Original Article

Prognostic Factors of Survival in Patients With Advanced Cancer Admitted to Home Care

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Abstract

Context. Data regarding prognostication of life expectancy in patients with advanced cancer are of paramount importance to patients, families, and clinicians. However, data regarding patients followed at home are lacking.

Objectives. The aim of this study was to evaluate the correlation between various factors recorded at the beginning of home care assistance and survival.

Methods. A sample of consecutive patients admitted to two home care programs was surveyed. A preliminary consensus was achieved as to the possible variables easy to be recorded at home. These included age at the time of home care admission, gender, residence, marital status, primary cancer diagnosis, Karnofsky Performance Status (KPS) score, measures of systolic blood pressure and heart rate, cyanosis, use of oxygen, and body temperature. The Edmonton Symptom Assessment System was used to record the intensity of each symptom. Patients were divided into two groups: patients with a survival of less than 10 days (short survival) and patients with a survival of 10 days or more (medium-long survival).

Results. Three hundred seventy-four consecutive patients admitted to home care programs were surveyed, of which 187 were male. The mean ± SD age was 72.1 ± 12.7 years. The mean survival was 56.2 ± 65 days. Mean survival was 71.5 ± 67 days (287 patients) and 5.6 ± 2.7 days (87 patients) in the short and medium-long survival groups, respectively. No association between type of tumor and survival was observed ($P = 0.162$). Univariate logistic regression analysis revealed that male gender ($P = 0.020$), older age ($P = 0.012$), lower KPS scores ($P < 0.0005$), systolic blood pressure less than 100 mm Hg ($P = 0.003$), heart rate greater than 100 beats per minute ($P = 0.0006$), delirium ($P = 0.004$), the use of oxygen ($P = 0.002$), intensity of fatigue ($P = 0.006$), drowsiness ($P < 0.0005$), anorexia ($P < 0.0005$), dyspnea ($P < 0.0005$), poor sense of well-being ($P < 0.0005$), and distress score ($P < 0.0005$) were associated with a survival of less than 10 days. Marital status, residence, cognitive function, fever, pain, depression,

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and anxiety were not found to be significantly correlated with survival. In a multiple logistic regression model, low systolic blood pressure and high heart rate, gender, delirium, use of oxygen, KPS score, drowsiness, anorexia, and dyspnea were significantly correlated with a shorter survival.

Conclusion. Low systolic blood pressure and high heart rate, male gender, poor KPS score, anorexia, and dyspnea were correlated with a shorter survival. Moreover, patients with low systolic blood pressure and high heart rate, male gender, poor KPS score, and greater intensity of anorexia and dyspnea are more likely to die within one week. The combination of physical symptoms from the Edmonton Symptom Assessment System and other parameters included in this study, which are simple to assess and are repeatable at home, should be further explored in future studies to provide a simple tool for use with patients with advanced cancer admitted to a home care program. J Pain Symptom Manage 2013;45:56–62.

Key Words
Home care, prognosis, survival, advanced cancer

Introduction

Prognostication of life expectancy in patients with advanced cancer is of paramount importance to patients, families, and clinicians. In the last several years, many studies have been done to identify possible predictors of survival in this population.[1–5] However, data regarding patients followed at home are lacking. Most studies of home care have focused on the probabilities of predicting a home death[6–8] rather than on survival. Indeed, communicating survival predictions is an important part of cancer care, even at home, where survival is assumed to be short.[8] Investigating possible factors associated with a shorter survival may help in planning communications and making therapeutic decisions.

The Home Care-Italy group recently has been established, with the intent to disseminate and implement information on cancer patients followed at home, given the paucity of existing data in this setting. As part of its scientific program, this study was undertaken to evaluate the correlation between various factors recorded at the beginning of home care assistance and survival.

Methods

Over a six-month period, we prospectively collected the charts of consecutive patients admitted to two home care programs in L'Aquila and Turin, which belong to the Home Care-Italy group. These two programs, which are representative of home care programs in Italy, have been shown to provide a similar level of assistance and have sufficient experience in collecting scientific data.[9] The patients received home visits from physicians (two or three weekly) and nurses (three to seven weekly) and also have access to on-call visits in case of need.

Ethics committee approval and informed consent were obtained from the University of Palermo. A preliminary consensus on the possible variables to be measured was achieved, not only on the basis of the literature[1–5] but primarily based on the feasibility, simplicity, and reproducibility of parameters to be measured at home (excluding biochemical data, for instance). Consensus regarding the final choices was reached after debating these issues at an investigators' meeting.

