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# Comprehensive Geriatric assessment and its clinical impact in oncology

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## ABSTRACT

Comprehensive geriatric assessment (CGA) is a process that consists of a multidimensional data-search and a process of analyzing and linking patient characteristics creating an individualized intervention-plan, carried out by a multidisciplinary team. In general, the positive health care effects of CGA are established, but in oncology both CGA and the presence of geriatric syndromes still have to be implemented to tailor oncological therapies to the needs of elderly cancer patients. In this paper the conceptualization of geriatric syndromes, their relationship to CGA and results of clinical studies using CGA in oncology are summarized. Geriatric syndromes are associated with increased vulnerability and refer to highly prevalent, mostly single symptom states (falls, incontinence, cognitive impairment, dizziness, immobility or syncope). Multifactorial analysis is common in geriatric syndromes and forms part of the theoretical foundation for using CGA.

In oncology patients, we reviewed the value of CGA on the following endpoints: recognition of health problems, tolerance to chemotherapy and survival. Most studies performed CGA to identify prognostic factors and did not include an intervention. The ability of CGA to detect relevant health problems in an elderly population is reported consistently but no randomized studies are available. CGA should explore the pre-treatment presence of (in)dependence in Instrumental Activities of Daily Living (IADL), poor or moderately poor quality of life, depressive symptoms and cognitive decline, and thereby may help to predict survival. However, if scored by the Charlson comorbidity-index, comorbidities are not convincingly related to survival. The few studies that included a CGA-linked intervention show inconsistent results with regard to survival but compared to usual care quality of life is improved in the surviving period. Functional performance scores and dependency at home appeared to be independent predictive factors for toxicity, similar to depressive symptoms and polypharmacy. Overall, CGA implements/collects information additional to chronological age and Performance Score. So far in oncology there are no prognostic validation studies reported using geriatric syndromes or information based on CGA in its decision making strategies.

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## 1. Introduction

Health care for older people is becoming increasingly important in industrialised nations. As the population ages, there is an emerging need to develop a means to characterize the 'functional age' of older patients in order to tailor treatment decisions based on factors other than chronological age and to develop interventions to optimize cancer treatment. Comprehensive geriatric assessment (CGA) is one of the procedures designed to improve the health of this population.<sup>1</sup> CGA is defined as a multidisciplinary evaluation in which the multiple problems of older people are uncovered, described and if possible explained, and in which the resources and strengths of the person are catalogued and a coordinated plan is developed to focus interventions on the individual person's problems.<sup>2</sup> Usually CGA starts with a multidimensional search for relevant medical, functional, mental and social parameters of older individuals. Often nutrition and drug-use are explicitly assessed as well. Secondly, an analysis of this information by a geriatrician and subsequently by a multidisciplinary team lead by this geriatrician leads to individualised goals and an integrated intervention-plan. The effects of implementing a CGA-based approach has been evaluated in a number of controlled studies, conducted in clinical and outpatient settings, as well as among community dwelling elderly people.<sup>3</sup> Positive effects of CGA are (among others) prevention of functional decline, less unplanned (re)hospitalisations and less nursing home admissions. Compared to usual care CGA detects a greater number of health problems.<sup>4</sup> Its impact on mortality is more robust for inpatients than for community-dwelling older people.<sup>5,6</sup> Key issue in the debate on effectiveness of CGA concerns the population characteristics of the elderly individuals to whom CGA is addressed. Patients should neither be terminally ill nor too fit. Patients who benefit most are classified as 'frail' or 'having geriatric syndromes'. Another essential issue for the effectiveness of CGA compared to usual care is the presence of control or follow-up by the intervention team.<sup>3–7</sup>

In oncology there is increasing interest in assessment techniques for elderly cancer patients, both to determine the most feasible cancer treatment as well as to create an integrated intervention plan to deal with the multiple health problems that coexist in many elderly cancer patients. Both the presence of a geriatric syndrome and CGA are used to tailor oncological therapies to the needs of elderly cancer patients.

In this article we focus first on the conceptualization of geriatric syndromes and CGA, secondly studies with CGA or CGA-like interventions in oncology are reviewed.

