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VALIDATION OF A MODIFIED-MULTIDIMENSIONAL PROGNOSTIC INDEX (m-MPI) INCLUDING THE MINI NUTRITIONAL ASSESSMENT SHORT-FORM (MNA-SF) FOR THE PREDICTION OF ONE-YEAR MORTALITY IN HOSPITALIZED ELDERLY PATIENTS

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Abstract

Background—The mortality prediction represents a key factor in the managing of elderly hospitalized patients. Since in older subjects mortality results from a combination of biological, functional, nutritional, psychological and environmental factors, a Multidimensional Prognostic Index (MPI) that predict short- and long-term mortality based on a standardized comprehensive geriatric assessment (CGA) has recently been developed and validated.

Objective—This study compares the accuracy in predicting the mortality of the MPI with a modified version of the MPI (m-MPI) that included the Mini Nutritional Assessment-Short Form (MNA-SF) instead of the standard MNA.

Design—This prospective study with a one-year follow-up included 4088 hospitalized patients aged 65 years and older. A standardized CGA that included information on functional (Activities of Daily Living, ADL and Instrumental-ADL), cognitive (Short Portable Mental Status Questionnaire), risk of pressure sore (Exton-Smith Scale), comorbidities (CIRS Index), medications, living status and nutritional status (MNA and MNA-SF) was used to calculate the MPI using a previously validated algorithm.

Results—Higher MPI values were significantly associated with higher mortality rates with a close agreement between the estimated and the observed mortality both after 1-month

(MPI1=2.8% versus m-MPI1=2.8%, $p=0.946$; MPI2=8.9% versus m-MPI2=9%, $p=0.904$; MPI3=21.9% versus m-MPI3=21.9, $p=0.978$) and 1-year of follow-up (MPI1=10.8% versus m-MPI1=10.5%, $p=0.686$; MPI2=27.3% versus m-MPI2=28%, $p=0.495$; MPI3=52.8% versus m-MPI3=52.7%, $p=0.945$). The estimated areas under the receiver operating characteristics (ROC) curves suggested a clinically negligible difference between the two indices.

Conclusion—The m-MPI is as sensitive as the MPI in stratifying hospitalized elderly patients into groups at varying risk of short- and long-term mortality, but with fewer items.

Keywords

Multidimensional Prognostic Index (MPI); Mini Nutritional Assessment Short Form (MNA-SF); mortality; prognosis; Comprehensive Geriatric Assessment (CGA); survival

Introduction

The mortality prediction represents a key factor in the managing of elderly hospitalized patients. Since in older subjects mortality results from a combination of biological, functional, nutritional, psychological and environmental factors, tools that successfully identify older patients with different life expectancy should be multidimensional in nature (1, 2). Recently, a Multidimensional Prognostic Index (MPI) to predict mortality based on a standardized comprehensive geriatric assessment (CGA) including information on functional (Activities of Daily Living, ADL and Instrumental-ADL), cognitive (Short Portable Mental Status Questionnaire, SPMSQ) and nutritional status (Mini Nutritional Assessment, MNA), as well as on risk of pressure sore (Exton-Smith Scale), comorbidities (CIRS Index), medications and living status has been developed and validated in two independent cohorts of elderly patients hospitalized for acute disease or relapse of a chronic disease (3). This CGA-based MPI resulted excellent in predicting short- and long-term mortality in older patients with specific diseases such as gastrointestinal bleeding (4), pneumonia (5), heart failure (6), liver cirrhosis (7) or dementia (8) demonstrating a prognostic accuracy significant higher than accuracy of prognostic tools based on organ-specific functions (5–7).

Unfortunately, a potential limitation of the CGA-based MPI is that is time consuming to administer, with an interview taking up to half an hour to complete (3). We have therefore developed a modified version of the MPI (m-MPI) that is quicker and easier to administer. In the m-MPI we have substituted the standard form of the MNA (9) with a short form of the MNA (MNA-SF) (10) reducing the number of items and thus the time of administration. The MNA-SF is a diagnostic tool consisting of 6 items, instead of 18 items of the standard MNA, that has been validated in several populations and can be administered like a stand-alone instrument or in a 2-step process, using complete examination with the MNA only if the final score is under 11 (11).