Patients were then followed at home according to local policies and protocols. The following information was collected (other than survival time): age at the time of home care admission, gender, residence, marital status, primary cancer diagnosis, Karnofsky Performance Status (KPS) score, systolic blood pressure and heart rate, cyanosis, use of oxygen, and body temperature. Symptom severity was recorded using the Edmonton Symptom Assessment System (ESAS). The ESAS is a validated and reliable assessment tool, commonly

used in cancer patients to screen for symptom severity.[10] With the ESAS, patients rate the severity of the following symptoms: pain, fatigue, nausea, depression, anxiety, drowsiness, lack of appetite, well-being, and shortness of breath. The sum of the patient's responses is the ESAS distress score. Delirium was evaluated by the clinical judgment of the home care palliative care specialists and by the Mini-Mental State Examination (scores less than 24 of 30 were considered to indicate that delirium was present).[11]

Patients were divided into two groups: patients with a survival of less than 10 days (short survival) and patients with a survival of 10 days or more (medium-long survival). This was considered by the panel to be an important interval to provide useful information in terms of communication and therapeutic planning.

Statistical Analysis

Statistical analysis of quantitative and qualitative data, including descriptive statistics, was performed for all items. Continuous data are expressed as mean ± SD, unless otherwise specified. One-way analysis of variance was conducted to analyze the possible relationship between clinical variables and survival. Odds ratios and their 95% CIs were calculated using the univariate and multivariate model of logistic regression analysis. Model performance was evaluated using the Hosmer-Lemeshow test for goodness of fit. The continuous variables that were independently prognostic of survival were assessed in univariate and multivariate linear regression models, and slope coefficients with their SEs are presented. Data were analyzed by Epi Info software, version 6.0 (CDC, Atlanta, GA) and SPSS software, version 14.0 (SPSS, Inc., Chicago, IL). All *P*-values were two-sided, and *P*-values less than 0.05 were considered to indicate statistical significance.

Results

Three hundred seventy-four consecutive patients admitted to home care programs in L'Aquila and Turin were surveyed. The mean age was 72.1 ± 12.7 years; 187 patients were male. Primary tumor frequency is reported in Table 1.

Overall mean survival was 56.2 ± 65 days. Mean survival was 71.5 ± 67 days (287 patients) and 5.6 ± 2.7 days (87 patients) in the short and medium-long survival groups, respectively. No association between type of tumor and survival was observed ($P = 0.162$). On univariate logistic regression analysis, male gender ($P = 0.020$), older age ($P = 0.012$), lower KPS score ($P < 0.0005$), systolic blood pressure less than 100 mm Hg ($P = 0.003$), heart rate more than 100 beats per minute ($P = 0.0006$), delirium ($P = 0.004$), use of oxygen ($P = 0.002$), intensity of fatigue ($P = 0.006$), drowsiness ($P < 0.0005$), appetite loss ($P < 0.0005$), dyspnea ($P < 0.0005$), poor sense of well-being ($P < 0.0005$), and high distress score ($P < 0.0005$) (Tables 2 and 3) were associated with a survival of less than 10 days. Marital status, residence, cognitive function, fever, pain, depression, and anxiety were not found to be significantly correlated with survival.

Table 1
Primary Tumors

Tumor Type	*n* (%)
Gastrointestinal	82 (21.9)
Lung	64 (17.1)
Genitourinary	46 (12.3)
Head and neck	42 (11.2)
Breast	35 (9.4)
Liver	28 (7.5)
Pancreas	26 (6.9)
Non-solid tumors	19 (5.1)
Sarcoma	8 (2.1)
Melanoma	7 (1.9)
Unknown	6 (1.6)
Others	11 (3.0)

In a multiple logistic regression model, low systolic blood pressure and high heart rate, gender, delirium, use of oxygen, poor KPS score, drowsiness, appetite loss, and dyspnea were significantly correlated with a shorter survival (Tables 2 and 3). The Hosmer-Lemeshow goodness-of-fit test for the final model yielded a *P*-value of 0.640, suggesting the model fits the data well.

