HHS Public Access

Author manuscript

Curr Geriatr Rep. Author manuscript; available in PMC 2018 February 21.

Published in final edited form as:

Curr Geriatr Rep. 2017 December ; 6(4): 247–254. doi:10.1007/s13670-017-0227-8.

Comorbidity, Physical Function, and Quality of Life in Older Adults with Acute Myeloid Leukemia

Susan Storey, PhD, RN, AOCNS [Assistant Professor],
Indiana University School of Nursing, Indianapolis, IN 46202

Tamryn Fowler Gray, RN, MSN, BMTCN, CNL [PhD Candidate], and
Johns Hopkins University, School of Nursing

Ashley Leak Bryant, PhD, RN-BC, OCN [Assistant Professor]
School of Nursing, The University of North Carolina at Chapel Hill, 401 Carrington Hall, #7460, Chapel Hill, NC 27599, Office: 919-966-5628

Abstract

Purpose of review—To describe the pathology, impact of comorbidities, functional limitations, symptoms, and quality of life (QOL) related to treatment of acute myeloid leukemia (AML) in older adults.

Recent findings—AML is a rare aggressive hematologic disease that occurs most often in older adults. The prognosis for older patients with AML is markedly worse due to genetic mutations and patient characteristics such as comorbidities and functional limitations. Patient characteristics may influence treatment decisions, as well as impact symptoms, functional ability, health-related outcomes and (QOL).

Summary—As the population continues to age, the number of people diagnosed with AML is expected to increase. Better management of comorbidities is imperative to improving QOL and other treatment related outcomes. Prospective, longitudinal and multi-site studies are warranted to further understand the interaction between these characteristics on symptoms, outcomes and QOL.

Keywords

Acute myeloid leukemia; older adults; patient reported outcomes; symptoms; physical function; quality of life; comorbidities

Introduction

Acute myeloid leukemia (AML) is a rare aggressive hematologic disease that afflicts 3–4 persons per 100,000 individuals annually (1, 2). In the United States, estimates predict 21,830 new cases of AML with approximately 10,590 AML related deaths in 2017 (3). The risk for AML increases with age, and recent Surveillance Epidemiology and End Results Data (SEER) indicates that over 70% of new AML cases are diagnosed in adults ≥ 55 years of age with the median age of diagnosis being 67 years of age (1, 4). The prognosis for older

Correspondence to: Ashley Leak Bryant.

patients diagnosed with AML is notably worse due to poor cytogenetic characteristics, genetic mutations that confer resistance to chemotherapy and patient clinical characteristics such as comorbidities and physical function (5, 6).

AML is a disease of the hematopoietic system in the bone marrow resulting in a transformation of leukocytes and leukocyte precursors into malignant cells (7). A large number of these immature, abnormal cells proliferate rapidly and accumulate in the bone marrow suppressing the hematopoietic system (7). The etiology of leukemia is unknown, environmental exposure, genetic characteristics and the process of aging can cause a gradual deterioration of the immune system (immunosenescence), increasing the risk for the development of AML (8). The normal aging process creates a milieu of persistent low-grade inflammation, known as “inflammaging” which is characterized by increased levels of circulating pro-inflammatory cytokines, (IL-1, IL-6 and TNF-α) (9, 10). These pro-inflammatory cytokines facilitate cellular aberrations that decrease the ability of the immune system to conduct its usual surveillance and immune-editing activities when exposed to foreign pathogens and/or self-antigens (11, 12). Continuous exposure of cells to systemic inflammation throughout the aging process is a contributing factor in the increased vulnerability to cancer, infectious diseases, diabetes, heart disease, neurodegeneration and other age related chronic comorbid diseases (9, 10, 13). Additionally, environmental exposures to benzene and ionizing radiation have also been associated with an increased risk for leukemias (14).