## 2. Geriatric syndromes

Geriatric syndromes play an important role in medicine of older patients such as clinical practice, teaching, research and management.<sup>8</sup> Some authors state that presence of geriatric syndromes is important in the decision-making process in cancer treatment, especially in deciding whether a life-pro-

longing treatment should be offered to a patient.<sup>9</sup> However validation studies regarding the prognostic value of geriatric syndromes are lacking in decision making strategies within oncological care.

What does a syndrome mean to clinicians and how do we use the word syndrome in medicine in contrast to a disease (e.g. *E. Coli* cystitis)? Commonly the term syndrome is defined as a nosological entity consisting of signs, symptoms and manifestations clarified by medical techniques. A syndrome often refers to a (partly) uncertain pathological entity; in contrast a disease refers to a clinical entity, well defined in its pathogenesis and aetiology. Three types of clinical syndromes are described in Fig. 1. In the first type combinations of symptoms and signs are grouped together without evidence of aetiology or pathogenesis (e.g. chronic fatigue syndrome). In the second type symptoms and signs are grouped only with evidence of aetiology (e.g. Marfan's syndrome). In the last type there is only evidence of pathogenesis, but without a known aetiology (e.g. Cushing's syndrome).<sup>10</sup> In contrast a geriatric syndrome refers to highly prevalent, mostly single symptom states, caused by accumulated impairments in multiple systems. In a recent review pressure sores, incontinence, delirium, falls en functional decline, turned out to be evidence based geriatric syndromes, while the multifactorial aetiology of other geriatric problems (e.g. cognitive impairment, dizziness, and syncope) still remains to be studied. In case of a geriatric syndrome, there is no single pathogenetic pathway which causes the symptom(s). The leading symptoms are linked to a number of diseases or aetiological factors, often concerning multiple organs. There is also an overlap in aetiological factors in different geriatric syndromes and often patients suffer from more than one geriatric syndrome. Diagnostic workups of geriatric syndromes consist of a search for disease(s) and a multiple risk factor assessment.

The multifactorial analysis of geriatric syndromes, with their interacting pathogenetic pathways and multiple aetiological factors, forms (part of) the theoretical foundation for using the comprehensive geriatric assessment (CGA). Clinical studies on geriatric syndromes such as delirium, urinary incontinence, falls, dizziness and syncope provide evidence for the effectiveness of performing CGA as a multifactorial analysis if a multi-targeted intervention-plan forms part of it.<sup>11–13</sup>

On theoretical grounds the presence of geriatric syndromes can be used in oncology to recognise the need for multifactorial analysis and incorporate this analysis in diagnostic procedures or clinical pathways. The occurrence of a geriatric syndrome could be a banner for increased vulnerability in elderly patients e.g. heralding an increased incidence of adverse events, or even a reduced response rate or decreased survival. In cancer care high prevalences of geriatric syndromes have been reported in a population of patients with prostate, breast or colorectal cancer receiving home care.<sup>14</sup> Outside oncology there is overt evidence that geriatric syndromes are associated with increased vulnerability and adverse events but its value in oncology is yet unclear.<sup>15,16</sup>