The purpose of this study was to compare the sensitivity of the MPI and m-MPI in stratifying hospitalized elderly patients into groups at varying risk of short- and long-term mortality.

Methods

Subjects

Patients aged 65 years and older admitted from January 2005 to December 2007 to the Geriatrics Unit of the Casa Sollievo della Sofferenza Hospital (IRCCS, San Giovanni Rotondo, Italy) because of an acute disease or a relapse of a chronic disease were screened for eligibility. Inclusion criteria were: 1) age ≥ 65 years; 2) a complete CGA during hospitalization; 3) ability to provide an informed consent or availability of a proxy for the informed consent.

At baseline, the following parameters were collected by a systematic interview, clinical evaluation and review of records from the patients' general practitioners: date of birth, gender, clinical history, current pathologies and medication history. All patients admitted to our Unit received a standard CGA. Vital status up to December 31, 2008 was assessed by directly contacting the participants or consulting the Registry Offices of the cities where the patients were residents at the time of hospital admission. When a patient moved to a different city the Registry Office of the new city of residence has been contacted. Dates of death were identified from death certificates.

The Comprehensive Geriatric Assessment (CGA)

Functional status was evaluated by Activities of Daily Living (ADL) index (12), which defines the level of dependence/independence in 6 daily care activities including bathing, toileting, feeding, dressing, continence and transferring and by Instrumental Activities of Daily Living (IADL) scale (13) which assess independence in 8 activities that are more cognitively and physically demanding than ADL, including managing finances, taking medications, using telephone, shopping, using transportation, preparing meals, doing housework and washing.

Cognitive status was assessed by the Short Portable Mental Status Questionnaire (SPMSQ), a 10-item questionnaire that assesses orientation, memory, attention, calculation and language (14).

Co-morbidity was examined using the Cumulative Illness Rating Scale (CIRS) (15). The CIRS uses a 5-point ordinal scale (score 1–5) to estimate the severity of pathology in each of 13 systems, including cardiac, vascular, respiratory, eye-ear-nose-throat, gastrointestinal, hepatic, renal, genitourinary, musculo-skeletal, skin, nervous system, endocrine-metabolic and psychiatric behavioural disorders. Based on the ratings, the Comorbidity Index (CIRS-CI) score which reflects the number of concomitant diseases was derived from the total number of categories in which moderate or severe levels (grade 3–5) of a chronic disease were identified (range 0–13).

Nutritional status was explored with the MNA, which include information on a) anthropometric measures; b) lifestyle, medication and mobility; c) number of meals, food and fluid intake and autonomy of feeding; and d) self perception of health and nutrition. For this study both the MNA (9) and the MNA-SF (10) scores were calculated.

The Exton Smith Scale (ESS) was used to evaluate the risk of developing pressure sores. This 5-item questionnaire determines physical and mental condition, activity, mobility, and incontinence. For each item, a score from 1 to 4 is assigned (16).

Medication use was defined according to the Anatomical Therapeutics Chemical Classification code system and the number of drugs used by patients at admission was recorded. Co-habitation status, i.e. living with family (with spouse and/or other relatives and/or a caregiver), institutionalized or living alone, was also recorded. The approximate time required for collecting data for the CGA was 30 minutes (range from 25 to 35 minutes per person).

The Multidimensional Prognostic Index (MPI)

We used the MPI developed and validated in two independent cohorts of elderly hospitalized patients as previously reported (3). Briefly, a cluster analysis on CGA data was initially made for evaluating the independence of variables and identifying the most relevant domains of the CGA in predicting mortality outcome. Following a step-wise method, the domains of the CGA, one at a time, were progressively included in the model and Cox and logistic regression analyses performed. Thus an “eight domain” MPI, was developed that included a total of 63 items and yielded the best index for predicting one-year mortality. For each domain a 3-level score was used, i.e. 0 = no problems, 0.5 = minor problems, and 1 = major problems as previously reported (Table 1).

