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REVIEW

Impact of comprehensive geriatric assessment on the risk of adverse events in the older patients receiving anti-cancer therapy: a systematic review and meta-analysis

Min-Hsiang Chuang[1], Jui-Yi Chen[2,3], Wen-Wen Tsai[4], Chia-Wei Lee[5], Mei-Chuan Lee[6,7], Wen-Hsin Tseng[8], Kuo-Chuan Hung[9,10]

[1]Department of Internal Medicine, Chi Mei Medical Center, Tainan City, Taiwan
[2]Division of Nephrology, Department of Internal Medicine, Chi Mei Medical Center, Tainan City, Taiwan
[3]Department of Health and Nutrition, Chia Nan University of Pharmacy and Science, Tainan City, Taiwan
[4]Department of Education, Chi Mei Medical Center, Tainan City, Taiwan
[5]Department of Neurology, Chi-Mei Medical Center, Tainan City, Taiwan
[6]Department of Pharmacy, Chi Mei Medical Center, Tainan City, Taiwan
[7]Department of Public Health, College of Medicine, National Cheng Kung University, Tainan City, Taiwan
[8]Division of Urology, Department of Surgery, Chi Mei Medical Center, Tainan City, Taiwan
[9]Department of Anesthesiology, Chi Mei Medical Center, Tainan City, Taiwan
[10]Department of Hospital and Health Care Administration, College of Recreation and Health Management, Chia Nan University of Pharmacy and Science, Tainan City, Taiwan

Address correspondence to: Kuo-Chuan Hung, MD. Tel: +886 6 281 2811; Fax: +886 6 283 3806. Email: ed102605@gmail.com

Abstract

Background: to assess the efficacy of comprehensive geriatric assessment (CGA) for preventing treatment-related toxicity in older people undergoing non-surgical cancer therapies.
Methods: MEDLINE, EMBASE and Cochrane library databases were searched from inception till January 2022 to identify randomised controlled trials (RCTs) on the incidence of toxicity measured by the Common Terminology Criteria for Adverse Events (primary outcome) and that of therapeutic modifications, early treatment discontinuation, progression-free survival, overall survival and hospitalisation (secondary outcomes).
Results: analysis of six RCTs published from 2016 to 2021 recruiting 2,126 participants (median age: 71–77) who received chemotherapy as the major therapeutic approach revealed 51.7% and 64.7% of Grade 3+ toxicity in the CGA and control (i.e. standard care) groups, respectively (RR = 0.81, 95% CI: 0.7–0.94, $P = 0.005$, $I^2 = 65\%$, certainty of evidence [COE]: moderate). There were no significant differences in the incidence of early treatment discontinuation (RR = 0.88, $P = 0.47$; $I^2 = 63\%$,1,408 participants, COE: low), initial reduction in treatment intensity (RR = 0.99, $P = 0.94$; $I^2 = 83\%$, 2055 participants, COE: low), treatment delay (RR = 1.06, $P = 0.77$, $I^2 = 0\%$, 309 participants, COE: moderate), hospitalisation (RR = 0.86, $P = 0.39$, $I^2 = 41\%$, 914 participants, COE: moderate), progression-free and overall survival with or without CGA. However, there was an association between CGA and a lower incidence of dose reduction during treatment (RR = 0.73, $P < 0.00001$, 956 participants, COE: moderate).
Conclusions: our results demonstrated that comprehensive geriatric assessment may be associated with a lower incidence of treatment-related toxicity and dose reduction compared to standard care in older people receiving non-surgical cancer treatments. Further large-scale studies are warranted to support our findings.

Keywords: anti-cancer therapy, chemotherapy, geriatric assessment, toxicity, older people

Key Points

- This study demonstrated an association of comprehensive geriatric assessment (CGA) with a reduction in the incidence of Grade 3+ toxicity.
- The incidence of dose reduction during treatment was also reduced in the CGA group compared to standard care.
- No significant differences were observed in early treatment discontinuation and initial reduction of treatment intensity between patients with CGA and those receiving standard care.

Introduction

Not only do the majority of cancer diagnosis and mortality occur in older patients ≥65 years [1] but comorbidities and disabilities as well as an increased susceptibility to chemotherapy-related toxicity and a decreased tolerance to cancer therapies are also prevalent in this population [2–4]. Nevertheless, older patients are usually underrepresented in clinical trials [5, 6] and offered less aggressive interventions compared to their younger counterparts [7–9]. Although age commonly serves as the basis for defining the geriatric population in clinical trials for subgroup analyses, chronological age alone is not always associated with the physiological and functional status of older adults [6, 10]. Therefore, there is a lack of solid evidence to support clinical decisions regarding cancer treatment for older adults, highlighting the importance of thorough and individualised assessment.

