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Original Research

Impact of comprehensive geriatric assessment on short-term mortality in older patients with cancer—a follow-up study



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Abstract Purpose: The aim of this study was to evaluate the impact of comprehensive geriatric assessment (CGA) linked to intervention on identified problems on 90-day mortality in older patients with cancer.

Patients and methods: Eligible patients were 70 years or older and referred to the Oncology Department at Aarhus University Hospital in order to receive treatment for head and neck cancer (HNC), lung cancer (LC), upper gastrointestinal tract (UGI) cancer or colorectal cancer (CRC). All patients were intendedly invited for CGA. Patients for the study were identified by the oncology department. CGA evaluated six domains: comorbidity, autonomy, mental, cognitive, nutritional status and medication. Intervention was proposed if deficits were detected. Follow-up was performed 90 days after inclusion.

Results: From January 1st 2016 through July 31st 2018, 781 patients were identified. Sixty-seven patients were excluded. Median age: 76 (interquartile range: 72–80) years. Primary tumour sites: 5% HNC, 46% LC, 20% UGI and 29% CRC. A total of 407 patients had CGA, 307 had no CGA. Geriatric intervention was proposed in 325 patients (80%) and initiated in 319 patients (78%) in the CGA group. Within 90 days, 142 patients (20%) died. In the non-CGA group, 74 patients died (24%), versus 68 patients (17%) in the CGA group. A potential reduction of death in the CGA group was detected: crude odds ratio (OR): 0.63 (95% confidence interval: 0.43; 0.91), $p = 0.014$. Adjusted OR: 0.62 (95% confidence interval: 0.39; 1.00), $p = 0.05$.

Conclusion: A CGA linked to oncology evaluation may reduce short-term mortality in older patients with cancer referred for oncological treatment.

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1. Introduction

Cancer is primarily a disease of the older part of the population [1,2]. An increase in cancer incidence is anticipated due to increasing longevity [3]. Older patients are underrepresented in cancer treatment trials [4], leaving a gap of knowledge of how best to assess and treat them.

Patients with cancer are routinely assessed clinically by performance status (PS) [5]. PS is known to predict survival [6]. It has been proposed that PS has reduced predictive value in older patients with cancer, as some chronic conditions may influence PS, but not survival [7]. This calls for an alternative method of assessing older patients with cancer.

A comprehensive geriatric assessment (CGA) collects information on a person's health status in multiple domains. CGA is a multidisciplinary evaluation including identification and quantification of the problems of older patients followed by personalised interventions [8]. CGA has been reported to improve survival and physical performance in older patients [9]. Others reported an increased probability of living in their own home following CGA but found little or no effect on survival [10]. Soubeyran *et al.* [11] demonstrated that malnutrition and poor mobility predicted 6-month survival in older patients with cancer. Recently, elements of CGA have been identified as predictors for short-term mortality in older patients with cancer [12].

The potential of CGA to detect limitations in functional ability, not identified by PS, has been demonstrated previously [13]. CGA may reveal impairments in geriatric domains even in patients with a favourable PS. From previous studies, we know that frail older patients with cancer have a high risk of dying within 3 months [12,14]. However, it remains uncertain if CGA can affect short-term mortality in older patients with cancer.

The objective of this study was to compare 90-day mortality between two groups of older patients with cancer, one group with CGA and one without at the first visit to the department of oncology (DO).

1.1. Hypothesis

CGA reduces 90-day mortality in older patients with cancer.

Tailored follow-up on the problems identified during CGA affects short-time mortality.

2. Methods

The study is as a cohort study with follow-up 90 days after inclusion.

Patients were referred to the DO outpatient clinic at Aarhus University Hospital for cancer treatment.

Patients would qualify for participation if they were aged 70 years or more and living in Aarhus Municipality, Denmark, or one of the three surrounding municipalities.

Patients should have a diagnosis of head and neck cancer (HNC), lung cancer (LC), upper gastrointestinal tract (UGI) or colorectal cancer (CRC).

The DO was responsible for identifying patients and informing of the planned CGA. If patients were not identified by the DO or if invited patients did not respond to invitation, they were defined as non-CGA patients.