Discussion

This is the first study to examine factors correlated with a short survival in patients with advanced cancer followed at home. It also was a first attempt to identify some simple variables, easy to measure at home, that can be evaluated in larger studies. Moreover, analysis was based on intensity of symptoms, as

Table 2
Univariate and Multivariate Multiple Regression Analyses in Survival Groups

Variables	Survival ≥10 Days, Mean (±SD)	Survival <10 Days, Mean (±SD)	Univariate Regression Analysis, Coefficient (SE); *P*	Multivariate Regression Analysis, Coefficient (SE); *P*
Age (yr)	71.1 (13.1)	75.1 (10.9)	0.004 (0.002); 0.012	0.002 (0.001); 0.229
KPS score	47.5 (17.1)	35.1 (12.1)	−0.008 (0.001); <0.0005	−0.004 (0.001); 0.002
Pain	2.8 (2.6)	2.9 (2.8)	0.0007 (0.008); 0.933	
Fatigue	6.5 (3.9)	7.7 (2.5)	0.016 (0.006); 0.006	−0.0008 (0.006); 0.888
Nausea	1.5 (2.4)	1.9 (2.5)	0.011 (0.009); 0.209	
Depression	3.8 (2.9)	4.4 (3.3)	0.011 (0.007); 0.124	
Anxiety	3.2 (2.7)	3.8 (3.2)	0.013 (0.007); 0.095	
Drowsiness	2.8 (2.7)	5.1 (2.9)	0.045 (0.007); <0.0005	0.021 (0.008); 0.011
Appetite loss	4.7 (3.1)	6.8 (3.1)	0.036 (0.006); <0.0005	0.025 (0.008); 0.0021
Well-being	5.1 (2.8)	6.5 (2.9)	0.029 (0.007); <0.0005	−0.003 (0.010); 0.743
Dyspnea	2.0 (2.6)	3.9 (3.4)	0.037 (0.007); <0.0005	0.020 (0.007); 0.009
ESAS distress score	31.5 (14.8)	42.1 (16.1)	0.008 (0.001); <0.0005	0.0008 (0.002); 0.740

KPS = Karnofsky Performance Status score; ESAS = Edmonton Symptom Assessment System.

measured by the ESAS, rather than on the mere presence or absence of symptoms.

Numerous factors have been found to be implicated in short survival. A high level of symptom burden is likely to be associated with a shorter survival[12] as well as other signs, such as tachycardia and low systolic blood pressure, which are indirect signs of autonomic dysfunction. All factors implicated in respiratory function (dyspnea, cyanosis, the use of oxygen) were associated with a shorter survival, whereas psychological factors or pain intensity

Table 3
Univariate and Multivariate Logistic Regression Analyses in Survival Groups

Variables	Survival ≥10 Days (*n* = 287), *n* (%)	Survival <10 Days (*n* = 87), *n* (%)	Univariate Logistic Regression, OR (95% CI); *P*	Multivariate Logistic Regression, OR (95% CI); *P*
Gender				
Male	134 (46.7)	53 (60.9)	1.8 (1.1–2.9); 0.02	1.9 (1.1–3.3); 0.024
Female	153 (53.3)	34 (39.1)		
Residence				
Town	199 (69.8)	53 (60.9)	0.7 (0.4–1.1); 0.104	
Village	86 (30.2)	34 (39.1)		
Delirium				
Yes	7 (2.6)	9 (10.7)	4.51 (1.5–13.9); 0.004	3.8 (1.3–11.6); 0.018
No	263 (97.4)	75 (89.3)		
Fever				
Yes	10 (3.6)	5 (6.0)	1.7 (0.5–5.6); 0.350	
No	266 (96.4)	79 (94.0)		
Heart rate				
≥100	23 (8.1)	19 (22.1)	3.2 (1.7–6.2); 0.0006	3.1 (1.4–6.9); 0.005
<100	262 (91.9)	67 (77.9)		
Cyanosis				
Yes	7 (2.4)	5 (5.7)	2.4 (0.7–7.8); 0.125	
No	280 (97.6)	82 (94.2)		
Use of oxygen				
Yes	27 (9.4)	19 (21.8)	2.7 (1.4–5.1); 0.002	2.3 (1.1–4.9); 0.038
No	260 (90.6)	68 (78.2)		
Hospitalization				
Yes	23 (19.8)	2 (8.3)	0.4 (0.1–1.7); 0.181	
No	93 (80.2)	22 (91.7)		
Systolic blood pressure				
<100	26 (9.0)	18 (20.7)	2.6 (1.3–5.3); 0.003	2.7 (1.6–5.9); 0.002
≥100	261 (91.0)	69 (79.3)		
Marital status				
Divorced	8 (2.8)	0 (0.0)	0.9 (0.6–1.4); 0.754	
Single	20 (7.0)	4 (4.7)		
Widow	75 (26.1)	27 (31.8)		
Married	184 (64.1)	54 (63.5)		

OR = odds ratio.

were not determinant. In a multivariate analysis, low systolic blood pressure and high heart rate, gender, delirium, the use of oxygen, lower KPS scores, drowsiness, appetite loss, and dyspnea were confirmed to be correlated with a survival of less than 10 days. These factors are meaningful and easy to assess.

