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Geriatric assessment with management in cancer care: Current evidence and potential mechanisms for future research

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Abstract

Older adults with cancer represent a complex patient population. Geriatric assessment (GA) is recommended to evaluate the medical and supportive care needs of this group. “GA with management” is a term encompassing the resultant medical decisions and interventions implemented in response to vulnerabilities identified on GA. In older, non-cancer patients, GA with management has been shown to improve a variety of outcomes, such as reducing functional decline and health care utilization. However, the role of GA with management in the older adult with cancer is less well established. Rigorous clinical trials of GA with management are necessary to develop an evidence base and support its use in the routine oncology care of older adults. At the recent U-13 conference, “Design and Implementation of Intervention Studies to Improve or Maintain Quality of Survivorship in Older and/or Frail Adults with Cancer,” a session was dedicated to developing research priorities in GA with management. Here we summarize

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identified knowledge gaps in GA with management studies for older patients with cancer and propose areas for future research.

Keywords

Geriatric assessment with management; Cancer; Geriatric oncology; Geriatric assessment intervention

1. Introduction

Older patients with cancer are a heterogeneous group, and chronologic age does not necessarily reflect physiologic age in this population. GA should be utilized in determining a patient's fitness for cancer treatment and developing a personalized treatment plan.[1] GA is a set of tools to assess a variety of domains that commonly impact older adults, including physical function, comorbidity and polypharmacy, nutrition, cognitive function, social support, and psychological status. GA can provide a comprehensive assessment of a patient's overall health status and identify potential areas of vulnerability. In non-cancer patients, geriatricians recognize these areas of vulnerabilities and develop goal-directed interventions in response to GA impairments to potentially improve outcomes. "GA with management" describes the resultant medical decisions and interventions implemented in response to vulnerabilities identified on GA. In older patients with cancer, GA can be incorporated into routine oncology evaluation. Items contained in the GA predict chemotherapy toxicity, and GA has been shown to influence decision making for cancer treatments. However, GA has not yet been routinely used to develop goal-directed interventions and guide management in older patients with cancer. Although there are data to support the benefit of GA with management interventions in the non-cancer population, the optimal approach for developing and implementing these interventions in older patients with cancer is not established. Because oncologists are not always familiar with the geriatrics literature and may not be willing to extrapolate information from the non-cancer population, knowledge about the feasibility and benefit of GA with management in oncology will be important to move the field forward. Data supporting the impact of GA with management on cancer-specific as well as non-cancer-specific outcomes will be necessary to support utilization of geriatric assessment and management as a standard of care for older patients with cancer. Here we summarize research priorities for GA with management discussed at the recent U-13 conference "Design and Implementation of Intervention Studies to Improve or Maintain Quality of Survivorship in Older and/or Frail Adults with Cancer." We will review current knowledge on the use of geriatric assessment in cancer care, discuss the evidence supporting GA with management in the non-cancer population, and summarize knowledge gaps regarding GA with management in older patients with cancer and propose mechanisms to fill these knowledge gaps.

1.1. What is Known

1.1.1. Geriatric Assessment in Oncology Care—It is feasible to incorporate GA into routine oncology practice. Hurria and colleagues developed a cancer-specific GA, the majority of which is completed solely by the patient within 27 min.[2] It is also feasible to

incorporate GA into a private oncology practice model and community oncology clinics.[3,4] Elements of the GA have also been shown to be predictive of chemotherapy toxicity.[5,6] The Cancer and Aging Research Group (CARG) developed a predictive model for chemotherapy toxicity that includes several GA measures as well as cancer and treatment-specific factors. The model was developed in 500 patients with cancer aged ≥65 years and found that geriatric-specific risk factors, such as history of falls and needing assistance with taking medications, were predictive of grade 3 to 5 chemotherapy toxicity.[5] Extermann and colleagues also developed a chemotherapy toxicity risk prediction model, the Chemotherapy Risk Assessment Scale for High-Age Patients (CRASH) score. The CRASH model also included several GA risk factors, such as needing assistance with Instrumental Activities of Daily Living (IADL) (e.g., meal preparation or housework) and impaired cognition (Mini Mental Status Exam [MMSE] score < 30), which were predictive of chemotherapy toxicity.[6] GA is influential in clinical decision making. Hamaker and colleagues conducted a systematic review of the effect of GA on treatment decision making in older patients with cancer. They identified six studies that addressed a change in oncologic treatment and found that the initial treatment plan was modified in 39% of patients based on GA results.[7]