Comprehensive geriatric assessment (CGA) is a tool that typically encompasses the evaluations of functional status, comorbidities, cognitive function, psychological status, social support, nutrition and medications [11, 12]. Previous studies have demonstrated the feasibility and potential benefits of CGA in predicting treatment outcomes [3, 13–16], assisting clinical decision [17, 18], enhancing communication [19] and providing additional information not identified by standard performance status scales [20, 21]. Incorporation of CGA into oncology practice is recommended by several organisations and societies including the American Society of Clinical Oncology (ASCO) and the International Society of Geriatric Oncology [11, 22].

On the other hand, the beneficial impacts of CGA on the reduction of serious adverse events from non-surgical cancer treatments remain controversial. Despite the demonstration of a reduction in Grade 3 or more (3+) toxicities associated with the use of CGA in two previous observational studies, the results were not statistically significant [23, 24]. Similarly, although a systematic review reported a trend towards a beneficial effect of CGA against treatment-related toxicities or complications, the high heterogeneity of study design and type of cancer treatment precluded a robust conclusion [25]. Three recent randomised controlled trials (RCTs) also demonstrated inconsistent findings. While two studies reported a statistically significant reduction in Grade 3–5 toxicities in the CGA group [26, 27], the other failed to produce the same results [28]. This systematic review and meta-analysis aimed at pooling evidence from the published RCTs to evaluate whether implementation of CGA could reduce serious treatment-related toxicities as measured by the Common Terminology Criteria for Adverse Events (CTCAE) in older patients undergoing non-surgical cancer treatments.

Methods

This meta-analysis was reported according to the recommendations of PRISMA 2020 statement Appendix 1 and was registered with the International Prospective Register of Systematic Reviews (CRD42022306462).

Eligibility criteria

Studies that assessed the impact of CGA on the risk of non-surgical adverse outcomes in older people receiving nonsurgical anti-cancer therapy were considered eligible. Included trials were those that met the predefined PICO (i.e. population, interventions, comparison and outcome) framework: (i) Patient population: older patients (i.e. age ≥ 65 years) receiving nonsurgical anti-cancer therapy (e.g. chemotherapy or targeted therapy), (ii) Intervention: CGA-based interventions that provided patient management recommendations or multidisciplinary care for geriatric patients. Trials in which CGA was used for guiding clinical decision regarding anti-cancer therapy was also included, (iii) Comparison: standard care, (iv) Outcomes: the primary outcome was the incidence of Grade 3 or more (3+) adverse events, which were graded based on the CTCAE. No restriction was placed on language, sample size or publication date.

Exclusion criteria were (i) non-RCTs; (ii) CGA served exclusively as a tool to predict adverse events or other outcomes; (iii) studies not published in peer-reviewed journals or those published only as abstracts or letters; and (iv) those in which information about primary outcome was unavailable.

Information sources and search strategy

The following databases were searched from the inception dates till 24 January 2022: MEDLINE, Cochrane CENTRAL register of controlled trials and Embase. The following free text words and medical subject headings (i.e. MeSH terms in Medline) were combined for searching: ('cancer*' or 'tumour*' or 'neoplasm*' or 'carcinoma' or 'Malignancy') and ('comprehensive geriatric assessment' or 'CGA' or 'Geriatric

Assessment' or 'geriatric intervention') and ('Toxicity grading scales' or 'Common Terminology Criteria for Adverse Events' or 'CTCAE' or 'Adverse events' or 'common toxicity criteria' or toxicity). Related reviews and reference lists of the retrieved trials were examined for potentially eligible articles to reduce the possibility of omissions. The search strategy of one of the databases is shown in Appendix 2.

Selection process and data collection

Two reviewers inspected the titles and abstracts of the retrieved articles to determine their eligibility based on study design, participants, intervention and outcomes before the conduction of independent full-text reviews. We resolved disagreements by consulting a third author.

The following data were independently retrieved by the two reviewers from each study: first author, publication year, patient characteristics (e.g. age), study setting, sample size, type and modification of anti-cancer therapies, type of cancers, clinical stage of cancer, adverse events, progression-free survival (PFS), overall survival (OS), and incidence of hospitalisation.

Outcomes and definitions of data items

The primary outcome was the incidence of Grade 3 or more (3+) adverse events which were graded based on the CTCAE. The secondary outcomes included the incidence of therapeutic modifications (i.e. initial reduction in treatment intensity and dose reduction during treatment), early treatment discontinuation, PFS, OS, treatment delay and hospitalisation. The definitions of secondary outcomes were based on those of the individual studies. If the secondary outcome in a study was not defined or was expressed in a term consistent with but not identical to that used in the current meta-analysis, the data were adopted from that study without modifications.