Males had a shorter survival. This result was not expected and only can be explained by later admission to home care in comparison with women, rather than to diseases prevalent in males, as no differences were found in primary diagnosis. Of interest, in a multiple logistic regression model, the ESAS distress score did not influence survival, underscoring the relevance of some specific physical symptoms over others. Finally, it is likely that some parameters, which were found altered only in a small number of patients, might possibly interfere with survival when analyzed in a larger sample of patients. Thus, these parameters should be better assessed in a prognostic model in studies with greater numbers of home care cancer patients.

Studies of cancer patients admitted to home care programs are lacking in the literature, so we were not able to make any comparisons. Many studies published in the last few years, performed in different settings, have allowed the development of various tools to estimate survival, such as clinical prediction of survival, principally based on experience and subject to many biases; the Palliative Prognostic Score; the Palliative Performance Index; and others. Some of these tools require biological markers, which are unreliable or difficult to perform at home.[11]

Recent reviews provide information about predicting survival in patients with advanced disease in the general population.[2–4] Irrespective of the underlying type of malignancy, most patients with advanced cancer experience a prolonged period of gradual decline and then a short phase of accelerated decline in the last weeks of life. The main indicators of this final phase are poor performance status; weight loss; symptoms such as appetite loss, breathlessness, or confusion; and abnormalities on some laboratory parameters, including high white cell count, lymphopenia, hypoalbuminemia, and elevated lactate dehydrogenase or C-reactive protein.[4,5,13] Recently, a two-week survival prognostic model that incorporated both biochemical markers and the presence of appetite loss, dyspnea, and edema[14] was used in a palliative care unit.

Prognostic methods also have been reported, based only on clinical signs. The ESAS, which has been used to assess symptom burden and monitor changes after clinical interventions,[15,16] was used in the present study, and as it is validated in different languages, it may be useful for home care teams as a means of survival prediction. Recently, ESAS scores have been found to worsen in the last four weeks before death compared with those in the previous months.[17] Shortness of breath has been associated with a higher risk of dying in an acute palliative care unit but was unevaluable on multivariate analysis because of a large number of missing data. The observation that tachypnea and oxygen use were both significant highlights the prognostic importance of respiratory failure and its accompanying signs.[11] However, these data were predictors of inpatient mortality rather than length of survival.

In a recent study, fatigue, shortness of breath, lack of appetite, and feeling sad, as assessed by the M. D. Anderson Symptom Inventory, were found to be independent prognostic factors for survival time in hospitalized cancer patients, with a mean survival of 49 days.[18] Similarly, appetite loss, drowsiness, dyspnea, and fatigue were found to be associated with time to death, with a mean survival of 36 days.[12] These data were obtained, however, in the hospital or outpatient clinic setting, and symptoms were evaluated at the last assessment in the palliative care clinic, which was, on average, about five weeks before death.

Of interest, psychological symptoms were not significantly associated with survival, as observed in the present study performed at home. This finding was expected, possibly because psychological symptoms are persistent in the different phases of disease, even when physical symptom burden is less prominent. Similar results have been reported in recent studies using the ESAS.[12,19] The ESAS, however, may not be a reliable or specific measure for psychological symptoms.[20] In another study, for example, depressive symptoms were studied longitudinally using the Beck Depression Inventory, a validated measure for depression. In contrast to the flat pattern found with the ESAS, depression increased in a curvilinear

fashion toward the end of life.[21] The limited psychometric evidence supports the need for further ESAS validation studies.[22]

Surprisingly, hemodynamic values have never been included in previous prognostic models, despite the likelihood that these parameters are meaningfully associated with a short survival and are worthy of appropriate assessment. Of interest, tachycardia was associated with death in an acute palliative care unit.[11]

This study has obvious limitations, given the exploratory nature of this approach and the limited number of patients recruited in two home care programs. These findings need further evaluation in larger prospective studies. However, the findings of this trial may provide useful information for new prognostic models to be tested and validated for use with those patients followed at home.

