How old is too old? Frailty and geriatric assessments of older patients undergoing allogeneic HCT

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Allogeneic hematopoietic cell transplantation (HCT) is a curative-intent treatment for many hematologic malignancies but carries a significant risk of morbidity and mortality. An increasing number of older adults are receiving HCT, but current pretransplant evaluations overlook the unique vulnerabilities that older adults face. Oncology-specific geriatric and frailty assessments provide a comprehensive evaluation of older adults, help better weigh the risks of HCT with patients, and guide personalized optimization strategies to minimize vulnerabilities. Geriatric assessments evaluate seven domains: comorbidities, physical function, mental health, cognition, nutrition, medications, and social support. Frailty indices provide unique evaluations into a patient's overall status. Various standardized measures have been used to evaluate these areas in older adults prior to HCT. Different care models exist for the integration of geriatrics and geriatric principles into HCT evaluation: a multidisciplinary consultative clinic, a geriatrician alongside the HCT clinic, or a primary geriatric hematologist/transplant physician. Future studies are needed to investigate the use of geriatric assessments in selecting the conditioning regimen and intensity and measuring the impact of geriatric assessment–driven interventions on quality of life and toxicities post transplant.

LEARNING OBJECTIVES
- Describe the domains of a geriatric assessment
- Assess for vulnerabilities in HCT recipients utilizing standardized measures

CLINICAL CASE

Jane is a 71-year-old woman with acute myeloid leukemia with a complex karyotype. Treatment was initiated with venetoclax and azacitidine. She achieved a complete response, and reduced-intensity matched unrelated peripheral blood allogeneic hematopoietic cell transplantation (HCT) was pursued. She underwent HCT evaluation per institutional standards, including a geriatric assessment.

Geriatric and frailty assessments in HCT

HCT is a curative treatment for many hematologic malignancies but carries a significant risk of morbidity and mortality. With advances in disease treatment, transplant techniques, and supportive measures, an increasing number of older adults are receiving HCT. Current evaluation for HCT eligibility is standardized regardless of age, overlooking the unique vulnerabilities older adults face. The lack of standardized evaluation of older adults has led to physicians arbitrarily determining eligibility for HCT.

Oncology-specific geriatric and frailty assessments provide in-depth evaluations of older adults, with a growing evidence base in HCT.[1] These assessments help better weigh the risks of HCT and guide personalized optimization strategies. Geriatric assessment-driven interventions decrease toxicities and falls in the nontransplant geriatric oncology population.[2,3] An area not evaluated by these assessments is the transplant ecosystem, which has recently been published.[4] Here, I focus on geriatric and frailty assessments and touch on models to incorporate into clinical practice. An in-depth discussion of care models and interventions are outside the scope of this article.

Geriatric assessment

Oncology-specific geriatric assessments typically comprise 7 domains (Table 1). The Practical Geriatric Assessment is

Table 1. Geriatric assessment domains, measures, and possible interventions

Domains	Tools	Interventions[5,10,40]
Comorbidity	HCT-CI Cumulative Illness Rating Scale-Geriatric OARS comorbidity	Referral to specialist familiar with transplant
Physical function	ADLs IADLs TUG 4-meter gait speed 6MWT	Physical therapy Occupational therapy Address uncontrolled pain
Psychological	PHQ-9 Hospital Anxiety and Depression Scale Mental Health Inventory-17 Short Form-36 (mental component summary) PROMIS Anxiety Geriatric Depression Screen	Referral to psychiatry Cognitive behavioral therapy Initiate antidepressants
Cognition	MiniCog Mini-Mental Status Exam MoCA Blessed-Orientation-Memory-Concentration Test	Review medications for possible contributing cause Address depression if present Delirium precautions when admitted
Nutritional status	MNA Preoperative Nutrition Screen Albumin Weight loss[a]	Refer to dietician Encourage nutrition supplement use Address possible contributing factors
Polypharmacy and potentially inappropriate medications	≥7 medications Beers Criteria	Stop potentially inappropriate and unnecessary medications Review medications for possible drug-drug interactions Consult pharmacist
Social support	Medical Outcomes Study Social Support Survey	Complete health care power of attorney Identify short-term and long-term needs

[a]Over the preceding 3 months.

