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**ORIGINAL ARTICLE**

# Prognostic factors for the feasibility of chemotherapy and the Geriatric Prognostic Index (GPI) as risk profile for mortality before chemotherapy in the elderly

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## ABSTRACT

**Background.** Comprehensive geriatric assessment (CGA) is a multidimensional method to detect frailty in elderly patients. Time saving could be accomplished by identifying those individual items that classify elderly cancer patients at risk for feasibility of chemotherapy and for mortality.

**Material and methods.** Patients older than 70 years of age were assessed before the first chemotherapy administration. GA consisted of the Mini Nutritional Assessment (MNA), Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE), Groningen Frailty Indicator (GFI) and Mini Mental State Examination (MMSE). Predictive individual items for feasibility of chemotherapy and mortality were entered in the multivariable logistic regression and Cox-regression models, and a three-item sum scale was constructed: the Geriatric Prognostic Index (GPI).

**Results.** The 494 patients had a median age of 75 years (range 70–92 years). The majority of the patients had malignancies of the digestive tract (41.7%) followed by hematological tumors (22.3%). Three items of the MNA ('psychological distress or acute disease in the past three months', 'neuropsychological problems' and 'using $>3$ prescript drugs') independently predicted for feasibility of chemotherapy. Two items of the MNA and one of the GFI ('declining food intake in past 3 months', 'using $>3$ prescript drugs', and 'dependence in shopping') independently predicted for mortality. In comparison with patients without any positive item on the three-item GPI, patients with one, two or three positive items had hazard ratios (HRs) of 1.58, 2.32, and 5.58, respectively (all $p<0.001$).

**Conclusions.** With only three items of the MNA, feasibility of chemotherapy can be predicted. The three-item GPI may help to identify elderly cancer patients at elevated risk for mortality.

The majority of persons with cancer is older than 65 years of age, and 70% of cancer mortality occurs in this age cohort [1]. As a result of demographic changes, the demand for care and treatment of older people with cancer will strongly increase in the coming decades.

Comprehensive geriatric assessment (CGA) is a multidimensional method to provide objective information on comorbidity, functional status, social support, polypharmacy, nutritional- and psychosocial status [2]. As geriatric problems increase sharply after 70 years of age in cancer patients, the guidelines

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of the International Society of Geriatric Oncology (SIOG) recommend that all patients with cancer and an age above 70 years should undergo some form of GA [3]. However, to conduct a full CGA is time consuming and associated with high costs. Therefore, a two-step approach could be a pragmatic alternative by using a brief screening tool. Well known examples of screening tools are formed by abbreviated CGA (aCGA) [4], Vulnerable Elders Survey (VES-13) [5], the Geriatric 8 (G8) [6], Groningen Frailty Indicator (GFI) [7], Flemish version of the Triage Risk Screening Tool (fTRST) [8] and others [9]. Nevertheless, further time saving might be accomplished by identifying the essential items of such screening tools. For example, this has been shown to be applicable for the Mini Nutritional Assessment (MNA) [10]. The study of osteoporotic fractures (SOF) index was developed from frequently cited physiologic domains in the frailty literature [11,12] and appeared accurate in comparison with CGA for the detection of frailty in cancer patients [13]. The geriatric vulnerability score (GVS) appeared applicable for elderly patients with advanced ovarian cancer treated with carboplatin [14].

The present cohort of elderly cancer patients, collected in the region of the Comprehensive Cancer Center West in the Netherlands, offered the opportunity to analyze and determine which elements of the chosen geriatric screening program were independently predictive for feasibility of chemotherapy and mortality.

## Material and methods

Patients older than 70 years of age with various types of cancer ($N = 520$) were prospectively assessed before chemotherapy administration with either curative or palliative intent. The decision for treatment with chemotherapy had already been made by the treating (hemato)-oncologist on clinical grounds. The patients had been considered to be fit enough to receive chemotherapy. The collection of data was accomplished between May 2004 and February 2010 in three general and one university hospital: the hospital of the Reinier de Graaf Groep in Delft, Groene Hart hospital in Gouda, Haga hospital in The Hague, and the Leiden University Medical Center in Leiden. After February 2010 no more funding was available for data management, thus prohibiting further inclusion of patients in this prospective registration cohort. We excluded 25 patients because they did not start with chemotherapy and one patient because of age.