The treatment regimen for AML is aggressive and associated with high acuity, fluctuating symptoms and a high financial cost. Standard regimens involve cycles of induction chemotherapy, consolidation chemotherapy, and when appropriate, allogeneic hematopoietic cell transplantation; with the goal of achieving complete remission with possible cure of the disease (15, 16). Older individuals, often do not tolerate aggressive therapies and are more likely to experience poor health outcomes such as longer neutropenia (low white blood cell count), increased rates of infection and longer hospital length of stay (17–19). Additionally, older patients with AML are less likely to achieve complete remission and remain relapse free compared to their younger counterparts (15, 20). The disparity in these outcomes among younger versus older patients (< 60 years of age vs ≥ 60 years of age) may be due to differences in cytogenetics, subsequent resistance to chemotherapy, treatment-related toxicity, immune suppression resulting in increased vulnerability to bacterial and fungal infections, decreased physical functional reserve, organ dysfunction and/or comorbidities (6, 8, 20–24). Changes to physical and functional abilities may be exacerbated due to the treatment regimens for AML. Side effects from treatment, in addition to managing comorbidities, can affect health outcomes and overall quality of life (QOL). Managing comorbidities, improving health outcomes, and maintaining QOL for older patients with AML is important to consider during and after treatment. Little is known regarding the impact of comorbidities, physical function, and symptoms on the QOL and health outcomes of older patients receiving treatment for AML. Therefore, the purpose of this short review is to describe comorbidity, symptoms and QOL experienced by older adults with AML. Specifically, this review will focus on the comorbidities and measures used in AML, and QOL related to treatment in older adults with AML.

Comorbidities and AML

Advanced age is often accompanied by frailty and comorbidities, which have an important impact on the tolerance that older patients diagnosed with AML may have to intensive treatment modalities (1). Treatment choice also depends on a variety of factors, including age, performance status, and comorbidities (25). Studies have shown older patients with AML can benefit from standard therapy regimens; however, there is often reluctance among clinicians especially in the presence of comorbidities due to the difficulty of predicting risk/benefits of available therapies (11, 17, 26). Concern of treatment toxicity and/or mortality may influence clinicians' decisions regarding treatment regimen and/or reduction in the intensity of treatment (21).

Researchers have demonstrated that comorbidities are an independent predictor of all-cause mortality in patients with AML (24, 27, 28). In one prospective observational study examining change in QOL scores and their association with therapy and survival in older adults with AML, researchers found at least one comorbid disease was present in 70% patients with AML in the palliative treatment group and 48% of those in the intensive treatment group (15). Several important prognostic factors for AML such as age, gender, and socioeconomic status are associated with comorbidity, and these factors may potentially explain the adverse effect of comorbidity on prognosis (29).

There are also health-related outcomes to consider when examining treatment related to older adults with AML. For example, studies of older adults with AML have shown a relationship between increased comorbidity burden and worse outcomes including toxicity, hospital readmission rates, 30-day mortality, and worse overall survival (24, 28, 30). Although the initial therapy for AML has been standardized and forms the backbone of clinical trials, some patients do not receive conventional therapy at diagnosis due to existing or potential comorbidities which may also impact prognosis and health outcomes (8).

Diabetes is a common comorbidity that occurs with aging (31). Older patients with comorbid diabetes and cancer have been found to have poorer health outcomes than cancer patients without diabetes (32–34). In older patients with AML, diabetes was found to be adversely associated with 30-day survival rates (30). Hyperglycemia defined as a blood glucose ≥ 140 mg/dL (35), has been noted to occur in up to 38% of hospitalized patients including those with a diagnosis of diabetes and those without diabetes (36). The onset of hyperglycemia can occur in those with and without a diagnosis of diabetes, a recent review noted 11% of inpatients with no prior history of diabetes experienced hyperglycemia (37).Diabetes and/or hyperglycemia are often exacerbated by the administration of glucocorticosteroids as part of the chemotherapy treatment regimen (38). Standard screening of patients with AML prior to the onset of treatment could be beneficial in predicting and managing those patients who may be a higher risk for exacerbation of their diabetes and/or the development of hyperglycemia. Independent of a diagnosis of diabetes, hyperglycemia has been shown to impact the health outcomes of patients with cancer (39, 40). For example, patients with AML who experienced hyperglycemia were found to have a greater risk for infection, (19, 41), sepsis, (42), longer hospital length of stay (18) and mortality. However,

inconsistencies in definitions and measurement practices between studies make it difficult to interpret the full impact of hyperglycemia on health outcomes(43).

