Prediction survival of Egyptian patients with advanced gastrointestinal malignancies using the Chuang ‘s prognostic score

Thesis Submitted in the partial fulfilment of

Master degree in Clinical Oncology

BY

Abha Ali Abdullah Mohammed

Resident of Clinical Oncology

Faculty of medicine, Cairo university

Under the supervision of

Prof .Dr. Omar Al-Farouk Zaki

Professor of clinical oncology

Clinical oncology department

Faculty of medicine, Cairo university

Prof.Dr. Amr Yehia Sakr

Professor of clinical oncology

Clinical oncology department

Faculty of medicine, Cairo university

Dr.Dina Ezz EL-Dain Farag

Lecturer of clinical oncology

Clinical oncology department

Faculty of medicine, Cairo university

Faculty of Medicine

Cairo University

2015

Acknowledgment

First, before all, thanks be to GOD this work has been accomplished. I would like to express my deepest thanks are sincerely offered to all my professors and colleagues for their encouraging attitude.

First, I wish to offer my sincere thanks to Dr. Omar Zaki, Dr. Amr Sakr, Dr.Samy Alsirafy.

Professors of Clinical Oncology, Cairo University, and Dr. Dina Ezz lecture of clinical oncology, Cairo University for their valuable assistance and support, which have always been beyond description.

Thanks all my family for my Mom and my sisters and brothers and all my family. I would like to special thank with all my respect and love to my brother in law (Salah Ali) to give me this chance to complete my graduate studies by his support. And (Ali Saleh Al-shaibi) for his support me in the absence of my family in cairo.

I specialized thanks for, all my friends in NEMROCK For their care and for all love in my special life and in my work and for continuous encouragement.

Finally all my deepest thanks are for my lovely city (CAIRO) for all moments where I have lived.

Abha

Abstract

Background and aim:

With the increasing number of agents active against cancer, advanced cancer patients including metastatic colorectal cancer (MCC) patients may continue receiving palliative systemic anticancer therapy (PSAT) near the end-of-life. Validated palliative prognostic models may be helpful in identifying MCC patients with limited survival who are unlikely to benefit from PSAT. One of these models in the Chuang's prognostic score (CPS) which was developed to predict survival in terminal cancer patients.

Methods:

The CPS was prospectively assessed in 39 patients with MCC who were receiving PSAT. It is based on eight items: ascites, edema, cognitive impairment, liver and lung metastases, performance status, tiredness and weight loss. The total CPS score ranges from 0 to 8.5 with the higher score indicating worse prognosis.

Results:

For the whole group of patients, the median survival from the date of CPS assessment was 103 days (95%CI: 75-131) and the median CPS score was 4.5 (range: 2 – 8). Patients were divided into two groups using a CPS cutoff socre of 5, group 1 with a CPS score ≤5 and group 2 with a CPS score >5. Group 1 patients had a significantly (p=0.014) longer median survival of 149 days (95%CI: 77-221) in comparison to group 2 patients who had a median survival of 61 days (95%CI: 35-87). Using the same cutoff score, 3-month mortality was predicted with a positive predictive value of 71%, a negative predictive value of 76%, a sensitivity of 63%, a specificity of 83% and an overall accuracy of 74%.

Conclusions:

The CPS may be useful in identifying MCC patients with relatively shorter survival who are unlikely to benefit from continuing PSAT. Further studies to explore the role of the CPS and other palliative prognostic models in predicting survival in incurable cancer patients receiving PSAT are needed.

Keywords: Colorectal cancer, Metastases, Palliative systemic anticancer therapy, Prognosis, Chuang's prognostic scale, End-of-life care

Table of Contents

List of Table

List of Figure

List of Abbreviations

CPS	**Chuangs prognostic score**
ECOG	**Eastern Co-operative Oncology Group**
KPS	**KPS Karnofsky Performance Status**
PaP Score	**The Palliative Prognostic Score**
PPI	**Palliative Prognostic Index**
PPS	**Palliative Performance Status**
PPV	**Positive Predictive Value**
QOL	**Quality of Life**
GIT	**Gastrointestinal tract**
TCP Score	**Terminal Cancer Prognostic Score**
(CACS)	**Cachexic anorexia syndrome**
ChPS	**The Chinese Prognostic Scale**
NPV	**Negative Predictive Value**
PCMU	**Palliative Care Medicine Unit**
NEMROCK	**Kasr El Einy Centre of Clinical Oncology and Nuclear Medicine**
MCRC	**Metastatic colorectal carcinoma**
HCC	**Hepatocellular carcinoma**