GA consisted of the MNA, Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE), GFI and Mini Mental State Examination (MMSE). These tests were selected for performing a GA with a minimum of overlap between the domains, and a maximum duration of 45 minutes to complete the interview. The tests have been described in detail previously [15]. Details of the MNA are given in Supplementary Addendum 1 (available online at http://informahealthcare.com/doi/abs/10.3109/0284186X.2015.1068446). Supplementary Addendum 2 (available online at http://informahealthcare.com/doi/abs/10.3109/0284186X.2015.1068446) provides details on the GFI. Patients scoring 4 or more points were considered to have a moderate to severe frailty. The IQCODE screens for cognitive decline over the last 10 years by interviewing family members or caregivers. We used the short 16 items Dutch translation IQCODE-N [16]. The MMSE has been tested extensively and is considered to be a standard test for current cognitive function.

Feasibility of chemotherapy was defined by the inability to complete the intended number of cycles of chemotherapy: at least four cycles. This number was arbitrarily chosen as a surrogate endpoint, realizing that four cycles cannot be considered as the standard number of cycles. It was considered likely, that if at least four cycles could be administered, then patients could be treated with the intended total dose of chemotherapy. The small group of patients with aggressive non-Hodgkin lymphoma stage I who were treated with the intended number of three cycles of chemo(-immuno)therapy and involved field radiotherapy, were grouped under the heading of four or more cycles of chemotherapy.

The duration of the follow-up was defined as the difference between the date of the first GA and 1 January 2013 or the date of death. Vital status and last follow-up date were recorded from the patient's medical record. If indicated by the test results, a dietician or a geriatrician was consulted.

### *Statistical analysis*

To identify the most relevant individual items of the MNA, GFI, IQ-CODE and MMSE, every single item was dichotomized. Details are given in Supplementary Addendum 3 (available online at http://informahealthcare.com/doi/abs/10.3109/0284186X.2015.1068446).

Categorical variables are presented as numbers with percentages and continuous variables as medians with their range. Logistic regression analysis and Cox regression analysis on (items of) the MNA, GFI, IQCODE and MMSE for the prediction of feasibility of chemotherapy and mortality obtained odds ratios (OR) and hazard ratios (HR), respectively. To avoid type I errors in multiple testing, a p-value $< 0.01$ was considered statistically significant. All multivariable models were adjusted for sex, age, purpose of

treatment, and type of malignancy. Those questionnaires of the MNA, GFI, IQCODE and MMSE that independently predicted for feasibility of chemotherapy or mortality ($p < 0.01$) were used in further analyses with the dichotomized composite items. When individual items were predictive for feasibility of chemotherapy and mortality ($p < 0.01$), these were included in multivariable logistic regression and Cox-regression models. Forward stepwise procedures were used in both the logistic and Cox regression models, with an entry criterion of $p < 0.01$ and the removal criterion of $p > 0.10$. As sensitivity analysis, the variable selection procedures were rerun using backward stepwise selection. Subsequently, the independent predictive items for mortality were summed, and this sum score was analyzed using the multivariable adjusted Cox regression model. In stratified analyses, the predictors for mortality were tested separately in the palliative treated and adjuvant/curative treated groups. The models were internally validated by calculating c-statistics, which are measures for the discriminative performance of the models, using bootstrapping to take into account that the models were developed and validated on the same data [17]. For logistic regression the c-statistic is equal to the area under the curve of a ROC curve. Statistical tests and analyses were performed using SPSS 21 for Windows® (SPSS inc. Chicago, IL, USA) and R 3.1.0 [18] using package rms (Regression Modeling Strategies) [19].

## Results

A total of 494 patients with various types of cancer were evaluated. Table I shows the baseline characteristics of the patients.

The scores of the GA are shown in Table II. Roughly one third of the patients showed shortcomings with the MNA and the GFI, and some 10% of the patients had cognitive problems. In total 353 patients were treated with four or more cycles of chemotherapy, of whom 61% were treated with full dose and 39% with an adapted dose. A total of 141 patients (29%) could not complete at least four cycles of chemotherapy. In this group, 69% of the patients were treated with full dose, and 31% received an adapted dose (a decision of the treating oncologist). The reasons for early treatment withdrawal were complications of chemotherapy (50%), deteriorating general condition (11%), ineffectiveness of chemotherapy (10%), worsening comorbidity (2%) and others (27%). Supplementary Addendum 4 (available online at http://informahealthcare.com/doi/abs/10.3109/0284186X.2015.1068446) gives information on applied chemotherapy regimens. Of course, this shows a large variety in this cohort of patients.

