Comprehensive geriatric assessment in older patients with cancer: an external validation of the Multidimensional Prognostic Index in a French prospective cohort study

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Abstract

Background: Older patients with cancer require specific and individualized management. The Multidimensional Prognostic Index (MPI) based on the Comprehensive Geriatric Assessment (CGA) has shown a predictive interest in terms of mortality.

Methods: From 2015 to 2017, consecutive patients ≥75 years old with cancer in Poitiers University Hospital referred to an oncogeriatric consultation. Patients underwent CGA with MPI that is categorized into three risk groups of mortality at one year.

Results: Overall, 433 patients were included (women 42%; mean age 82.8±4.8 years). Most common tumor sites were prostate (23%), skin (17%), colorectum (15%) and breast (12%); 29% patients had a metastatic disease; 231 patients (53%) belonged to "MPI-1" group, 172 (40%) to "MPI-2" group and 30 patients (7%) were classified in "MPI-3" group. One-year mortality rate was 32% (23% in MPI-1, 41% in MPI-2 and 53% in MPI-3, p=0.024). All domains of MPI except cognition and living status were significantly associated with mortality at one-year, as well as tumor sites and metastatic status. Cox proportional hazard regression analysis, adjusted on age, gender, tumor sites and metastatic status, validated MPI as being associated with a higher mortality risk (p<0.0001). The prognostic value of MPI was confirmed by the area under the ROC curve at 0.826 (P <0.0001).

Conclusion: Our study confirmed the predictive value of MPI for one-year mortality in older patients with cancer. This practical prognostic tool may help to optimize the management of these vulnerable patients.
Background

Individuals over 65 years old are the fastest growing segment of the population, and will represent about 20% of Americans and 25% of Europeans by 2030 [1]. The incidence of cancer continues to increase worldwide: it is estimated at 23.6 million/year by 2030, namely an increase of 68% cases compared with 2012 [2]. The incidence of cancer is 11 times higher in people over 65 years old, and people aged 70 and older have a higher risk of developing invasive cancer [3]. The older population is characterized by a very heterogeneous profile, especially in terms of frailty, geriatric characteristics, and comorbidities, which explains the need for specific and adapted care [4-5]. Nevertheless, scientific data are scarce because older subjects are often underrepresented in oncological clinical trials that set the standards of antineoplastic treatment [6-7].

Over the last three decades, the five-year survival rate for all types of cancer has increased particularly in individuals aged 50 to 64 [3, 8]. Still, older patients have more risk of toxicity of anti-cancer therapies as chemotherapy, and require a benefit/risk assessment prior to treatment [4]. A comprehensive geriatric assessment (CGA) is thus recommended in these patients to diagnose comorbidities and optimize geriatric interventions, to improve the functional state and possibly the survival rate, by ensuring a better tolerance to treatment [9-10]. CGA has also shown a predictive value in identifying elderly patients with cancer who are exposed to a poor prognosis, including a higher risk of death during hospitalization [11]. Among the CGA-based assessment tools, the Multidimensional Prognostic Index (MPI) has shown a predictive interest in mortality at six months and 12 months in Italian patients aged 70 years and older with advanced cancers [12-15].
The main objective of our study was to validate the performances of the MPI to predict mortality one-year after diagnosis in an external French cohort of elderly patients with cancer. The secondary objective was to find the major risk factors associated with 12-month mortality in these patients.

Methods
Study population

This prospective single-center cohort study enrolled from March 2015 to March 2017, all patients with cancer, aged 75 years and older, who were referred to the geriatric oncology clinic of Poitiers University Hospital, prior to anti-cancer treatment plan. Socio-demographic data and cancer-related information were collected during the consultation, including age, sex, marital status, social environment, type of cancer, metastasis status, and cancer-specific treatment. The CGA was performed by a senior geriatrician specialized in oncology, and provided necessary data for MPI.