For calculating the m-MPI we used the following cut-off values of the MNA-SF: MNA-SF $\geq 12 = 0$; MNA-SF < 12 and $\geq 8 = 0.5$, MNA-SF $< 8 = 1$. In agreement with a recent study that evaluated a modified version of the MPI-SF (17), these cut-off values were obtained from a statistical analysis using receiving operating curves (ROC) in order to optimize sensitivity for the upper limit (Sensitivity 90.4, Specificity 86.4 and area under the ROC curve: 0.95) and specificity for the lower (Sensitivity 92.4, Specificity 92.6 and area under the ROC curve: 0.98). Thus the m-MPI included 51 items in 8 domains.

The sum of the calculated scores from the eight domains was then divided by 8 to obtain a final score between 0 to 1, both for MPI and the m-MPI. As previously reported (3), three grades of severity risk to stratify the examined population were considered: low risk (MPI-1 and m-MPI-1 values ≤ 0.33), moderate risk (MPI-2 and m-MPI-2 values between 0.34 and 0.66) and severe risk (MPI-3 and m-MPI-3 values > 0.66) of mortality.

Statistical analysis

Continuous variables were summarized as mean and standard deviation, and categorical variables as frequencies and percentages. Comparisons between men and women were made using Mann-Whitney U test or Pearson's chi-square test for continuous or categorical variables respectively. Kruskal-Wallis and Mantel-Haenszel chi-square tests were used to compare age, gender, education level and mortality across the MPI groups. Correlation analysis of total scores of the MPI and the m-MPI was carried out with the non-parametric Spearman's coefficient. The classification agreement between the two indices was measured and tested by the kappa coefficient as introduced by Cohen.

Time to death predictivity of MPI score group was tested using age- and sex-adjusted Cox proportional hazards regression models. The same models were used to compute the estimated mortality. Time to death was calculated as the time between admission and time of death or the end of follow-up, whichever come first. The proportionality of the hazard assumption was graphically checked by plotting log $[-\log(\text{survival function})]$.

Age- and sex-adjusted logistic models were carried out on the individual parameters of the MPI and the MPI itself to test the prognostic value for mortality after 1 month and 12 months of follow-up.

The predictive ability of the models was assessed by calculating the area under the receiver operating characteristics (ROC) curves, along with their 95% confidence intervals, for the MPI and the m-MPI. Since our large sample size (n° 4088) was statistically highly powered, able to detect differences between areas under the ROC curves of just 0.005 (with a power equal to 90%, and a Type I error of 5%) (18), to compare the predictive power of the MPI vs m-MPI we used a test for equivalence. The test was implemented assuming that the two indices were clinically equivalent if the difference between the two areas under the ROC curves lies within a $-0.025 - +0.025$ interval.

A p value < 0.05 was considered for statistical significance. Statistical analyses were performed using the SPSS version 16 software for Windows (SPSS Inc., Chicago, Illinois).

Results

Study population

During the enrolment period 4412 elderly patients were screened for the inclusion in the study. Of these, 4088 patients, 1972 men (48.2%) and 2116 women (51.8%) with a mean age of 78.1 years ($\pm$ 7.1) and a range from 65 to 100 years, fulfilled the admission criteria and were included in the study.

Table 2 shows the characteristics of patients included in the study, divided according to gender. Women were older ($p<0.001$) and had significantly higher disability in the ADL ($p<0.001$), cognitive impairment at SPMSQ ($p<0.001$), lower Exton-Smith score ($p<0.001$) and MNA score ($p<0.001$) than men. As expected, women were using more medications ($p<0.001$), had higher MPI mean values ($p<0.001$) and demonstrated lower mortality rates after both 1 month and 12 months of follow-up ($p<0.001$) than men.