Patients were excluded if they were referred to specialised palliative care or participated in another geriatric study at the time of referral to the DO.

Both patients with newly diagnosed cancer and patients with a relapse from a previously treated cancer were included. Patients would qualify for participation, regardless of the stage of the cancer or initiation of specific cancer treatment. Patients who responded to the invitation for CGA were preferably assessed on the day of their first oncologic consultation.

Potential patients for this study were identified by a weekly review of lists of planned consultations in the DO outpatient clinic, available in the electronic medical file. By repeating this procedure, retrospectively patients who did not attend CGA were identified and registered (see Fig. 1).

Data recorded from medical files at baseline included age, gender, primary tumour site, tumour-node-metastasis status and PS. The Charlson Comorbidity index score was calculated by review of medical files. Information on cumulated exposure to smoking was estimated in all patients based on information from medical files.

Patients responding to invitation had a complete CGA at baseline. CGA was performed by a geriatric specialist or a senior resident in geriatric medicine and a trained geriatric nurse. Validated instruments were used for the CGA assessing six domains of health: autonomy: Activities of Daily Living by Barthel-100 [15] and Instrumental Activities of Daily Living (IADL) by Functional Activities Questionnaire (FAQ) [16,17], nutrition: Mini Nutritional Status [18], cognition: Mini Mental State Examination [19], mood: Geriatric Depression Scale 15-item [20], comorbidity: Cumulative Illness Rating Scale-Geriatrics [21] according to the modified guidelines [22] and polypharmacy: the number of daily medications.

According to the results of the CGA, patients were categorised as 'fit', 'vulnerable' or 'frail' as previously published [14]. Initiation of intervention based on the CGA was registered in four categories: medical, nutritional, physical or social. Tailored follow-up on the identified problems was performed by the multidisciplinary team on a subgroup of patients also

