https://doi.org/10.1093/jnci/djad207 Editorial

Editorial

Geriatric assessment and management: is decreasing treatment toxicity good enough?

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The majority of new cancer cases occur in older adults. Geriatric assessment and management (or comprehensive geriatric assessment) refers to the use of various validated tools to assess an older adult's health status and guides subsequent therapeutic and supportive care interventions. It is important to note that there are 2 steps to geriatric assessment and management: the evaluation of an older adult's aging-related health conditions (ie, physical performance, cognition) and management through adjusting cancer plan in response to knowledge about aging-related conditions and/or implementing aging-sensitive interventions to address aging-related conditions (eg, physical therapy referral for falls and balance issues), which is recommended by several professional organizations including the American Society of Clinical Oncology, National Comprehensive Cancer Network, and International Society of Geriatric Oncology (1-3). Earlier studies demonstrated that aging-related vulnerabilities uncovered on geriatric assessment are associated with higher morbidity and mortality (4,5), and geriatric assessment measures can predict treatment toxicity (6,7). However, earlier guidelines were not able to establish a defined role for geriatric assessment and management because of a limited number of large, well-designed randomized controlled trials (RCTs). Since 2020, several clinical trials have been conducted to assess the effects of geriatric assessment and management, and a number of systematic reviews have been performed (8-11). Only one was a meta-analysis by Chuang et al. (12) focusing on treatment toxicity, and none included cost-effectiveness data.

In this issue, Anwar et al. (13) extended the literature by performing a systematic review and meta-analysis on the effectiveness of comprehensive geriatric assessment among older adults receiving curative or palliative treatments. It included 17 RCTs that studied the following outcomes: mortality, hospitalization, readmission, treatment toxicity, change in treatment, quality of life, functional status, and cost (13). Of note, trials were included if geriatric assessment was done and recommendations were provided with or without subsequent implementation. Models of care varied, for instance, centralizations where comprehensive geriatric assessment was performed by a geriatrician, a geriatric oncologist, a trained nurse, or a multidisciplinary geriatric team vs decentralization where comprehensive geriatric assessment was performed by research personnel using validated tools and criteria, results of which were then provided to the treating oncology team. Seven studies had variable or as-needed follow-up visits. One study also incorporated a palliative care intervention with comprehensive geriatric assessment. Trials included older adults undergoing various treatments including chemotherapy, targeted therapy, immunotherapy, radiation, and surgery. Overall, pooled results revealed statistically significant lower treatment toxicity (assessed using clinician-related Common Terminology Criteria for Adverse Events [CTCAE]) in the comprehensive geriatric assessment arm compared with the control or usual care arm. Although there was differential effects of comprehensive geriatric assessment on hospitalization, readmission, change in treatment, and quality of life within specific trials, meta-analysis did not reveal differences between the comprehensive geriatric assessment and control arms. Meta-analysis of results on functional status, postoperative complications, and satisfaction were not feasible because of various definitions. Of these 3 outcomes, satisfaction was better in the comprehensive geriatric assessment compared with the control arm in one study (14). There were no studies on cost-effectiveness of comprehensive geriatric assessment. Results by Anwar et al. (13) are consistent with the metaanalysis by Chung et al. (12) that showed lower treatment toxicity in the comprehensive geriatric assessment arm.

It is important to point out that Anwar et al. (13) included a predefined set of outcomes. RCTs have demonstrated that comprehensive geriatric assessment improved other outcomes important to patients such as decreased number of falls over 3 months as well as increased medication discontinuation (14), completion of advanced directives (15), and completion of goals of care discussion (16). In addition to CTCAE, one study also demonstrated that comprehensive geriatric assessment decreased toxicity assessed on the patient-reported outcome version of the CTCAE, which evaluates patient perspective of treatment tolerability (17).