1.1.2. Geriatric Assessment with Management Intervention—GA with management improves a variety of outcomes in older, non-cancer patients. In a study by Frese and colleagues of 1620 community-dwelling adults aged 70 years and over, individuals randomized to GA with management interventions had a 22.3% decreased risk of death. The risk of nursing home placement was also lower in the intervention group.[12] The DEED II study demonstrated that GA with implementation of geriatric management interventions for community-dwelling older adults with a recent Emergency Room (ER) visit produced lower rates of hospitalization at 30 days and 18 months following the initial ER visit. The management intervention group maintained better physical and mental function at 6-month follow-up than the control group.[13] A Cochrane meta-analysis evaluated the benefit of comprehensive GA with management program in hospitalized patients and included 10,315 patients in six countries. It showed that GA with management improved the likelihood that patients would be alive and functionally independent in the community at 6-month and 12-month follow-up. Rates of institutionalization were lower for patients receiving GA with management.[14]

Other studies have shown less robust benefits from GA with management in the non-cancer population. Cohen and colleagues evaluated the impact of inpatient and outpatient GA in 1388 patients randomized to receive inpatient GA versus usual care, with or without outpatient GA follow-up. They found no significant effects on overall survival with the intervention; however, the intervention group had significant reductions in functional decline and improvements in mental health without an increase in cost.[15]

Several domain-focused GA with management programs have also been shown to improve outcomes in older, non-cancer patients. Multiple studies have evaluated the impact of physical function interventions and have been shown to improve a variety of outcomes including mobility,[16,17] strength,[18] balance,[19] gait speed[19,20] and decrease risk of falls.[21] Focused nutritional interventions have demonstrated improvement in Mini-Nutritional

Assessment (MNA) scores and serum albumin levels.[22] Keeler and colleagues demonstrated that GA with management interventions are cost effective.[23]

An expert panel of U.S.-based geriatric oncologists recommend incorporation of GA with management into clinical care.[30] A Delphi process was utilized to develop consensus regarding GA with management interventions among experts in the field. The experts met consensus on multiple, high-priority GA with management recommendations; however, many of these recommendations have not yet been tested in older adults with cancer. GA with management recommendations based upon this expert consensus are summarized in Table 1.

2. Current Gaps in Knowledge and Mechanisms for Filling Gaps

2.1. Gap 1: What is the Feasibility of Developing and Implementing ga with Management Interventions in Cancer Care?

A recent British study evaluated the impact of GA with management in older patients with cancer undergoing chemotherapy. In this study, a cohort of patients deemed to be high-risk based upon a screening questionnaire (CGA-GOLD) underwent evaluation by a geriatrician with implementation of geriatric management interventions. Outcomes of interest included grades 3–5 chemotherapy toxicity, rate of completion of cancer treatment as planned, treatment modifications, early treatment discontinuation, and death at 6 months. Outcomes of the intervention group were compared to a previously evaluated observational cohort. The authors determined that patients who received GA with management were more likely to complete cancer treatment and required fewer treatment modifications than the observational cohort. The overall grade 3–5 chemotherapy toxicity rate was not significantly different between the two groups. On average, patients received 6.2 ± 2.6 geriatric management interventions (range 0–15).[24] However, this model of care relied upon geriatrician management, and the feasibility of developing and implementing such interventions independent of direct geriatrics involvement is not established.