Risks of bias assessment

Independent assessment of the risk of bias across the included RCTs was performed by two authors who employed the Cochrane's tool (RoB 2) to evaluate the possibility of different biases, namely, allocation, performance, attrition, measurement, reporting biases, and overall bias [29]. Disagreement between the two authors was settled through arbitration that involved a third reviewer.

Effect measures and data synthesis

The Cochrane Review Manager (RevMan 5.3; Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014) was used for data synthesis. For an outcome, data from at least two trials were pooled. Due to the potential heterogeneity in clinical setting and population across the included studies, dichotomous outcome data were analysed using the Mantel–Haenszel random-effects model and presented as risk ratios (RR) with 95% confidence intervals (CIs). For all continuous variable outcomes, we reported mean differences (MD) and 95% CIs. Using the I^2 statistic, heterogeneity was estimated with significance predefined at $I^2 > 50\%$ [30]. For a specific outcome reported in 10 or more studies, the potential publication bias was assessed through visual inspection of a funnel plot. The potential influence from the findings of an individual trial on the overall result was assessed with sensitivity analysis (i.e. leave-one-out approach). Two-tailed tests were performed on all comparisons. A P-value under 0.05 was considered statistically significant.

Certainty assessment

Based on the probabilities of publication bias, study limitations, consistency of effects, indirectness, and imprecision included in GRADE, two review authors independently weighed the certainty of the evidence regarding the primary and secondary outcomes by assigning a study to one of four grades (i.e. high, moderate, low and very low). Disagreements on certainty ratings were resolved through discussion.

Results

Study selection and characteristics

A literature search identified 808 potentially eligible articles. After removing 122 duplications, 686 records were screened based on title and abstract. Of the 14 reports that underwent full text screening, eight were excluded (Figure 1). Finally, six RCTs [26–28, 31–33] published from 2016 to 2021 with a total of 2,126 participants were included. All studies investigated the impact of CGA on outcomes in older people receiving non-surgical cancer treatments.

The characteristics of studies are shown in table 1. Five studies recruited patients aged ≥70 years [26, 28, 31–33], while one trial recruited participants aged ≥65 years [27]. The median or mean age of the participants was over 70 years with a proportion of male ranging from 39.9% to 74.5%. The type of cancer included solid malignant tumour (three trials) [27, 32, 33], non-small cell lung cancer (one trial) [31], colorectal cancer (one trial) [28], and solid malignant tumour or lymphoma (one trial) [26]. The anti-cancer treatments of the six RCTs included in the current meta-analysis comprised chemotherapy, chemo-radiotherapy and targeted therapy. Of the five trials that provided the proportions of patients receiving the three treatment modalities [26–28, 31, 33], all participants in three studies [27, 28, 31] and between 88% and 94% of patients in the other two studies [26, 33] received chemotherapy. However, one pilot study [32] that enrolled 71 patients who underwent the three treatments did not give details regarding patient prevalence for each modality. In four RCTs, CGA-based intervention alone was implemented to reduce treatment-related toxicity [26–28, 32]. In one study, CGA served as a screening tool for allocating patients (i.e. frail or fit) to different chemotherapy regimens [31]. In the other study, Geriatric-8 screening tool was used to identify older people who would benefit from