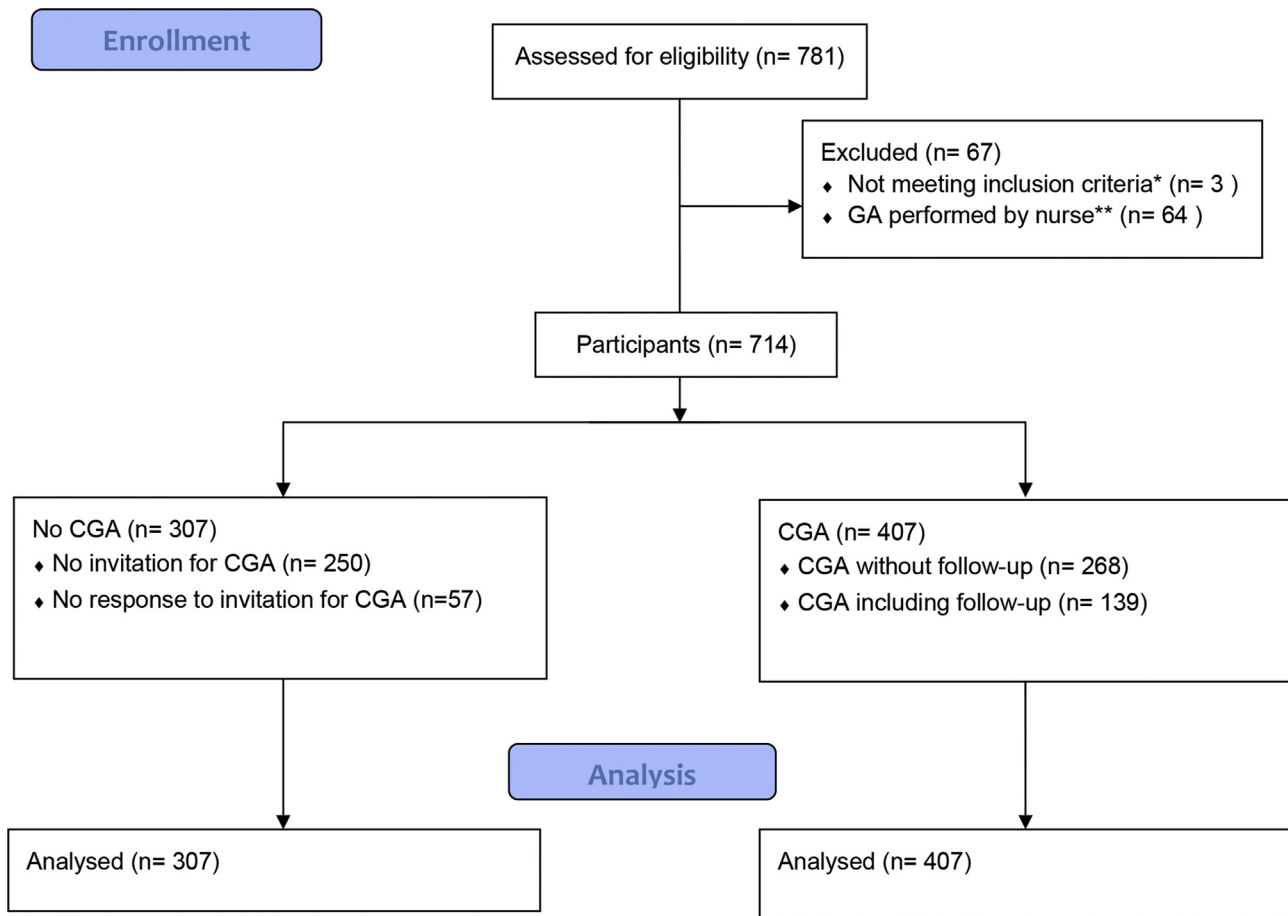


Fig. 1. Study recruitment and follow-up. *Owing to referral to specialised palliative (n = 2) care or participation in another geriatric study (n = 1). **Owing to the absence of the primary investigator because of participation in courses, vacation and so on. These patients had a brief evaluation by a geriatric nurse. CGA, comprehensive geriatric assessment.

included in the intervention arm in an ongoing controlled randomised study (Clinical Trials.gov: NCT02837679).

Selection of patients for CGA was not influenced by the study group. Patients were identified by staff in the DO solely from information on age, primary tumour site and geography.

There were two reasons for not attending CGA: non-identification by the staff in the DO or non-response to the invitation. Potentially, this could bias the results if the populations differed in baseline variables.

Information on potential confounders, e.g. smoking exposure and comorbidity, was collected prospectively by the multidisciplinary team in the CGA group, whereas similar information was collected retrospectively in the non-CGA-group. Information on death was obtained from the electronic medical file. Death was registered in the medical file if the patients died in hospital or at home.

Patients were consecutively included from January 1st, 2016, through July 31st, 2018.

Distant metastasis was registered as present or not. Exposure to tobacco smoking was categorised into

never smoker, moderate exposure (1–30 pack-years) and heavy exposure (>31 pack-years).

Death within 90 days was the primary end-point. Secondary end-point was additional effect of tailored follow-up by the multidisciplinary team.

2.1. Statistical methods

Baseline characteristics were analysed using comparative statistics. Fisher's exact test or chi-square test was used as for categorical data as appropriate. For continuous data, Student's t-test was used for parametric data and the Wilcoxon rank sum test for non-parametric data. Owing to a lack of data regarding T-stage and N-stage in numerous patients, these data were omitted from the analyses.

In order to identify factors that may influence 90-day mortality, a multiple logistic regression model was constructed with a stepwise variable selection. Initially, a univariate logistic regression model was used to select baseline variables ($p \leq 0.20$) for the multivariate analysis. Primary tumour site, presence of metastases, PS, and initial treatment goal were included in the

Table 1

Baseline characteristics of patients and total population in the two exposure groups.

