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Prognostication in palliative cancer care: Both probabilities and uncertainties must be taken into account

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Abstract

Prognosticating survival in palliative cancer patients has been a longstanding challenge. While different tools and approaches may ease prognostication, biological variability limits their accuracy. Assessment of physical status is important for prognostication, along with evaluating the degree of systemic inflammation and patient-reported symptom burden. The distribution of survival was examined among palliative cancer patients with different functional status (Eastern Cooperative Oncology Group Performance Status), inflammation-related markers (modified Glasgow prognostic score [mGPS]), and self-reported symptom intensities (the eleven-point numeric rating scale [0 – 10]). Physical status and biomarkers of systemic inflammatory responses yielded important prognostic information in patients with advanced cancer. Among 147 hospitalized patients, median survival was longer for those continuing anti-cancer treatment, those with better functional status, and those with normal levels of C-reactive protein and/or albumin. Regarding the functional status categories, patients with PS 2 exhibited the widest range of survival. All categories, except PS 4, included patients with actual survival of almost 1 year or more. In terms of inflammatory markers, the widest survival range was observed among patients with mGPS 0. All categories included patients with actual survival of more than half a year, and mGPS 0 and 1 included patients with survival of more than one and a half years. No statistically significant differences in survival were identified between patients with mild and higher intensities of the symptoms under investigation. A wide range of survival outcomes at the group level makes prognostication for individual patients particularly challenging.

Keywords: Prognostication; Palliative cancer care; Probabilities and uncertainties

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1. Introduction

More than 50 years ago, a highly ranked medical journal stated that the survival of cancer patients not receiving active treatment is difficult to predict and that lifespan estimates should be interpreted with great caution.[1] However, prognostication is considered a core clinical skill important for robust decision-making.[2] To address both challenges and requirements, many different procedures have been developed to improve forecasting accuracy.[3] Prognoses may be communicated by a variety of techniques and can be expressed as, for instance, anticipated remaining lifespan, possibility of death, or probability of survival within a defined time frame.[3] In addition, survival prediction is a continuous process, as prognostic factors may change throughout the disease trajectory.[4] The most common prognostic approach is clinician prediction of survival (CPS).[3] Clinical prediction of survival represents a complex process that, based on expertise and experience, attempts to estimate the patients' expected lifespan.[4,5] As prognostic accuracy varies by the patient population under consideration, setting, and time frame, CPS may be supplemented by designated and appropriate instruments.[3,6] Many specific prognostic tools include objective observations, but also subjective symptom scores may be relevant in prognostication, as cancer patients experience a higher intensity of certain symptoms towards the end of life.[4,7-9]

The European Society for Medical Oncology (ESMO) has published a clinical practice guideline for prognostic evaluation in patients with advanced cancer.[6] This guideline emphasizes the importance of CPS and promotes clinical predictions with varying degrees of supplementary information from prognostic factors and multivariable models. For patients receiving disease-modifying treatment (DMT), additional assessments of physical function and inflammation are recommended, whereas the use of multivariable prognostic models is considered optional. For patients no longer receiving DMT and being closer to death, CPS remains important, along with relevant measures of prognostic factors and clinical signs of impending death.[6] In everyday clinical practice, the traditional diagnostic work-up consists of patient-reported information, physical examination, and laboratory findings.[10] Consequently, information on performance status (PS), biomarkers of systemic inflammatory responses, and PROMs may also be routinely available for prognostication purposes.

Formal assessments of physical function, such as the Karnofsky Performance Scale Index and the Eastern Cooperative Oncology Group PS (ECOG PS), were originally developed to evaluate chemotherapy tolerability and responses.[11,12] Although calibrated differently, both systems share the fundamental idea of evaluating patients' ability to carry out normal activities and their dependence on nursing care. For years, these scales have been found relevant and applicable in the prognostication process.[13-15] PS independently predicts survival, and some authors have been described it as a cornerstone of prognosis in advanced cancer.[14] A frequently cited paper, based on data from more than 1,600 participants, reported that patients with advanced cancer and ECOG PS 1 had a median survival of just under 200 days; those with PS 2, approximately 100 days; those with PS 3, approximately 50 days; and patients with end-stage cancer and PS 4, a median remaining lifespan of approximately 25 days.[13]