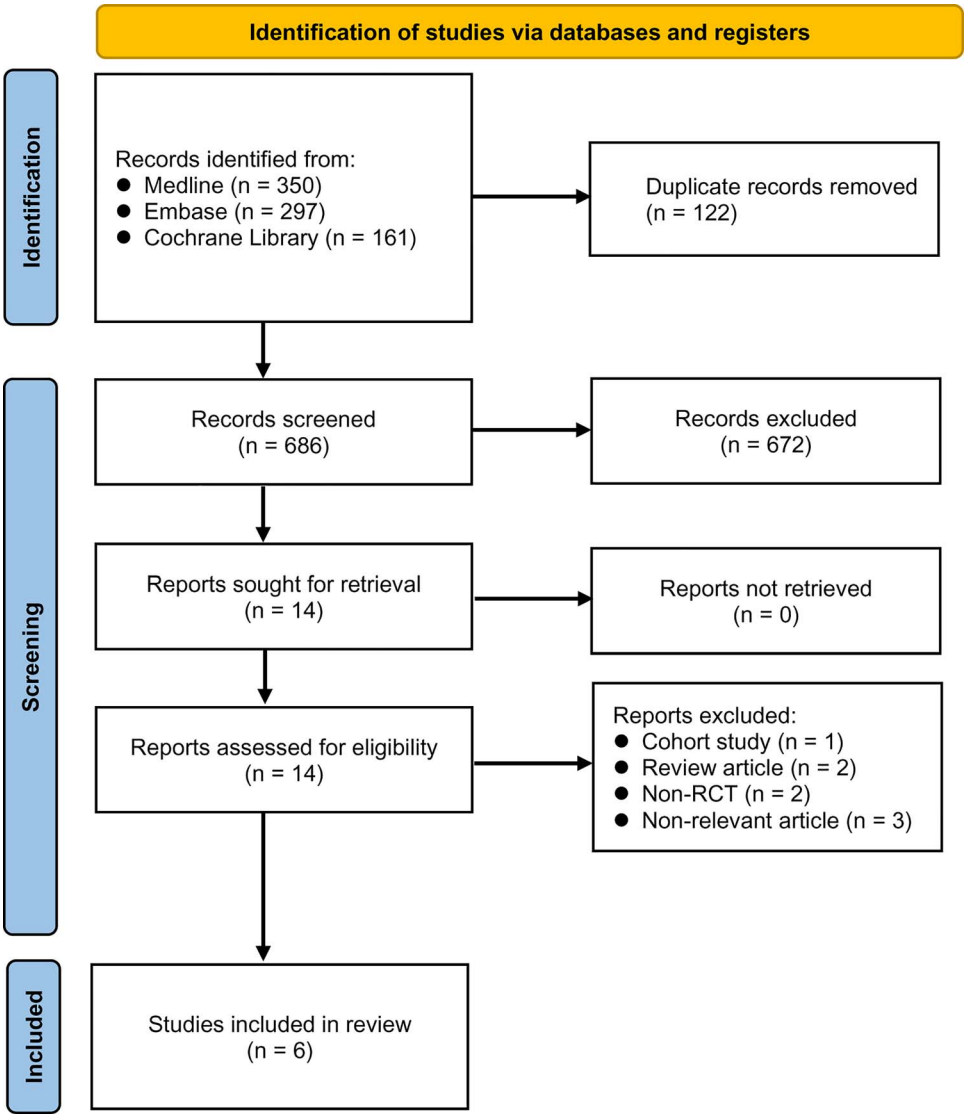

Figure 1. PRISMA flow diagram of study selection for the current meta-analysis.

CGA (i.e. Geriatric-8 score ≤ 14) before the implementation of CGA [33]. Although polypharmacy screening was performed in all of our six included trials using CGA, details on drug–drug or drug–disease interactions were unavailable in all studies. All studies were published in the English language. The six included trials were conducted in four countries, including one conducted in France and Spain [31], three in the USA [26, 27, 32] and two in Denmark [28, 33].

Risk of bias assessment

The risk of bias assessment is demonstrated in Figure 2. Regarding the risk of bias arising from the randomisation process, we had some concerns for three trials [28, 31, 33], while one study was considered to be at high risk [32] and two were deemed at low risk [26, 27]. For deviations from intended intervention, we had concerns for three RCTs [28, 32, 33]. For risk of selection of the reported results, we had concerns for one trial [32]. The overall risk of bias was judged to be low in two RCTs [26, 27] and high in one study [32], while three trials still had some concerns regarding their overall risk of bias [28, 31, 33].

Results of syntheses

Primary outcome: impact of CGA on incidence of treatment-related toxicity

Six trials with 2,126 participants reported the incidence of Grade 3+ treatment-related toxicity which was graded based on the CTCAE version 4.0. The incidence of Grade 3+ toxicity was 51.7% and 64.7% in the CGA and control groups, respectively. By adopting a random-effects model, CGA-based interventions were associated with a lower incidence of Grade 3+ toxicity compared

Table 1. Characteristics of included studies ($n = 6$)

Study	Country	Number[a]	Age (median, years)[a]	Male (%)[a]	Cancer type	Cancer Stage	Anti-cancer therapy (% of patients)	Intervention	Control	Follow-up (months)
Corre 2016	France and Spain	243 vs. 251	77 vs. 76	74 vs. 74	NSCLC	IV	CT (100)	Allocation of CT regimens based on CGA	Allocation of CT regimens based on age and PS	4.5[b]
Li 2021	USA	402 vs. 203	71 vs. 72	42 vs. 40	SMT[c]	I–IV	CT (91.4) CT + TT (8.6)	CGA-directed interventions	Standard of care	6
Lund 2021	Denmark	71 vs. 71	75 vs. 75	61 vs. 54	CRC	II–IV	CT (100)	CGA-directed interventions	Standard of care	27[b]
Magnuson 2018	USA	37 vs. 34	76[d]	59 vs. 54	SMT	III–IV	CT, CRT or TT (NR)	CGA-directed interventions	Standard of care	3
Mohile 2021	USA	349 vs. 369	77 vs. 77[d]	58 vs. 55	SMT, lymphoma	III–IV	CT (67.1) CT + others (21)[e] Others (11.8)[e]	CGA-directed interventions	Standard of care	3
Nadaraja 2020	Denmark	49 vs. 47	74 vs. 77	53 vs. 51	SMT	III–IV	CT (93.6) TT (6.4)	CGA-directed interventions[f]	Standard of care	14.1[b]