Comparison between MPI versus m-MPI

Higher grades of both MPI and m-MPI were significantly associated with elevated mortality after both 1 month (MPI-1 2.8% vs m-MPI-1 2.8%, $p=0.946$; MPI-2 8.9% vs m-MPI-2 9%, $p=0.904$; MPI-3 21.9% vs m-MPI-3 21.9, $p=0.978$) and 12 months of follow-up (MPI-1 10.8% vs m-MPI-1 10.5%, $p=0.686$; MPI-2 27.3% vs m-MPI-2 28%, $p=0.495$; MPI-3 52.8% vs m-MPI-3 52.7%, $p=0.945$). As shown in Table 3 no significant difference was found between the estimated and the observed mortality by the MPI and the m-MPI after both 1 month and 12 months of follow-up. The logistic regression analyses demonstrated that both the MPI and the m-MPI were significantly associated with the 1-month and 12-

month mortality rates. The MPI and the m-MPI also presented odds ratio values higher than that of all its components (Table 4); again similar results were shown by the MPI and the m-MPI.

Table 5 shows patients divided according to the MPI and the m-MPI grades. A very close agreement was observed in the distribution of patients according to the MPI and the m-MPI scores, i.e. MPI-1 53.8% vs m-MPI-1 53.9%, ; MPI-2 37.1% vs m-MPI-2 37%; MPI-3 9.1% vs m-MPI-3 9.1%. Since the differences in the distribution of patients according to the MPI and the m-MPI grades were negligible (Cohen $k=0.95$, $p<0.0001$), the construction of separate survival curves to compare the two models was unnecessary. A Spearman correlation between the MPI and m-MPI demonstrated an r value of 0.964 ($p<0.001$).

The areas under the ROC curves calculated for the MPI and the m-MPI were 0.762 (95%CI = 0.7328–0.7912) and 0.748 (95%CI = 0.7191–0.7769) at 1 month and 0.7173 (95%CI = 0.6970–0.7375) and 0.7097(95%CI =0.6895–0.7298) at 12 months, respectively. For both the endpoints (one month and 12 months), the two indexes showed to be equivalent, since the 95%CI of the AUC difference lies within the clinical interval for equivalence [1 month: 0.0140 (0.0048–0.0232); 12 months: 0.0076 (0.0020–0.0132)]. The estimated areas under the ROC curve suggested a clinically negligible difference between the two indices.

Discussion

The data of the present study show that the m-MPI, which includes a MNA-SF instead of the standard MNA, was as sensitive as the MPI in predicting short- and long-term mortality risk in a large population of elderly patients admitted to a geriatric ward for an acute disease and/or a relapse of a chronic disease. Higher MPI and m-MPI values were significantly associated with higher mortality rates with a close agreement between the estimated and the observed mortality both after 1-month and 1-year of follow-up. Logistic regression analysis and the analysis of the area under the ROC curves demonstrated that the MPI is as sensitive as the m-MPI in predicting mortality. In addition, the correlation between the MPI and the m-MPI was very high (r value = 0.96). Our findings further demonstrate that the MPI is a sensitive prognostic tool in predicting mortality in a large group of hospitalized elderly patients, and that the m-MPI is also an excellent predictor of short- and long-term mortality, but has the advantage of being easier and less time consuming to administer.

Malnutrition is one of the most important clinical conditions that affect the prognosis in elderly patients. It has been estimated that approximately 35–65% of hospitalized elderly patients and 25–60% of institutionalized patients without acute diseases are malnourished (19, 20, 21). Malnutrition is associated with increased morbidity and prolonged hospital stays (22, 23), and with a mortality rate three-fold higher than in well-nourished patients (24). Indeed, the evaluation of nutritional status cannot be excluded from a CGA (25). The findings of this study are in agreement with the results of previous studies (3–8), and demonstrate that the prognostic value of the aggregate indices of the CGA in both the MPI and the m-MPI, was superior to the prognostic value of the individual parameters used to construct the MPI. These findings support the concept that considering multidimensional aggregate information is very important for predicting short-and long-term mortality in

hospitalized older patients. These findings are in agreement also with recent studies (1, 2, 26) carried out in non-hospitalized older individuals that demonstrated that cumulative indexes of health deficiencies can significantly predict health outcomes and death.