6MWT, 6 minute walk test; ADLs, activities of daily living; IADLs, instrumental activities of daily living; MNA, mininutrition assessment; MoCA, Montreal cognitive assessment; OARS, Older Americans Resources and Services; PHQ-9, patient health questionnaire-9; TUG, timed up and go.

Adapted from Jayani et al.[1]

a concise tool built to overcome barriers to implementation.[5] The Practical Geriatric Assessment provides a foundation for more in-depth assessments of vulnerabilities in older adults undergoing intensive therapies, including HCT. Summarized below are the standardized measures utilized in HCT.

Comorbidities

Standard HCT evaluation includes an assessment of comorbidities, most commonly using the Hematopoietic Cell Transplantation-Comorbidity Index (HCT-CI).[6] This tool calculates a weighted score of comorbidities and organ function that is predictive of nonrelapse mortality (NRM) and overall survival (OS).[6] It was originally validated in a cohort of young patients and was updated to incorporate chronologic age with the Comorbidity-Age Index.[7] The advantage of this tool in patients beyond their sixth decade of life remains uncertain.[8] In addition, this tool has yet to be validated with the recent advancements in HCT such as posttransplant cyclophosphamide-based graft-versus-host disease prophylaxis.

Physical function

Two categories of physical function measures have been studied: patient-reported and objective measures.

Patient-reported measures

Activities of daily living (ADLs) and instrumental activities of daily living (IADLs). ADLs are activities needed to independently care for one's self; IADLs are activities needed to independently live in the community. Impairments in these measures are frequently seen in older adults prior to HCT, with reports of impairments in ADLs and IADLs as high as 42% and 50%, respectively.[9,10] These findings indicate that prior to HCT, the majority of older adults require assistance to care for themselves or live in the community. Multiple single-institution studies have shown that older adult HCT recipients with impairments in ADLs and/or IADLs have increased NRM, decreased OS, and decreased progression-free survival.[11-13] However, these findings were not replicated in a multicenter retrospective study.[14]

Health-related quality of life (QOL). Up to 42% to 64% of older adults report low physical function prior to HCT, which has been correlated with inferior survival outcomes.[11-13,15] These findings are also seen in adults of all ages, suggesting that patient-reported physical function provides an additional perspective into a patient's function not otherwise captured.[15,16] However, these studies utilize different measures. Some measures focus on physical function in terms of health-related quality of life (QOL)—for example, the Short Form-36 (SF-36)—while others, such as the International Physical Activity Questionnaire, focus on the level of activity.

The National Institutes of Health–sanctioned Patient-Reported Outcomes Measurement Information Systems (PROMIS) aims to overcome this variability by standardizing the collection and reporting of patient-reported measures.

Objective measures

Objective measures of physical function are not subject to recall bias and may measure a patient's physical function with more accuracy and reproducibility, but these measures have not consistently correlated with survival post transplant. Studied measures range from evaluation of fall risk to cardiopulmonary fitness. The 6-minute walk test (6MWT) is not predictive of post-transplant survival despite evaluating cardiopulmonary fitness.[17,18] However, studies show that a decline in 6MWT early post transplant identifies patients at risk of inferior survival. Additionally, these studies, which included adults of all ages, found that the majority of patients scored lower than age-matched norms. This finding raises the need for a threshold specific for adults (or older adults) with hematologic malignancies that may be more predictive of outcomes.