The key question here is, is decreasing treatment toxicity good enough? We would argue that the answer is yes. Treatment toxicity is included as an endpoint in all therapeutic trials, and a therapeutic drug that treats the disease but leads to severe or fatal toxicities is not an effective option. Therefore, decreasing treatment toxicity is an important outcome, especially in the older adult population. This also brings up the concept of tolerability (ie, the degree to which overt adverse events can be tolerated by the patient) (18). We know older adults are concerned

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about side effects of cancer treatment, and side effects are associated with worse functional status, cognition, and quality of life. Many older adults prioritize these outcomes over survival (19). Survival may not be a meaningful endpoint by itself in a trial evaluating comprehensive geriatric assessment, because patientcentered outcomes are prioritized by patients. In older adults with competing risk factors, outcomes such as mortality, hospitalization, readmission, and change in treatment may not accurately reflect treatment tolerability. Therefore, trials need to consider incorporating tolerability outcomes that are patientcentered and clinically meaningful.

Anwar et al. (13) aimed to pool data on cost-effectiveness of comprehensive geriatric assessment, however, there were no studies that conducted these analyses. In settings of limited resources, cost-effectiveness analyses assist in directing resources in areas of highest yield. It is an important area of consideration in the implementation and dissemination of an intervention.

So where do we go from here? We highlight several areas for future research to promote uptake of comprehensive geriatric assessment: 1) conduct cost-effectiveness of comprehensive geriatric assessment as part of an RCT; 2) incorporate novel and combined endpoints in RCTs of comprehensive geriatric assessment such as treatment tolerability; 3) promote uptake of comprehensive geriatric assessment through methods such as dissemination and implementation science or customer discovery approach in the business world (20); and 4) study various models of care for comprehensive geriatric assessment in specific populations (including different delivery methods as well as variable follow-up times) and how they differentially affect outcomes. Beyond research, the American Society of Clinical Oncology has recently updated its guideline to include a more streamlined version of the geriatric assessment (ie, practical geriatric assessment with management recommendations) (21,22). Through generation of high-quality evidence from research that ultimately leads to development and dissemination of guidelines in comprehensive geriatric assessment, in collaboration with stakeholders, we are one step closer to providing tailored and patient-centered care to our growing older adults with cancer.

Data availability

No new data were generated or analyzed for this editorial.

Author contributions

Kah Poh Loh, MBBS (Conceptualization; Writing – original draft) and Supriya Gupta Mohile, MD (Writing – original draft).

Funding

No funding was use for this editorial.

Conflicts of interest

KPL has served as a consultant for Pfizer and Seagen and has received honoraria from Pfizer. SGM has no disclosures.

References

1. Wildiers H, Heeren P, Puts M, et al. International Society of Geriatric Oncology consensus on geriatric assessment in older

patients with cancer. J Clin Oncol. 2014;32(24):2595-2603. doi:10.1200/jco.2013.54.8347