SMT: solid malignant tumour; CRC: colorectal cancer; CT: chemotherapy; CRT: chemoradiotherapy; TT: targeted therapy; NR: not reported; PS: performance status. [a]Presented as intervention vs. control groups. [b]Presented as median. [c]Cancer types included gastrointestinal (202 [33.4%]), breast (136 [22.5%]), lung (97 [16.0%]), genitourinary (91 [15.0%]), gynecologic (54 [8.9%]), and other (25 [4.1%]). [d]Presented as mean. [e]Eligible regimens had to include at least one chemotherapy agent or have a more than 50% prevalence of grade 3–5 toxic effects as determined by the primary oncologist with review and approval by a clinical team masked to the study group. [f]Patients were referred to CGA-intervention if Geriatric-8 (G8) ≤ 14.

to that in the control group (RR = 0.81, 95% CI: 0.7–0.94, $P = 0.005$, $I^2 = 65\%$) (Figure 3). Sensitivity analysis revealed no change in the strength of evidence by excluding one study at a time. During sensitivity analysis, exclusion of one trial [31] in which CGA was used as a decision tool for allocation of chemotherapy regimens resulted in a substantial reduction in heterogeneity ($I^2 = 16\%$) without changing the overall results (RR = 0.76, 95% CI: 0.68–0.86, $P < 00001$).

Secondary outcome: association of CGA with incidence of early discontinuation of treatment

Among the five trials that reported the incidence of early discontinuation of treatment [27, 28, 31–33], three attributed the early discontinuation to treatment toxicity [28, 31, 33] and two did not specify the reasons [27, 32]. Forest plot demonstrated no significant difference in this outcome with or without CGA (RR = 0.88, 95% CI: 0.62–1.25, $P = 0.47$; $I^2 = 63\%$,1,408 participants) (Figure 4). Sensitivity analysis showed a stable result.

Secondary outcome: impact of CGA on treatment modification

The incidence of initial reduction in treatment intensity was reported in five trials [26–28, 31, 33]. Merged results demonstrated no notable impact of CGA on this outcome (RR = 0.99, 95% 0.77–1.28, $P = 0.94$, 2,055 participants) (Appendix 3A). There was substantial heterogeneity ($I^2 = 83\%$) among the five studies. Removing the study by Mohile *et al*. [26] decreased the heterogeneity (i.e. $I^2 = 7\%$), leading to a lower incidence of reduced intensity treatment in the CGA group compared to that in the control group (RR = 0.88, $P = 0.03$).

Information regarding the incidence of dose reductions during treatment was available in three trials [26, 28, 33]. Forest plot revealed an association between CGA and a lower incidence of dose reduction during treatment (RR = 0.73, 95% 0.63–0.83, $P < 0.00001$, 956 participants) with no heterogeneity ($I^2 = 0\%$) (Appendix 3B). Sensitivity analysis demonstrated a stable result regarding this outcome.

Secondary outcomes: impact of CGA on treatment delay and hospitalisation

Three trials provided information regarding the impact of CGA on treatment delay [27, 32, 33]. Forest plot showed no difference in the incidence of treatment delay between the two groups (RR = 1.06, 95% CI: 0.73–1.52, $P = 0.77$, $I^2 = 0\%$, 309 participants) (Appendix 4A). Sensitivity analysis supported a consistent result.

The incidence of hospitalisation was available in four RCTs [27, 28, 32, 33]. Forest plot demonstrated no association between CGA and a lower incidence of hospitalisation compared to that in the control group (RR = 0.86, 95% CI: 0.6–1.22, $P = 0.39$, $I^2 = 41\%$, 914 participants) (Appendix 4B). Sensitivity analysis confirmed the robustness of this result.

Secondary outcomes: impacts of CGA on progression-free and overall survival

Details regarding OS (available in five trials) [26–28, 31, 33] and PFS (available in three trials) [28, 31, 33] are shown in Appendix 5 and Appendix 6, respectively. Among these studies, none reported a significant difference in the two outcomes between the CGA and the control groups.