Comorbidity Measures in AML

There are risk assessments that help to measure the potential impact of comorbidities on health outcomes related to survival and mortality rates. The Charlson Comorbidity Index (CCI) and Hematopoietic Cell Transplantation-Specific Comorbidity Index (HCT-CI) are frequently used to measure comorbidities (44). The CCI assigns point values for certain comorbidities, some of which are stratified for severity (44). The original CCI has been revised slightly for use in older adults with AML (44). A single-center retrospective study showed that patients with a CCI score >1 had a significantly lower chance of attaining a complete remission compared to those with a score of 0 or 1 (35 versus 63%, respectively) (44). The group with higher CCI scores also showed a trend toward higher 8-week mortality and lower 2-year survival (44). The HCT-CI was developed to improve the sensitivity of the CCI in the stem cell transplant setting, but has been evaluated as a tool to predict outcomes with intensive induction chemotherapy for AML as well (44). Overall, the importance of comorbidities has not been well established in older patients with AML. However, it has been shown that AML cancer survivors who have comorbid disease(s) experience lower levels of QOL, (45) have poorer physical function, and less able to self-manage their disease (46). The assessment of comorbidities prior to treatment is critically important to better facilitate choice of treatment options. More research is necessary to determine which comorbid risk assessment tool best identifies the comorbidity or cluster of comorbid conditions that exert the most influence on the health outcomes of older patients with AML. The impact of comorbidities on the severity of symptoms experienced by older patients with AML is unknown. Future research should examine the interaction between a diagnosis of AML, comorbidities, and normal aging health related issues on symptom severity.

Symptom and Physical Function Changes for Older Adults with AML

Fatigue has been found to be the most common, distressing symptom that has been reported by more than 90% of adults with AML during treatment (47, 48). Fatigue significantly impacts QOL, leading to restrictions in activities of daily living (ADLs), and is particularly severe during chemotherapy (48, 49). Hospitalization can be detrimental to adults with AML as it can reduce functional abilities, endurance, and overall health (50, 51). Functional decline is a major concern for older adults with AML. Irrespective of previous physical ability or frailty, older adults who are hospitalized are at an increased risk for disability (52). Furthermore, hospital length of stays can be up to 35% longer for those who require assistance from basic activities, such as dressing and bathing, to more complex activities like pain management (53). A central focus of cancer rehabilitation is improvement of body function, fatigue and overall QOL (54–56). Therefore, exercise has been introduced to various cancer populations during and post-treatment due to its positive impact on physical health, fatigue, symptoms and functioning.

The American College of Sports Medicine published exercise guidelines for cancer survivors which recommend that survivors of cancer achieve 150 minutes of moderate to

vigorous intensity aerobic activity weekly (57). There are several physical (symptom reduction) and psychological benefits (decreased anxiety and depressive symptoms) associated with exercise for survivors (57–59). Before a patient starts to exercise, a functional assessment is recommended to be completed by professionals such as occupational therapists, physical therapists, recreational therapists, exercise physiologists, or a registered nurse. Common functional measures used in practice and research are Eastern Cooperative Oncology Group (ECOG), clinician or patient rated Karnofsky Performance Scale (KPS) that quantify and capture how well an individual is able to engage in daily activities while having AML and determine how well the individual will be able to tolerate. The geriatric assessment is a more comprehensive approach to assess function as ECOG and KPS are crude assessments of function (Table 1).

Five exercise studies conducted in patients with AML have shown beneficial effects on cardiorespiratory fitness, muscle strength and functional mobility (47, 60–63). These benefits are critical in ensuring that the patient remains active and functional during their hospitalization and after hospital discharge. Most of these studies involved small sample sizes (10–35), and statistically significant improvements in symptoms such as fatigue, anxiety, depression or QOL were found (5, 47, 60, 64)(Table 2).

Quality of Life in AML

Recognized as one of the most important patient-reported outcomes, QOL includes physical, psychological, emotional,, spiritual, and sexual function domains (7,51,(65). An AML diagnosis may significantly impact QOL of affected individuals, which is underscored by the fact that 97% of patients older than 60 years with AML report that QOL is more important than length of life (65). Given the short life expectancy of many older patients with AML and the low likelihood of cure, patients may wish to consider the impact of cancer therapy on their QOL (66). Therefore, maximizing QOL should be an important goal when treating this population and eliciting patient preferences and goals of treatment are necessary to formulate a personalized treatment plan. The optimal target should be to cure the disease without compromising on patient’s QOL, as well as maintaining general functioning and cognition in the long term (1).