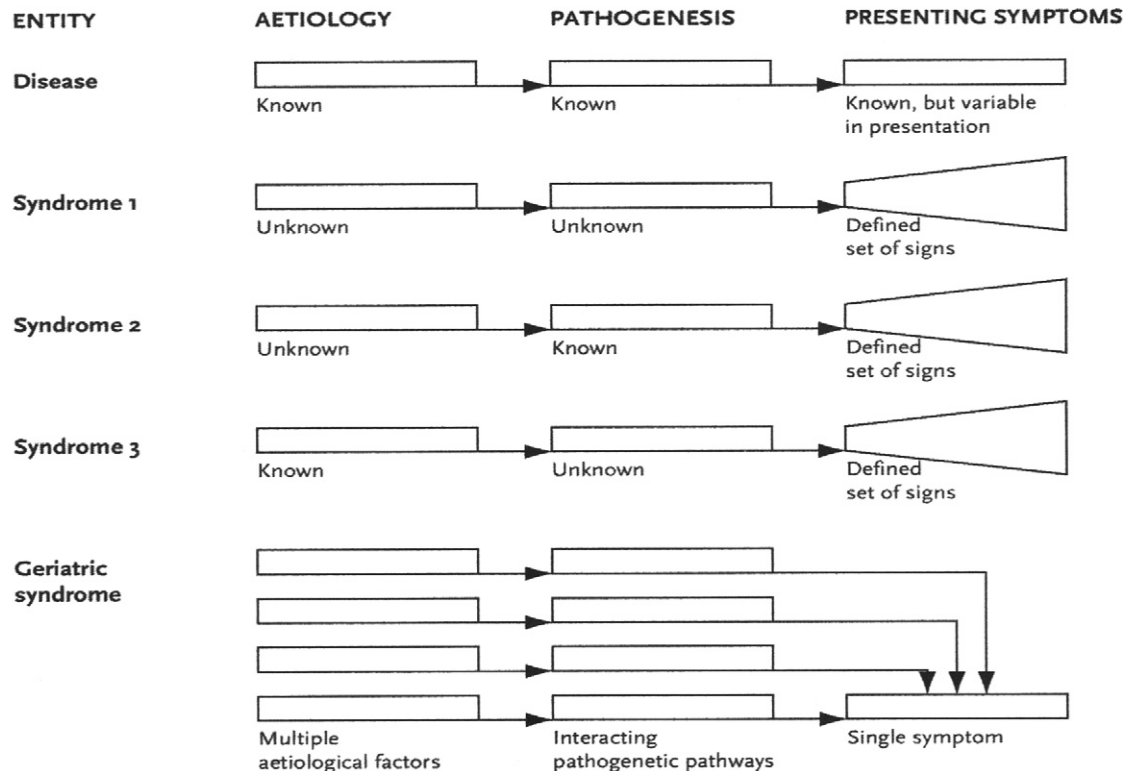


Fig. 1 – Differentiating clinical syndromes.

### 3. CGA, multidimensional assessment techniques and their impact

As mentioned in the introduction, CGA consists of four key-features: a multidisciplinary team, a multidimensional data-search, a process of analysing and linking patient characteristics together and the creation of an individualised intervention-plan. The value of CGA in oncology can be appraised by using different and heterogeneous endpoints: survival, functional decline, preventing (re)hospitalisations or nursing home admissions, number of unrecognised health problems, tolerance to or toxicity from oncological treatment, quality of life, etc. We conducted a review of the value of CGA on the endpoints survival, toxicity and recognition of health problems. The review was based on a systematic search in Pubmed using the following Medical Subject Headings (MeSH) terms: 'geriatric assessment' and the free text search terms: 'geriatric care', 'multidimensional assessment', each combined with MeSH-terms: cancer, oncology or carcinoma. Reports presented at annual American Society of Clinical Oncology-meetings concerning CGA were reviewed. Only clinical trials, meta-analyses and randomised controlled trials published before March 1<sup>st</sup> 2007 were included in this review.

Studies were grouped according to the endpoints mentioned above and special attention was drawn on CGA key-features. Furthermore, we discriminated between studies only conducting a multi-dimensional data-search and studies which also incorporated a multidisciplinary intervention-plan.

### 4. CGA and unrecognised health problems

A pilot study using CGA in elderly early breast cancer patients (mean age 79 yrs) showed that a high number of new health problems were detected and on average 1.5 new medical problem per patient required an intervention. Information delivered by CGA influenced oncological treatment directly in about one third of the patients. Pharmacological, nutritional, mental and social issues were highly prevalent and relevant in this study.<sup>17</sup> Their interventions led to an improvement in quality of life. A prospective study on CGA (mean age 72 yrs) emphasized that even in patients with a good Eastern Conference Oncology Group-Performance Status (PS) almost ten percent had limitations in Activities of Daily living (ADL); more than one third had limitations on Intermediate or Instrumental Activities of Daily Living (IADL) and 13% had two or more comorbidities.<sup>18</sup> A recent retrospective study (mean age 74 yrs) reported on an interdisciplinary model of care in an Oncology-Acute Care for Elders unit.<sup>19</sup> Patients underwent a CGA focused on geriatric syndromes: dependence in ADL and IADL was common; 29% had cognitive impairment in whom 36% was not documented in the medical records during hospitalisation and in the majority of cases this was not known before hospitalisation. Furthermore, restricted diets were present in 38% of the patients with weight loss. A French study showed in a somewhat older population (median age 78 yrs) that, although the majority (83%) had a Karnofsky-score above 60, many health problems were uncovered by CGA: only 44% of this group was fully ADL-independent and 13% IADL-independent; cognitive disorders and

depressive symptoms were present in almost half of the patients; malnutrition, polypharmacy and dangerous drug-interactions were common.<sup>20</sup> All studies had an open design and led to an in-depth analysis of the clinical impact of CGA in oncology. Conclusions of these studies were almost identical, advocating the value of CGA to detect relevant health issues in older cancer patients. Unfortunately no randomized study on this topic has been published.