Geriatric-specific objective physical function measures show impairments in 3% to 45% of older adults prior to HCT.[11-14,19,20] These measures include the 4-meter gait speed, timed up-and-go (TUG), and short physical performance battery (SPPB). The 4-meter gait speed is a timed measure of gait over 4 meters. TUG is a timed measure assessing gait and balance. The SPPB evaluates 3 components of physical function: balance, gait speed, and lower extremity strength. A slow 4-meter gait speed has been associated with decreased OS.[11] There are mixed reports on the correlation between an abnormal TUG and survival outcomes post HCT.[12-14,19] There are limited data on the prognostication of SPPB in HCT; however, older adults with AML and low SPPB prior to intensive chemotherapy have inferior survival.[21]

Mental health

Increased rates of depression and anxiety are seen in those with cancer, and HCT recipients are no exception. Uncontrolled depression and anxiety in older adults with cancer are associated with treatment nonadherence, decreased health-related QOL and survival, and increased hospital length of stay.[22,23] These mental health disorders are often overlooked, with up to 56% of older adults reporting uncontrolled depression or anxiety prior to HCT.[11]

The tools currently utilized focus on patient-reported measures, with discordant findings on the impact of uncontrolled depression or anxiety on transplant outcomes. These differences may in part be due to the varying measures used. The Patient Health Questionnaire (PHQ_) evaluates depression symptoms but has some limitations. It focuses on symptoms that older adults may not present with and does not evaluate anxiety.[24] Measures like the Hospital Anxiety and Depression Scale evaluate for anxiety and depression. Yet other measures evaluate global mental health, including the Mental Health Inventory and SF-36. Of these, only the SF-36 Mental Component Summary has been associated with decreased OS post transplant. Here again, the PROMIS measures help decrease the variability in measures used.

Cognition

The risk of cognitive impairment increases with age and is seen in up to 20% of older adults prior to HCT.[19] A number of tools exist to screen for cognitive impairment. These range from the MiniCog, which consists of a clock drawing and 3-word recall, to the Montreal Cognitive Assessment (MoCA), covering 8 domains of cognitive function. The MoCA detects subtle changes in cognition, such as mild cognitive impairment. Thus, the MoCA may identify patients at increased risk of complications such as delirium who would benefit from additional support. In a single-institution study of adults of all ages undergoing autologous or allogeneic HCT, the MoCA was not predictive of posttransplant outcomes, but extrapolation to older adults is limited.[25] However, impaired cognition identified by the 6-item Blessed Orientation-Memory-Concentration Test correlated with decreased OS in a multicenter retrospective study.[14]

Nutrition

Malnutrition places older adults at increased risk of inferior survival with many medical procedures, including HCT.[13,26] Prior to HCT, up to 36% of older adults are malnourished, and 76% are at risk.[13,27] In addition, malnutrition increases during the first 6 months post transplant.[27] Various measures of malnutrition have been investigated in the older adult HCT population. These range from simple measures such as serum albumin to more extensive tests such as the Perioperative Nutrition Screen and the Mini-Nutrition Assessment (MNA). The Perioperative Nutrition Screen focuses on weight loss, body-mass index, and oral intake, whereas the 6-item MNA incorporates neuropsychiatric and physical components. Low scores on these measures have been associated with inferior survival post-transplant.[11,13,26]

Polypharmacy and potentially inappropriate medications

The definition of polypharmacy varies, from 5 or more to 9 or more medications. Regardless, the concerns with polypharmacy remain the same: increased risk of adverse events and drug-drug interactions. Post-transplant medication regimens are complex and include medications with a narrow therapeutic index and the risk of severe and long-term consequences of noncompliance, such as acute and severe chronic graft-versus-host disease (GHVD). Polypharmacy in older adults prior to HCT is associated with lower OS, regardless of age and comorbidities.[28] With older adults on a median of 7 medications prior to HCT, ongoing efforts in deprescribing and the impact on HCT-related outcomes are needed.[28]

Older adults are also at increased risk of adverse effects from medications that may overshadow the potential benefit. Resources are available to help identify these so-called potentially inappropriate medications—for example, the American Geriatric Society Beer's Criteria.[29] Some of these medications are commonly used during HCT (Table 2). Nearly 50% of older adults are taking potentially inappropriate medications prior to or during HCT, which has been associated with inferior survival and increased severe toxicities post-transplant.[28,30,31]

Social support

HCT recipients are required to relocate close to the transplant center with an informal caregiver for the early posttransplant period. During this time and even after returning home, many remain on immunosuppression with increased risk of infection. As a result, many isolate themselves to decrease this risk. However, social isolation places older adults at increased risk of additional issues, including dementia. Additionally, informal