The psychosocial burden of disease as a psychosocial construct in terms of the in older patients with AML is huge for the patient, especially during active treatment (1). In the context of this paper, the psychological burden of disease refers to the emotional stress of living with a diagnosis of cancer and its treatment, fear of recurrence, and the distress imposed by living with the day-to-day physical problems that can create new or worsen preexisting psychological distress for people living with cancer, their families, and other informal caregivers (67).

Cancer is a stressful time for both patients and family members who are often expected to deal with cancer-related symptoms (68). Spirituality, a fundamental element of human experience that encompasses the individual’s search for meaning and purpose in life, could be an important factor that helps a person in coping with the disease process (69). Quality of life may be influenced by an individual’s previous health status prior to the cancer diagnosis.

Evidence suggests that for “fit” patients, older age is associated with QOL and physical function similar to those of younger patients during and after intensive chemotherapy (20). Furthermore, coping strategies are an integral role in survivorship, and interventions to enhance effective coping are instrumental to improve adaptation and leukemia survivors’ QOL (70).

Since intensive chemotherapy is known to be rarely beneficial for frail older adults or those with poor-risk disease, AML may be better-managed using palliative care approaches that focus on QOL and symptom management (15, 44). Despite the poor prognosis associated with AML, palliative care and hospice services are rarely used (66). This population could benefit from early referral to palliative care concurrently while pursuing induction chemotherapy (66). For example, patients who are deemed too frail for myelosuppressive therapy because of multiple comorbidities, may benefit from low-intensity therapies (such as low-dose cytarabine) in conjunction with palliative care (71, 72). Early integration of palliative care improves QOL and symptom burden and decreases health service utilization in patients with solid malignancies. Employing a similar strategy in older adults with AML may prove valuable in improving QOL and health care delivery.(66). However, the absence of a clear transition between the curative and palliative phases of disease for older patients with AML may hamper the receipt of hospice services (66). Research comparing health care utilization and end-of-life care in older patients with AML found that only a minority of patients dying of AML utilized Hospice services. The frequent need for blood product support, which many hospice organizations do not permit because of financial constraints, likely contribute to lower rates of hospice referrals (66). More research is needed to assess the availability and impact of palliative care and hospice services on QOL in this population.

Older adults with AML are commonly underrepresented in clinical trials, often due to poor performance status, abnormal organ function, or active infection (73, 74). Poor representation in clinical trials leads to inadequate evidence and knowledge about responses of older patients to medications (2, 75). Major medical breakthroughs in cancer could not happen without the generosity of clinical trial participants young and old; therefore, it is important for research to include participants of different age, sex, race, and ethnicity (75). The lack of recruitment and participation of older adults in clinical trials results in medical decisions for older adults being routinely based on data derived from studies of younger adults (76). Older adults represent the fastest-growing population nationwide. Therefore, the evaluation of new treatment therapies in the older adult population is becoming a major issue.

The National Comprehensive Cancer Network, an alliance of leading cancer centers, explicitly state clinical trials as the preferred option in patients with untreated AML who are aged 60 years and older (73). With longer life expectancy, there is an anticipation that treatments will cure and improve QOL (75). Hence, there is a clear need for evidence-based interventions for older adults. Evidence-based data ensures that therapies are prescribed to the older patient when they may offer a meaningful gain in survival, QOL or both, and avoided in situations in which they may not be beneficial (77).

Conclusions

Caring for the patient holistically is the goal of patient centered care—better management of comorbidities and symptoms can lead to improved physical function, ultimately enhancing QOL. Currently, AML remains a high mortality disease for adults. Additionally, only a few drug studies have incorporated patient reported outcomes (PROs) and even less have tracked how these change over time. More clinical trial studies that incorporate PROs from older adults with AML are needed to increase our knowledge about ways to improve physical function and maximize QOL because maintaining or improving function during treatment is critical. Inclusion of patients in clinical trials who are frail, unfit or who have high-risk disease should be strongly encouraged by providers. We encourage oncology providers to incorporate more comprehensive patient assessments tailored to older adults to assess fitness and develop personalized strategies with the interdisciplinary team to improve the care of older adults with AML.