## 5. CGA and survival

Our search revealed seven studies reporting on CGA and its impact on survival (Table 1). The age of the study populations was 'young' in geriatric terms with a mean age between 72 and 75 years. Five studies were designed to detect prognostic factors on survival by using CGA as a multidimensional data-search.<sup>21–25</sup>

Two studies<sup>22,23</sup> were phase II pharmacological studies with small numbers of patients. One study found that ADL-dependency was associated with a shorter progression free survival compared to those with ADL-independency. The second (not mentioned in Table 1) was closed prematurely because of high toxicity and therefore a statistical analysis could not be performed. A study<sup>21</sup> on older patients with different cancer types showed that an increased risk of death appeared in case of ADL-dependency (Hazard Ratio 2.0, CI 1.3–2.9) and IADL-dependency (HR 1.5, CI 1.1–2.0). In chemotherapeutically treated advanced non-small-cell lung cancer patients IADL-dependency and moderate or poor quality of life at baseline were independently associated with the risk of death.<sup>24</sup> Age, ADL-dependency and comorbidity were not associated with an altered risk of dying in this population with an overall limited life expectancy. In advanced ovarian cancer patients, an increased mortality risk was found when depressive symptoms occurred before treatment with chemotherapy.<sup>25</sup> Only this study reported explicitly on cognitive impairment and cognitive deficits were not related to a significantly decreased survival.

Two other studies focused on a direct comparison between usual care and CGA, in which CGA also included an intervention-plan.<sup>26,27</sup> In a prospective study comparing geriatric care to usual care a posthoc analysis was done in the group of patients with malignancies.<sup>27</sup> No significant differences were found in survival or hospital costs. With regard to quality of life, inpatients on the geriatric unit showed a better performance on pain, emotional and mental limitations and ADL-functioning at 6 months, whereas the outpatients performed better on mental limitations. After 1 year only the effect on pain was sustained. A larger randomised controlled trial on newly diagnosed cancer patients with solid tumours showed an increased mortality in the usual care group (HR 2.0, CI 1.3–3.1).<sup>26</sup> This effect was only established in the group with advanced cancer. In the intervention-group (including a large number of patients with advanced cancer) quality of life remained comparable to patients with early stages. It should be taken into account that CGA was conducted in the postoperative period and specialised home visits were structurally applied.

Overall CGA reveals information that is relevant to predict survival in cancer patients, the results are consistent in high-

lighting the impact of IADL-dependency and depressive symptoms on survival. Evidence for improving survival by performing CGA is less clear. Unfortunately there are only two studies in cancer medicine including intervention-plans in their study-design. Both studies that included an intervention plan showed improved quality of life in their intervention-groups. On the survival endpoint, no robust conclusions can be drawn, although the one study primarily designed to study elderly cancer patients gave positive results. This study incorporated a follow-up to their recommendations, and resulted in findings in line with positive results in studies on CGA outside oncology.

Comparison from CGA data derived from oncology studies with studies on CGA in general health care reveals some major differences: firstly, age in the above-mentioned study populations is substantially younger than in other studies of CGA. The oldest old (age above 80 years) are poorly requested. Secondly, the functional status of newly diagnosed cancer patients seems to be similar to an age-cohort that is ten years younger.<sup>28</sup> This fact may diminish the potential effect of CGA that primarily focuses on more or less dependent or frail patients. Furthermore, it is remarkable that cognitive impairment was not associated with an increased mortality. However, cognitive decline is mentioned as one of the important elements in geriatric syndromes.<sup>29</sup> In general medicine functional measures, including cognitive impairment, predicted 90-day and 2-year mortality in a group of hospitalized elderly patients.<sup>30</sup> We can only speculate about this striking difference. Referral bias to an oncology department may occur, and in patients with cognitive impairment physicians may show a diminished tendency to perform diagnostic procedures to establish the diagnosis cancer. Overall data from intervention studies remain scarce, so the value of CGA in oncology on the endpoints of 'survival/mortality' needs to be addressed in a prospective fashion before conclusions can be made. Special attention needs to be drawn to interventions made within the CGA-procedure.