Multidimensional Prognostic Index

The MPI, based on a CGA, was calculated after administration of standardized and validated tests exploring eight domains (Table 1). The living status was categorized as “living with family”, “institutionalized” or “alone”, and functional status was evaluated by Activities of Daily Living (ADL) ranging from 0 (total dependence) to 6 (independence) and Instrumental ADL (IADL) (16–17]. Nutrition was assessed by Mini Nutritional Assessment-Short Form (MNA-SF) questionnaire; cognitive status was evaluated by Short Portable Mental Status Questionnaire (SPMSQ) [18–19]. The Exton-Smith Scale (ESS) estimated the risk of pressure ulcer [20]. The comorbidities were evaluated by Cumulative Illness Rating Scale (CIRS) which scores the severity
of 14 organic systems, ranging from 0 (absent) to 4 (most severe) [21]. Based on this scale, a comorbidity index (CIRS-CI) records the number of moderate to severe organ pathologies (CIRS scores 2 to 4) [22]. The number of medication is classified in three groups: “≤3 drugs a day”, “4 to 6 drugs” or “≥7 drugs”.

The MPI was scored by matching the results of these tests. A value of "0", "0.5" or "1" was assigned according to the conventional cutoff points, considering “0” as no problem, “0.5” minor problem and “1” major problem (Table 1). The sum was then divided by 8 to obtain the final MPI score, which was categorized into 3 groups: the "MPI-1" group (final score below 0.34, defining patients with low mortality risk at one year), the "MPI-2" group (0.34–0.66, moderate risk) and the "MPI-3" group (group > 0.66, higher risk).

| Assessment tests (range) | No problem (value = 0) | Minor problem (value = 0.5) | Severe problem (value = 1) |
|--------------------------|------------------------|-----------------------------|---------------------------|
| ADL (0–6)                | ≥ 5                    | 4 – 3                        | ≤ 2                       |
| IADL (0–8)               | ≥ 3                    | 5 – 4                        | ≤ 3                       |
| SPMSQ (0–10)             | ≤ 3                    | 4-7                          | ≥ 8                       |
| CIRS-CI (0–14)           | 0                     | 1-2                          | ≥ 3                       |
| MNA-SF (0–17)            | ≥ 12                   | 8-11                         | ≤ 7                       |
| ESS (5–25)               | ≥ 16                   | 10-15                        | 5-9                       |
| Number of medications    | 0–3                   | 4-6                          | ≥ 7                       |
| Living status            | living with family    | Institutionalized            | living alone              |

Abbreviations: ADL: Activities of Daily Living; IADL: Instrumental Activities of Daily Living; SPMSQ: Short Portable Mental Status Questionnaire; CIRS-CI: Cumulative Illness Rating Scale Comorbidity Index; MNA-SF: Mini Nutritional Assessment Short Form; ESS: Exton Smith Scale.

a Number of errors

b Number of pathologies

A systematic follow-up was performed by the same clinical research assistant. All the clinical and biological data were collected and recorded in a cohort database.
Statistical analysis

Descriptive statistics were reported as mean ± standard deviation (SD) for continuous variables or absolute number and percentage for categorical variables. A logistic regression was used for univariate and multivariate analyses to explore the relationship between the various risk factors and the overall mortality rate: all the variables with p-value < 0.20 in univariate analyses, in addition to age and sex, were included in multivariate analyses where a p-value < 0.05 (χ² test) was defined as statistically significant. A Cox proportional hazard regression method was used for multivariate analysis, using step-by-step regression procedure. It took in account age, sex, metastatic status, tumor sites, and the MPI groups; a second multivariate analysis included the eight elements of MPI, adjusted on age, sex, tumor sites and metastatic status.

The discriminatory power of the MPI index on the prediction of one-year mortality was evaluated by the calculation of the area under the Receiver Operating Characteristic (ROC) curve in the logistic regression models.

All analyses in this study were performed with SAS 9.4 (SAS Institute, Cary).

Results

Characteristics of study population

During the recruitment period, 433 eligible patients aged 75 years and older were included, mostly males (n = 252, 58%), with a mean age of 82.8 ± 4.8 years (Table 2). The most common tumor sites were prostate (23%), skin (17%) and breast (12%); 29% patients had a metastatic disease. Anti-cancer treatment included chemotherapy in 162 patients (37%), surgery in 137 (32%) and radiotherapy in 109 (25%). Patients had comorbid conditions regarding the CIRS-scale and medication,
and were frequently malnourished (29%) (Table 2). In this cohort, 231 patients (53%) were classified in "MPI-1" group, 172 patients (40%) in "MPI-2" and 30 patients (7%) in "MPI-3". Except for metastatic status and antineoplastic treatments, all variables of interest differed between the three MPI groups (p ≤ 0.02).