Inflammation represents another cornerstone of prognosis in advanced cancer.[14] While PS assessments include elements of subjective judgment and clinical evaluation, biomarkers of systemic inflammatory responses are strictly objective measures.[14,16,17] The presence of a systemic inflammatory response may be due to increased disease activity and cancer progression, and research has shown that combined assessment of C-reactive protein (CRP) and serum albumin has independent prognostic value.[18] This combination was named as the Glasgow prognostic score (GPS).[19] Both the GPS and the modified GPS (mGPS) utilize CRP and albumin levels to score patients into three different categories, and the system has been extensively validated for different cancer diagnoses.[14,18,20-22] Higher scores correspond to a more dismal prognosis, and the mGPS is recommended by the ESMO for prognostic evaluation in patients with advanced cancer receiving DMT.[6]

The presence of certain clinical signs and symptoms, such as some of the anorexia-cachexia syndrome, dyspnea, and delirium or cognitive failure, has been demonstrated to carry prognostic significance in patients with advanced cancer.[23] Accordingly, the existence of particular clinical signs and symptoms are incorporated to varying extents into prognostic tools for this group of patients.[7,24] A study of more than 10,000 cancer patients followed over the last 6 months of their lives showed that the PROMs for tiredness, loss of appetite, reduced well-being, and drowsiness increased dramatically towards the end of life.[8] In fact, most of the patients described the intensities of these four symptoms as moderate to severe during the last weeks of life.[8] Additionally, dyspnea tends to intensity as death approaches and is used in several prognostic tools for patients with advanced cancer.[7,8,25] The optimal thresholds for classifying symptom intensity as mild or moderate on the eleven-point numeric rating scale (NRS 0 – 10) are debated.[26,27] For the Edmonton Symptom Assessment

Scale (ESAS), optimal thresholds may even differ by symptom.[26] Personalized NRS 0 – 10 symptom goals for patients with advanced cancer have been investigated, and it is demonstrated that NRS 3 represents a symptom goal for many patients.[28] Additionally, a symptom intensity of NRS 4 or higher has been recommended as a trigger for further measures.[26] This threshold may thus be relevant for distinguishing between mild and more severe symptom intensities.

Despite clinical skills and access to both laboratory results and PROMs, prognostication of the remaining lifespan is encumbered with inaccuracy, as the exact timing of death cannot be predicted with certainty.[4] The introduction of novel treatments, such as targeted anticancer therapy and immunotherapy, has further complicated prognostication.[29] Patients receiving such interventions may experience either major temporary improvements or sustained long-term responses.[29] Furthermore, when prognosticating median survival, defined as the midpoint in an organized dataset, approximately half of the patients will live shorter and half longer than the anticipated time frame.[4] Therefore, clear measures of variability may provide information equally important as measures of central tendency, both in terms of fostering hopes and establishing realistic expectations for the individual patient.[30] Hence, information on expected survival may be challenging to formulate and even more difficult to apprehend.[31] In addition, various prognostic assessments may be considered as tests with defined sensitivities, specificities, and positive and negative predictive values.[32] For practitioners, this implies that results must be interpreted from a clinical perspective and delivered both with caution and careful consideration. Awareness of the potential for contradictory information to arise can further promote sound clinical practice.

By using our previously published data, we aimed to study the inherent uncertainties of commonly used prognostic methods in patients with advanced cancer.[33] Survival was examined across different ECOG PS categories, separate mGPS groups, and among patients with mild or higher intensities of self-reported symptoms known to increase towards the end of life. Additionally, characteristics of patients with both short and longer survival durations were further described.

2. Methods

2.1. Design

The current paper is based on data from a study published by the research group in 2021.[33] The primary study reported on interventions conducted and symptom relief achieved in patients with advanced cancer admitted to an acute palliative care unit (APCU) at a tertiary cancer clinic. The palliative care unit at the cancer clinic, St. Olavs Hospital, Trondheim University Hospital, Norway, comprises 12 beds and receives approximately 450 admissions each year. The clinic has for years been a certified ESMO-designated center of integrated oncology and palliative care. In the primary study, all patients admitted to the APCU between January 15, 2019, and January 15, 2020, were assessed. This paper presents secondary and supplementary analyses of the data collected.