## 6. CGA and tolerance to chemotherapy

A major topic in geriatric oncology is the question as to whether CGA can predict the risks and benefits of chemotherapy in a heterogeneous elderly population in the pre-treatment phase. Selecting fit elderly individuals to receive standard treatment is the goal of most clinicians. Other goals may be to achieve a well structured and individualized risk assessment that can be used to inform and advise on a patients health problems including the maximal feasible cancer treatment. Selecting the unfit elderly e.g. for adjusted chemotherapeutical regimes or supportive care can be a further objective if CGA is relevant in predicting tolerance to chemotherapy.

Our literature search revealed five studies that evaluated the value of CGA in predicting tolerance to chemotherapy (Table 2). Two studies were phase II studies with limited numbers of patients.<sup>22,23</sup> A prospective study to identify prognostic factors using CGA showed that both depression and dependence at baseline were significant predictors for toxicity in advanced ovarian cancer patients treated with carboplatin-cyclophosphamide.<sup>31</sup> This study was retrospectively extended with a

**Table 1 – Endpoint: Mortality/survival**

Author	Population, department + setting	Study-design + intervention	Results: geriatric factors as effect modifiers	Comment
Zagonel et al. 2002 <sup>21</sup>	Oncology department N = 252 Mean age 72 yr, range 65-92 yrs	Prospective observational study Identifying the prognostic role on survival of ADL and IADL dependency Follow up unknown	Increased risk of death in ADL-dependency (HR 2.0, CI 1.3-2.9) and IADL-dependency (HR 1.5, CI 1.1–2.0)	<ul style="list-style-type: none"> <li>- IADL and ADL scores were dichotomized</li> <li>- results were irrespective of Performance Status or type of cancer</li> </ul>
McCorkle et al. 2000 <sup>26</sup>	Surgical oncological academic department N = 375 Age: 60-92 yr early stage: N = 255 advanced stage N=120	RCT Postoperative CGA with consecutive home visits Mean follow up 24 months	No benefit on survival in early stage group. Benefit in advanced stage group, risk of death doubles: 2.0 (1.3-3.1) in usual care group vs intervention group	<ul style="list-style-type: none"> <li>- home care was delivered by advanced practice nurses.</li> <li>- quality of life remained in surviving intervention-group</li> </ul>
Rao et al. 2005 <sup>27</sup>	Veterans Administration Medical Center N = 99 Mean age 74, range nknown	Post hoc analysis in a subset of a randomized 2 × 2 factorial trial. Geriatric inpatient unit, outpatient clinic versus non-geriatric in- and outpatient services, Follow up 1 yr	No difference on mortality	<ul style="list-style-type: none"> <li>- strictly defined frailty characteristics,</li> <li>- no difference in hospital costs</li> <li>- geriatric care improved quality of life, only the effect on pain sustained after 1 yr</li> </ul>
Del Mastro et al. 2005 <sup>22</sup>	Medical Oncology department, Women >= 70 yrs with stage III and IV breast cancer N = 48 Mean age 74 yr, range 70-87 yrs	Phase II study to evaluate activity and toxicity of weekly paclitaxel. Post hoc factor analysis within pre-treatment CGA (comorbidity, functional status, mental health, age)	At least one inability in the ADL-scale was associated with a lower probability of response (p = 0.009) and a shorter progression free survival (p = 0.04) Charlson ADL- and IADL scales: not predictive on activity or toxicity	<ul style="list-style-type: none"> <li>- 63% Charlson score = 0</li> <li>- 26% one ADL-dependency</li> <li>- no report on the impact of incomplete cytotoxic regimens</li> <li>- mean overall survival 36 months, mean progression free survival 9.7 months</li> </ul>
Maione et al. 2005 <sup>24</sup>	Multicenter, oncology department Stage IIIB or IV non- small-cell lung cancer, PS ≤ 2 N = 566 Median age 74 yrs, range 70–84 yrs	Preplanned analysis within MILES-study, a phase III study with randomization to vinorelbine, gemcitabine or both; to identify prognostic role of baseline levels of comorbidity, functional status and QoL measured by CGA	Increased risk of death in <ul style="list-style-type: none"> <li>- Performance Score 2: p = 0.06 (HR 1.2–1.9)</li> <li>- worse IADL-score: p = 0.04 (HR 1.0–1.7)</li> <li>- intermediate + worse QoL score: p = 0.003 (HR 1.3–2.4)</li> </ul>	<ul style="list-style-type: none"> <li>- age, ADL-score and Charlson score did not correlate with an increased risk of death</li> <li>- short life expectancy due to advanced lung cancer may cover up factors which may be relevant to survival in case of a longer life expectancy</li> </ul>
Tredan et al. 2007 <sup>25</sup>	Oncology department Advanced ovarian cancer FIGO III/IV N = 155 Age > 70 yr Mean age 75 yr, range 70–90 yrs	Retrospective observational study to identify prognostic factors using CGA Carboplatin-cyclophosphamide or carboplatin/paclitaxel Follow-up 30 months	Performance Status was not a significant predictor of mortality (p = 0.06), depressive symptoms at baseline were highly significant (p < 0.001)	<ul style="list-style-type: none"> <li>- CP-group had at baseline better prognostic factors; high toxicity due to paclitaxel</li> <li>- Part of the study population was reported before<sup>26</sup>; also polypharmacy (&gt;6 drugs per day) was predictive on survival (p = 0.04)</li> </ul>