Table 2. Examples of potentially inappropriate medications commonly used post transplant[a]

Promethazine
Scopolamine
Lorazepam
Oxybutynin
Dicyclomine
Cyclobenzaprine
Proton pump inhibitors[b]
Sliding scale insulin
Diphenhydramine[b]

[a]Potentially inappropriate medications based on American Geriatric Society Beers Criteria.[29]

[b]May be appropriate in certain circumstances.

caregivers have other responsibilities or burdens. Children often have other commitments such as work or their own families. Spouses or siblings may have medical conditions or be frail as well. A limited number of studies have evaluated the impact of social support on HCT outcomes in older adults. After transplant, the majority of older adults report inadequate social support and decreased social well-being.[27,32]

Frailty index

Two models of frailty index exist, with different theoretical constructs.

Fried Frailty Index

The Fried Frailty Index evaluates patients as frail, prefrail, or fit.[33] This index consist of 3 patient-reported (weight loss, energy, physical activity) and 2 objective hand grip, gait speed) measures with adaptations (Table 3).[27,33-35] Up to a quarter of older adults undergoing HCT are frail, and over half are prefrail.[11,19,27] Although the Fried Frailty Index has not consistently been shown to predict OS in older adults, a study of adult HCT recipients showed that frailty predicted for an increased risk of severe or life-threatening nonhematologic toxicities and mortality.[11,27,35]

Cumulative Frailty Index

The Cumulative Frailty Index focuses on the accumulative impact of health deficits.[36] This index includes symptoms, comorbidities, laboratory values, and disabilities. It has been associated with hospitalization and survival in the general older adult population. Further studies are needed to understand the advantage of this frailty model in evaluating HCT recipients.

CLINICAL CASE (continued)

We return to Jane, our 71-year-old woman with high-risk AML. Her standard HCT evaluation revealed a history of coronary artery disease, supraventricular tachycardia, a normal echocardiogram, and a low forced expiratory volume and diffusing capacity of lung for carbon monoxide. Her HCT-CI score was 4. Her geriatric assessment revealed additional areas of vulnerability. She reported low physical function and was found to have an abnormal TUG and low 6MWT. The PHQ-9 identified severe depression symptoms. The PROMIS Anxiety measure showed no increased anxiety symptoms. The MoCA revealed mild cognitive impairment. On review of her medications, she was found to be on 12 medications, with the use of a potentially inappropriate medication, zolpidem.

Table 3. Fried Frailty Index

Component	Original Tool[33]	Adapted measures[27-35]
Exhaustion	Effort for and difficulty starting activities over preceding week (from Center for Epidemiologic Studies Depression Scale)	Need for assistance or unable to carry out normal activity or work or Self-reported weakness
Low physical activity	Kilocalorie expenditure over a week	Rapid Assessment of Physical Activity MOS-SF-10 physical function or Minnesota Leisure Time Activity Questionnaire- short version or Frequency of intensive exercise over preceding week
Weight loss	Self-report	Self-report
Low grip strength/ weakness	Grip strength	Ability to lift and carry groceries. or Self-reported upper extremity weakness
Slow gait speed	15-feet walk time	3-meter walk or TUG or Self-report of health limiting walking

MOS-SF-10, Medical Outcomes Survey Short Form 10-Item.

Table 4. Care models for implementation of geriatrics into HCT

Model type	Description
Multidisciplinary consultative clinic	Patient is evaluated by multiple disciplines in 1 day or separate days Allows for more patients to be seen Limited follow-up Treatment plan finalized by primary hematologist/transplant physician Resource intensive
Geriatrician alongside HCT clinic	Allows patients to be seen longitudinally by geriatrics or with new geriatric syndromes
Shared care	Division of medical management of medical care between the geriatrician and transplant physician Providers located in different clinic spaces with different support staff
Embedded	Incorporation of the geriatrician within the same clinical space as the transplant team May take on a consultative role
Geriatric hematologist/transplant physician primary provider	Evaluated prior to HCT and geriatric syndromes addressed early Monitor and address new geriatric syndromes Treatment modifications as appropriate

Models for integration of geriatrics into HCT

Different care models exist for integrating geriatrics and geriatric principles into the care of older adults with cancer and have shown improvement in treatment outcomes in transplant and nontransplant patients (Table 4).[2,3,10,37-39] This integration may also benefit younger HCT recipients who experience accelerated aging.[34] Each health care system has unique needs best addressed by different care models. In these models, evaluations may be completed through a combination of patient-reported tools, objective measures, and clinical evaluation.