Survival analysis

Among the 433 patients, twelve were lost to follow-up (3%). Mean follow-up was 13.7 ± 6.4 months.

The overall mortality at 12 months was 32% (23% in MPI-1, 41% in MPI-2 and 53% in MPI-3, p = 0.024) (Fig. 1). Survival analysis, adjusted on age, sex, tumor sites and metastatic status, confirmed that compared to MPI-3 group, patients of the MPI-1 and MPI-2 groups had a lower risk of one-year mortality (adjusted Hazard ratio (aHR) of 0.204, 95% confidence interval (95% CI) [0.114–0.366], and aHR of 0.467, 95% CI [0.268–0.814], respectively, p < 0.0001) (Table 3).

| Table 3 |
|------------------|------------------|------------------|------------------|------------------|
| | Univariate analysis | | Multivariate analysis | |
| | HR (95% CI) | p | aHR (95% CI) | p |
| Age | 1.006 (0.973–1.040) | 0.73 | - | - |
| Sex: female | 1.096 (0.781–1.537) | 0.60 | - | - |
| Tumor sites | - | 0.0005 | - | 0.002 |
| Metastatic status | 2.015 (1.434–2.833) | < 0.0001 | 1.863 (1.282–2.706) | < 0.0001 |
| MPI groups (compared to MPI-3) | | < 0.0001 | | < 0.0001 |
| MPI-1 | 0.271 (0.154–0.474) | | 0.204 (0.114–0.366) | |
| MPI-2 | 0.582 (0.338–1.002) | | 0.467 (0.268–0.814) | |

Abbreviations: HR: hazard ratio; CI: confidence interval; MPI: Multidimensional Prognostic Index

Risk factors associated with one-year mortality
To test the relationship between risk factors and the one-year mortality, a logistic regression was applied: multivariate analysis showed an independent association between one-year mortality and metastatic status (aHR 1.863, 95% CI [1.282–2.706], p = 0.001), tumor sites (p = 0.002) and malnutrition (aHR 0.798, 95%CI [0.743–0.857], p < 0.0001).

Predictive performance of MPI

The discriminate power of MPI using the 12-month survival was statistically significant (Table 4). The logistic regression model adjusted by age, sex, tumor sites and metastatic status was the best model to predict one-year mortality (p < 0.0001), with the area under the ROC curve at 0.826.

| Predictive performance of MPI during a 12-month follow-up |
|----------------------------------------------------------|
| unadjusted model | 0.723 | 0.012 |
| age adjusted model | 0.732 | 0.013 |
| age and sex adjusted model | 0.732 | 0.020 |
| age and sex adjusted model + others mortality predictors | 0.826 | < 0.0001 |

a AUC ROC: area under the receiver operating characteristics curve

b metastasis of cancer and type of cancer

Discussion

Our study confirmed the predictive value of the multidimensional prognostic index: older patients with cancer in the MPI group with a higher risk were significantly exposed to two- to five-fold higher rate of one-year mortality. In our cohort, the discriminate power of MPI predictive performance in our cohort was good, and comparable to the literature [23].

Estimation of patient survival at time of the therapeutic decision is required to assess the balance of benefits and risks of performing or not specific oncologic
interventions, considering the cancer-specific mortality. Clinicians may need to know if their patient will die of cancer or with cancer, when comorbidities or geriatric syndromes are challenging. Several scales have been created and validated in large epidemiologic cohorts for estimating overall survival, notably at twelve months for Carey and Walter indexes [5, 24-25]. These two scores consider dependency, comorbidities with cancer, malnutrition. None of these tests were specifically developed in cohorts with individuals with cancer, and may not be informative enough to reflect the clinical and functional variability in daily care, to provide personalized corrective interventions. Recent evidence reported positive impact of geriatric interventions and monitoring in survival increase, improvement of quality of life, and completion of chemotherapy [26-27]. The MPI then differs from other mortality indexes because it is based on a CGA, with each of the eight tests assessing one geriatric domain. Giantin and collaborators confirmed the good discriminatory power for 12-month mortality in a cohort of 160 cancer patients older than 70, and validated higher mortality prediction compared to a standard CGA [13]. Use of the MPI in clinical practice may provide a rapid and comprehensive evaluation of patients, to adapt the decision-making in oncology.