**Table 2 – Endpoint: toxicity to chemotherapy**

Author	Population + setting, department	Study-design + intervention	Results: geriatric factors as effect modifiers	Comment
Freyer et al. 2005 <sup>30</sup>	Advanced ovarian cancer FIGO III/IV, age > 70 yr N = 83 Median age 76 yr, range 70–90 yrs Oncology department	Open multicenter prospective study to identify prognostic factors using CGA Carboplatin- cyclophosphamide	- depression at baseline $p = 0.006$ - dependence $p = 0.04$ - Performance Score $\geq 2$ $p = 0.03$	- 72% received six cycles with no S-toxicity and no tumor progression - few geriatric conditions in study population - dependence dichotomized
Tredan et al. 2007 <sup>25</sup> (Freyer 2005 extended)	Advanced ovarian cancer FIGO III/IV, Age > 70 yr N = 155 Mean age 75 yr, range 70–90 yrs Oncology department	Retrospective observational study to identify prognostic factors using CGA Carboplatin-/cyclophosphamide or carboplatin/paclitaxel	No predictive factors in paclitaxel group	- CP-group had at baseline better prognostic factors; high toxicity due to paclitaxel
Extermann et al. 2002 <sup>31</sup>	Diverse cancers and chemotherapies N = 60 mean age 75 yr, range 70–87 yrs Tertiary cancer centre	Open prospective pilot study on predictors of tolerance to chemotherapy Using a multidimensional assessment	Higher diastolic blood pressure, MAX2, lactate dehydrogenase, marrow invasion related to toxicity ( $p < 0.1$ ); Charlson-index did not predict toxicity	- baseline functional, mental and mental status were not reported in relation to toxicity - 47% of the patients showed grade 4 hematological or grade 3/4 non-hematological toxicity
Del Mastro et al. 2005 <sup>22</sup>	Women $\geq 70$ yr with stage III and IV breast cancer N = 48 Mean age 74 yr, range 70–87 yrs Oncology department	Phase II study to evaluate activity and toxicity of weekly paclitaxel. Post hoc factor analysis within pre-treatment CGA (comorbidity, functional status, mental health, age)	Charlson-index, ADL- and IADL scales were not predictive on toxicity	- 63% Charlson score = 0 - 26% one ADL-dependency - no report on the impact of incomplete cytotoxic regimens - mean overall survival 36 months, mean progression free survival 9.7 months
Freyer et al. 2004 <sup>23</sup>	Women with hormonal-resistant metastatic breast cancer, age > 70 years, Performance Status 0–2 N = 26, mean age and range unknown Oncology department	Open multicentre phase II study with Idarubicin. Geriatric assessment to identify factors predicting tolerance	No statistical analysis could be performed. Multi-dimensional geriatric assessment seemed not to be indicative to poor outcomes	- premature ending of the study because of high toxicity and lack of efficacy