In conclusion, information about survival in patients with advanced cancer followed at home is of the utmost importance to patients, families, and clinicians, and assessment of simple parameters associated with short survival may be helpful. Low systolic blood pressure and high heart rate, gender, low KPS score, appetite loss, and dyspnea were correlated with a survival of less than 10 days. The combination of physical symptoms of the ESAS and other parameters included in this study, which are simple to assess and repeatable at home, should be further explored in future studies with larger numbers of patients to construct survival models.

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References

1. Viganò A, Dorgan M, Buckingham J, Bruera E, Suarez-Almazor M. Survival prediction in terminal cancer patients: a systematic review of the medical literature. Palliat Med 2000;14:363–374.

2. Stone P, Lund S. Predicting prognosis in patients with advanced cancer. Ann Oncol 2007;18:971–976.

3. Glare P, Sinclair C, Downing M, Stone P, Maltoni M. Predicting survival in patients with advanced disease. Eur J Cancer 2008;44:1146–1156.

4. Maltoni M, Caraceni A, Brunelli C, et al. 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 2005;23:6240–6248.

5. Gripp S, Moeller S, Bolke E, et al. Survival prediction in terminally ill cancer patients by clinical estimates, laboratory tests, and self-rated anxiety and depression. J Clin Oncol 2007;25:3313–3320.

6. Ahlner-Elmqvist M, Jordhoy M, Jannert M, Fayers P, Kaasa S. Place of death: hospital-based advanced home care versus conventional care. Palliat Med 2004;18:585–593.

7. Chvetzoff G, Garnier M, Perol D, et al. Factors predicting home death for terminally ill cancer patients receiving hospital-based home care: the Lyon comprehensive cancer center experience. J Pain Symptom Manage 2005;30:528–535.

8. Ikezaki S, Ikegami N. Predictors of dying at home for patients receiving nursing services in Japan: a retrospective study comparing cancer and non-cancer death. BMC Palliat Care 2011;10:3.

9. Mercadante S, Valle A, Porzio G, et al. How do cancer patients receiving palliative care at home die? A descriptive study. J Pain Symptom Manage 2011;42:702–709.

10. Chang VT, Hwang SS, Feuerman M. Validation of the Edmonton Symptom Assessment Scale. Cancer 2000;88:2164–2171.

11. Elsayem A, Mori M, Parsons H, et al. Predictors of inpatient mortality in an acute palliative care unit at a comprehensive cancer center. Support Care Cancer 2010;18:67–76.

12. Cheung W, Barmala N, Zarinehbaf S, et al. The association of physical and psychological symptom burden with time to death among palliative care outpatients. J Pain Symptom Manage 2009;37:297–304.

13. Kikuchi N, Ohmori K, Kuriyama S, et al. Survival prediction of patients with advanced cancer: the predictive accuracy of the model based on biological markers. J Pain Symptom Manage 2007;34:600–606.

14. Ohde S, Hayashi A, Takahasi O, et al. A 2-week prognostic prediction model for terminal cancer patients in a palliative care unit at a Japanese general hospital. Palliat Med 2010;25:170–176.

15. Elsayem A, Swint K, Fisch MJ, et al. Palliative care inpatient service in a comprehensive cancer center: clinical and financial outcomes. J Clin Oncol 2004;22:2008–2014.

16. Modonesi C, Scarpi E, Maltoni M, et al. Impact of palliative care unit admission on symptom control evaluated by the Edmonton Symptom Assessment System. J Pain Symptom Manage 2005;30:367–373.

17. Zeng L, Zhang L, Culleton S, et al. Edmonton Symptom Assessment scale as a prognosticative indicator in patients with advanced cancer. J Palliat Med 2011;14:337–342.

18. Liu Y, Xi Q, Xia S, et al. Association between symptoms and their severity with survival time in hospitalized patients with far advanced cancer. Palliat Med 2011;25:682–690.

19. Seow H, Barbera L, Sutradhar R, et al. Trajectory of performance status and symptom scores for patients with cancer during the last six months of life. J Clin Oncol 2011;29:1151–1158.

20. Vignaroli E, Pace E, Willey J. The Edmonton Symptom Assessment System as a screening tool for depression and anxiety. J Palliat Med 2006;9: 296–303.

21. Lo C, Zimmermann C, Rydall A, et al. Longitudinal study of depressive symptoms in patients with metastatic gastrointestinal and lung cancer. J Clin Oncol 2010;28:3084–3089.

22. Nekolaichuk C, Watanabe S, Beaumont C. The Edmonton Symptom Assessment System: a 15-year retrospective review of validation studies. Palliat Med 2008;22:111–122.