	Total N = 714	Non-CGA n = 307 (43%)	CGA n = 407 (57%)	P-value
Age, years				
Median (IQR)	76 (72–80)	76 (73–81)	75 (72–79)	
Range	70–95	70–95	70–91	0.007
Gender				
Female, n (%)	324 (45)	144 (47)	180 (44)	0.476
Cancer type, n (%)				
Head and neck	39 (5)	24 (8)	15 (4)	
Lung	325 (46)	164 (53)	161 (40)	
Upper gastrointestinal tract	139 (20)	45 (15)	94 (23)	
Colorectal	211 (29)	74 (24)	137 (33)	< 0.001
Dissemination of cancer, n (%)				
T-stage 0	4 (1)	3 (1)	1 (–)	
1	78 (11)	37 (12)	41 (10)	
2	90 (13)	43 (14)	47 (11)	
3	177 (25)	69 (23)	108 (27)	
4	167 (23)	62 (20)	105 (26)	
Missing	198 (28)	93 (30)	105 (26)	0.155
N-stage 0	185 (26)	80 (26)	105 (26)	
1	92 (13)	36 (12)	56 (14)	
2	150 (21)	64 (21)	86 (21)	
3	67 (9)	27 (9)	40 (9)	
4	1 (–)	1 (–)	0 (–)	
Missing	219 (31)	99 (32)	120 (30)	0.825
Metastatic disease	338 (47)	138 (45)	200 (49)	0.267
Performance status, ECOG				
0–1	420 (59)	167 (54)	253 (62)	
2	178 (25)	80 (26)	98 (24)	
>2	116 (16)	60 (20)	56 (14)	0.059
Charlson comorbidity score				
Median (IQR)	1 (0–2)	1 (0–2)	1 (0–2)	
Range	0–8	0–8	0–8	0.849
Smoking, pack-year, n (%)				
Never smoker	217 (31)	74 (24)	143 (35)	
1–30	245 (18)	108 (35)	137 (34)	
>30	252 (24)	125 (41)	127 (31)	0.003
Initial oncology treatment intention				
Curative	261 (37)	118 (38)	143 (35)	
Palliative	328 (46)	138 (45)	190 (47)	
None	125 (17)	51 (17)	74 (18)	0.643
Geriatric characteristics				
ADL independent, n (%)			377 (93)	
IADL independent, n (%)			266 (37)	
Nutritional status (MNA): well nourished, n (%)			161 (40)	
Normal cognition (MMSE), n (%)			385 (95)	
GDS normal, n (%)			308 (75)	
Comorbidity: total CIRS-G-score			11 (4.5)	
Number of affected organ systems, mean (SD)			5 (2.0)	
Number of daily medications, mean (SD)			6.0 (3.1)	

'Non-CGA' had no comprehensive geriatric assessment. 'CGA' had CGA at the first visit to the oncology outpatient clinic.

CGA, comprehensive geriatric assessment, IQR, interquartile range, SD, standard deviation, ECOG, Eastern Cooperative Oncology Group, ADL, Activities of Daily Living, IADL, Instrumental Activities of Daily Living, MNA, Mini Nutritional Assessment, MMSE, Mini Mental State Examination, GDS, Geriatric Depression Scale 15-item, CIRS-G, Cumulative Illness Rating Scale-Geriatrics. Bold values represent statistical significance ($p < 0.05$).

multivariate analysis. In the subgroup of patients having CGA, a logistic regression analysis was performed in order to evaluate the effect of a tailored follow-up by the multidisciplinary team for 90 days. This analysis was adjusted for the frailty status of patients and initial

treatment goal. Inclusion of further variables in the model was restricted by the number of events.

As no deaths occurred in the patients with HNC, this group was omitted from the multivariate regression analyses.

A p-value of 5% or less was considered statistically significant. STATA version 15 was used for the statistical analyses.

Study data were collected and managed using REDCap electronic data capture tools hosted at Aarhus University [23].

2.2. Ethical considerations

The study was evaluated by the regional ethics committee who considered it to be a medical database research project without intervention or collection of biological material. So a formal approval was not deemed necessary and informed consent was not necessary. The study was conducted in accordance with the Declaration of Helsinki and Good Clinical Practices. The study was approved by the Danish Data Protection Agency (1-16-02-3-14) and registered at Clinical Trials.gov: NCT03814213.

3. Results

A total of 781 eligible patients were identified. We excluded three patients referred for specialised palliative care at time of CGA or participating in another geriatric research programme. Owing to logistical issues, 64 patients did not have a CGA by the multidisciplinary team. These patients had a brief geriatric assessment performed by a nurse. Of the remaining 714 patients, the DO failed to identify 250 patients before their first consultation, and they did not receive an invitation for CGA. A total of 464 patients received an invitation for CGA, but 57 patients did not respond. Follow-up was performed in all patients after 90 days (Fig. 1).