Introduction

Estimating survival of advanced cancer patients is important for many reasons (**Glare *P et al, 2004***). It facilitates communication with patients and their families and assists in decision making in addition to other cancer care applications **(Glare *P et al, 2004*).**

A number of factors may be useful in predicting survival in advanced cancer patients. Although physicians' prediction of survival is generally inaccurate(***Glare P et al, 2003***), it was found to be an independent predictive value in multivariate analysis **(*Pirovano M et al, 1999*)** Performance status scoring systems like the Eastern Cooperative Oncology Group (ECOG) and Karnofsky scale and a number of quality of life measurement scales were found to be of predictive value as well **(Glare *P et al, 2004*)**. Some symptoms, as well, like tiredness, dyspnea and anorexia independently predicted survival **(*Maltoni M et al.1997, Chuang R-B et al, 2004*).**

In addition, a number of biological parameters were found to be independently predictive of survival of advanced cancer patients like the total white blood cell count and the lymphocyte percentage **(*Maltoni M et al.1997*).**

In order to overcome inaccurate prediction when using the above mentioned factors individually, a number of prognostic models incorporating many predictive factors were developed like the Chuang prognostic score (CPS), palliative prognostic (PaP) score and the palliative prognostic index (PPI) **(*Stone PC et al 2007, Ripamonti CI 2009*)**.

The CPS (**Table 1**) was developed by Chuang et al in 2004 **(*Chuang R-B et al, 2004)*.**

It is based on eight parameters, lung metastasis, liver metastases, tiredness, ascites, edema, cognitive impairment, weight loss in the last 3 months and the ECOG performance status.

The CPS did not include biological parameters and predicted survival near the end of life. It is a simple score; however, it is expected to be of value very near the end-of-life **(*Stone PC et al 2007*)**. The total score ranges from 0 (best prognosis) to 8.5 (worst prognosis). Using a cut off point of ≥ 3.5 predicted 2-week survival with a positive predictive value of 63% and a negative predictive value of 60% **(*R-B et al, 2004*)**.

In addition to the developers, only one study validated the CPS in a different setting in Saudi Arabia and found it useful in predicting survival and in-hospital mortality of patients with advanced cancer **(*Al-Zahrani AS et al, 2013*)**.

Aim of the work

The aim of this study is to do Prospectively observation study to assess the value of the CPS in an advanced GIT cancer of Egyptian cancer patients referred to the Palliative Care Medicine Unit (PCMU) of Kasr Al-Aini Center of Clinical Oncology and Nuclear Medicine (NEMROCK).

Chapter I

Principle of prognostication in advanced cancer patients

Estimating prognosis is one of the most difficult tasks the oncologist encounters, particularly for patients with incurable malignancies whose life expectancies may vary between days and years. A physician's ability to formulate accurate estimate of prognosis among patients with advanced, incurable cancers is essential to medical decision-making, such as whether to pursue chemotherapy, clinical trials, or hospice care. In the United States, Canada, and many European countries, hospice referrals require a physician-predicted prognosis of 6 months or less.

Furthermore, advanced cancer patients who hold overly optimistic perceptions of their prognosis are more likely to want futile, aggressive care **(*Weeks JC et al, 1998*)**.

When physicians provide prognostic information during end-of-life discussions, advanced cancer patients are more likely to avoid aggressive medical care that is associated with lower quality of life near death, greater medical care costs, and worse caregiver bereavement outcomes **(*Wright AA et al, 2008. Zhang B et al, 2009. Temel JS et al 2010*)**.

This review discusses data informing prognostication in patients with advanced, incurable GIT tumours, including physician assessment of life expectancy, prognostic factors, and prognostic models in this patient population.

Prognosis is a generic term related to predicting any health outcome.