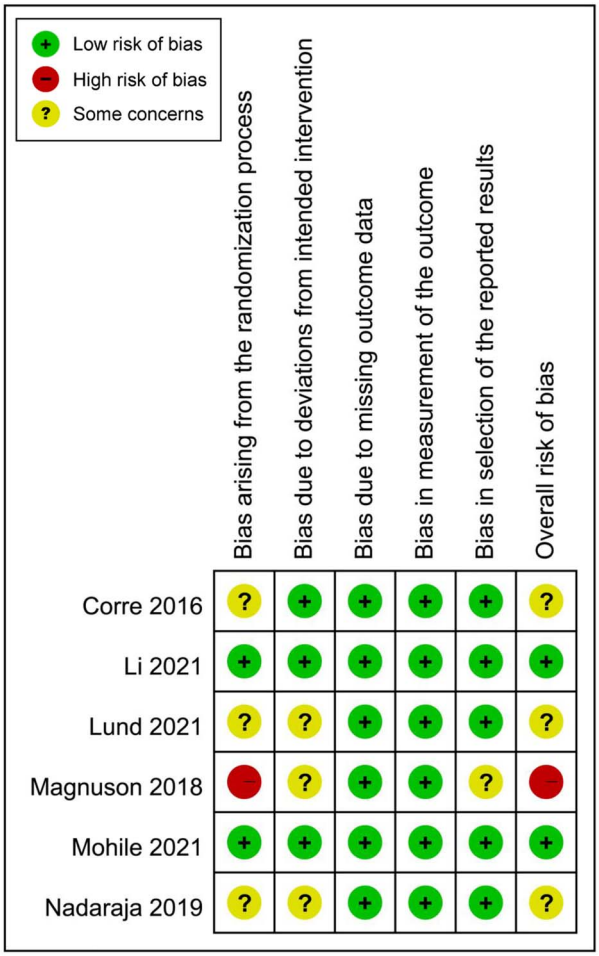

Figure 2. Summary of different categories of risk of bias of the included studies.

Certainty of evidence

The quality of evidence for outcome measures according to the GRADE system is presented in Appendix 7. The levels of evidence of the primary and the secondary outcomes were graded as low to moderate. The level of evidence was downgraded due to a high degree of inconsistency and imprecision.

Discussion

This systematic review and meta-analysis of six RCTs evaluating 2,126 older people undergoing non-surgical cancer treatments demonstrated an association of CGA-based interventions with a reduction in the incidence of Grade 3+ toxicity and dose reduction during treatment compared to standard care without compromising overall or progression-free survival. No significant differences were observed in the incidence of early treatment discontinuation, initial reduction of treatment intensity, treatment delays or hospitalisation.

In the general population, geriatric assessment and management have been reported to reduce serious adverse drug reactions and suboptimal prescriptions [34–36]. Previous studies have also shown that older inpatients are more likely to be discharged to their own homes instead of nursing homes if they received CGA with no differences in mortality or the incidence of re-admission compared with those receiving standard care [37, 38]. In surgical oncology, results regarding the risk of complications were mixed with one RCT reporting a reduction [39] but no difference in another two [40, 41]. A number of recent studies have demonstrated the value of identifying impairments in some CGA domains in the prediction of an increased risk of complications or mortality in older people with cancer [15, 16, 42–44].

Our study supported that CGA and CGA-based interventions could reduce Grade 3+ toxicities from non-surgical cancer treatments compared to standard care. Among the six included studies, the clinical and methodological heterogeneity of the one by Corre *et al*. [31] was deemed high because of its exclusive enrollment of patients with stage IV cancer, its use of CGA specifically for predefined chemotherapy allocation, and exclusion of patients with Grade 5 toxicity (i.e. treatment-related death). Since chemotherapy allocation by geriatric assessment falls under the broad definition of CGA-based interventions and treatment-related death was reportedly low (0.9% among fit patients treated with a carboplatin doublet in the CGA arm and similar percentage in the standard arm), we considered it appropriate to be included in the current meta-analysis. Although the statistical heterogeneity would be reduced if this trial was excluded, the conclusion remained unchanged. Consistent with our finding, two small observational studies reported reduced 3+ toxicity in the CGA group, though the result was either statistically nonsignificant [23] or not analysed [24]. Despite the demonstration of a trend towards a beneficial effect against treatment-related toxicity or complications in two reviews [25, 45], no statistical analysis was conducted and their included studies were highly heterogeneous in terms of study design and cancer treatments that included both surgery and non-surgical strategies. Our study provided evidence in support of the beneficial effect of CGA on reducing severe treatment-related toxicities.