Future Directions

As the population grows older, the number of estimated cases for AML will also rise. Integration of electronic symptoms into routine electronic records and care remains a high priority. Future large scale, multi-centered longitudinal randomized trials are warranted to measure the effects of comorbidities on physical and psychological variables of interest, in addition to QOL. Studies that test self-management interventions such as exercise are also needed to assess its impact on the management of comorbidities, and subsequent improvement of symptoms and physical function, thereby improving QOL for older patients with AML.

References

1**. Almeida AM, Ramos F. Acute myeloid leukemia in the older adults. Leukemia research reports. 2016; 6:1–7. This study provides evidence for how the most frail and oldest among the oldest will have the least net benefit from chemotherapy or hematopoietic transplantation, even if they receive the best available treatment, while the fittest and youngest patients will benefit most. [PubMed: 27408788]

2. Krug U, Buchner T, Berdel WE, Muller-Tidow C. The treatment of elderly patients with acute myeloid leukemia. Deutsches Arzteblatt international. 2011; 108(51–52):863–70. [PubMed: 22259641]

3. American Cancer Society. Cancer Facts & Figures. 2017. Available from: https://www.cancer.org/research/cancer-facts-statistics/all-cancer-facts-figures/cancer-facts-figures-2017.html

4. NC, I. SEER Stat Fact Sheets: acute myeloid leukemia (AML). Bethesda, MD: National Cancer Institute; Available from: 2015http://seer.cancer.gov/statfacts/html/amyl.html

5. Klepin HD, Danhauer SC, Tooze JA, Stott K, Daley K, Vishnevsky T, et al. Exercise for older adult inpatients with acute myelogenous leukemia: a pilot study. Journal of geriatric oncology. 2011; 2(1): 11–7. [PubMed: 23843929]

6**. Sanford D, Ravandi F. Management of Newly Diagnosed Acute Myeloid Leukemia in the Elderly: Current Strategies and Future Directions. Drugs & aging. 2015; 32(12):983–97. This study suggests the importance of assessing fitness for intensive induction therapy in older adults using a standardized approach that incorporates performance status, burden of comorbidities, and patient preferences, as well as assessment for enrollment in clinical trials when available and feasible in the management of AML in older adults. [PubMed: 26446152]

7. American Cancer Society. What is Acute Myeloid Leukemia?. 2017. Available from: https://www.cancer.org/cancer/acute-myeloid-leukemia/about/what-is-aml.html

8. Vey N. Targeting age-related changes in the biology of acute myeloid leukemia: is the patient seeing the progress? Interdisciplinary topics in gerontology. 2013; 38:73–84. [PubMed: 23503517]

9. Baylis D, Bartlett DB, Patel HP, Roberts HC. Understanding how we age: insights into inflammaging. Longevity & healthspan. 2013; 2(1):8. [PubMed: 24472098]

10. Pawelec G, Goldeck D, Derhovanessian E. Inflammation, ageing and chronic disease. Current opinion in immunology. 2014; 29:23–8. [PubMed: 24762450]

11**. Klepin HD. Elderly acute myeloid leukemia: assessing risk. Current hematologic malignancy reports. 2015; 10(2):118–25. Physiologic changes of aging that decrease treatment tolerance also influence outcomes and vary among patients of the same chronologic age so improving risk prediction for older adults is important in improving the chances that older adults will tolerate and benefit from therapies. [PubMed: 25939828]

12*. Wang ES. Treating acute myeloid leukemia in older adults. Hematology American Society of Hematology Education Program. 2014; 2014(1):14–20. Treatment of older adults with AML is challenging because there is no consensus regarding optimal therapy. [PubMed: 25696830]

13. Fulop T, et al. Aging, frailty and age-related diseases. Biogerontology. 11(5):547–63.

14. American Cancer Society. What Are the Risk Factors for Acute Myeloid Leukemia?. 2017. Available from: https://www.cancer.org/cancer/acute-myeloid-leukemia/causes-risks-prevention/risk-factors.html

15. Oliva EN, Nobile F, Alimena G, Ronco F, Specchia G, Impera S, et al. Quality of life in elderly patients with acute myeloid leukemia: patients may be more accurate than physicians. Haematologica. 2011; 96(5):696–702. [PubMed: 21330327]

