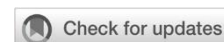


Prognostication in patient with terminal stage of cancer

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Abstract

Prognosis is one of the most critical factors affecting clinical decision in medical practice. In terminal illness where patients are only less than months to live, prognostication is essential to provide an appropriate plan, particularly to avoid futile treatment and to arrange palliative care referral. Prognostication is a process of foreseeing and foretelling, which enable the health care team, patients and family to be involved in the decision making. Determining prognosis is a challenge for doctors as lack of knowledge and skills and fear of the response of the patients and their families. Prognostication is essential in decision making among terminally ill patients, as the risks of adverse effects, energy, time and cost potentially outweighs the benefit of survival, quality of life, functional gain and hope. The benefit of prognostication is not only for the doctors, but particularly to the patients, their families, as well as to institution and health care system. In daily practice a subjective judgment made by doctor based on clinical assessment is usually overoptimistic. A tool is needed to make a better prognostication. Palliative Prognostic Index (PPI) and Palliative Prognostic Score (PaP score) are the most common tools used in palliative care setting.

Keywords: cancer, prognostication, terminal stage, tools

Abstrak

Dalam praktek kedokteran, prognosis adalah salah satu faktor yang sangat penting dalam pengambilan keputusan. Pada stadium terminal, pasien diperkirakan memiliki harapan hidup beberapa bulan atau kurang, sehingga prognosis sangat penting dalam merencanakan perawatan yang tepat untuk menghindari tindakan yang sia-sia dan dapat melibatkan perawatan paliatif dalam penatalaksanaan selanjutnya. Penentuan prognosis merupakan proses memperkirakan harapan hidup dan mengomunikasikan kepada pasien dan keluarga sehingga dapat terlibat dalam pembuatan keputusan. Membuat prognosis merupakan tantangan bagi dokter, karena kurangnya pengetahuan dan ketrampilan serta kekhawatiran terhadap respons pasien dan keluarga. Penentuan prognosis penting untuk pasien dengan penyakit stadium lanjut, karena risiko efek samping, tenaga, waktu, dan biaya berpotensi melebihi manfaat dari harapan hidup, kualitas hidup, status fungsional, dan harapan yang bisa dicapai. Manfaat penentuan prognosis tidak hanya bagi dokter, tetapi terutama bagi pasien, keluarga, dan institusi serta sistem kesehatan. Dalam praktek klinik, prognosis yang dibuat dokter biasanya melebihi yang sebenarnya. Dibutuhkan sebuah alat untuk menentukan prognosis dengan lebih baik. *Palliative Prognostic Index (PPI)* dan *Palliative Prognostic Score (PaP score)* merupakan alat yang paling umum digunakan pada pasien kanker stadium terminal.

Kata kunci: alat, kanker, prognosis, stadium terminal

Background

Formulating prognosis and estimating survival are as important as making diagnosis of cancer. On the contrary, not defining prognosis or incorrectly defining prognosis is as dangerous as misdiagnosis.¹ An accurate prognosis is required to provide an appropriate and specific clinical plan of care and for ethical reasons such as prevention of inappropriate or futile treatment in vulnerable patients, as well as organizational intent.² Prognosis gives us a timeframe and leads us to design a realistic goal of treatment.³ This paper discusses about the advantages of prognostication, process of prognostication in advanced or terminal stage of cancer and prognostication tools in advanced/terminal stage of cancer.