Table I. Baseline characteristics of 494 elderly cancer patients.

| | Median (range) | *N* (%) |
|---|---|---|
| Age | 75 (70–92) | |
| • 70–74 years | | 237 (48.0) |
| • 75–79 years | | 170 (34.4) |
| • ≥80 years | | 87 (17.6) |
| Male gender | | 246 (49.9) |
| Type of malignancy: | | |
| • Upper digestive tract | | 64 (13.0) |
| • Lower digestive tract | | 142 (28.7) |
| • Hematological | | 110 (22.3) |
| • Breast | | 61 (12.3) |
| • Gynecological | | 38 (7.7) |
| • Prostate | | 29 (5.9) |
| • Lung | | 21 (4.3) |
| • Urinary tract | | 11 (2.2) |
| • Other | | 18 (3.6) |
| Purpose of treatment: | | |
| • Adjuvant/ curative | | 206 (41.7) |
| • Palliative | | 288 (58.3) |

The median follow-up was 17 months (range 1–101) for all patients, and 61 months (range 44–101) for the 99 survivors. The most common cause of death was cancer progression (84.0%). Other causes were treatment related (3.1%), cardiovascular mortality (2.3%), or unknown causes (10.6%).

The effect of the MNA, GFI, IQCODE and MMSE on feasibility of chemotherapy and mortality are given in Table III. Patients with adverse scores on the MNA and GFI had a higher odds to stop chemotherapy before the fourth cycle with ORs of 2.21 [95% confidence interval (CI) 1.48–3.31; $p < 0.001$] and 1.71 (95% CI 1.13–2.58; $p = 0.01$), respectively. After adjusting for gender, age, purpose of treatment and type of malignancy only the

Table II. Results of the geriatric assessments of 494 elderly cancer patients.

| Test | Score | *N* (%) |
|---|---|---|
| MNA* | well nourished | 316 (64.5) |
| | (risk of) malnutrition* | 174 (35.5) |
| | unknown | 4 |
| GFI | <4 pts | 344 (69.8) |
| | ≥4 pts | 149 (30.2) |
| | unknown | 1 |
| IQCODE | ≤3.30 pts | 418 (87.1) |
| | >3.30 pts | 62 (12.9) |
| | unknown | 14 |
| MMSE | >24 pts | 445 (91.0) |
| | ≤24 pts | 44 (9.0) |
| | unknown | 5 |

*(Risk of) malnutrition defined as a score of ≤11 on the MNA screening section or less than 24 pts on the assessment section (see Addendum 1).

Table III. Outcome of geriatric assessment of MNA ($N = 490$), GFI ($N = 493$), IQCODE ($N = 480$) and MMSE ($N = 489$) for feasibility of chemotherapy and overall mortality in elderly cancer patients.

| Feasibility | $N = 353 \geq 4$ cycles, *n* (%) | $N = 141 < 4$ cycles, *n* (%) | Univariable analysis, odds ratio (95% CI) | p-Value | Multivariable analysis*, odds ratio (95% CI) | p-Value |
|---|---|---|---|---|---|---|
| MNA | | | | | | |
| Well nourished | 245 (69.8) | 71 (51.1) | ref | | ref | |
| (Risk of) malnutrition | 106 (30.2) | 68 (48.9) | 2.21 (1.48–3.31) | $<0.001$ | 2.30 (1.48–3.58) | $<0.001$ |
| GFI | | | | | | |
| Not frail | 258 (73.1) | 86 (61.4) | ref | | ref | |
| (risk of) frailty | 95 (26.9) | 54 (38.6) | 1.71 (1.13–2.58) | 0.01 | 1.68 (1.08–2.62) | 0.02 |
| IQCODE | | | | | | |
| Normal risk | 300 (87.0) | 118 (87.4) | ref | | | |
| Cognitive decline | 45 (13.0) | 17 (12.6) | 0.96 (0.53–1.75) | 0.90 | – | |
| MMSE | | | | | | |
| No cognitive dysfunction | 322 (92.3) | 123 (87.9) | ref | | | |
| Cognitive dysfunction | 27 (7.7) | 17 (12.1) | 1.65 (0.87–3.13) | 0.13 | – | |