Multidisciplinary consultative clinic

A clinic involving providers from other disciplines such as geriatrics, physical therapy, occupational therapy, social worker, or psychiatry, among others, may be ideal in assessing older adults prior to HCT. This model might require multiple trips or a lengthy clinic day for patients but is aligned with traditional comprehensive geriatric assessments. This model is more resource intensive but has been shown to improve OS and NRM in single-institution retrospective studies.[10,39] These clinics are typically consultative clinics where patients are evaluated, recommendations are made, and final treatment plans rest with the treating hematologist/transplant physician. A limitation to this approach is that these clinics may focus on evaluation and optimization prior to transplant due to limited resources, but there is a need to support older adults post transplant as well. However, one benefit to this approach is the expanded access for patients. This model can be incorporated into the standard institutional HCT evaluation of older adults or as a referral through the use of geriatric screening tools to identify patients at highest risk of vulnerabilities.

Geriatrician alongside HCT clinic

Another care model is to incorporate geriatricians into HCT clinics, which may be done in 2 ways: 1) shared care, 2) embedded. Both methods allow longitudinal geriatrics support for older adult HCT recipients, including for new geriatric syndromes that arise post transplant. The shared care model comprises a division of medical management between the geriatrician and transplant physician, who may be located in different offices with different support staff. The embedded model incorporates a geriatrician within the same offices as the transplant team but who may take on a consultative role.

Primary geriatric hematologist/transplant physician

Another model is to have a geriatric-hematologist/transplant physician as the primary provider for the patient. In this model, the primary provider evaluates patients prior to transplant, addresses geratric syndromes prior to transplant and any that arise after, and treatment modifications are made where appropriate. This model is limited by the number of geriatric-trained hematologists/transplant physicians.

CLINICAL CASE (continued)

Based on the vulnerabilities identified on the geriatric assessment, prior to HCT Jane was referred to physical therapy to build muscle strength and improve her physical function and to psychiatry for management of depression. The zolpidem was stopped and melatonin trialed. By HCT, her physical function had improved both on the TUG and in self-report, and her depression symptoms had significantly improved. Other than one planned 3-day admission, she completed the majority of her transplant care as an outpatient. She had an initial decline in 6MWT post transplant but recovered by Day+ 100. She and her caregiver were provided written instructions with any medication changes. Unfortunately, she relapsed at Day+ 180. Her salvage treatment course was complicated by recurrent infections. She ultimately developed progressive disease, at which point she transitioned to hospice and passed at 1 year post-transplant.

Conclusion

In conclusion, geriatric and frailty assessments identify vulnerabilities in older adult HCT candidates not captured on routine HCT assessment. These vulnerabilities place them at increased risk of poor outcomes, but oncology-specific geriatric assessments can guide interventions to minimize vulnerabilities. Different care models exist for implementing geriatrics into HCT evaluations. Future studies are needed to investigate the use of geriatric assessments in selecting the conditioning regimen and intensity and the impact of geriatric assessment-driven interventions on QOL and toxicities post-transplant.

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Reena V. Jayani: no competing financial interests to declare.

Off-label drug use

Reena V. Jayani: nothing to disclose.