Participants had a median age of 76 (interquartile range: 72–80) years. The oldest participant was 95 years old. The CGA group was 1 year younger than the non-CGA group. The most prevalent primary tumour site was the lung. More patients in the non-CGA group had LC and fewer had UGI or CRC. Only 5% of patients had HNC. Information on T- and N-stage was missing in between 25 and 30% of patients, especially in patients referred for palliative treatment. Patients in the CGA group had been less exposed to tobacco. For further details including geriatric characteristics in the CGA group, see Table 1. In the non-CGA group, non-responders to invitation for CGA were more often not offered treatment for their cancer disease as compared to patients with no invitation for CGA, see Supplementary material S1.

Mean time to perform the CGA was 69 (± 19) minutes. Geriatric intervention was needed in 325 patients (80%) of patients in the CGA group. Intervention was initiated in 319 (78%) of patients. The reason for not initiating the intervention in the remaining 6 patients was non-acceptance by patients (Table 2). Intervention

was initiated by the multidisciplinary team; additional support from geriatric physiotherapy and occupational therapy was available.

3.1. Complete follow-up regarding mortality was obtained

During the 90-day follow-up, 142 patients (20%) died. In the non-CGA group, 74 patients died (24%), while 68 patients (17%) in the CGA group died. Fig. 2 illustrates the mortality rate. The reduction in the death rate in the CGA group was statistically significant: crude odds ratio (OR): 0.63 (95% confidence interval [CI]: 0.43; 0.91), $p = 0.014$. In the multivariate analysis, significance was just lost, OR: 0.62 (0.39; 1.00), $p = 0.05$. Presence of metastases, primary tumour site, PS status and primary treatment goal contributed significantly to the model. A subgroup of patients had a tailored follow-up on CGA in an attempt to improve compliance to intervention based on CGA. This may have influenced the effect of CGA. Therefore, a supplementary analysis was performed omitting the tailored follow-up group. Crude OR: 0.61 (95% CI: 0.40; 0.93), $p = 0.021$. In the multivariate analysis, significance is lost: OR: 0.77 (95% CI: 0.45; 1.31), $p = 0.334$.

The estimated within-CGA group effect of a follow-up on the CGA is small: crude OR 0.91 (95% CI: 0.52; 1.58), $p = 0.732$. Adjusting for baseline variables with statistically significant uneven distribution, frailty status and initial treatment goal, indicates a possible more profound effect of tailored follow-up: OR 0.72 (95% CI: 0.39; 1.32), $p = 0.289$.

4. Discussion

In this cohort of older patients with cancer, 20% of patients died within 90 days from the first visit to the DO. Having a CGA seems to reduce short-term mortality. In the multivariate analysis, however, the statistical significance is lost. A subgroup analysis indicates that a tailored follow-up on the problems identified during CGA may have an additional positive effect on lowering the short-term mortality. To our knowledge, this is the first study to demonstrate a possible effect on short-term mortality of CGA including interventions in a population of older patients with cancer. Previous studies have shown inconsistent results regarding the effect of CGA on survival in older patients with cancer.

Table 2

Initial geriatric interventions based on findings in comprehensive geriatric assessment (CGA) in the 407 older patients with cancer assessed by CGA.

Geriatric intervention indicated, n (%)	325 (80)
Geriatric intervention initiated, n (%)	319 (78)
Medical changes, n (%)	283 (70)
Nutritional interventions, n (%)	141 (35)
Physical interventions, n (%)	120 (29)
Social interventions, n (%)	57 (14)