| Mortality | Alive, *N* (%) | Deceased, *N* (%) | Univariable analysis, hazard ratio (95% CI) | p-Value | Multivariable analysis*, hazard ratio (95% CI) | p-Value |
|---|---|---|---|---|---|---|
| MNA | | | | | | |
| Well nourished | 75 (76.5) | 241 (61.5) | ref | | ref | |
| (Risk of) malnutrition | 23 (23.5) | 151 (38.5) | 1.68 (1.37–2.06) | $<0.001$ | 1.86 (1.48–2.34) | $<0.001$ |
| GFI | | | | | | |
| Not frail | 75 (76.5) | 269 (68.1) | ref | | ref | |
| (risk of) frailty | 23 (23.5) | 126 (31.9) | 1.47 (1.19–1.82) | $<0.001$ | 1.77 (1.41–2.22) | $<0.001$ |
| IQCODE | | | | | | |
| Normal risk | 86 (88.7) | 332 (86.7) | ref | | | |
| Cognitive decline | 11(1.3) | 51 (13.3) | 1.12 (0.83–1.50) | 0.46 | – | |
| MMSE | | | | | | |
| No cognitive dysfunction | 90 (92.8) | 355 (90.6) | ref | | | |
| Cognitive dysfunction | 7 (7.2) | 37 (9.4) | 1.36 (0.97–1.91) | 0.08 | – | |

Hazard and odds ratios [with 95% confidence intervals (CI)] were calculated using either Cox regression or logistic regression analysis.
*Adjusted for sex, age, purpose of treatment, type of malignancy.

MNA was significantly related to feasibility with a p-value $< 0.01$: OR 2.30 (95% CI 1.48–3.58; $p < 0.001$). The MNA remained a significant predictor after additional adjustment for GFI [OR 2.12 (95% CI 1.33–3.39; $p = 0.002$)]. With respect to mortality, an adverse score for MNA and GFI was associated with increased HRs for mortality of 1.68 (95% CI 1.37–2.06; $p < 0.001$) and 1.47 (95% CI 1.19–1.82; $p < 0.001$), respectively. After adjustment for gender, age, purpose of treatment and type of malignancy, these HRs remained significant (1.86; 95% CI 1.48–2.34; $p < 0.001$; and 1.77; 95% CI 1.41–2.22; $p < 0.001$, respectively).

Table IV shows the univariable significant individual items (with $p < 0.01$) of MNA for feasibility of chemotherapy and of the GFI and MNA for mortality. In the stepwise selection procedure, three items of the MNA independently predicted feasibility ['psychological distress' (MNA-D), 'neuropsychological problems' (MNA-E) and 'using > 3 prescript drugs' (MNA-H)], with ORs of 2.10 (95% CI 1.31–3.38; $p = 0.002$), 3.44 (95% CI 1.50–7.90; $p = 0.004$) and 1.96 (95% CI 1.27–3.03; $p = 0.002$), respectively. Two items of the MNA ['declining food intake in past 3 months' (MNA-A) and 'using > 3 prescript drugs' (MNA-H)] and one item of the GFI ['dependence in shopping' (GFI-Q1)] independently predicted for mortality, with HRs of 1.82 (95% CI 1.47–2.24; $p < 0.001$), 1.38 (95% CI 1.12–1.71; $p = 0.003$) and 1.77 (95% CI 1.31–2.40; $p < 0.001$), respectively. In sensitivity analyses a backward stepwise selection procedure resulted in the same three items. Table V shows the c-statistic of the different models. For mortality the outcome increased from 0.66 to 0.70 when adding MNA(A), MNA(H) and GFI(Q1) to the model. This indicates that these three dichotomous variables gave additional predictive value to the model. Similarly, the items MNA(D), MNA(E), and MNA(H) added predictive value to the outcome variable feasibility, increasing the c-statistic from 0.61 to 0.69.