Our study demonstrated no significant difference in early treatment termination between the CGA and control groups. In contrast, one previous RCT showed a reduction in early treatment termination in the CGA arm [46], while another prospective cohort study reported no difference in this outcome between the intervention and control groups [23]. Although the reasons for early treatment termination were not specified in the aforementioned studies and in two of the trials included in our meta-analysis [27, 32], variations in study population may have played a role. While over half of early treatment discontinuations were attributed to disease progression in the study by Corre *et al.* [31] that enrolled patients with stage IV non-small cell lung cancers (NSCLC), Nadaraja *et al*. [33] reported unacceptable toxicity as the primary cause of early treatment termination in their participants comprising all-stage NSCLC, gynecologic or

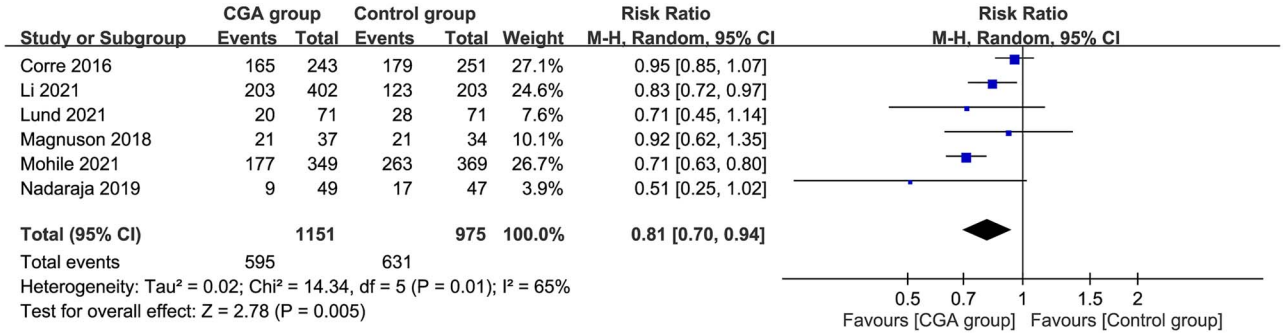

Figure 3. Forest plot comparing the incidence of Grade 3 or higher treatment-related toxic effects between CGA and control groups. M-H, Mantel–Haenszel; CI, confidence interval.

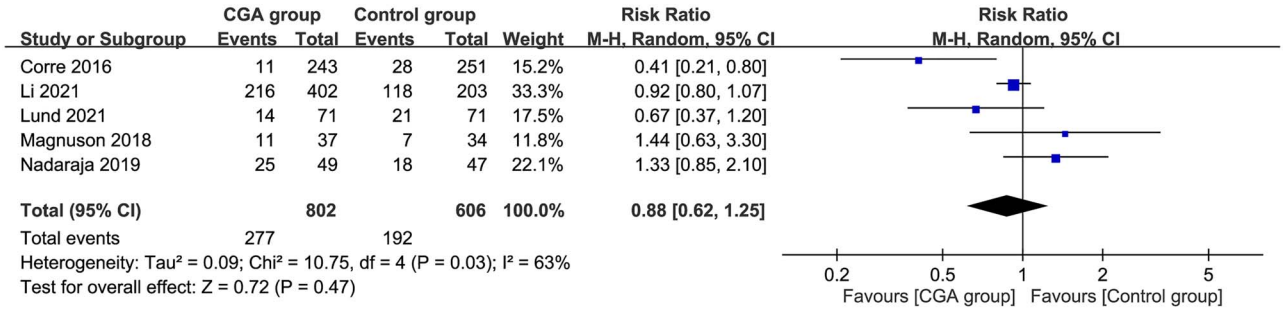

Figure 4. Forest plot comparing the incidence of early discontinuation of anti-cancer therapy between CGA and control groups. M-H, Mantel–Haenszel;CI, confidence interval.

urologic cancers. Considering the potential contribution of this variation to the inconsistency and heterogeneity among the included studies in our meta-analysis, caution is warranted when interpreting the results. In addition, whether the higher rate of treatment completion in the CGA group compared to that in the controls in some studies was attributable to treatment modifications or non-oncological interventions, or both, remains to be clarified [45].

Regarding the modification of oncologic treatments, although our study showed no significant difference in the initial reduction in treatment intensity between the two groups, this finding was of low certainty considering its high statistical heterogeneity and inconsistency across the included trials. For instance, the strategy for chemotherapy allocation in the study by Corre *et al*. [31], which relied exclusively on geriatric assessments, differed from the rest of the studies. Compared with the control group, they showed more patients in the CGA group receiving doublet therapy [31]. In contrast, Mohile *et al*. [26] reported more patients being given reduced-intensity treatments in the CGA group. This bidirectional effect of geriatric assessment may partly contribute to the high heterogeneity ($I^2 = 83\%$) in our meta-analysis. Discrepancies in patient population (e.g. cancer type, stage), definition of reduced-intensity regimen (e.g. dose reduction or omission of some agents), and study design (e.g. conduction and implementation of geriatric assessment) may also be potential confounders.