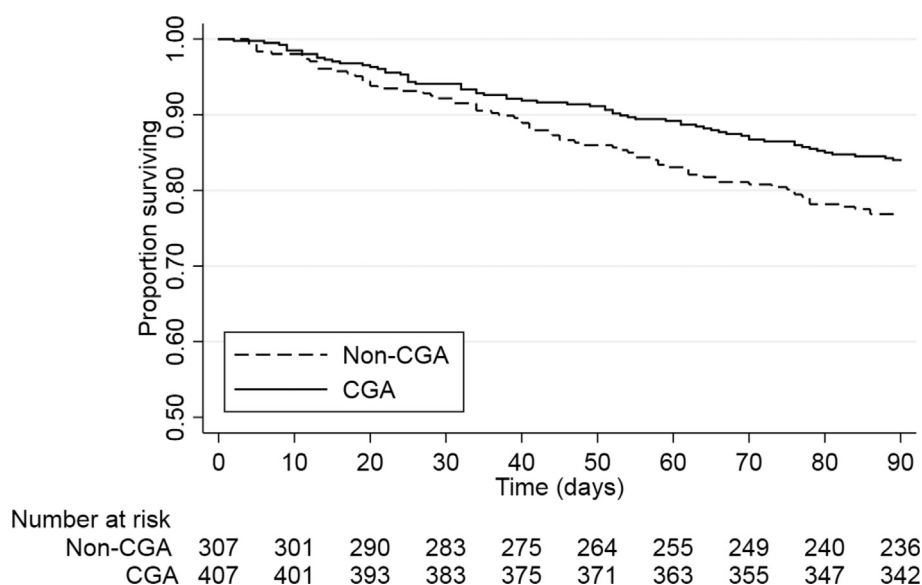


Fig. 2. Proportion of patients surviving. CGA, comprehensive geriatric assessment.

In a study by Corre *et al.* [24], no effect on survival was demonstrated in a population of older patients with advanced non-small-cell LC. In that study, CGA was used to allocate anticancer treatment strategy, and the protocol did not include interventions based on CGA. Rao *et al.* [25] found no effect on survival by CGA offered after discharge from hospital. McCorkle *et al.* [26] demonstrated an increased survival in a population of postsurgical patients with cancer offered specialised home care interventions compared to standard care. The effect was only present in late-stage cancers. We found no difference in the effect of CGA in relation to stage. The suggested additional benefit of a tailored follow-up for 90 days is in line with previous studies concluding that CGA programmes including control of medical recommendations and extensive ambulatory follow-ups are more likely to be effective(9). A study of implementation of geriatric recommendations without close follow-up reveals that one or more geriatric recommendations were performed in 52% of patients covering only 35% of all given recommendations [27]. This emphasises the need for follow-up on recommendations based on CGA. Furthermore, it has previously been documented that patient adherence to CGA recommendations was associated with the importance of the proposed interventions [28]. A positive association between the number of identified problems and adherence to recommendations was found, but at the same time, a negative association between adherence and the number of recommendations was demonstrated. No patients with HNC died during the follow-up. This may be due to selection as patients with HNC were evaluated clinically at a multidisciplinary conference before referral to the DO. By this process, the frailest patients may have been excluded from the study population in advance.

This single-centre study has several limitations. First and most importantly, the comparability of the two groups can be questioned as no geriatric baseline data (e.g. G-CODE [29]) were registered in non-CGA patients. We did, however, adjust for potential confounders like PS in the analyses. Retrospective collection of baseline information in the non-CGA-group may have biased the accuracy of the information in the groups. Furthermore, as smoking exposure is an important risk factor for LC, this information in patients with LC may be more detailed than in other patients. The present study included only a limited number of primary tumour sites. This limits the external validity with regard to other tumour sites. Verification of the results in a preferably multicentre randomised design including more primary tumour sites is desirable.

As patients with a variety of primary tumour sites and stages were included, a difference in treatment strategy and side-effects can be anticipated. On the other hand, anticancer treatment is guided by cancer stage, PS [30] and patient preference. Adjustments for stage and primary tumour site were performed in the analyses.

From previous studies of older patients with cancer, we know that some patients are fit and need no geriatric intervention [14](27). The present study included patients who needed no geriatric intervention; this may have diluted the results.

5. Perspectives

The present study adds to the knowledge of the effect of CGA offered to older patients with cancer. It emphasises that interventions linked to CGA may be needed in order to have an impact. An issue to address in future studies is whether a possible

explanation for the additional effect of a close follow-up is due to an increased adherence to cancer treatment. A screening tool with the ability to identify older patients with cancer in need of geriatric intervention would enable a more specific selection of patients for CGA. Quality of life linked to CGA and to possible life expectancy gain is another important factor to address in future studies.

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Conflicts of interest statement

The authors declare no conflict of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ejca.2019.05.003>.

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