A sum score, the Geriatric Prognostic Index (GPI), was constructed using the three items with increased HRs for mortality. With one positive item the HR was 1.58 (95% CI 1.24–2.02; $p < 0.001$), with two positive items 2.32 (95% CI 1.76–3.06; $p < 0.001$), and with all three items 5.58 (95% CI 3.48–8.61; $p < 0.001$), in comparison with no

Table IV. Independent effects of MNA and GFI items for feasibility of chemotherapy and overall mortality in 494 elderly cancer patients.

| Feasibility | Present *N* (%) | ≥4 cycles, % | <4 cycles, % | Univariable analysis, odds ratio (95% CI) | p-Value | Multivariable analysis, odds ratio (95% CI) | p-Value |
|---|---|---|---|---|---|---|---|
| MNA | | | | | | | |
| Declining food intake in past 3 months (A)* | 217 (44.2%) | 39.3% | 56.4% | 2.00 (1.34–3.00) | 0.001 | – | – |
| Weight loss in past 3 months (B) | 179 (36.5%) | 32.3% | 47.1% | 1.88 (1.26–2.80) | 0.002 | – | – |
| Psychological stress or acute disease in past 3 months (D) | 120 (24.4%) | 19.7% | 36.4% | 2.34 (1.52–3.61) | <0.001 | 2.10 (1.31–3.38) | 0.002 |
| Dementia or depression (E) | 35 (7.1%) | 4.6% | 13.6% | 3.29 (1.64–6.60) | 0.001 | 3.44 (1.50–7.90) | 0.004 |
| Using >3 prescript drugs (H) | 181 (36.6%) | 31.7% | 48.9% | 2.06 (1.38–3.07) | <0.001 | 1.96 (1.27–3.03) | 0.002 |
| Self-view of nutritional status (O) | 99 (20.0%) | 17.0% | 27.7% | 1.87 (1.18–2.96) | 0.008 | – | – |
| Poor self-rated health (P) | 129 (26.1%) | 22.1% | 36.2% | 2.00 (1.31–3.06) | 0.001 | – | – |
| **Mortality** | **Present *N* (%)** | **Alive, %** | **Deceased, %** | **Univariable analysis, hazard ratio (95% CI)** | **p-Value** | **Multivariable analysis, hazard ratio (95% CI)** | **p-Value** |
| MNA | | | | | | | |
| Declining food intake in past 3 months (A) | 217 (44.2%) | 32.7% | 47.1% | 1.63 (1.33–1.98) | <0.001 | 1.82 (1.47–2.24) | <0.001 |
| Psychological stress or acute disease in past 3 months (D) | 120 (24.4%) | 14.3% | 27.0% | 1.38 (1.11–1.73) | 0.004 | – | – |
| Using >3 prescript drugs (H) | 181 (36.6%) | 24.2% | 39.7% | 1.58 (1.29–1.94) | <0.001 | 1.38 (1.12–1.71) | 0.003 |
| Declining protein intake (K) | 90 (18.2%) | 12.1% | 19.7% | 1.49 (1.16–1.91) | 0.002 | – | – |
| Intake ≤5 cups of fluid per day (M) | 35 (7.1%) | 2.0% | 8.4% | 1.76 (1.23–2.52) | 0.002 | – | – |
| Self-rated nutritional problems (N) | 99 (20.0%) | 11.1% | 22.3% | 1.81 (1.42–2.30) | <0.001 | – | – |
| Poor self-rated health (P) | 129 (26.1%) | 18.2% | 28.1% | 1.62 (1.30–2.02) | <0.001 | – | – |
| GFI | | | | | | | |
| Dependence in shopping (Q1) | 59 (12.0%) | 4.1% | 13.9% | 2.02 (1.51–2.69) | <0.001 | 1.77 (1.31–2.40) | <0.001 |
| Dependence in (un) dressing (Q3) | 12 (2.4%) | 0.0% | 3.0% | 2.34 (1.31–4.16) | 0.004 | – | – |
| Poor self-rated physical fitness (Q5) | 196 (39.8%) | 29.6% | 42.3% | 1.42 (1.16–1.74) | 0.001 | – | – |
| Weight loss in past 6 months (Q8) | 191 (38.7%) | 32.7% | 40.3% | 1.38 (1.13–1.69) | 0.002 | – | – |

Hazard and odds ratios [with 95% confidence intervals (CI)] were calculated using either Cox regression or logistic regression analysis. Independent predictors in a multivariable Cox-regression model using a stepwise procedure with an entry criterion of $p < 0.01$, while adjusted for sex, age, purpose of treatment, and type of malignancy.
*A: Item A of MNA, Q5: question 5 of GFI.

positive item. The median survival with the GPI was 2.26 years with score 0, 1.34 years with score 1, 0.95 years with score 2 and 0.56 years with score 3 (Figure 1).