A small number of trials evaluating GA with management interventions focusing on a single GA domain has been conducted in older patients with cancer. A French study evaluated the impact of a nutritional counseling program for patients aged ≥70 receiving chemotherapy for solid tumor malignancies that were at risk based upon MNA score. The authors found that dietary counseling was efficient at increasing caloric intake in this population but had no significant effect in mortality or chemotherapy outcomes.[25] For older women with breast cancer, the impact of a nurse case management intervention program was evaluated in a randomized trial. The authors found that patients randomized to the intervention group were more likely to receive standard of care therapy (increased rates of breast conserving therapy, radiation therapy, reconstruction, and chemotherapy). The effect of the intervention was most pronounced in women with indicators of poor social support.[26] McCorkle and colleagues evaluated the impact of a specialized home care intervention program in older post-surgical cancer patients. The intervention involved a 4-week program of home visits and telephone calls delivered by advanced practice nurses. The authors found that the nurse-based intervention improved overall survival, with impact most pronounced in individuals

with advanced disease.[27] Other studies have demonstrated that GA with management improves quality of life and pain management in older cancer patients.[28,29]

The current evidence for using GA with management in cancer patients is minimal, and it is unclear if such interventions can be developed and implemented in an oncology setting independent of geriatrician assessment. In the majority of oncology care settings, the involvement of geriatricians in cancer care is limited at best. Therefore, models of care need to be developed to optimize inclusion of geriatric management principles into oncology practice. Feasibility studies need to be developed evaluating various implementation rates of GA with management recommendation in various models of care.

In prior studies, implementation rates of GA-based management recommendations were a limiting factor. In the systematic review of geriatric assessment by Hamaker and colleagues, implementation rates of geriatric management interventions were highest in trials that had a standardized intervention protocol or a geriatric consultation. However, in the one study that relied on the cancer specialist to implement suggested interventions, only 26% of patients received any of the recommendations.[7] Clearly, supportive mechanisms for implementing recommendations should be developed and evaluated. For geriatric management interventions that are referral based (such as physical therapy or home health services), the referral process could be automated using electronic health record technology. Multidisciplinary members of the oncology care team, such as social workers or nurses, could be engaged to implement the geriatric management interventions. For management interventions that are education based, for example counseling on fall precautions, videos or web modules could be developed and utilized.

2.2. Gap 2: How Does the Benefit of Geriatric Interventions Vary Based Upon Cancer Prognosis?

The role of geriatric assessment with management interventions may vary based upon cancer prognosis. In patients who are receiving curative intent cancer treatment, or who have a longer prognosis, the benefits of GA with management interventions may be similar to those in the non-cancer population. For these patients, estimated life expectancy will be of sufficient duration to derive the full potential benefit of the proposed intervention. Thus, in this group of patients, GA with management interventions may maintain independence and reduce functional decline. Amore important and relevant question in this population may be how to incorporate GA with management recommendations into clinical care. As cancer treatments become increasingly effective and patients are living longer with cancer and cancer treatments, GA with management interventions may become a valuable tool for optimizing independence and function during cancer therapy and survivorship.

It is also important to understand if GA with management interventions improves the tolerance and efficacy of treatments for patients who are receiving cancer therapy. For example, in vulnerable patients receiving adjuvant chemotherapy, regimens frequently need to be modified or dose reduced due to adverse events. It is unknown if GA with management interventions may improve tolerability, thus allowing patients to receive standard of care treatment and therefore potentially improving cancer-related outcomes. Randomized studies

will be required to determine the impact of GA with management interventions on the tolerance and efficacy of cancer therapy regimens.

For patients with shorter cancer-specific survivals (i.e., <1 year), studies of GA with management interventions may focus on outcomes such as improvement in quality of life and prolongation of active life expectancy.

Therefore, the outcomes of interest vary based upon the clinical setting for GA with management. Clinical trial end points should reflect this variability as well. Clinical trials in oncology usually have the primary end point of survival, and perhaps this is appropriate in the curative intent setting. However, given the supportive care focus of GA with management, alternative end points such as chemotherapy toxicity, completion of planned therapy, rates of hospitalization, or quality of life may also be appropriate end points. Geriatric-specific and patient-centered outcomes, such as physical function or cognition, may also be appropriate outcomes for domain-specific GA studies.