group of patients treated with carboplatin/paclitaxel. In this combined non-randomized cohort no predictive factors were found for the occurrence of side effects.<sup>25</sup> Authors suggest that the failure to determine predictive factors might be due to the high toxicity of paclitaxel, especially since pre-treatment patient characteristics in the paclitaxel group were somewhat better compared to the cyclophosphamide group. An American study used a multidimensional assessment to predict toxicity in an elderly group with diverse cancers. The index on published toxicity (MAX2), higher diastolic blood pressure, bone marrow invasion and serum lactate dehydrogenase levels were predictors for toxicity. The Charlson comorbidity index was not a good predictor.<sup>32</sup> Also in the other studies neither the Charlson index nor the most prevalent comorbidities were predictive of tolerance to chemotherapy.<sup>22–31</sup> Comorbidity itself or an accumulation of comorbidities may give no additional information unless

the severity of comorbid conditions is taken into account. In patients with cancer and a short survival, comorbidity is less relevant.<sup>33</sup>

PS and dependency at home were independent predictive factors for toxicity. As expected, statistical analysis showed no predictive strength in studies where the prevalence of high grade PS or dependency were low. We found no study in which an intervention was performed that ameliorated relevant items and then reviewed the effects.

A surplus value of CGA in detecting relevant factors on toxicity lies probably in exploring dependency, emotional status and polypharmacy. This is in line with studies that focused on one of these items separately: Blower stressed the importance of co-medication in cancer treatment in elderly patients and its consequence for toxicity.<sup>34</sup> Jatoti found no prediction of toxicity using the PS in elderly lung cancer patients while an activity-score predicted toxicity very well.<sup>35</sup> Chen

underlined the association between severe toxicity and, independent from each other, PS, depressive symptoms and IADL dependency.<sup>36</sup> Studies on different cytotoxic regimens stressed the importance of cognitive decline as an adverse event following chemotherapy. Also a high prevalence of pre-existing cognitive impairment has been reported.<sup>37</sup> If substantial cognitive deficits occur, these may affect self-management capacities, life expectancy and interfere with cancer treatment. In our search only two studies analysed the relation between cognitive malfunctioning and severe toxicity. Although the prevalence of cognitive impairment was between 8 and 18%, cognitive impairment was no predictor for toxicity.<sup>25–31</sup> To our knowledge no studies are available primarily studying the association between cognitive impairment and overall tolerance to chemotherapy.

## 7. Clinical impact and future directions

CGA seems highly valuable in describing populations of elderly cancer patients in trials e.g. to determine whether results can be translated to the heterogeneous population of elderly patients. Data concerning CGA and its ability to detect relevant health problems in elderly cancer patients are consistent and promote the application of CGA in everyday practice. The high prevalence of geriatric syndromes in oncology underlines its importance. CGA is also promising in revealing domains associated with a high incidence of adverse effects when chemotherapy is being considered. Information obtained is additional to just chronological age and the Performance Score. Emotional, cognitive function, functional dependency and polypharmacy are the most relevant domains to explore. With regard to survival, CGA also uncovers relevant items, especially IADL-dependency, moderate quality of life and depressive symptoms at baseline. Data on comorbidities explored by CGA (and collected by Charlson index) and ADL-dependency are not however convincingly related to survival. Although CGA convincingly reveals extra information, its definite place in cancer medicine has not been elucidated yet.