The effect of the three predictive items for mortality was studied separately in the palliative ($N = 288$) and adjuvant/curative ($N = 206$) treated patients. The three items (MNA-A, MNA-H and GFI-Q1) remained significant in the palliative treated group with HRs of 2.02 (95% CI 1.54–2.65; $p < 0.001$), 1.54 (95% CI 1.19–2.00; $p = 0.001$) and 1.89 (95% CI 1.30–2.74; $p = 0.001$), respectively. In the adjuvant/curative treated group the GFI-Q1 remained associated with mortality [HR 2.22 (95% CI 1.28–3.83; $p = 0.004$)], but the effect of MNA-A and MNA-H was smaller [HR 1.31 (95% CI 0.90–1.93; $p = 0.17$) and 1.30 (95% CI 0.89–1.92; $p = 0.18$), respectively).

Table V. C-statistic coefficients of the different additional models for feasibility of chemotherapy and mortality.

| Model | Feasibility | Mortality |
|---|---|---|
| Gender, age, purpose of treatment, and type of malignancy | 0.61 | 0.66 |
| MNA + GFI, dichotomized | 0.65 | 0.69 |
| MNA-D + MNA-E + MNA-H | 0.69 | – |
| MNA-A + MNA-H + GFI-Q1 | – | 0.70 |
| GPI score | – | 0.70 |

MNA-A, declining food intake in past 3 months; MNA-D, psychological stress or acute disease in past 3 months; MNA-E, dementia or depression; MNA-H, using >3 prescript drugs; GFI-Q1, dependence in shopping.

## Discussion

In this study among 494 elderly cancer patients the result of the MNA test was predictive for the risk of premature discontinuation of chemotherapy. Furthermore, a three-item GPI was constructed, that predicted for mortality. It has to be stressed that these 494 patients were considered to be fit for treatment with chemotherapy before the GA was performed.

CGA is an evidence-based method to evaluate deficits and frailty in elderly cancer patients [3]. This diagnostic tool provides information for the process leading up to the treatment plan and may recognize previously unaddressed problems, creating opportunities to improve functional status and resources of old cancer patients [3]. It may even contribute to prolonged survival and may help to weigh the benefits against the risks of chemotherapy and identify patients that may be too frail to profit from this demanding form of treatment [3].

Already, the literature of geriatric oncology highlighted scoring systems for the toxicity of chemotherapy [20,21]. Hurria et al. identified three risk strata for grade 3–5 toxicity, with 11 risk factors [21], while the CRASH score of Extermann et al. identified four risk factors for hematologic and non-hematologic toxicity each, discerning four risk categories for grade 4 hematologic toxicity and grade 3–4 non-hematologic

