (24)
Symptoms and signs at ER Presentation	
Abdominal distention	17 (4)
Dyspnea	68 (17)
Fatigue	28 (7)
Zubrod score ≥3	43 (11)
SBP ≥170 or ≤90 mm Hg	32 (8)
DBP ≤50 mm Hg	20 (5)
HR ≥110 or ≤60	129 (33)
RR≥28 breaths per minute	17 (4)
Outcomes	
Admitted to the hospital	160 (40)
Died within 14 days	21 (5)
Died within 90 days	86 (22)
Died within 180 days	120 (30)
Vital status unknown	24 (6)
Alive at 180 days	252 (64)

N=396
ER emergency room, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *HR* heart rate, *RR* respiratory rate
[a]Mean, 54; median, 56

Table 2 Selected characteristics of patients with and without disease progression

Clinical characteristics	With disease progression (*N*=97)	Without disease progression (*N*=299)
Mean age (±SD)	54 (±14)	55 (±14)
History of metastases (%)	53 (55)	34* (11)
Severe pain (score ≥7) (%)	25 (26)	22** (7)
Temp ≥38.5 or ≤35.5°C (%)	28 (29)	16** (5)
Systolic BP ≥170 or ≤90 mm Hg (%)	9 (9)	8 (3)
HR ≥110 or ≤60 (%)	40 (41)	30** (10)
Zubrod score ≥3 (%)	20 (21)	8*** (3)
Dyspnea (%)	18 (19)	17 (6)
Constipation (%)	10 (10)	4** (1)
Nausea and vomiting (%)	25 (26)	20 (7)
Fatigue (%)	7 (7)	7 (2)
Outcomes		
Admitted to the hospital (%)	51 (53)	37** (12)
Survival, mean days	92.4	153.6
Survival, median days	77.0	180.0
Survival, interquartile days	28.0–180.0	155.0–180.0
Died within 14 days (%)	16 (16)	5* (2)
Died within 90 days (%)	47 (48)	39* (13)
Died within 180 days (%)	59(61)	61* (20)

SD standard deviation, *Temp* temperature, *BP* blood pressure, *HR* heart rate
*P<0.001; **P<0.05; ***P<0.01

metastases, and symptoms and signs associated with 90- or 180-day deaths on bivariate analysis. The presenting symptom of dyspnea was significantly associated with death within 90 days [odds ratio (OR) 3.05, 95% confidence interval (CI) 1.03, 9.04] as well as death within 180 days (OR 3.13, 95% CI 1.25, 7.80). The only other significant predictor for each of these outcomes was the presence of disease progression, with odds ratios of 3.97 (95% CI 1.44, 10.94) and 4.34 (95% CI 1.87, 10.09) for 90- and 180-day deaths, respectively.

Discussion

In this study, we showed that disease progression was a significant predictor of short-term mortality in acutely symptomatic cancer patients. Disease progression in such cancer patients was associated with death within 14, 90, and 180 days of their ER presentation. Furthermore, the results from the regression analyses support the hypothesis

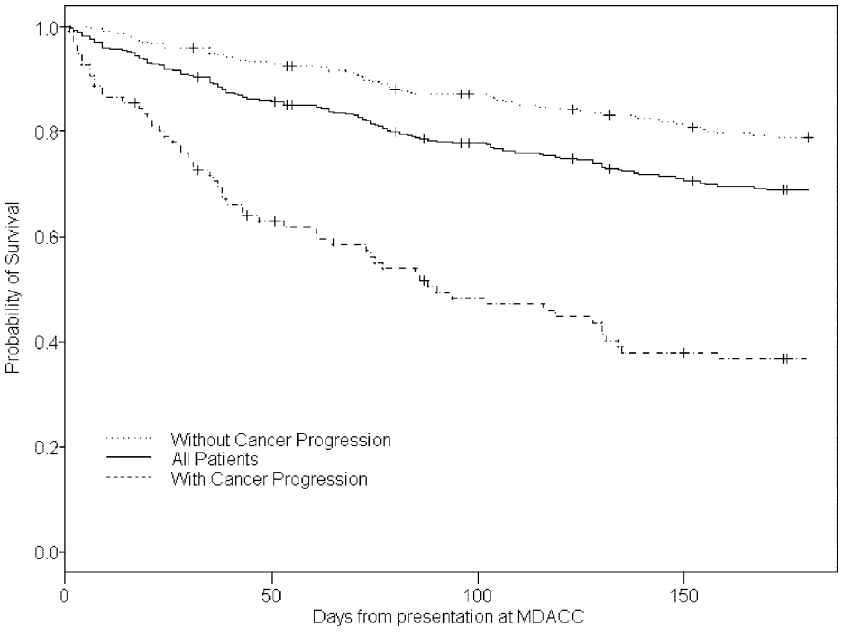

Fig. 1 Kaplan–Meier curves for overall survival and by disease progression for the 180-day outcome