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References

1. Jayani R, Rosko A, Olin R, Artz A. Use of geriatric assessment in hematopoietic cell transplant. *J Geriatr Oncol*. 2020;11(2):225-236.
2. 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.
3. 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.
4. Wall SA, Olin R, Bhatt V, et al. The transplantation ecosystem: a new concept to improve access and outcomes for older allogeneic hematopoietic cell transplantation patients [published online ahead of print 1 May 2023]. *Transplant Cell Ther*.
5. 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.
6. Sorror ML, Maris MB, Storb R, et al. Hematopoietic cell transplantation (HCT)-specific comorbidity index: a new tool for risk assessment before allogeneic HCT. *Blood*. 2005;106(8):2912-2919.
7. Sorror ML, Storb RF, Sandmaier BM, et al. Comorbidity-Age Index: a clinical measure of biologic age before allogeneic hematopoietic cell transplantation. *J Clin Oncol*. 2014;32(29):3249-3256.
8. Backhaus D, Brauer D, Pointner R, et al. A high Hematopoietic Cell Transplantation Comorbidity Index (HCT-CI) does not impair outcomes after non-myeloablative allogeneic stem cell transplantation in acute myeloid leukemia patients 60 years or older. *Bone Marrow Transplant*. 2023; 58(1):30-38.
9. Lin RJ, Shahrokni A, Dahi PB, et al. Pretransplant comprehensive geriatric assessment in hematopoietic cell transplantation: a single center experience. *Bone Marrow Transplant*. 2018;53(9):1184-1187.
10. Derman BA, Kordas K, Ridgeway J, et al. Results from a multidisciplinary clinic guided by geriatric assessment before stem cell transplantation in older adults. *Blood Adv*. 2019;3(22):3488-3498.
11. Muffly LS, Kocherginsky M, Stock W, et al. Geriatric assessment to predict survival in older allogeneic hematopoietic cell transplantation recipients. *Haematologica*. 2014;99(8):1373-1379.
12. Huang LW, Sheng Y, Andreadis C, et al. Functional status as measured by geriatric assessment predicts inferior survival in older allogeneic hematopoietic cell transplant recipients. *Biol Blood Marrow Transplant*. 2020; 26(1):189-196.
13. Deschler B, Ihorst G, Schnitzler S, Bertz H, Finke J. Geriatric assessment and quality of life in older patients considered for allogeneic hematopoietic cell transplantation: a prospective risk factor and serial assessment analysis. *Bone Marrow Transplant*. 2018;53(5):565-575.
14. Olin RL, Fretham C, Pasquini MC, et al. Geriatric assessment in older alloHCT recipients: association of functional and cognitive impairment with outcomes. *Blood Adv*. 2020;4(12):2810-2820.
15. Jayani RV, Pidala J, Jim H, Whiting J, Mo Q, Mishra A. Association of patient-reported physical activity on allogeneic hematopoietic cell transplant outcomes. *Clin Hematol Int*. 2021;3(1):34-39.
16. Wood WA, Le-Rademacher J, Syrjala KL, et al. Patient-reported physical functioning predicts the success of hematopoietic cell transplantation (BMT CTN 0902). *Cancer*. 2016;122(1):91-98.
17. Jones LW, Devlin SM, Maloy MA, et al. Prognostic importance of pretransplant functional capacity after allogeneic hematopoietic cell transplantation. *Oncologist*. 2015;20(11):1290-1297.
18. Mishra A, Pidala J, Thapa R, et al. Objective and subjective physical function in allogeneic hematopoietic stem cell transplant recipients. *Bone Marrow Transpl*. 2021;56(12):2897-2903.
19. Rodrigues M, de Souza PMR, de Oliveira Muniz Koch L, Hamerschlak N. The use of comprehensive geriatric assessment in older patients before allogeneic hematopoietic stem cell transplantation: a cross-sectional study. *J Geriatr Oncol*. 2020;11(1):100-106.
20. Holmes HM, Des Bordes JK, Kebriaei P, et al. Optimal screening for geriatric assessment in older allogeneic hematopoietic cell transplantation candidates. *J Geriatr Oncol*. 2014;5(4):422-430.