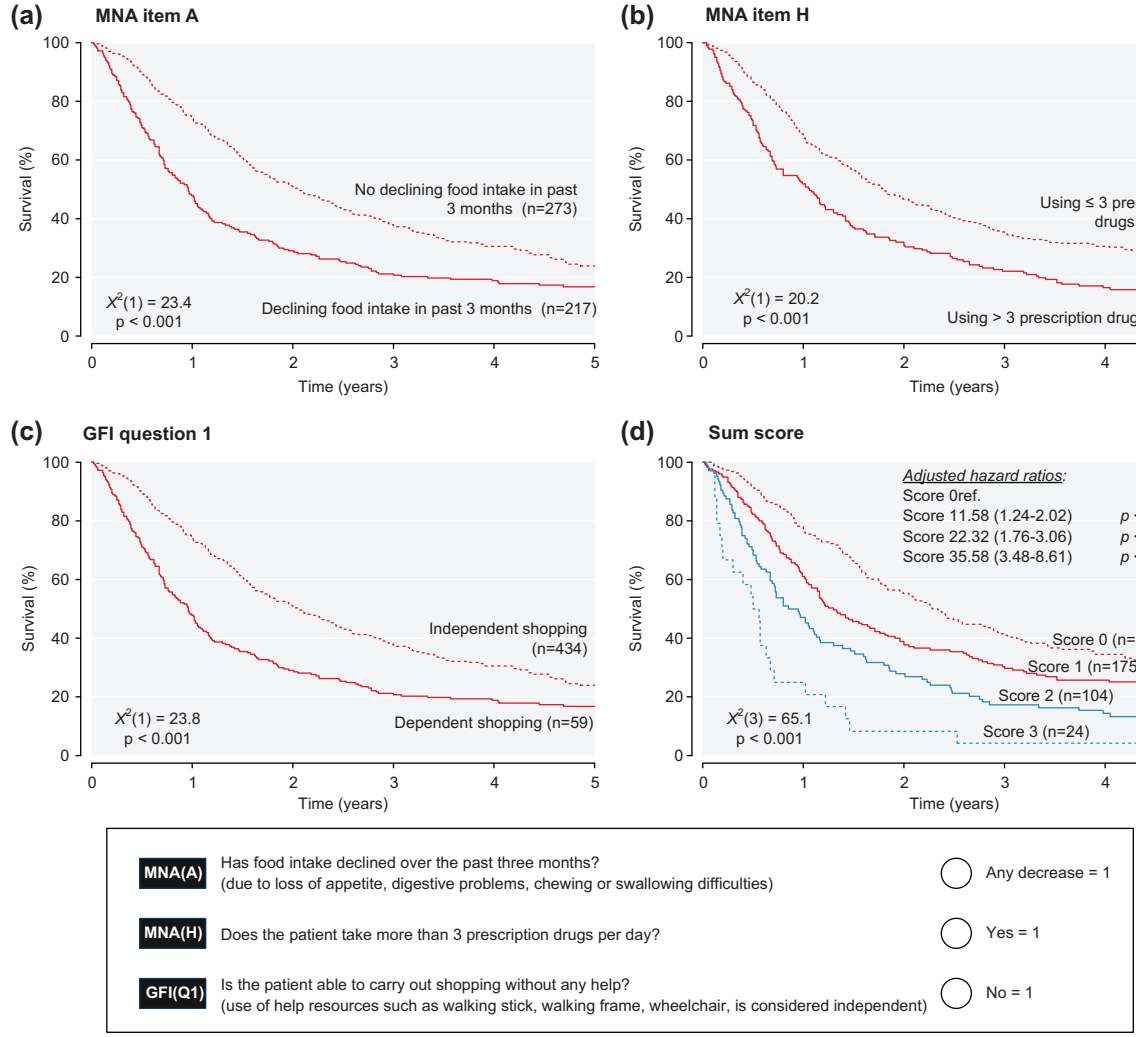


Figure 1. Kaplan–Meier curves of overall survival in 494 elderly patients with various types of cancer according to: [A] MNA item A, [B] MNA item H, [C] GFI question 1 and [D] sum score of these three items.

toxicity [20]. Hoppe et al. identified depression and dependence for instrumental activity of daily living (IADL) as risk factors for early functional decline during chemotherapy [22]. The GVS showed increased toxicity with three or more risk factors of albumin, lymphocyte count, and scores of ADL, IADL and Hospital Anxiety and Depression Scale, for patients with advanced ovarian cancer and treatment with carboplatin [14]. The present study concentrated on the inability to complete at least four cycles of chemotherapy and showed that in the case of (risk of) malnutrition by MNA the chance not to complete chemotherapy increased more than two-fold. The large variety of chemotherapy regimens, shown in Supplementary Addendum 4 available online at http://informahealthcare.com/doi/abs/10.3109/0284186X.2015.1068446, precluded analyses of specific schedules. However, for all schedules given adequate dose intensity is essential, whether it is given for palliative or curative reasons. The reasons for early treatment withdrawal in our study form common reasons in general oncology practice to decide on stopping chemotherapy. And of course it is legitimate to ask the question, whether one should have started chemotherapy at all, when this only results in toxicity and early treatment withdrawal [2,3,23,24].

Others concentrated in their research on risk factors for mortality [24,25]. Kanesvaran et al. developed a Clinical Scoring System (CSS) in an Asian population, consisting of the factors age, albumin, ECOG performance status, depression, stage of disease and nutritional index. A nomogram predicted overall survival rate [25]. Soubeyran et al. identified male gender, advanced stage, poor MNA and decreased mobility as risk factors for early death [24]. The GVS showed significantly worse survival with the same risk factors as shown for toxicity [14]. As previously shown in a smaller cohort [15], the present study identified poor MNA and poor GFI as risk factors for mortality. In general, CGA contains components that predict for mortality [23]. These data show the importance of the nutritional status and frailty score as part of pre-treatment assessment to select patients who might benefit from interventions.