that disease progression at the time of cancer patients' ER visits is an independent clinical predictor of death within 90 and 180 days, after controlling for a number of symptoms known to be common among such patients, such as dyspnea, fatigue, and abdominal distention [16, 20, 21, 24]. To our knowledge, this is the first study to demonstrate the potential use of such a clinical predictor of short-term mortality among patients with advanced cancer.

We believe the clinical measure of disease progression could greatly assist clinicians who care for cancer patients. We examined its application across a group of patients with diverse cancers. At a time when cancer treatment can often stabilize or even reduce the burden of metastatic disease, patients with advanced cancer can sometimes live for many months. Patients with metastatic breast, colorectal, or prostate cancer in particular can live for years [8, 19, 21, 26]. Thus, the burden of disease itself does not predict short-term mortality. In contrast, progressive disease despite therapy is likely to cause increasing problems for the cancer patient. By studying cancer patients presenting to an ER with acute symptoms, we selected a subset of cancer patients who had a higher likelihood of disease progression and short-term mortality. The majority of acutely symptomatic patients in our study who were

Table 3 Characteristics of patients who died within 14, 90, or 180 days

Clinical characteristics	14 days (missing 6)		90 days (missing 17)		180 days (missing 24)	
	21 dead	369 alive	86 dead	293 alive	120 dead	252 alive
Age (mean)	58.3	54.4	57.0	53.7	57.6	53.9*
Disease progression (%)	76	21**	55	15**	49	12**
History of metastases (%)	71	36*	52	34***	51	32**
Abdominal distention (%)	19	4*	13	2***	10	2**
Abdominal pain (%)	23	14	23	13*	18	13
Fatigue (%)	10	7	12	5*	10	5*
Dyspnea (%)	43	16***	29	14***	24	15*
Zubrod score ≥3 (%)	24	10*	20	9***	17	9
SBP ≥170 or ≤90 mm Hg (%)	24	7*	14	6***	12	7
HR ≥110 or ≤60 (%)	38	33	40	32***	38	32***
RR ≥28 breaths per minute (%)	10	4	6	4	5	4
Admitted from ER (%)	48	40	49	38	51	35*

Within each of the three mortality outcomes, the asterisks denote statistically significant differences in the prevalence of the clinical characteristic for cases that survived vs those that died

SBP systolic blood pressure, *DBP* diastolic blood pressure, *HR* heart rate, *RR* respiratory rate, *ER* emergency room

*P<0.05; **P<0.001; ***P<0.01

Table 4 Multivariate analysis of predictors of patient death within 90 or 180 days

Clinical characteristic	Death in 90 days			Death in 180 days		
	Beta	OR	95% CI	Beta	OR	95% CI
Dyspnea	1.116	3.05	1.03, 9.04	1.140	3.13	1.25, 7.80
Disease progression	1.379	3.97	1.44, 10.94	1.469	4.34	1.87, 10.09

These models control for patient age, metastases, and the presence of the following signs and symptoms: extreme systolic BP or HR abnormalities, low diastolic BP, Zubrod performance status score ≥3, fatigue, abdominal distention, and (in the 180-day-death model) admission to the hospital

OR odds ratio, *CI* confidence interval, *BP* blood pressure, *HR* heart rate

assessed as having progressive malignant disease died within 6 months of their ER presentation.

Although an acute-care setting such as the ER would not be considered the best place for a discussion of prognosis and advance care planning (ACP), a study by Lamont and Siegler suggests this may merit further evaluation [14]. In their study of 111 cancer patients admitted to a tertiary care medical center, patients generally did not want to discuss ACP with their oncologists until they were "seriously ill." In addition, they also found that more patients were willing to discuss this topic with a house officer than with their own oncologist [14]. Future research could explore the role of non-oncologist providers in discussing prognosis and ACP with cancer patients with advanced disease.