Prognostication in Terminal Stage of Cancer

Prognosis in early stage of cancer is defined based on pathology results, proper diagnostic and treatment. In advanced or terminal stage, however, clinical condition is the main factor in determining the prognosis.⁴ Determining prognosis is a challenge. It may create distress and induce fear due to patient's or family's response. Many doctors refuse to response or unclearly explain the prognosis or overoptimistic.⁵ Studies in the USA found doctors are lacking of knowledge and skills in prognostication and communication about prognosis.⁵ According to Aaboom et al, most doctors do not clearly determine terminal stage for their cancer patients.⁶ In Denmark, only 1/3 of terminally stage patients was diagnosed as terminal stage which result in high mortality rate in hospital. Hui and Bruera argue, that is not only biological factor to define prognosis, but also psychological aspect, financial and logistic availability.⁷ European Association of Palliative Care suggest that prognosis is required to set a plan of care whether a patient should receive palliative treatment intent to prolong survival or approach for comfort.⁸

The Benefit of Application of Prognostication in Clinical Practice

Decision making in clinical practice is critically based on prognosis. It directs the approach of investigations and treatment which is tailored to many other biological, psychosocial, logistical, and financial factors. Terminally ill patients are those who are expected to live for months or less. Having knowledge of short survival is essential in decision making among these specific patients, as the risks

of adverse effects, energy, time and cost potentially outweighs the benefit of survival, quality of life, functional gain and hope. The benefit of prognostication for the patients and families include having change to consider aggressive measures, to say good bye, to finish unfinished business, to use the remaining life according to their values, and to provide advanced directives. The absence of prognostication in advanced stage and terminally ill patients will cause more suffering due to futile treatment and inefficiency particularly during the National Health Insurance (Jaminan Kesehatan Nasional) era. In Indonesian culture, fighting to the end and the value of giving the best are tightly held. It will be difficult for clinicians to withdraw or withhold futile treatment if prognostication is not formulated. Prognostication in terminally ill patients will assist the clinician to avoid futile treatment and to arrange palliative care referral aims to improve quality of the remaining life, to relieve suffering, to achieve peaceful, comfort and dignified death as well as to lighten the burden of the family. These factors are considered to the need of prognostication.⁷

Generally, the risk of getting complication and side effect from treatment significantly increased, and the potential of benefit dramatically decreased. Therefore, less aggressive approach is recommended. In the end of life, the goal of care changes from to prolong life to care for comfort. For those who have few weeks of survival, one week of hospitalization may take a long period of their remaining life. They may prefer to be cared for at home despite receiving less effective treatment. Delirium is a barrier of being able to express symptoms, make decision and choose the treatment. Therefore, the family should make the decision on behalf of them. Difficulty in prognostication results in dilemma of recommendation. Terminally ill patients usually are complicated by comorbidities which hinder diagnosis procedure and treatment. At the end of life, diagnostic tests aim to confirm diagnosis without treatment change should be avoided. Therapy to prevent long term complications may not be appropriate. However, therapy with short onset and symptomatic is highly recommended. Hospital discharge can be based on survival.

Prognostication as a Process of Foreseeing and Foretelling

Prognostication is a process not an event, consisting of two components namely foreseeing and foretelling. Foreseeing is formulating the probability of a patient

to achieve response in certain period, while foretelling is communicating the prognosis to the oncology team, the patient or the family. Foreseeing can be based on subjective judgment using intuition or objective assessment using prognostic factors or prognostication tools, such as Palliative Prognostic score (PaP Score) and Palliative Prognostic Index (PPI).⁷ Prognosis is not merely estimation of survival, but also probability treatment response, cancer progressiveness or recurrence, death, disability, toxicity and cost.⁵

The components of prognostication include Clinical Prediction of Survival (CPS), Performance Status (PS), symptoms and laboratory results and other factors, including organ metastasis, tumor response, disease progression, and multiple organ failure.⁴

Clinical Prediction of Survival (CPS)

CPS is a subjective judgment made by doctor based on clinical assessment. It has limitation in its capacity when it is used alone. It becomes an independent value if combined with other prognostic factors or prognostic tools. According to a system review, CPS is 45% overoptimistic towards Actual Survival (AS). It has 25% accuracy in estimating one week of survival, 20-30% in answering the question how long this patient will live and 90% in responding question of would you be surprised if this patient dies in a week.^{5,7}

Performance Status (PS)

Karnofsky Performance Scale (KPS) and The Eastern Cooperative Oncology Group Performance Status (ECOG-PS) are widely used performance status tools in oncology. KPS describes patient functional and family or society burden. It does not directly show the prognosis rather the disease state, comorbidity and the impact of both in the patient's vitality. It needs other assessment to determine survival. Low score of KPS becomes a sensitive predictor of poor prognosis but not in vice versa.⁸ ECOG is commonly used in oncology. Compared to KPS, ECOG is less sensitive at the low performance status.