The innovation of the MPI is that the index was developed on CGA data routinely collected in elderly patients hospitalized in acute wards. The present MPI includes parameters that particularly characterize the hospitalized elderly patient, such as comorbidity, nutritional status, risk of pressure sores and drug use, while functional and cognitive parameters, i.e. the basal ADL and IADL and the SPMSQ, were derived from sensitive instruments that have been validated in several settings of geriatric populations. Indeed, in clinical practice there may be strong motivations to use a structured approach for data collection as the CGA. The benefits resulting from this approach are precision and reproducibility that are enhanced by the use of standardized and validated questionnaires that require the respondent to choose from a limited number of answers.

This MPI has some limitations. Since the index focused on hospitalized older patients, it is likely that it is not applicable to institutionalized or community-dwelling subjects. Indeed, in a more healthy group of elderly subjects, the MPI would probably include other predictor variables that take into account of the different setting populations.

Even if the use of the MNA-SF couldn't fully substitute the standard MNA for diagnosis of malnutrition, the findings of this study demonstrated that in this setting of elderly hospitalized patients the MNA-SF may be included for the calculation of the MPI without loss in its prognostic accuracy and making the m-MPI easy and user-friendly to clinical practitioners.

In conclusion the m-MPI, that included a MNA-SF instead of the standard MNA, accurately stratified hospitalized elderly patients into groups at varying risk of short- and long-term mortality with the same degree of accuracy as the original MPI but with fewer items.

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Table 1

Multidimensional Prognostic Index Score Assigned To Each Domain Based On The Severity Of The Problems

Assessment	No (Value=0)	Problems Minor (Value=0.5)	Severe (Value=1)
Activities of Daily Living (ADL) ^a	6–5	4–3	2–0
Instrumental IADL (IADL) ^a	8–6	5–4	3–0
Short Portable Mental Status Questionnaire (SPMSQ) ^b	0–3	4–7	8–10
Comorbidity-Index (CIRS-CI) ^c	0	1–2	3
Mini Nutritional Assessment (MNA) ^d	24	17–23.5	< 17
Exton-Smith Scale (ESS) ^e	16–20	10–15	5–9
Numbers of Medications	0–3	4–6	7
Co-habitation status	Living with Family	Instituzionalized	Living Alone

^aNumber of active functional activities;^bNumber of errors;^cNumber of diseases;^dMNA score: 24, satisfactory nutritional status; 17–23.5, at risk of malnutrition; <17, malnutrition;^eESS score: 16–20, minimum risk; 10–15, moderate risk; 5–9 high risk of developing scores.

Table 2

Baseline Characteristics of the population included in the study by Sex

	All	Males	Females	P value
Patients, No. (%)	4088(100)	1972(48.2)	2116(51.8)	
Age				
Mean (SD), y	78.1(7.7)	77.4(7)	78.7(7.1)	<0.001
Range, y	65–100	65–100	65–100	
ADL, mean (SD), score	4.3(2.3)	4.5(2.2)	4.13(2.3)	<0.001
IADL, mean (SD), score	4.2(3.1)	4.2(3)	4.2(3)	0.637
SPMSQ, mean (SD), score	2.2(2.5)	1.9(2.4)	2.5(2.6)	<0.001
ESS, mean (SD), score	16.2(3.5)	16.6(3.4)	15.8(3.5)	<0.001
CIRS-CI, mean (SD), score	2.9(1.7)	3(1.7)	2.9(1.7)	0.642
MNA, mean (SD), score	21.4(5.7)	22(5.7)	20.8(5.6)	<0.001
MNA-SF, mean (SD), score	10.5(3.1)	10.8(3.1)	10.3(3.1)	<0.001
Number of Medications, mean (SD), No.	4.2(2.8)	4(2.8)	4.3(2.7)	<0.001
MPI, mean (SD), score	0.38(0.2)	0.34(0.2)	0.40(0.2)	<0.001
Mortality, No. (%)				
at 1 month	287(7)	156(7.9)	131(6.2)	<0.001
at 6 months	595(14.6)	321(16.3)	274(12.9)	<0.001
at 12 months	787(19.3)	422(17.2)	365(19.3)	<0.001

Abbreviation: 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; CIRS-SI, Cumulative Illness Rating Scale - Severity Index; MNA, Mini-nutritional assessment; MNA-SF Mini-nutritional assessment Short Form; MPI, Multidimensional Prognostic Index.