Our study had a number of limitations, one being a small sample size. For example, only 5% of the study population died within 14 days, making regression analysis not feasible in that particular group of patients. Similarly, the numbers of patients with individual types of cancer were small; therefore, we may not have had sufficient numbers of cases to control for certain cancers that one would expect to be associated with the greatest short-term mortality (i.e., lung cancer). We were unable to determine vital status for a small number of patients, could not confirm that all of the deaths were due to cancer, and were also missing Zubrod scores for many patients, preventing a complete analysis of the role of performance status in this patient population. The retrospective nature of our study is a likely cause of the missing data and the lack of a clinician's estimate of expected patient survival. It is possible that clinicians' prediction of survival includes an assessment of cancer patients' disease progression. This measure has been identified as having some predictive power for prognosis, along with performance status and the presence of some symptoms associated with advanced cancer, such as the anorexia–cachexia syndrome, dyspnea, delirium, and some laboratory abnormalities such as elevated C-reactive protein [17]. Finally, the definition of disease progression was challenging because of the diverse malignancies included in our study and the inclusion of patients at varying points in their cancer trajectory. A prospective study of well-defined cancer cohorts could more thoroughly explore the prediction of survival based on disease progression as well as other clinical factors that appear to have predictive power [17].

Our patients received their initial acute assessment and care in the ER of a comprehensive cancer center, so our findings may not be applicable to patients in other clinical settings. We were able to review the medical records of all of the ER patients, including their recent diagnostic tests and progress notes as recorded in the hospital computer system. Such records are also available to our ER physicians. Health care providers in other acute-care settings may not have access to such records and therefore might find it difficult to determine whether a patient's cancer is stable or progressing. Nevertheless, it should be possible to develop and test a simple instrument that assesses this. All patients in our study who were recently diagnosed and had not begun treatment or who had just started a new treatment regimen irrespective of the extent of their disease were considered to not have disease progression. It might be possible in the acute-care setting to ask patients or their treating oncologists about the status of their cancer, but further study is needed to confirm this. We believe new measures are needed if the goal is improved prognostication, particularly in patients who have not been referred for palliative care.

We acknowledge that new and more accurate prognostic measures themselves may not be sufficient to ease the process of dying for many cancer patients. The Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatments (SUPPORT) was unable to improve end-of-life care and decision making for seriously ill patients [1]. Having examined the SUPPORT findings, Lynn and colleagues suggest that it might be necessary to effect changes in the systems of care if the quality of care for the dying is to be improved [15]. This includes everything from availability of hospice services and reimbursement policies to prevailing local practice patterns that may include a lack of referral to hospice until no more cancer-specific therapy is provided [15, 18]. An additional obstacle may be the preferences of cancer patients and their families. Kapo and colleagues interviewed 274 cancer patients and/or their family members at hospice enrollment and found that most of these people did not believe the hospice referral and enrollment occurred too late [11]. Nevertheless, the fact that physicians have a duty to provide prognostic information

to patients who desire it means that continued research in this area is necessary [2, 17].

In conclusion, we have identified a new clinical measure, cancer disease progression, which may identify a subset of acutely ill cancer patients at increased risk for short-term mortality. Patients with this characteristic who received care in our ER were more likely to die within 14, 90, or 180 days than those without disease progression. Despite this, many of these patients still had weeks or months of life left during which they could have benefited from referral to palliative or hospice care services. We think that exploring prognostic estimates in acutely ill cancer patients may be beneficial. Physicians have long hoped that improved prognostication might help them identify patients who would benefit from palliative or hospice care in a more timely manner. The fact that a recent study found that one sixth of all elderly patients dying of cancer who chose hospice care did so within 3 days of death indicates there is much room for improvement in this practice [5]. We hope that future studies validate disease progression as a clinical predictor of short-term mortality and establish it as a useful measure for the broad range of health care providers who care for cancer patients.