Our search showed that most studies in geriatric oncology have focused on identifying prognostic factors detected by CGA and did not include an intervention in their design. The few studies that included an intervention showed an improvement in quality of life measures. Lack of intervention studies limits our conclusions about the value of CGA in oncology. Clinicians should be cautious to make an analogy with studies on CGA in general health care especially because age and functional status differ substantially between study-populations. Therefore, studies with an intervention strategy and including older cancer patients and especially 'the oldest old' cancer patients should be encouraged. Prognostic validation studies using geriatric syndromes or information added by CGA in decision making in oncology are lacking. If detection of health problems and risks are indeed the only objectives, the multiple health domains which are explored by CGA can be integrated into oncology practice. This working method reduces CGA to a multidimensional screening on pre-treatment risks, incorporating the multiple screening tools used in the CGA in oncology. It only leads to an individualized treatment plan if the process and results are structurally

implemented in elderly cancer patients. Implementing screening tools in clinical pathways can be an option and has been advocated to establish beneficial effects in multidisciplinary teams.<sup>38</sup>

To put CGA into everyday clinical practice some practical issues should be resolved. For example should clinicians only evaluate the patient's characteristics as fit or not fit for oncological treatment, and thus dichotomize the relevant parameters to apply them in clinical practice? Among others Freyer did dichotomize on dependency, defining every assistance for living at home as a 'dependency state'.<sup>31</sup> Quantifying or dichotomizing each parameter in decision making may be an option but require a great number of prognostic validation studies. Cut off points will probably differ significantly between each malignant disease, stages and every cytotoxic regimen. Furthermore, patients may act differently on several domains through either interacting or via independent pathways. For the present a qualitative use of data revealed by CGA probably is more valid in clinical practice, and reflects the lack of evidence.

A geriatric oncology taskforce stated that a two step approach is an alternative to deliver CGA to older cancer patients.<sup>39</sup> The first step should be a screening process of every older cancer patient to select the vulnerable patients who will benefit most from CGA. The second step is the actual performance of CGA in those who have highest chances to benefit. This two step approach is less time and manpower-consuming than using the CGA in every older cancer patient. Many screening instruments refer to vulnerability, in geriatrics known as 'frailty'. Frailty is associated with a high incidence of adverse health outcomes: increased dependency, death, hospitalisation and nursing home admission. Some authors use the term frailty-concept or frailty-syndrome.<sup>40</sup> Definitions of frailty have been proposed, but as yet there is no formal consensus. Definitions agree that a combination of factors influences peoples physiological state to the extent that its reserve is largely reduced. Subsequent exposure to minimal stresses may be sufficient to lead to adverse outcomes.<sup>41</sup> At present the annotation 'syndrome' is premature: signs and symptoms cannot unequivocally be grouped together, neither can frailty be defined as a single symptom state. Many factors are proposed as predictors of frailty and markers of neuromuscular function, cognition and inflammatory activity seem most relevant. Several indices of frailty have been constructed to use in clinical care and community dwelling elderly people. The clinical criteria by Fried,<sup>42</sup> the Edmonton Frailty Scale,<sup>43</sup> Groningen Frailty Indicator<sup>44</sup> are examples of frailty indices. Also the Vulnerable Elders' Survey-13 (assesses self-reported health, functional capacity and physical status) can be seen as a frailty screening tool. Preliminary findings suggest that these screening tools separate the fit from the frail elderly.<sup>45,46</sup> In screening situations the negative predictive value of frailty indices is probably the most important aspect since it leads directly to the proposal of standard treatment to fit elderly. A two-step approach stresses the necessity to determine which interventions and cancer decisions are made based on the CGA. Clinical studies are required to assess suitability and the benefits of implementing frailty-scales with a subsequent full-CGA in identified

frail patients. The present data suggest that interdisciplinary working methods between oncology and geriatric medicine teams are promising. Also physicians should however be aware that the optimal interdisciplinary design has not yet been determined in detail.<sup>47</sup>

## 8. Conclusion

Geriatric syndromes, as assessed by Comprehensive Geriatric Assessment (CGA), act as effect modifiers for the outcome of oncological treatment, with regard to quality of life and chemotherapeutic drug toxicity, though the effect on survival is insufficiently studied.

The introduction of CGA in routine oncology is probably most appropriate in a step wise procedure. First all elderly should be screened for frailty. The screening tool should be very effective in identifying fit patients in order to prevent undertreatment in this group. Next the frail elderly should receive multidisciplinary geriatric assessment, and finally oncological treatment should be adapted to the presence of one or more geriatric syndromes.

Cost-effectiveness studies need to be conducted to optimize CGA in oncology, but the increasing necessity of tailor made oncology in the heterogeneous elderly population now already warrants the application of basic geriatric screening and assessment procedures.

## Conflict of interest statement

None declared.

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