One recent multicenter observational study showed that geriatric assessment could have prevented undertreatment and overtreatment in 15% and 34% of patients, respectively [47]. Despite a lack of difference in treatment delay between the CGA and control groups in the current meta-analysis, such a beneficial impact of CGA was supported by a less frequent dose reduction during treatment in the former than that in the latter.

Our study showed no difference in the incidence of hospitalisation between the CGA and control groups, in line with the finding of a previous study on patients with hematologic malignancies [48] as well as that of previous investigations on the general population [37, 49]. Regarding the impact of CGA on overall patient survival, despite the infeasibility of conducting a meta-analysis because of the variety in outcome measures across the included studies (e.g. hazard ratio, survival probability, median duration), the lack of difference in overall survival in five trials [26–28, 31, 33] as well as progression-free survival in three studies [28, 31, 33] suggested no significant impact of CGA on patient survival. The result was consistent with that of previous studies on the general population [37, 49] and on cancer patients [25, 45].

In addition to age-related physiologic changes that render older adults vulnerable to physiologic stress from cancer and its treatment, clinical decisions for this population are often complicated by functional and cognitive disabilities as well as comorbidities and impaired social supports [12]. Consistently, previous studies have demonstrated an association of

frailty with an increased consumption of healthcare resources [50–53]. Not only has CGA been shown to aid clinical decision-making in cancer patients [12, 54, 55] but it has also been found to shorten hospital stay in the primary care setting [56].

Despite emerging evidence supporting its benefit, geriatric assessment remains underutilised in oncologic practice [57–59]. A recent survey by the American Society of Clinical Oncology (ASCO) revealed that only about half (53%) of the clinicians were aware of ASCO Guideline for Geriatric Oncology and that most geriatric assessment tools were used less than half of the time except those for the assessment of functional status and falls [57]. An underutilisation of geriatric assessment both in the oncologic setting and in general medical practice may partly be attributed to barriers including difficulty translating guidelines into real-world practice, healthcare providers' lack of familiarity, patients' perceptions and desires, team working challenges, lack of incentives and resources, need for organisational changes as well as social, legal and economic factors, which might be overcome by knowledge mobilisation techniques and collaborative research involving its potential users through multidirectional communication [60]. Suggestions from oncologic societies, which emphasise a bridging of knowledge gap, evidence-based practice, multidisciplinary collaboration and sharing of resources, largely followed a similar framework [57, 61].

This meta-analysis had some limitations that should be considered. First, all of the included trials were performed in developed European countries ($n = 3$) and the USA ($n = 3$), and composed almost entirely of patients with solid malignant tumours except 46 (2%) who had lymphomas. Therefore, our findings may not be extrapolated to countries with different healthcare systems and/or allocations of resources, or to patients diagnosed with hematologic malignancies. Second, the number of participants and studies for quantitative synthesis of dose reduction and treatment delay was relatively small, especially for treatment delay. In addition, the fact that some of the included studies were judged to be at high risk of bias or have some concerns may have biased our findings. Third, the moderate to high heterogeneity in some of the outcomes, especially in initial reduction of treatment intensity (i.e. $I^2 = 83\%$), warrants further studies for verification of our findings. Fourth, because the definitions of secondary outcomes for the current investigation were not mentioned in our included studies, potential variations in definitions may bias our results. Fifth, because potential drug–drug or drug–disease interactions [62, 63] were not assessed in all of our included studies, their impacts on our findings remain unclear. Finally, because the current study mainly recruited patients with advanced cancers, patients with early-stage malignancies in whom curative-intent treatments dominate and survival statistics significantly differ were underrepresented. The impacts of CGA on some important outcomes in this population such as cure rate, long-term survival, and sequelae of treatment remain to be addressed.

In conclusion, this systematic review and meta-analysis showed an association of comprehensive geriatric assessment with decreases in Grade 3+ toxicity and the incidence of dose reduction during treatment without significant impacts on the incidence of hospitalisation, treatment delay, survival, early treatment discontinuation, and initial reduction of treatment intensity. Our findings supported the use of comprehensive geriatric assessment in older people diagnosed with malignancies.

Supplementary Data: Supplementary data mentioned in the text are available to subscribers in *Age and Ageing* online.

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