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References

1. (1995) A controlled trial to improve care for seriously ill hospitalized patients. The study to understand prognoses and preferences for outcomes and risks of treatments (SUPPORT). The SUPPORT Principal Investigators. JAMA 274:1591–1598
2. Christakis NA (1999) Death foretold: prophecy and prognosis in medical care. 1st edn. University of Chicago Press, Chicago
3. Christakis NA, Lamont EB (2000) Extent and determinants of error in doctors' prognoses in terminally ill patients: prospective cohort study. BMJ 320:469–472
4. Daugherty CK, Steensma DP (2002) Overcoming obstacles to hospice care: an ethical examination of inertia and inaction. J Clin Oncol 20:2752–2755
5. Earle CC, Neville BA, Landrum MB, Ayanian JZ, Block SD, Weeks JC (2004) Trends in the aggressiveness of cancer care near the end of life. J Clin Oncol 22:315–321
6. Escalante CP, Martin CG, Elting LS, Cantor SB, Harle TS, Price KJ, Kish SK, Manzullo EF, Rubenstein EB (1996) Dyspnea in cancer patients. Etiology, resource utilization, and survival implications in a managed care world. Cancer 78:1314–1319
7. Escalante CP, Martin CG, Elting LS, Price KJ, Manzullo EF, Weiser MA, Harle TS, Cantor SB, Rubenstein EB (2000) Identifying risk factors for imminent death in cancer patients with acute dyspnea. J Pain Symptom Manage 20:318–325
8. Giordano SH, Buzdar AU, Smith TL, Kau SW, Yang Y, Hortobagyi GN (2004) Is breast cancer survival improving? Cancer 100:44–52
9. Hauser TH, Ho KK (2001) Accuracy of on-line databases in determining vital status. J Clin Epidemiol 54:1267–1270
10. Huang J, Boyd C, Tyldesley S, Zhang-Salomons J, Groome PA, Mackillop WJ (2002) Time spent in hospital in the last six months of life in patients who died of cancer in Ontario. J Clin Oncol 20:1584–1592
11. Kapo J, Harrold J, Carrol JT, Rickerson E, Casarett D (2005) Are we referring patients to hospice too late? Patients' and families' opinions. J Palliat Med 8:521–527
12. Lamont EB, Christakis NA (1999) Some elements of prognosis in terminal cancer. Oncology (Williston Park) 13:1165–1170; discussion 1172–1174:1179–1180
13. Lamont EB, Christakis NA (2002) Physician factors in the timing of cancer patient referral to hospice palliative care. Cancer 94:2733–2737
14. Lamont EB, Siegler M (2000) Paradoxes in cancer patients' advance care planning. J Palliat Med 3:27–35
15. Lynn J, Arkes HR, Stevens M, Cohn F, Koenig B, Fox E, Dawson NV, Phillips RS, Hamel MB, Tsevat J (2000) Rethinking fundamental assumptions: SUPPORT's implications for future reform. Study to Understand Prognoses and Preferences and Risks of Treatment. J Am Geriatr Soc 48:S214–S221
16. Maltoni M, Pirovano M, Scarpi E, Marinari M, Indelli M, Arnoldi E, Gallucci M, Frontini L, Piva L, Amadori D (1995) Prediction of survival of patients terminally ill with cancer. Results of an Italian prospective multicentric study. Cancer 75:2613–2622
17. Maltoni M, Caraceni A, Brunelli C, Broeckaert B, Christakis N, Eychmueller S, Glare P, Nabal M, Vigano A, Larkin P, De Conno F, Hanks G, Kaasa S (2005) Prognostic factors in advanced cancer patients: Evidence-based clinical recommendations—a study by the Steering Committee of the European Association for Palliative Care. J Clin Oncol 23:6240–6248
18. Meyers FJ, Linder J (2003) Simultaneous care: disease treatment and palliative care throughout illness. J Clin Oncol 21:1412–1415
19. Pound CR, Partin AW, Eisenberger MA, Chan DW, Pearson JD, Walsh PC (1999) Natural history of progression after PSA elevation following radical prostatectomy. JAMA 281:1591–1597

20. Reuben DB, Mor V, Hiris J (1988) Clinical symptoms and length of survival in patients with terminal cancer. Arch Intern Med 148:1586–1591
21. Solomayer EF, Diel IJ, Meyberg GC, Gollan C, Bastert G (2000) Metastatic breast cancer: clinical course, prognosis and therapy related to the first site of metastasis. Breast Cancer Res Treat 59:271–278
22. Steensma DP, Loprinzi CL (2000) The art and science of prognosis in patients with advanced cancer. Eur J Cancer 36:2025–2027
23. Vigano A, Dorgan M, Bruera E, Suarez-Almazor ME (1999) The relative accuracy of the clinical estimation of the duration of life for patients with end of life cancer. Cancer 86:170–176
24. Vigano A, Dorgan M, Buckingham J, Bruera E, Suarez-Almazor ME (2000) Survival prediction in terminal cancer patients: a systematic review of the medical literature. Palliat Med 14:363–374
25. Weeks JC, Cook EF, O'Day SJ, Peterson LM, Wenger N, Reding D, Harrell FE, Kussin P, Dawson NV, Connors AF Jr, Lynn J, Phillips RS (1998) Relationship between cancer patients' predictions of prognosis and their treatment preferences. JAMA 279:1709–1714
26. Wilke HJ, Van Cutsem E (2003) Current treatments and future perspectives in colorectal and gastric cancer. Ann Oncol 14(Suppl 2):ii49–ii55