Symptoms and signs

Various symptoms are related to prognosis in advanced or terminal stage of cancer. A systematic review by Trajkovic-Vidakovic in 2012 found the symptoms mostly related to survival in univariate analysis as follow: confusion, anorexia, fatigue, cachexia, loss of

weight, cognitive disturbance, drowsiness, breathlessness, dysphagia, dry mouth and depression.⁹

Laboratory result

Biological parameters are essential factor in prognostication for patients with early stage of cancer who are receiving cancer treatment such as tumor marker, hormonal status, epidermal growth factor receptor (EGFR), as well as simple parameters for examples sodium count, lymphocyte, albumin and bilirubin.¹⁰ Increased bilirubin count is an indicator of low survival among patients in palliative care. They were proven to be more important than the type of cancer, tumor site, site of metastases and tumor grade.^{5,10} Leukocytosis and lymphocytopenia consistently related to survival, while serum level of albumin, prealbumin, total protein, pseudocholinesterase, high percentage of neutrophil proteinuria fail to show as prognostic parameters.^{11,12} C-reactive protein is a prognostic factor of "sentinel event", a sudden poor condition toward death. Some of the causes of sentinel event are renal disfunction, bacteremia, post amputation, myocardial infarction, dysphagia in dementia, decubitus and aspiration.⁵ Death in early stage of cancer is related to increased C-reactive protein.¹³ Leukocytosis is found in many early stages of cancer. The pathophysiology is unclear, but it is related to tumor growth.¹² In a study conducted by Chong Liang et al, it was found that neutrophil, lymphocyte and thrombocyte are potential parameter to predict survival. Three of them become independent factors. Abnormality of two out of those three parameters shows a systemic change related to death. Neutrophil and lymphocyte count negatively related to survival, while thrombocyte shows a positive relation to survival.^{12,14}

Prognostication tools

Palliative Performance Status (PPS), Palliative Prognostic Score (PaP score), Delirium PaP (D-PaP) and Palliative Prognostic Index (PPI) are the most frequent tools used in palliative care.⁴

Palliative Performance Status (PPS)

PPS is a modification of KPS which include oral intake and consciousness state. PPS has a strong correlation with survival. The higher the score, the longer the survival.^{15,16,17} Study done by Myers showed 66% accuracy among outpatients. There are some limitations of PPS. Firstly, it is useful in assessing risk of death in population but not individual patient.¹⁸ Secondly, It cannot be used

alone in advanced stage or terminal stage of cancer as other factors are required in predicting survival such as quality of life, laboratory result, type of cancer, CPS and sentinel event.¹⁶ The application of

PPS is more useful in early discussion of goal of treatment. According to Myers, PPS 70, 60, 50 means median survival duration are 6 months, 3 months and 2 months, respectively.¹⁸

Table 1. Palliative Performance Status⁵

PPS level	Ambulation	Activity level and evidence of disease	Self-care	Intake	Level of Consciousness
100	Full	Normal activity and work, no evidence of disease	Full	Normal	Full
90	Full	Normal activity and work, some evidence of disease	Full	Normal	Full
80	Reduced	Normal with effort, some evidence of disease	Full	Normal or reduced	Full
70	Reduced	Can't do normal job or work, some disease	Full	Normal or reduced	Full
60	Reduced	Can't do hobbies or work, significance disease	Occasional assistance needed	Normal or reduced	Full/confusion
50	Mainly sit/lie	Can't do any work, extensive disease	Considerable assistance needed	Normal or reduced	Full/confusion
40	Mainly in bed	Can't do any work, extensive disease	Mainly assistance	Normal or reduced	Full/drowsy/confusion
30	Bed bound	Can't do any work, extensive disease	Total care	Reduced	Full/drowsy/confusion
20	Bed bound	Can't do any work, extensive disease	Total care	Minimal	Full/drowsy/confusion
10	Bed bound	Can't do any work, extensive disease	Total care	Mouth care only	Drowsy/coma
0	Death				