Table 3

Cumulative HR for mortality in MPI and m-MPI according to different grades of severity of MPI after 1 month and 12 months of follow-up

MPI grades	Months	MPI			m-MPI		
		EM	95% CI	OM	EM	95% CI	OM
1	1	0.028	0.022–0.034	0.027	0.001	0.022–0.034	0.027
	12	0.108	0.094–0.102	0.101	0.003	0.093–0.117	0.099
2	1	0.089	0.075–0.103	0.095	0.006	0.076–0.104	0.095
	12	0.273	0.251–0.295	0.262	0.011	0.258–0.302	0.262
3	1	0.219	0.179–0.259	0.221	0.002	0.179–0.259	0.222
	12	0.527	0.475–0.579	0.447	0.08	0.476–0.58	0.449

Abbreviation: MPI, multidimensional prognostic index; m-MPI, modified MPI; EM, estimated mortality; OM, observed mortality; Delta indicates the difference between EM and OM values.

Table 4

Mortality risk of the MPI, the m-MPI and the individual domains of the CGA after 1 and 12 months of follow-up

Risk Factors	1 Month		12 Months	
	OR (95% CI)	p value	OR(95% CI)	p value
MPI	3.17(2.67 – 3.77)	<0.001	2.77 (2.46 – 3.11)	<0.001
m-MPI	3.18(2.68 – 3.78)	<0.001	2.82 (2.5 – 3.18)	<0.001
Age	1.06 (1.04 – 1.08)	<0.001	1.07 (1.06 – 1.08)	<0.001
Sex (male)	1.3 (1.02 – 1.66)	0.032	1.3 (1.12 – 1.52)	0.001
ADL	1.45 (1.4 – 1.5)	<0.001	1.35 (1.31 – 1.38)	<0.001
IADL	1.34 (1.29 – 1.39)	<0.001	1.27 (1.24 – 1.3)	<0.001
SPMSQ	1.12 (1.07 – 1.18)	<0.001	1.12 (1.09 – 1.16)	<0.001
CIRS-CI	1.27 (1.2 – 1.36)	0.53	1.24 (1.19 – 1.3)	<0.001
MNA	1.15 (1.13 – 1.17)	<0.001	1.14 (1.13 – 1.15)	<0.001
MNA-SF	1.26(1.23 – 1.30)	<0.001	1.25 (1.22 – 1.27)	<0.001
Exton Smith Scale	1.32 (1.28 – 1.35)	<0.001	1.25 (1.23 – 1.28)	<0.001
No. of drugs	1.06 (1.02 – 1.11)	0.005	1.07 (1.04 – 1.1)	<0.001
Social Network	1.04 (0.78 – 1.38)	0.80	1.07 (0.89 – 1.28)	0.5

Abbreviation: MPI, Multidimensional-Prognostic; rMPI-SF, revised Multidimensional-Prognostic Index; 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, Mini-nutritional assessment; MNA-SF, Mini-nutritional assessment short form.

Table 5

Distribution of the patients according to the MPI and m-MPI grade

	MPI 1 No. Patients (%)	MPI 2 No. Patients (%)	MPI 3 No. Patients (%)
MPI	2198 (53.8%)	1519 (37.1%)	371 (9.1%)
m-MPI	2206 (53.9%)	1512 (37.0%)	370 (9.1%)

Cohen K = 0.95 p-value < 0.001; Abbreviation: MPI, Multidimensional Prognostic Index; m-MPI, modified Multidimensional Prognostic Index.