The MPI has been developed and validated in large cohorts of in and outpatients for many causes, to predict mortality but also length of hospital stay, care intensity, institutionalization, re-hospitalization, and access to homecare services [28-29]. This index may be used as a decision-making tree for cancer management, to select older patients with lower mortality risk for a standard treatment as younger counterparts, those for an adapted care, or exclusive supportive strategy in patients with limited life expectancy. This classification in three groups is comparable with the geriatric oncology algorithm of Balducci [4]. It defines three groups of patients
(robust, vulnerable and frail) according to seven criteria: age, dependence measured by ADL and IADL, comorbidities with CIRS-CI, cognition evaluated with MMSE (mini-mental state examination) or delirium, depressive mood, urinary and fecal incontinence, and falls in the last six months. More recent classifications were suggested to improve the global management in such individuals, including nutrition data [25].

Indeed, malnutrition is highly prevalent in geriatric oncology settings [30]. This geriatric syndrome is a well-known risk factor of early mortality. Our findings confirmed that one-year mortality is strongly associated with nutritional status and altered MNA in its short form. Some questions of this test were selected for the elaboration of the Geriatric-8 (G8) index, to screen for vulnerability in older patients with cancer, as recommended by the International society of geriatric oncology (SIOG) [31–32].

The findings of this study should be interpreted with caution. First of all, the design as an observational single-center study may limit the extrapolation of our results to general older population with cancer. Recruited patients in this cohort may not be representative, as cancer specialists may not refer all their patients to the geriatric oncology clinic, notably those screened as “not-vulnerable” in geriatric terms, as recommended by the SIOG and National Institute of Cancer in a two-step approach [31]. Cancer management of these patients may follow standard strategy, without a geriatric expertise. However, our results are consistent with existing findings in geriatric oncology settings.

Conclusions

Our research on the predictive value of MPI for one-year mortality of the elderly
patients with cancer is an important basis for future studies aiming to improve the therapeutic strategy for these patients. A major part of this strategy involves personalized geriatric interventions, such as specific care monitoring by nurse, physical rehabilitation. It has shown benefits for elderly cancer patients, but so far, no study has yet demonstrated their impact on the survival [33–35]. MPI appears to be a rapid assessment tool to optimize cancer care, guiding patient-tailored interventions, and predicting early mortality. These findings pave the way of prospective interventional studies, taking account of MPI groups for decision-making about cancer treatments and follow-up.

Declarations

Ethics approval and consent to participate
All eligible patients who had signed the consent form were included in the study.
The study protocol was validated by the ethics committee of our institution.
Consent for publication
Not applicable
Availability of data and materials
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.
Competing interests
The authors declare that they have no competing interests
Funding
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Authors’ contributions
CH, MP, SV and EL designed the study. SV, AJ, EL contributed to data acquisition. CH
and EL performed the data analysis. MP, EL draft the paper. CH, MP, SV, EL are
major contributors in writing the manuscript. All authors reviewed the manuscript
and approved the final version.

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Abbreviations

ADL: Activities of Daily Living
aHR: adjusted Hazard ratio
CGA: Comprehensive Geriatric Assessment
CI: Confidence interval
CIRS: Cumulative Illness Rating Scale
CIRS-CI: Cumulative Illness Rating Scale-comorbidity index
ESS: Exton-Smith Scale
G8: Geriatric 8
IADL: Instrumental Activities of Daily Living
MNA-SF: Mini Nutritional Assessment-Short Form
MPI: Multidimensional Prognostic Index
ROC: Receiver Operating Characteristic
SIOG: International society of geriatric oncology
SPMSQ: Short Portable Mental Status Questionnaire

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Table

Due to technical limitations, table 2 is only available as a download in the supplemental files section.
Figures

**Figure 1**

Kaplan-Meier survival analysis according to MPI groups (n=433)

Supplementary Files

This is a list of supplementary files associated with the primary manuscript. Click to download.

*table2.JPG*