- Dotan E, Walter LC, Browner IS, et al. NCCN guidelines[®] insights: older adult oncology, version 1.2021. J Natl Compr Canc Netw. 2021;19(9):1006-1019. doi:10.6004/jnccn.2021.0043
- Mohile SG, Dale W, Somerfield MR, et al. Practical assessment and management of vulnerabilities in older patients receiving chemotherapy: ASCO guideline for geriatric oncology. J Clin Oncol. 2018;36(22):2326-2347. doi:10.1200/jco.2018.78.8687
- Saad M, Loh KP, Tooze JA, et al. Geriatric assessment and survival among older adults receiving postremission therapy for acute myeloid leukemia. Blood. 2020;136(23):2715-2719. doi:10.1182/blood.2020005498
- Eriksen GF, Benth J, Grønberg BH, et al. Geriatric impairments are associated with reduced quality of life and physical function in older patients with cancer receiving radiotherapy - a prospective observational study. J Geriatr Oncol. 2023;14(1):101379. doi:10.1016/j.jgo.2022.09.008
- Hurria A, Togawa K, Mohile SG, et al. Predicting chemotherapy toxicity in older adults with cancer: a prospective multicenter study. J Clin Oncol. 2011;29(25):3457-3465. doi:10.1200/ jco.2011.34.7625
- Extermann M, Boler I, Reich RR, et al. Predicting the risk of chemotherapy toxicity in older patients: The Chemotherapy Risk Assessment Scale for High-Age Patients (CRASH) score. *Cancer*. 2012;118(13):3377-3386. doi:10.1002/cncr.26646
- Hamaker M, Lund C, Te Molder M, et al. Geriatric assessment in the management of older patients with cancer - a systematic review (update). *J Geriatr Oncol*. 2022;13(6):761-777. doi:10.1016/j. jgo.2022.04.008
- Puts MT, Santos B, Hardt J, et al. An update on a systematic review of the use of geriatric assessment for older adults in oncology. Ann Oncol. 2014;25(2):307-315. doi:10.1093/annonc/ mdt386
- Scheepers ERM, Vondeling AM, Thielen N, van der Griend R, Stauder R, Hamaker ME. Geriatric assessment in older patients with a hematologic malignancy: a systematic review. *Haematologica*. 2020;105(6):1484-1493. doi:10.3324/haematol.2019.245803
- Puts MT, Hardt J, Monette J, Girre V, Springall E, Alibhai SM. Use of geriatric assessment for older adults in the oncology setting: a systematic review. J Natl Cancer Inst. 2012;104(15):1133-1163. doi:10.1093/jnci/djs285
- Chuang MH, Chen JY, Tsai WW, et al. 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. Age Ageing. 2022;51(7): doi:10.1093/ageing/ afac145
- Anwar MR, Yeretzian WT, Ayala AP, et al. Effectiveness of geriatric assessment and management in older cancer patients: a systematic review and meta-analysis. J Natl Cancer Inst. 2023;115 (12):1483-1496.
- Mohile SG, Mohamed MR, Xu H, et al. Evaluation of geriatric assessment and management on the toxic effects of cancer treatment (GAP70+): a cluster-randomised study. *Lancet*. 2021;398(10314):1894-1904. doi:10.1016/s0140-6736(21)01789-x
- Li D, Sun CL, Kim H, et al. Geriatric Assessment-Driven Intervention (GAIN) on chemotherapy-related toxic effects in older adults with cancer: a randomized clinical trial. JAMA Oncol. 2021;7(11):e214158. doi:10.1001/jamaoncol.2021.4158
- DuMontier C, Uno H, Hshieh T, et al. Randomized controlled trial of geriatric consultation versus standard care in older

adults with hematologic malignancies. *Haematologica*. 2022;107 (5):1172-1180. doi:10.3324/haematol.2021.278802

- Culakova E, Mohile SG, Peppone L, et al. Effects of a geriatric assessment intervention on patient-reported symptomatic toxicity in older adults with advanced cancer. J Clin Oncol. 2023;41 (4):835-846. doi:10.1200/jco.22.00738
- ICH Harmonised Tripartite Guideline. Statistical principles for clinical trials. International Conference on Harmonisation E9 Expert Working Group. Stat Med. 1999;18(15):1905-1942.
- Loh KP, Mohile SG, Lund JL, et al. Beliefs about advanced cancer curability in older patients, their caregivers, and oncologists. Oncologist. 2019;24(6):e292-e302. doi:10.1634/theoncologist.2018-0890
- 20. Loh KP, Kaushik R, Mohile SG, et al. Speeding the dissemination and implementation of geriatric assessment: What we can learn from the business world. *J Geriatr Oncol.* 2020;11(7):1170-1174. doi:10.1016/j.jgo.2020.03.007
- Dale W, Klepin HD, Williams GR, et al. Practical assessment and management of vulnerabilities in older patients receiving systemic cancer therapy: ASCO guideline update. J Clin Oncol. 2023;41(26):4293-4312. doi:10.1200/jco.23.00933
- Williams GR, Hopkins JO, Klepin HD, et al. Practical assessment and management of vulnerabilities in older patients receiving systemic cancer therapy: ASCO guideline questions and answers. *J Clin Oncol Oncol Pract.* 2023;19(9):718-723. doi:10.1200/op.23.00263