2.2. Patients

The patients referred to the APCU are adult persons with advanced cancer, and for whom palliative care interventions are considered relevant and beneficial. Ongoing anti-cancer treatment does not preclude referral to the APCU, but patients with hematological, gynecological, and pulmonary malignancies are treated at their respective university hospital departments. These patients are only referred to the APCU for follow-up on neuraxial pain management. The present analysis included all patients with available ECOG PS registrations, relevant biomarkers of systemic inflammatory responses, and intensities of self-reported symptoms. Readmissions of previously included patients were excluded from the analysis.

2.3. Assessments

For the current research, data registered at the time of admission were used. ECOG PS registrations, the serum biomarkers CRP and albumin, and patient-reported symptom intensities for tiredness, loss of appetite, reduced well-being, drowsiness, and dyspnea (NRS 0 – 10) were retrieved. The assessment period for PROMs covered the past 24 h. In addition, information was collected on patient demographics, cancer diagnosis, metastatic status, care trajectory (ongoing anti-cancer treatment along with palliative care versus palliative care alone), and survival from admission.

2.4. Analyses

Descriptive statistics were used for demographics and to report survival (in days) for the entire cohort, across different care trajectories, and among different PS groups. Similarly, survival was calculated in patients classified into mGPS categories 0, 1, and 2, respectively.[6] Patients with CRP ≤ 10 mg/L scored 0, patients with CRP > 10 mg/L and albumin ≥ 35 g/L scored 1, and patients with CRP > 10 and albumin <35 g/L scored 2.[18] PROMs for tiredness, loss of appetite, reduced well-being, drowsiness, and dyspnea

were each dichotomized into scores of ≤3 (mild symptom intensities) and scores of ≥4 (higher symptom intensities), and survival was computed accordingly for patients with mild and higher symptom intensities.[8,26,28]

In accordance with ESMO guidance, patients were categorized based on survival time after admission into days (0 – 13 days), weeks (14 – 55 days), or months (≥56 days), with respect to care trajectories, ECOG PS categories, mGPS classes, and symptom intensity levels assessed for the study.[6] Patients with ECOG PS 3 surviving months or longer, and patients with PS 2 surviving only weeks, were further studied with respect to biomarkers of systemic inflammatory responses.

Due to the non-normal distribution of data, non-parametric tests were used for group survival comparisons. Medians were used as the measure of central tendency, and range as the measure of dispersion. The Mann–Whitney U test was used for comparisons between two independent groups, while the Kruskal–Wallis test was used for comparisons involving more than two groups. To investigate which pairs that were different, the Dunn procedure was performed. $p \leq 0.05$ were considered statistically significant.

All calculations were conducted using STATA v17 (Stata Corporation LP; College Station, TX, USA).

2.5. Ethics

The Regional Committee for Medical Research Ethics, Health Region Central Norway (REK) (2018/925/REK midt and 2021/212312/REK midt) defined the primary study and secondary analyses as healthcare improvement activities. In accordance with Norwegian health care legislation, explicit informed consent was not needed.

3. Results

3.1. Demographics

Altogether, 195 readmissions among 451 hospitalizations were excluded from the study. Of the 256 unique patients, 147 had recorded registrations of ECOG PS, CRP, albumin, and self-reported symptom registrations for tiredness, appetite, well-being, drowsiness, and dyspnea at admission. These 147 patients were included in the current analysis and their characteristics are presented in Table 1. The median age was 73 years, 67.3% were males, gastrointestinal and urological cancers were the most common diagnoses, 89.1% had metastatic disease, and 38.8% received anti-cancer treatment. Median overall survival was 52 days (range 3 – 708 days), with significantly longer median survival observed in those receiving anti-cancer treatment (Tables 1 and 2, Figure 1).

Table 1. Demographic and clinical characteristics

Characteristic	Sample	%
Age (median, range)	73 (29 – 92)	
Gender		
Male	99	67.3
Female	48	32.7
Cancer diagnosis		
Gastrointestinal	66	44.9
Breast	10	6.8
Prostate	22	15.0
Other urological	15	10.2
Other	34	23.1
Metastases		
Yes	131	89.1
No	16	10.9
Survival in days (median, range)	52 (3 – 708)	
Care trajectory		
Ongoing anti-cancer treatment	57	38.8
Palliative care alone	89	60.5
Missing	1	0.7
ECOG PS		
1	15	10.2
2	55	37.4
3	69	46.9
4	8	5.4
mGPS		
0	24	16.3
1	75	51.0
2	48	32.7

Abbreviations: ECOG PS: Eastern cooperative oncology group performance status; mGPS: Modified glasgow prognostic score.