In all GA with management research in the oncogeriatric population, the reasons underlying limited or failed intervention studies should be evaluated. Previous studies in older non-cancer patients' demonstrated multiple barriers to the development and implementation of GA with management in the clinical research setting. Table 2 outlines potential pitfalls in developing and executing clinical trials evaluating geriatric interventions.

2.3. Gap 3: What Clinical Trial Design is Optimal for Evaluation of ga with Management in Cancer Care?

In non-cancer patients, a design where geriatricians utilize GA to identify areas of vulnerability and develop specific management recommendations (protocol-based, GA-based management) to improve outcomes is called a standardly tailored intervention.[8,9] Examples of geriatric management include recommending physical therapy and home safety evaluation for an individual with history of falls,[10] or delirium prevention by avoiding high-risk medications in at-risk individuals.[11] Using GA to guide standardly tailored management interventions is a potential avenue for improving outcomes for older adults with cancer. Repeating GA at time points along the disease trajectory may also offer new opportunities for interventions as risk factors arise.

When designing a study evaluating GA with management in cancer care, several approaches can be considered. First, investigators could evaluate each specific geriatric management intervention separately. An example is a randomized trial evaluating the impact of exercise in patients with impaired physical function. Evaluating a specific geriatric management intervention independently allows for understanding of the individual impact of each specific intervention to ameliorate the risk factor and ultimately the ability to identify those management interventions that are of "highest impact," that are the most feasible to implement, and that provide the largest improvement in outcomes. A specific management intervention may actually provide benefit in more than one domain, as these domains are not necessarily biologically or psychosocially independent. For example, implementing "Meals on Wheels" services may help patients with impaired nutritional status as well as those with poor social support, mobility limitations, and difficulties accessing nutritious food. However,

there are several limitations to this approach. Management interventions are not typically developed in isolation in clinical practice. For example, for patients with a history of falls, a multicomponent intervention including physical therapy, home safety evaluation, and counseling on fall precautions may be recommended and may act additively or synergistically. Therefore, evaluating each management intervention individually may not reveal their combined overall impact. In complex older patients with cancer, individuals often have multiple impairments in GA domains at baseline, and evaluating a single management intervention in this population may underestimate the potential impact of a comprehensive, multicomponent management intervention.[9] Furthermore, these complex patients may develop new impairments over the course of a trial and should undergo a repeat GA at the time of blinded outcome assessment.

Alternatively, investigators could use a “domain-based” approach and study management interventions for a specific GA domain. For example, investigators could identify individuals with cognitive impairment and evaluate the benefit of a multicomponent management intervention including delirium prevention counseling, caregiver engagement, social work referral, and limiting treatment complexity. The benefit of investigating management interventions in a domain-based approach is that this strategy addresses an identified GA impairment in a more comprehensive fashion. However, this approach may limit the ability to determine which specific management intervention has the greatest benefit. Also, this approach does not address impairments in other GA domains that could be biologically linked (e.g., sarcopenia resulting from poor diet, mobility limitations, and cognition), thus potentially limiting impact.

Investigators may also consider evaluating the impact of a more comprehensive GA with management program, with multicomponent interventions targeting all domains. This strategy would involve a full baseline GA with development of management interventions that target any and all identified impairments. This application of GA with management allows for a global assessment of the patient, which may inform treatment decision making.

One design for evaluating impact of a GA with management program is to utilize an expert in geriatric oncology to develop and deliver the management interventions. This approach captures the finer nuances of clinical judgment utilized with complex, older patients with cancer. This population also commonly has comorbid conditions, which require careful consideration and management during cancer care. A clinician with expertise in evaluating and assessing the severity of the comorbid conditions and developing interventions to support the patient in this area may be helpful. GA with management encompasses not only the physical interventions (i.e., physical therapy, nutritional referral, etc.) but also the adaptive medical decision making (i.e., modifications in regimen or dosing due to comorbidity, absence of social support, etc.). Adaptive trials designs, such as sequential, multiple assignment, randomized trial (SMART[31]) designs, are used to construct adaptive management interventions and allows augmentation of initial treatment for non-responders. Benefits to assessing GA with management programs in this approach are that the magnitude of benefit from each intervention may be additive and adaptive medical decisions are responsive to change. One drawback to evaluating GA with management in this approach is that the relative lack of experts in geriatric oncology means that this strategy is

not readily applicable to routine clinical practice. Table 3 summarizes the various potential approaches to evaluating GA with management in cancer care.