In the incurable disease setting, prognostication is important for different reasons other than predicting survival **(Glare P et al 2004).**

A. Importance of prognostication in advanced disease*

To provide patients and their families with information about what the future is likely to hold so that they can set their goals, priorities, and expectations of care:

- To help patients develop insight into their dying.
- To assist clinicians in their decision-making.
- To establish patients eligibility for care programmes, including timely referral to hospice programmes and for clinical trials.
- For policy making with respect to appropriate resource utilization and allocation of support services, for example, frequency of contacts if home care is proposed.
- To provide a common language for health care professionals involved in the end of life care.

**** Adapted From Oxford Textbook Of Pallative Medicine 2004***

B. Formulating a Prognosis in Advanced Cancer

When prognosis is related to a potentially life-threatening illness such as cancer, it is closely related to diagnosis; the same clinical and pathological factors which are used to make a diagnosis are also relevant to the prognosis .Most of the literature dealing with prognosis in cancer concerns with factors that influences the probability of cure.

Traditional prognostic factors (e.g. stage and histology) can reasonably predict survival in early stage disease but don't provide an adequate short term prognosis in patients with advanced cancer (***Bruera E et al, 1992*****).**

There are various ways the practicing clinician can formulate a prognosis. One can rely on one's own experience, but this depends on having seen a lot of similar cases, having a reliable memory, and remaining dispassionate one‘s assessments.

One can consult an expert in the field but this is not always feasible and is subjected to the expert's own biases. One can consult textbook, but modern textbooks contain little or no information about relative probabilities of outcomes of interest. One can employ validated, published algorithms of variable ease of us **(*Teno JM et al ,2000*) .**

C. Physician prediction of prognosis

Physician assessment of prognosis—drawing upon clinical experience and comprehensive knowledge of the patient—is frequently utilized to assess prognosis. This mechanism of predicting prognosis among advanced cancer patients has been investigated in multiple studies demonstrating these estimates to be largely unreliable, with accuracy ranging from 20%-60%. **(*Christakis NA et al, 2000. Chow E et al, 2001. Glare P et al, 2003*. *Vigano A et al 1999*)**.

Glareet al reviewed 8 studies investigating the accuracy of physicians’ survival estimates in over 1500 terminal cancer patients; physicians’ prognostic estimates were correct 25% **(*Vigano et al, 1999)*** of the time to within 1 week of actual survival time, 43% to within 2 weeks, and 61% to within 4 weeks **(*Glare P et al, 2003*)** Studies suggest that physicians tend to overestimate life expectancy among advanced cancer patients. prospectively evaluated 210 advanced cancer patients and asked physicians to provide survival estimates based upon their clinical evaluations (median of 15 weeks before death). **(*Vigano et al, 1999*)**.

Physicians overestimated patient's survivals by a median of 1.1 months in a systematic review by Chow et al, clinicians 'estimates of survival tended to be in the overly optimistic direction in 9 of the 12 studies included (***Chow E et al, 2001***).

Furthermore, length of the patient-physician relationship has been shown to be associated with reduced accuracy of physician predictions. Each year a physician has known a patient, has been shown to increase the likelihood of making an erroneous prediction by 12% (***Christakis NA, 1998*****).** Additionally, accuracy of prediction has not been found to be dependent on length of clinical experience. In the aforementioned study by Gripp et al, both a young physician and a senior physician (greater than 10 years experience) demonstrated similar accuracies in predicting survival (accuracy of 60%). **(*Gripp S et al , 2007*)** Hence, a key next step in better estimating prognosis in advanced cancer patients is equipping physicians with prognostic tools that improve the physician accuracy in life expectancy predications.

D. Prognostic factors

Although factors such as tumour size, stage, grade, and genetics are important in determining prognosis for patients with no metastatic cancers, they do not appear to play as significant a role in predicting prognosis among cancer patients with incurable disease (***Hauser CA et al, 2006. Viganò A et al, 2000***) Several other potential prognostic factors have been studied in patients with incurable cancers, including symptoms, laboratory values and Karnofsky Performance Status.

Numerous studies have suggested that Karnofsky Performance Status (KPS) is a prognostic indicator in patients with advanced cancer **(*Lingjun Z et al, 2009. Suh SY et al, 2010. Trédan O et al, 2011*)**.