3.2. PS and survival

At admission, 15 patients (10.2%) were categorized as ECOG PS 1, 55 (37.4%) as PS 2, 69 (46.9%) as PS 3, and 8 (5.4%) as PS 4. Survival after admission for patients in each category is described in Table 2 and illustrated in Figure 2. Median survival varied across groups, with no statistically significant difference observed between patients with ECOG PS 1 and PS 2. The range for survival also varied and was largest for patients with PS 2. Except for those with PS 4, all categories included patients who survived almost 1 year or more. All categories also included patients who survived <1 month.

3.3. Biomarkers and survival

At admission, 24 patients (16.3%) were scored as mGPS 0, 75 (51.0%) as mGPS 1, and 48 (32.7%) as mGPS 2. Survival

Table 2. Care trajectory, performance status, biomarkers, symptom intensities, and days of survival

	n	Median	Range	*p*-value*
Care trajectory				
Ongoing anti-cancer treatment	57	82	3 – 629	<0.01
Palliative care alone	89	40	6 – 708	
Missing	1			
ECOG PS[2]				
1	15	122	19 – 368	ref. category
2	55	79	10 – 708	0.23
3	69	42	3 – 320	<0.01
4	8	19	6 – 33	<0.01
mGPS[3]				
0	24	68	13 – 708	ref. category
1	75	68	6 – 629	0.44
2	48	30	3 – 273	<0.01
Tiredness				
Mild symptom intensity	28	81	3 – 629	0.08
Higher symptom intensity	119	44	6 – 708	
Loss of appetite				
Mild symptom intensity	56	60	6 – 708	0.09
Higher symptom intensity	91	45	3 – 368	
Reduced well-being				
Mild symptom intensity	55	52	6 – 361	0.74
Higher symptom intensity	92	52	3 – 708	
Drowsiness				
Mild symptom intensity	40	75	3 –629	0.16
Higher symptom intensity	107	45	6 – 708	
Dyspnea				
Mild symptom intensity	84	64	6 – 708	0.13
Higher symptom intensity	63	42	3 – 439	

Note: *Variables with two categories were compared with the Mann–Whitney *U* test, and variables with more than two categories with the Kruskal–Wallis test and the Dunn procedure.
Abbreviations: ECOG PS: Eastern cooperative oncology group performance status; mGPS: Modified glasgow prognostic score.

after admission for patients with the respective scores is delineated in Table 2 and illustrated in Figure 2. Median

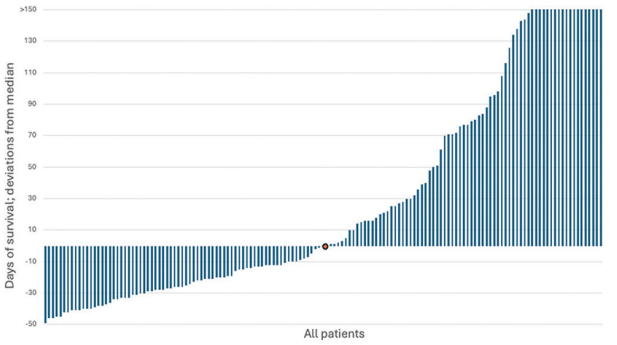


Figure 1. Survival variability in the study population. Zero on the y-axis represents median survival for the entire study population. The vertical bars represent negative and positive deviations from the median survival (in days) for each patient.

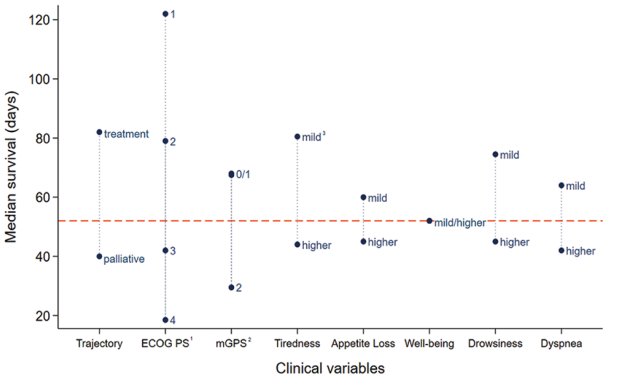


Figure 2. Selected patient characteristics and median survival for the respective groups
Notes: [a]Eastern cooperative oncology group performance status (ECOG PS); [b]Modified glasgow prognostic score (mGPS); [c]Mild and higher symptom intensities; [d]The dotted horizontal line represents the median survival for the entire study population; [e]Median survival was similar for patients with mGPS 0 and 1, as well as for those with mild and higher symptom intensities related to reduced well-being.