16. Preussler JM, Meyer CL, Mau LW, Majhail NS, Denzen EM, Edsall KC, et al. Healthcare Costs and Utilization for Patients Age 50 to 64 Years with Acute Myeloid Leukemia Treated with Chemotherapy or with Chemotherapy and Allogeneic Hematopoietic Cell Transplantation. Biol Blood Marrow Transplant. 2017; 23(6):1021–8. [PubMed: 28263920]

17. Oran B, Weisdorf DJ. Survival for older patients with acute myeloid leukemia: a population-based study. Haematologica. 2012; 97(12):1916–24. [PubMed: 22773600]

18**. Storey S, Von Ah D. Prevalence and impact of hyperglycemia on hospitalized leukemia patients. European journal of oncology nursing : the official journal of European Oncology Nursing Society. 2015; 19(1):13–7. The findings from this study provide preliminary evidence demonstrating hyperglycemia in the leukemia patient is common and has detrimental effects on clinical outcomes; specifically patients with hyperglycemia were 1.6 times more likely ($p < 0.01$) to experience neutropenia than those without hyperglycemia, and hospital length of stay was significantly longer in patients with hyperglycemia (2 days versus 15 days; $p < 0.001$). [PubMed: 25227459]

19**. Storey S, Von Ah D. Impact of Hyperglycemia and Age on Outcomes in Patients With Acute Myeloid Leukemia. Oncology nursing forum. 2016; 43(5):595–601. This study provides preliminary evidence that hyperglycemia may have harmful consequences during initial induction for AML, particularly among those ≥65; these patients had 5.6 ($p = .022$) times greater risk of infection than those < 65; more days of neutropenia were found but not statistically significant. [PubMed: 27541552]

20. Klepin HD, Rao AV, Pardee TS. Acute myeloid leukemia and myelodysplastic syndromes in older adults. Journal of clinical oncology : official journal of the American Society of Clinical Oncology. 2014; 32(24):2541–52. [PubMed: 25071138]

21. Klepin HD. Elderly acute myeloid leukemia: assessing risk. Current hematologic malignancy reports. 2015; 10(2):118–25. [PubMed: 25939828]

22. Etienne A, et al. Comorbidity is an independent predictor of complete remission in elderly patients receiving induction chemotherapy for acute myeloid leukemia. Cancer. 2007; 109(7):1376–83. [PubMed: 17326052]

23*. Nazha A, Ravandi F. Acute myeloid leukemia in the elderly: do we know who should be treated and how? Leuk Lymphoma. 2014; 55(5):979–87. This review highlights the challenges of treating older adults with AML (including combination of less toxic agents and other non-toxic

therapies, novel targeted agents, resource utilization and allocation, and identifying suitability among patients for aggressive treatment therapies) and the divergent views between physicians and patients about determining fitness for intensive chemotherapy. [PubMed: 23885839]

24**. Djunic I, Virijevic M, Novkovic A, Djurasinovic V, Colovic N, Vidovic A, et al. Pretreatment risk factors and importance of comorbidity for overall survival, complete remission, and early death in patients with acute myeloid leukemia. Hematology (Amsterdam, Netherlands). 2012; 17(2):53–8. The aim of this study was to detemine which factors are associated with poor prognosis in patients with AML of all ages, and results found that in patients aged 55 years, the most significant predictor of poor overall survival and early death was comorbidity.

25. Ofran Y, Tallman Martin S, Rowe Jacob M. How I treat acute myeloid leukemia presenting with preexisting comorbidities. Blood. 2016; 128(4):488–96. [PubMed: 27235136]

26. Thomas X, Caroline Lejeune. Blinatumomab in acute lymphoblastic leukemia. Expert Rev Anticancer Ther. 2016; 16(3):251–3. [PubMed: 26775917]

27. Etienne A, Esterni B, Charbonnier A, Mozziconacci MJ, Arnoulet C, Coso D, et al. Comorbidity is an independent predictor of complete remission in elderly patients receiving induction chemotherapy for acute myeloid leukemia. Cancer. 2007; 109(7):1376–83. [PubMed: 17326052]