PPS: palliative performance status
cited with modifications from reference 5

Palliative Prognostic Score (PaP score)

PaP score is combination of Clinical Prediction of Survival, Karnofsky Performance Scale, and symptoms of anorexia, breathlessness, leukocytes and lymphocyte count. PaP score is not suitable in hematology, myeloma and renal cancer.¹⁹ In this tool, the normal range of leukocyte is 4800 – 8500 cells/mm³, and leukocytosis >8500 – ≤ 11,000 is considered ≤30% change of normal range, and >11,000 is more than >30%. Normal range of lymphocyte is 20 – 40% of total leukocyte. It is

considered low if in the range of 12% - <20% (≤40% of normal range) and extremely low if <12% (>40% of normal range).

PaP score is used to calculate probability of 30-day survival.¹² Validation has been done in various palliative care settings in Italy including hospice, palliative care unit as well as in oncology inpatients.²⁰ In Australia, it has been validated in hospice.¹¹ The PaP score is significantly different between those three groups, with 97%, 57% and 25% probability of 30-day survival, therefore it is recommended.¹²

The interpretation of PaP score is as follows:¹⁹
 0-5,5 : 30 days survival > 70% (high)
 6-11 : 30 days survival 30-70% (moderate)
 11.5-17.5 : 30 days survival <30% (low)

PaP score was created in 2004. In 2015, it was modified by adding delirium, and then named D-PaP score. By adding 2 score for delirium the maximal score becomes 19,5.

Table 2. Palliative Prognostic Score¹⁹

Variables	Score
Breathlessness	
No	0
Yes	1
Anorexia	
No	0
Yes	1,5
KPS	
>40%	0
10-40%	2,5
CPS	
>12	0
11-12	2
7-10	2.5
5-6	4.5
3-4	6
1-2	8.5
Leukocyte count	
≤ 8.500	0
8.500 – 11.000	0.5
>11.000	1.5
Lymphocyte percentage	
20-40%	0
12-19,9%	1
<12%	2.5

KPS: Karnofsky performance scale, CPS: clinical prediction of survival
 cited with modifications from reference 19

Palliative Performance Index (PPI)

Palliative Performance Index (PPI) is a prognostic tool which includes PPS, oral intake, symptoms of edema, breathlessness, and delirium. This tool was created and validated in hospice setting in Japan. It is easy to use and applicable in various settings of palliative care service. It can be easily used by oncologists, palliative care physicians or general practitioners.¹⁰ Survival is divided into three groups, >6 weeks, 3-6 weeks and <3 weeks. Using score >6 as the cut-off point, 3 weeks survival has sensitivity 80% and specificity 77%.²¹

Table 3. Palliative Performance Index¹⁰

Variables	Score
PPS	
10-20%	4
30-50%	2.5
>50%	0
Delirium	4
Breathlessness at rest	3.5
Oral Intake	
1 spoon or less	2.5
Reduced but more than 1 spoon	1
Normal	0
Edema	1
Delirium (is not solely by a single medication)	4
Median survival 68 days (52-115 days)	0 – 4
Median survival 21 days (13-33 days)	5 - 6
Median survival 5 days (3-11 days)	7 – 15

PPS: palliative performance status
 cited with modifications from reference 10

Conclusion

Prognostication is essential in developing care plan for terminally ill patients. Therefore, having knowledge and skills in this area is required to achieve quality of life, quality of end of life care, and quality of death which become parameters of success in oncology. Both prognostication tools have been validated and widely used, therefore recommended to be used in Indonesia. If laboratory data is available and the clinician is confident to make CPS, PPI is more recommended.

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