survival was similar for patients with mGPS 0 and 1, but significantly different in patients with mGPS 2. The range for survival varied and was largest for patients with mGPS 0. All categories included patients who survived more than half a year, whereas those with mGPS 0 and 1 included patients who survived over one and a half years. All categories also included patients who survived <1 month.

3.4. Symptom intensity and survival

Details on dichotomized symptom intensities for tiredness, loss of appetite, reduced well-being, drowsiness, and dyspnea related to survival are depicted in Table 2 and illustrated in Figure 2. No statistically significant differences in survival were observed between patients with mild and higher intensities of these symptoms. Except for well-being, there was a non-significant trend

towards decreased survival for those with higher symptom intensity scores. All categories included patients who survived approximately a year or more, as well as patients who survived <1 week.

3.5. Characteristics of patients who survived days, weeks, and months

Fourteen patients (9.5%) survived 0 – 13 days, 65 patients (44.2%) survived 14 – 55 days, and 68 patients (46.3%) survived 56 days or more after admission. The distribution of the respective care trajectories, ECOG PS categories, mGPS classes, and symptom intensity levels assessed for the study purpose is shown in Table 3. Patients with longer actual survival had better functional status and less systemic inflammation, and anti-cancer treatment was withdrawn in most patients who survived only days. No patients with ECOG PS 4 lived for months, and no patients with PS 1 survived only days. However, 25 patients with ECOG PS 3 lived for months or longer, and 22 patients with PS 2 survived only weeks. Further analyses (not shown in the tables) demonstrated that the percentage of patients with mGPS 2 was similar (7/25 [28.0%] vs. 6/22 [27.3%], respectively) in these two groups and that almost one third (6/22 [27.3%]) of patients with PS 2 and only weeks of survival had mGPS 0.

Table 3. Characteristics of patients who survived days, weeks, and months

	Days (*n*=14)		Weeks (*n*=65)		Months (*n*=68)	
	n	%	*n*	%	*n*	%
Care trajectory						
Ongoing anti-cancer treatment	2	14.3	20	30.8	35	51.5
Palliative care alone	12	85.7	44	67.7	33	48.5
Missing			1	1.5		
ECOG PS						
1	0	0	4	6.2	11	16.2
2	1	7.1	22	33.8	32	47.1
3	10	71.4	34	52.3	25	36.8
4	3	21.4	5	7.7	0	0
mGPS						
0	1	7.1	11	16.9	12	17.6
1	3	21.4	29	44.6	43	63.2
2	10	71.4	25	38.5	13	19.1
Tiredness						
Mild symptom intensity	2	14.3	10	15.4	16	23.5
Higher symptom intensity	12	85.7	55	84.6	52	76.5
Loss of appetite						
Mild symptom intensity	3	21.4	25	38.5	28	41.2
Higher symptom intensity	11	78.6	40	61.5	40	58.8
Well-being						
Mild symptom intensity	5	35.7	24	36.9	26	38.2
Higher symptom intensity	9	64.3	41	63.1	42	61.8
Drowsiness						
Mild symptom intensity	3	21.4	16	24.6	21	30.9
Higher symptom intensity	11	78.6	49	75.4	47	69.1
Dyspnea						
Mild symptom intensity	6	42.9	34	52.3	44	64.7
Higher symptom intensity	8	57.1	31	47.7	24	35.3

Abbreviations: ECOG PS: Eastern cooperative oncology group performance status; mGPS: Modified glasgow prognostic score.

4. Discussion

4.1. Statement of principal findings

As demonstrated in previously published research, ECOG PS status and biomarkers of systemic inflammatory responses yielded important information for prognostication in patients with advanced cancer. Notably for the clinician, some patients with reduced functional status and systemic inflammation lived for months or longer, and some with better function or little inflammation survived only days. Although no patients with ECOG PS 4 lived for months and no one with PS 1 survived only days, the studied factors could not accurately predict the timing of death for the individual patient. In this single-center study with a limited number of patients included, statistically significant survival differences for patients with mild and higher intensities of the symptoms under investigation were not demonstrated.