28**. Mohammadi M, Cao Y, Glimelius I, Bottai M, Eloranta S, Smedby KE. The impact of comorbid disease history on all-cause and cancer-specific mortality in myeloid leukemia and myeloma - a Swedish population-based study. BMC Cancer. 2015; 15:850. Comorbidity increases overall mortality in patients diagnosed with hematological malignancies. The impact of comorbidity on cancer-specific mortality, taking competing risks into account, has not been evaluated. [PubMed: 26537111]

29. Ostgard LS, Norgaard JM, Sengelov H, Severinsen M, Friis LS, Marcher CW, et al. Comorbidity and performance status in acute myeloid leukemia patients: a nation-wide population-based cohort study. Leukemia. 2015; 29(3):548–55. [PubMed: 25092141]

30. Tawfik B, et al. Comorbidity, age, and mortality among adults treated intensively for acute myeloid leukemia (AML). Journal of geriatric oncology. 2016; 7(1):24–31. [PubMed: 26527394]

31. Giovannucci E, Harlan DM, Archer MC, Bergenstal RM, Gapstur SM, Habel LA, et al. Diabetes and cancer: a consensus report. CA Cancer J Clin. 2010; 60(4):207–21. [PubMed: 20554718]

32. Onitilo AA, Engel JM, Glurich I, Stankowski RV, Williams GM, Doi SA. Diabetes and cancer I: risk, survival, and implications for screening. Cancer Causes Control. 2012; 23(6):967–81. [PubMed: 22552844]

33. Renehan AG, Yeh HC, Johnson JA, Wild SH, Gale EA, Moller H, et al. Diabetes and cancer (2): evaluating the impact of diabetes on mortality in patients with cancer. Diabetologia. 2012; 55(6): 1619–1632. [PubMed: 22476948]

34*. Vissers PA, Falzon L, van de Poll-Franse LV, Pouwer F, Thong MS. The impact of having both cancer and diabetes on patient-reported outcomes: a systematic review and directions for future research. Journal of cancer survivorship : research and practice. 2016; 10(2):406–15. This systematic review demonstrates that the presence of both cancer and diabetes resulted in worse patient reported outcomes (heath-related quality life), compared to having either one of the diseases independently, and highlighting the need for more studies. [PubMed: 26428396]

35. Association AD. Standards of Medical Care in Diabetes. Diabetes Care. 2017; 40(1):S1–132. [PubMed: 27979885]

36. Umpierrez GE, et al. Management of hyperglycemia in hospitalized patients in non-critical care setting: an endocrine society clinical practice guideline. The Journal of Clinical Endocrinology & Metabolism. 2012; 97(1):16–38. [PubMed: 22223765]

37**. Brady VJ, Grimes D, Armstrong T, LoBiondo-Wood G. E355–365. Management of steroid-induced hyperglycemia in hospitalized patients with cancer : A review. Oncology nursing forum. 2014; 41(6):E355–65. This review of literature noted the occurrence of hyperglycemia in hospitalized patients with cancer irrespective of whether patients have a prior history of diabetes. [PubMed: 25355031]

38. Hammer MJ, Motzer SA, Voss JG, Berry DL. Glycemic control among older adult hematopoietic cell transplant recipients. Journal of gerontological nursing. 2010; 36(2):40–50.

39**. Storey S, Diane Von Ah. Impact of malglycemia on clinical outcomes in hospitalized patients with cancer: a review of the literature. Oncology nursing forum. 2012; 39(5) This review of literature examined the findings of 11 research articles that reported the impact of malglycemia (mostly hyperglycemia) on the various outcomes (infection, mortality, survival, toxicity and length of stay) among patients with heterogeneous types of cancer.

40*. Olausson JM, Marilyn J. Hammer, and Veronica Brady. The impact of hyperglycemia on hematopoietic cell transplantation outcomes: an integrative review. Oncology nursing forum. 2014; 41(5) This integrative review of published literature found associations between hyperglycemia and infection, time to engraftment, development of acute graft-versus-host disease, length of stay, and overall survival among HCT patients.