Screening tests have been developed to help for the identification of frailty and select the patients who might benefit from extensive CGA [9]. However, screening tools still contain 5–15 items [4,8], which may lead to a barrier against broad usage in clinical care. Many health workers aim for a balance between optimal health care and a minimal burden to patients and caregivers [5,6]. To improve pre-treatment assessment it is not always necessary to complete a full version of a (self-reported) questionnaire. The aCGA used seven of 16 ADL/IADL items for detection of shortcomings [4]. The three-item SOF index showed a sensitivity and specificity of 89.0 and 81.1, respectively, for the detection of disabilities in comparison with CGA [13]. The GVS score was developed for elderly patients with advanced ovarian cancer and treatment with carboplatin [14].

Regarding feasibility of chemotherapy, this study shows that three items of the MNA were predictive in multivariable analysis: "psychological stress or acute disease in the past three months", "neuro psychological problems" and "using more than three prescript drugs". These items seem comparable with items used by Hurria et al: "decreased social activity because of physical/emotional health, limited at least sometimes" and "taking medications with some help/unable" [21]. Depression was one of the risk factors for early functional decline, as shown by Hoppe et al. [22], and was also a risk factor of the GVS [14]. The MNA-score as a whole was one of the risk factors for non-hematologic toxicity, identified with the CRASH score [20].

The present study introduces the GPI as instrument for the prediction of mortality. Two items of the MNA (MNA-A and MNA-H) and one item of GFI (GFI-Q1) proved to be highly predictive for mortality. In comparison with no positive items the patients with all three items positive showed a HR for mortality of 5.58 (95% CI 3.48–8.61; $p < 0.001$). This holds especially for the palliative treated patients. The GPI can not be compared with the SOF index [13], which has not been correlated with mortality, nor with the CSS [25] (developed in an Asian population), nor with the GVS [14] (tumor- and treatment-specific score). The GPI concentrates on decreased food intake, polypharmacy and dependence in shopping. Poor score of MNA was identified as risk factor of early death by Soubeyran et al. but this study was not analyzed which factor(s) of the MNA contributed mostly [24]. Dependence in shopping was also identified by others as important risk factor for detection of disabilities [4].

The GPI could support the use of chemotherapy in patients with score 0–1, whereas a more thorough CGA would be warranted for those patients scoring 2 (median survival in this cohort almost one year) and the use of chemotherapy should be questioned in patients with score 3 (median survival of only six months). A potential form of bias exists for MNA-H, due to the fact that all patients with a normal screening score on the MNA were given score 1 (see Supplementary Addendum 1 available online at http://informahealthcare.com/doi/abs/10.3109/0284186X.2015.1068446). Therefore the GPI should be validated in an independent study population of elderly cancer patients.

Some limitations have to be mentioned. First, a variety of cancer types were included. However, we adjusted for cancer type in our multivariable models. Another source of heterogeneity may have been the fact that different chemotherapy regimens were given of which not all were given in the full doses. Second, the selected patients underwent a GA after they were considered to be fit to undergo chemotherapy by their oncologist, thereby introducing selection bias. Nevertheless, considerable shortcomings appeared to be present at baseline regarding GFI and MNA. Third, we tested the individual items of the MNA, GFI, IQCODE and MMSE resulting in a three-item GPI. Type I errors occurs in multiple testing and therefore we selected only individual items that were predictive in crude models with a p-value $< 0.01$ and in forward stepwise regression models with an entry criterion of $p < 0.01$. Fourth, models were developed and validated on the same dataset. The GPI therefore needs to be validated in future studies of elderly cancer patients. One strength of the study is that we did analyze separately the adjuvant/curative and the palliative treated patients for the effect of the GPI on mortality.

In conclusion, our results show that a poor MNA score was predictive for not completing four cycles of chemotherapy and poor MNA- and GFI scores were predictive for mortality of elderly patients with various types of cancer. 'Psychological stress', 'neuropsychological problems' and 'number of drugs taken' were predictive items of MNA for feasibility of chemotherapy. 'Declining food intake', 'number of drugs taken' and 'dependence in shopping' were the three predictive items for a higher risk of mortality, resulting in the GPI. Hazard ratios for mortality increased linearly with sum scores increasing from 0 to 3 points. The GPI can help to identify the elderly patient at an increased risk for mortality, who beforehand is considered to be fit enough to receive treatment with chemotherapy.

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## Supplementary material available online

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