21. Klepin HD, Geiger AM, Tooze JA, et al. Geriatric assessment predicts survival for older adults receiving induction chemotherapy for acute myelogenous leukemia. *Blood*. 2013;121(21):4287-4294.
22. Arrieta Óscar, Angulo LP, Núñez-Valencia C, et al. Association of depression and anxiety on quality of life, treatment adherence, and prognosis in patients with advanced non-small cell lung cancer. *Ann Surg Oncol*. 2013;20(6):1941-1948.
23. Klepin HD, Sun CL, Smith DD, et al. Predictors of unplanned hospitalizations among older adults receiving cancer chemotherapy. *JCO Oncol Pract*. 2021;17(6):e740-e752.
24. Weinberger MI, Roth AJ, Nelson CJ. Untangling the complexities of depression diagnosis in older cancer patients. *Oncologist*. 2009;14(1):60-66.
25. Root JC, Campbell C, Rocha-Cadman X, et al. Pretransplantation cognitive dysfunction in advanced-age hematologic cancers: predictors and associated outcomes. *Biol Blood Marrow Transplant*. 2020;26(8):1497-1504.
26. Lew MV, Ren Y, Lowder YP, et al. Geriatric assessment reveals actionable impairments in hematopoietic stem cell transplantation candidates age 18 to 80 years. *Transplant Cell Ther*. 2022;28(8):498.e1-498498.e9.
27. Ombres R, des Bordes JKA, Popat UR, et al. Serial frailty assessments following allogeneic stem cell transplant in older adults: a pilot study. *J Geriatr Oncol*. 2022;13(2):194-199.
28. Sugidono M, Lo M, Young R, et al. Impact of polypharmacy prior to allogeneic hematopoietic stem cell transplantation in older adults. *Transplant Cell Ther*. 2021;27(4):344.e1-344344.e5.
29. 2023 American Geriatrics Society Beers Criteria® Update Expert Panel. American Geriatrics Society 2023 updated AGS Beers Criteria® for potentially inappropriate medication use in older adults. *J Am Geriatr Soc*. 2023;71(7):2052-2081.
30. Lin RJ, Hilden PD, Elko TA, et al. Burden and impact of multifactorial geriatric syndromes in allogeneic hematopoietic cell transplantation for older adults. *Blood Adv*. 2019;3(1):12-20.
31. Bhargava D, Arora M, DeFor TE, et al. Use of potentially inappropriate medications in older allogeneic hematopoietic cell transplantation recipients. *Biol Blood Marrow Transplant*. 2020;26(12):2329-2334.
32. Huang LW, Sheng Y, Andreadis C, et al. Patterns and predictors of functional decline after allogeneic hematopoietic cell transplantation in older adults. *Transplant Cell Ther*. 2022;28(6):309.e1-309309.e9.
33. Fried LP, Tangen CM, Walston J, et al; Cardiovascular Health Study Collaborative Research Group. Frailty in older adults: evidence for a phenotype. *J Gerontol A Biol Sci Med Sci*. 2001;56(3):M146-M156.
34. Arora M, Sun CL, Ness KK, et al. Physiologic frailty in nonelderly hematopoietic cell transplantation patients: results from the bone marrow transplant survivor study. *JAMA Oncol*. 2016;2(10):1277.
35. Pamukcuoglu M, Bhatia S, Weisdorf DJ, et al. Hematopoietic cell transplant–related toxicities and mortality in frail recipients. *Biol Blood Marrow Transplant*. 2019;25(12):2454-2460.
36. Rockwood K, Andrew M, Mitnitski A. A comparison of two approaches to measuring frailty in elderly people. *J Gerontol A Biol Sci Med Sci*. 2007;62(7):738-743.
37. Chapman AE, Elias R, Plotkin E, Lowenstein LM, Swartz K. Models of care in geriatric oncology. *J Clin Oncol*. 2021;39(19):2195-2204.
38. Magnuson A, Dale W, Mohile S. Models of care in geriatric oncology. *Curr Geri Rep*. 2014;3(3):182-189.
39. Ngo-Huang A, Ombres R, Saliba RM, et al. Enhanced recovery stem-cell transplantation: multidisciplinary efforts to improve outcomes in older adults undergoing hematopoietic stem-cell transplant. *JCO Oncol Pract*. 2023;19(3):e417-e427.
40. 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.

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