3. Conclusion

It is feasible to incorporate GA into routine oncology care. GA is influential in decision making, and elements of the GA can predict chemotherapy toxicity. However, utilization of GA in oncology clinical practice remains limited, likely because geriatric management interventions have not been robustly studied in this heterogeneous population. GA with management is effective at improving outcomes in older non-cancer patients, and randomized clinical trials are needed to evaluate the potential feasibility and impact in the oncogeriatric population. Several clinical trial design options are available, with varying advantages and limitations as outlined above. The field of geriatric oncology is poised to move forward to investigate the benefit of GA with management in this population.

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Table 1

Summary of GA management recommendations from U.S.-based geriatric oncology experts through Delphi process.[30]

GA domain impaired	Examples of GA impairment	GA with management recommendations by Delphi consensus
Physical function	• History of falls • Impaired objective physical performance testing • Impaired ADLs or IADLs	• Physical therapy • Occupational therapy • Home safety evaluation • Fall risk assessment • Modification of cancer treatment regimen • Improving function prior to treatment initiation
Nutrition	• Recent weight loss or anorexia • Positive Mini-nutritional Assessment screen	• Nutrition consult • Oral care • Dietary recommendations • Evaluating drug tolerance
Cognition	• Abnormal cognitive testing (e.g., Mini Mental Status Examination [MMSE], Montreal Cognitive Assessment [MOCA])	• Involvement of caregivers • Delirium prevention • Social work referral • Capacity evaluation • Healthcare proxy designation • Limiting treatment complexity • Assessing the presence of caregiver support
Social support	• Patient lives alone or without significant family involvement	• Social work referral • Home health referral • Transportation assistance • Caregiver support services • Home safety evaluation • Consideration of modified treatment
Psychological	• Positive Geriatric Depression Scale (GDS) screen • Positive distress screen	• Social work referral • Counseling referral • Psychiatry/psychology referral

Table 2

Potential pitfalls in clinical trials evaluating GA with management.

Potential pitfalls in clinical trials evaluating GA with management	
1	GA Results are not initially captured
2	GA results and management recommendations are not delivered to the treating provider
3	GA management recommendations are not implemented by the treating provider
4	Patients refuse intervention/do not participate
5	GA with management has limited impact
6	Outcome measurements are not sensitive to detect the impact of GA with management interventions

Table 3

Summary of potential approaches to evaluating GA with management in cancer care.

Method	Example	Advantage		Disadvantage	
Intervention-based approach	Evaluation of counseling referral for patients with positive depression screen	**1**	Determine the impact of each individual intervention	**1**	Impairments in other domains not addressed
				2	Multiple interventions may be considered for a single impairment thus implementing only one may limit impact
GA domain-based approach	Evaluating impact of nutrition consult, nutritional supplements, and oral care for patients with impaired nutrition	**1**	Determine impact of each individual GA domain	**1**	Does not account for impairments in GA domains not addressed which may limit impact
		2	Accounts for multiple interventions being utilized for single impairment		
Full GA with multicomponent intervention using geriatrician/geriatric oncologist	Geriatrician/geriatric oncologist reviews GA findings, develops multicomponent intervention plan and implements interventions	**1**	Incorporates all potential impairments	**1**	Not readily transferrable to routine clinical practice given limited number of geriatricians/geriatric oncologists
		2	Accounts for clinical judgment as geriatrician/geriatric oncologist is evaluating full impact of GA		
		3	High likelihood of intervention implementation based upon prior literature		
Full GA with multicomponent intervention using algorithm	Support staff administers and scores GA, algorithm used to identify appropriate interventions based upon GA impairments	**1**	Incorporates all potential impairments	**1**	Does not account for clinical judgment of full GA
		2	Model could be used in routine clinical practice where geriatric oncology expert not available	**2**	Low likelihood of intervention implementation based upon prior literature