4.2. Appraisal of methods

As evidence-based practice is an important basis for palliative cancer care, appreciating the study design employed to answer a particular research question is critical.[34] Retrospective analyses exhibit important design limitations that should be considered.[34] However, they have a place in research, earn their utility, and contributed to important discoveries, such as the association between smoking and lung cancer.[34,35] However, retrospective studies are subjected to biases and are unable to display causal relationships.[34] The results should be interpreted with caution but may provide hypotheses for future prospective studies.[34] The current paper presents secondary analyses of data collected with the intent to describe interventions and symptom relief in an APCU.[33] Consequently, the data were gathered for purposes other than to address the study objectives.[36] In addition, this study did not investigate the recommended use of combinations of techniques to improve prognostication accuracy.[6] Furthermore, the

small sample size and study context, with a single-center design and a highly selected patient population, represent other factors affecting the risk of false results, incorrect associations, and limited external validity.[37,38] Moreover, the current study included patients from two different care trajectories with significantly different prognoses, and both sample size and survival variability affect statistical power.[39]

4.3. Comparison with previous work

Prognostic information is important at several levels for patients, their families, and health care providers.[6] For patients and their next of kin, it may guide and facilitate realistic future planning when time is limited, addressing both opportunities and limitations. For health care providers, prognostic information may represent a valuable tool for optimizing resource utilization and ensuring quality of care.[6] Therefore, previous research conducted to improve the accuracy and precision of prognostication methods and to describe associations with quality of life is highly relevant.[23,40-43]

Clinicians should use their clinical experience to predict the survival of patients with advanced cancer, and it is suggested that they supplement their judgment with input from multiple professionals.[6] In addition, over the years, it has become increasingly evident that combining several factors improves prognostication accuracy.[6,23,40,44] The ESMO Clinical Practice Guideline on prognostic evaluation in patients with advanced cancer in the last months of life also endorses this practice.[6] After the development of the Palliative Performance Scale, which is a modified Karnofsky Performance scale, more complex scoring systems and predictor models have been developed.[45-49] To varying degrees, comprehensive tools such as the palliative prognostic index, the palliative prognostic score, the Feliu prognostic nomogram, and the prognosis in palliative care study incorporate knowledge based on patient-reported information, laboratory findings, as well as physical examination and evaluations.[7,48] The goal was neither to validate established approaches nor to suggest new ones; the focus was solely to underline that prognostication implies dealing with uncertainties that must be considered from a clinical point of view.[1,31,50,51]Properly addressing these uncertainties includes gauging the patients' baseline understanding of their prognosis and gathering knowledge about the type of information they would like to discuss.[6]

Patients with advanced cancer may suffer from sudden and unexpected worsening and clinical crises, often regarded as oncological emergencies.[52] In the dataset on which the current study is based, 302 out of 451 admissions (67%) were due to emergencies, and during 57 hospitalizations (13%) the patient died.[33] With emerging therapies, more oncology patients are expected to live longer but also face the risk of undergoing a rapid and unpredicted decline.[29,53] This emphasizes the importance of available contextual information in the prognostication process.

Functional performance typically dwindles as cancer patients are approaching death, and ECOG PS is strongly associated with survival in patients with late-stage disease.[8,54] PS is incorporated into existing tools and evaluated for its prognostic capacity across different clinical settings.[6,7,14,40,55-58] The ESMO clinical practice guideline on prognostic evaluation in patients with advanced cancer during the last months of life also recommends the use of PS for prognostication purposes.[6] However, variability in individual survival within each ECOG PS group has been demonstrated in populations with both shorter and longer median survival than reported in the current study.[13,54] These findings, combined with the current results, underscore the challenges of using group data to treat or prognosticate individuals.[59] Nevertheless, communicating prognosis based on declined functional performance may represent an easily understandable starting point for both shared decision-making and advance care planning.[6]

