3rd Research Forum of the European Association for Palliative Care

"Methodology for Palliative Care Research"

Stresa, Lago Maggiore (Italy) 3-6 June 2004

Working Group on Prognostic Factors in Advanced Cancer Patients

Interim Working Draft

Working group Participants

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Background

The use of well identified prognostic factors (PFs) could allow for most appropriate intervention to the patient, avoiding the risks of over and under-treatment, as regards both therapeutic aspects and planning of care (ie, timing of palliative care program referral) (1). Moreover, knowledge of PFs can allow to advise the family and to accompany it in the difficult task of accepting t he course of the disease.

On the other hand, it must be remembered that prognostic information has only a probabilistic value and great caution has to be used in every single case (2). Moreover, patients must be protected by the temptation of health managers of using prognostic capacity not in avoiding futile therapies, but in denying appropriate therapies ("the cheapest patient, is the dead patient")

Open Questions

Some open questions about prognostication deserved to be focused and discussed by an EAPC expert group, to examine them closely and get a consensus to be spread and published.

First, it remains to be evaluated the real prognostic power of Clinical Prediction of Survival: some Authors report a low correlation with Actual Survival with an excess of optimistic previsions (3,4), while others have shown a low percentage of errors and a good balance between overoptimistic and over-pessimistic errors (5).

Second, there is not consensus about which clinical, laboratory, and socio-demographic PFs can be considered "evidence based", and which have less convincing proofs of prognostic capacity (6).

In particular, the role of Prognostic Scores has to be clarified, since in recent times we have assisted to an uncontrolled proliferation of scores built with methodologically doubtful procedures.

In fact, the third point to be faced is that many shortcomings have been described in the studies reviewing the methodology issues of published papers on PFs. In particular, lack of a well-identified "inception cohort" and of a Palliative Care Unit case-mix classification have been claimed (3).

Forth, difficulties in expressing and communicating prognosis seem to prevent from utilizing it in an appropriate way. What to do with patients that do not want to know, and how to help them to take part in clinical decision-making are just two of the emerging problems in this field (7,8)

Working Group Workshop

For the mentioned reasons,the Steering Committee of the Research Network of the EAPC a working group on PFs in advanced cancer patients, convened in a workshop in Courmayeur, Italy on February 2004, with the aim of identifying which topics have a sufficient **level of evidence** and which deserve more quantitative or qualitative research.In particular, the role of **Prognostic Scores** was to be clarified. **Ethic implications** and **appropriate use of PFs** hold a special interest.

The workshop results should also suggest researchers a minimum standard of **methodologic requirements**, to reduce the number of studies not easily interpreteable or difficult to compare, in particular as far as **population of interest** is concerned

Methods

The working group followed the SIGN (Scottish Intercollegiate Guideline Network) method for developing clinical practice guidelines and the Centre for Evidence Based Medicine, Oxford Grading system following this scheme:

1. Identification of key points

The core recommendations closely reflects the main key points emerging from the group discussion

2. Systematic literature search

TABLE 1 SYSTEMATIC LITERATURE SEARCH

Limits: human studies and English language

#1	STRATEGY FOR SEARCHING PAPERS ON ADVANCED CANCER PATIENTS: (Neoplasms (MesH term all subheadings) OR cancer (tw) OR tumor (tw) OR tumour (tw) OR oncolog*(tw) AND (terminal care (MesH term all subheadings) OR terminally ill (MesH term all subheadings) OR palliative care (MesH term all subheadings) OR hospices (MesH term all subheadings)
#2	STRATEGY FOR SEARCHING PAPERS ON PROGNOSIS (FROM ALTMAN 2001) incidence (MesH term) OR mortality (MesH term all subheadings) OR follow-up studies (MesH term) OR mortality (subheading) OR prognos* (tw) OR predict (tw) OR course (tw)
#3	ONE OF THE FOLLOWING STRATEGIES FOR SEARCHING PAPERS ON SPECIFIC TOPIC: BIOLOGICAL FACTORS SYMPTOMS AND CLINICAL AND PSYCHOSOCIAL VARIABLES
	CLINICAL PREDICTION
	PROGNOSTIC SCORES

#1 AND #2 AND #3 .

3. Assigning the level of evidence

Studies selected after the systematic literature search were evaluated for quality and type in order tobe classified according to the following grid

TABLE 2

		NUMBER OF QUALITY CHECKLIST CRITERIA SATISFIED							
		7	6	5	4	3	2	1	0
IMPACT STUDIES	V		1a+				1a+		
META-ANALYSIS	IV		1b+				1b-		
CONFERMATORY STUDIES	III								
EXPLORATORY STUDIES	II		2+				2-		
INVESTIGATIVE STUDIES	I		3+				3-		
NON-ANALYTIC STUDIES						4			
EXPERT OPINION						5			

4. Formulating the recommendations and assigning strength

The grading system proposed below is based on the SIGN grading system, modified to adapt for prognostic factors studies

1a+	Impact studies
1b+	High quality meta analyses, systematic reviews or confirmatory studies with a very low risk of bias
1b -	Meta analyses, systematic reviews or confirmatory studies with a high risk of bias
2+	Exploratory studies with a very low risk of bias
2 -	Exploratory studies with a very high risk of bias
3+	Investigative studies with a very low risk of bias
3-	Investigative studies with a very high risk of bias
4	Non-analytic studies, e.g. case reports, case series
5	Expert opinion

Preliminary core recommendations

1) **An accurate prognostication of life expectancy in patients is useful from a clinical and organization point of view.**

2) **Clinicians should continue to use prediction of survival based on their clinical judgement ONLY WHILE considering that a number of factors* limit its accuracy;**
   a. CPS are more than twice as likely to be overoptimistic than overpessimistic
   b. CPS is subject to an horizon effect
   c. Lack of Experience in oncology and palliative care reduces accuracy therefore a second opinion by a more experienced professional can be useful
   d. Clinicians should consider using CPS in combination with other prognostic factor to improve the accuracy of their predictions

3) **Clinicians can use a number of clinical signs and symptoms showed associated with life expectancy in this patients population such as:**
   a. Anorexia, weight loss, troubled swallowing or dysphagia
   b. Dyspnea
   c. Delirium

4) **Clinicians can use some laboratory variables associated with life expectancy in this patients population, which give additional prognostic information independently from clinical prediction of survival, performance status and some clinical signs and symptoms.**
   a. Low Vitamin B12
   b. HighC reactive eprotein
   c. High Bilirubin
   d. Leucocytosis
   e. Lymphocytopenia
   f. Low pseudocholinesterase

5) **Clinicians can use prognostic scores to improve their ability to prognosticate life expectancy in the terminally ill with cancer**

6) **Clinicians can assume that prognostication of life expectancy in advanced cancer is feasible at least in probabilistic terms, excessive negativism in this area of prognostication is not warranted on the basis of the available evidences**

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