Inflammation and tumor progression are closely linked, and from a prognostic perspective, CRP and albumin have been studied in thousands of patients.[18,60] These two measures constitute the components of the mGPS, with increased CRP levels recognized as a reliable negative prognostic factor, particularly when accompanied by decreased albumin levels.[6,18,40] The ESMO clinical practice guideline on prognostic evaluation in patients with advanced cancer during the last months of life also advises the inclusion of systemic inflammation markers in the prognostic assessment.[6] Nevertheless, as observed for ECOG PS categories, a large individual variability in survival exists within each mGPS group. Furthermore, median survival values for groups do not allow precise predictions for individual patients. Additionally, palliative cancer patients face a high risk of serious infections, and alternative explanations for the presence of systemic inflammatory biomarkers should also be considered.[61]

Patients with advanced cancer may experience a multitude of symptoms.[62] Many of these symptoms are clustered, with four common groupings identified: Anxiety-depression, nausea-vomiting, nausea-appetite loss, and fatigue-dyspnea-drowsiness-pain.[62] Both the presence and severity of certain symptoms, as well as overall symptom intensity scores, have been shown to negatively correlate to survival.[58,63] However, when interpreting results on symptom burden and survival, it is important to consider

that even the mere exposure of NRS 0 – 10 assessments may be positively associated with survival.[64] Nonetheless, higher symptom scores are associated with an increased risk of death, and many patients report increased tiredness and drowsiness, decreased appetite and well-being, and dyspnea towards the end of life.[8,9] Based on the limited number of patients with a wide range in survival times, statistically significant differences between low and higher symptom intensities could not be demonstrated for symptoms previously demonstrated to increase near the end of life.[8,39] With a large sample size and a different patient population, the results may have been different.

The remaining lifespan of palliative care patients varies, and although predictions are often inaccurate, survival may be expressed and presented as median days, weeks, or months.[6,49,61,65] To fully convey prognostic information, it is essential to present not only measures of central tendency but also interpretable and understandable measures of biological variability.[66] In this context, the range provides information into both the minimum and maximum expected survival times.[66] Effectively communicating the uncertainty, limitations, and unreliability of prognostic information is an important clinical skill.[2,6] To illustrate the intrinsic restrictions of established methods of prognostication, this study examined functional status, systemic inflammation, and self-reported symptoms in patients who survived for days, weeks, or months after admission to an APCU. Although functional status and degree of systemic inflammation provide important prognostic information, outliers complicate the clinical interpretation and reduce the predictive value of parameters registered at a single time point when estimating the remaining lifespan for individual patients.

4.4. Future work

Directions for future research on prognostication in advanced cancer have been published.[3] These include ten important themes with the potential to advance prognostication science. Emphasis is placed on improving prognostication accuracy while acknowledging inherent uncertainty and considering how prognostic information can be used in everyday clinical practice.[3] For tools to be relevant to palliative care physicians, they must be simple enough for practicality and complex enough to be effective.[67,68] This study illustrated the limitations and pitfalls of using variables recorded at a single time point to prognosticate the dynamics trajectory of palliative cancer care.[8] For instance, dynamic changes in systemic inflammatory markers may provide important information regarding cancer aggressiveness.[69] Employing information from repeated assessments is considered as good clinical practice in palliative cancer care and may be widely utilized in prognostication research.[70] Such an approach would also be more robust in accounting for intercurrent events that can affect functional status, laboratory findings, and symptom presentation.

5. Conclusion

Commonly used prognostic markers have demonstrated utility at the population level. However, for individual patients, statistical measures of central tendency may have limited clinical value. Palliative cancer care patients who present with favorable prognostic factors may live shorter than expected, whereas others with disadvantageous markers may outlive the expectancy. Prognostic communication should acknowledge and incorporate this inherent uncertainty.

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Conflict of interest

The authors declare that they have no competing interest.

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Writing – original draft: All authors
Writing – review & editing: All authors

Ethics approval and consent to participate

This investigation containing both primary study and secondary analyses was approved by The Regional Committee for Medical Research Ethics, Health Region Central Norway (REK) (2018/925/REK midt

and 2021/212312/REK midt). In accordance with the Norwegian health care legislation, explicit informed consent was not needed.

Consent for publication

On specific request, The Regional Committee for Medical Research Ethics, Health Region Central Norway (REK) stated that addressing patients or relatives of deceased patients for consent for publication would constitute a burden without benefit, as the presented data are completely anonymized and by no means suitable for identifying individual patients. Thus, a request of consent for publication was not recommended or needed.

Availability of data

All the primary data and all the analyzes are stored at an institutional server and can be obtained from the corresponding author at reasonable request.

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