41. Matias Cdo N, Lima V, Teixeira HM, Souto FR, Magalhaes V. Hyperglycemia increases the complicated infection and mortality rates during induction therapy in adult acute leukemia patients. Revista brasileira de hematologia e hemoterapia. 2013; 35(1):39–43. [PubMed: 23580883]

42. Ali NA, O'Brien JM Jr, Blum W, Byrd JC, Klisovic RB, Marcucci G, et al. Hyperglycemia in patients with acute myeloid leukemia is associated with increased hospital mortality. Cancer. 2007; 110(1):96–102. [PubMed: 17534900]

43. Storey S, Von Ah D, Hammer MJ. Measurement of Hyperglycemia and Impact on Health Outcomes in People With Cancer: Challenges and Opportunities. Oncology nursing forum. 2017; 44(4):E141–e51. [PubMed: 28632250]

44. Pettit K, Olatoyosi Odenike. Defining and treating older adults with acute myeloid leukemia who are ineligible for intensive therapies. Frontiers in oncology. 2015

45. Deschler B, Ihorst G, Platzbecker U, Germing U, Marz E, de Figuerido M, et al. Parameters detected by geriatric and quality of life assessment in 195 older patients with myelodysplastic syndromes and acute myeloid leukemia are highly predictive for outcome. Haematologica. 2013; 98(2):208–16. [PubMed: 22875615]

46. Hershey DS, Given B, Given C, Corser W, von Eye A. Predictors of diabetes self-management in older adults receiving chemotherapy. Cancer Nurs. 2014; 37(2):97–105. [PubMed: 23519039]

47. Alibhai SM, O'Neill S, Fisher-Schlombs K, Breunis H, Brandwein JM, Timilshina N, et al. A clinical trial of supervised exercise for adult inpatients with acute myeloid leukemia (AML) undergoing induction chemotherapy. Leukemia research. 2012; 36(10):1255–61. [PubMed: 22726923]

48. Leak Bryant A, Lee Walton A, Shaw-Kokot J, Mayer DK, Reeve BB. Patient-reported symptoms and quality of life in adults with acute leukemia: a systematic review. Oncol Nurs Forum. 2015; 42(2):E91–E101. [PubMed: 25806895]

49. Dombret H, Seymour JF, Butrym A, Wierzbowska A, Selleslag D, Jang JH, et al. International phase 3 study of azacitidine vs conventional care regimens in older patients with newly diagnosed AML with >30% blasts. Blood. 2015; 126(3):291–9. [PubMed: 25987659]

50. Krumholz HM. Post-hospital syndrome--an acquired, transient condition of generalized risk. N Engl J Med. 2013; 368(2):100–2. [PubMed: 23301730]

51. Mariano C, Williams G, Deal A, Alston S, Bryant AL, Jolly T, et al. Geriatric Assessment of Older Adults With Cancer During Unplanned Hospitalizations: An Opportunity in Disguise. Oncologist. 2015; 20(7):767–72. [PubMed: 26032136]

52. Gill TM, Allore HG, Holford TR, Guo Z. Hospitalization, restricted activity, and the development of disability among older persons. Jama. 2004; 292(17):2115–24. [PubMed: 15523072]

53. Chuang KH, Covinsky KE, Sands LP, Fortinsky RH, Palmer RM, Landefeld CS. Diagnosis-related group-adjusted hospital costs are higher in older medical patients with lower functional status. J Am Geriatr Soc. 2003; 51(12):1729–34. [PubMed: 14687350]

54. Law M, Sandy Steinwender, Leanne Leclair. Occupation, health and well-being. Canadian Journal of Occupational Therapy. 1988; 65(2):81–91.

55. Law M. Participation in the occupations of everyday life. The American journal of occupational therapy : official publication of the American Occupational Therapy Association. 2002; 56(6): 640–9. [PubMed: 12458856]

56. Vessby K, Anette Kjellberg. Participation in occupational therapy research: a literature review. British Journal of Occupational Therapy. 2010; 73(7):319–26.
57. Schmitz KH, Courneya KS, Matthews C, Demark-Wahnefried W, Galvao DA, Pinto BM, et al. American College of Sports Medicine roundtable on exercise guidelines for cancer survivors. Medicine and science in sports and exercise. 2010; 42(7):1409–26. [PubMed: 20559064]
58. Mustian KM, Sprod LK, Palesh OG, Peppone LJ, Janelsins MC, Mohile SG, et al. Exercise for the management of side effects and quality of life among cancer survivors. Curr Sports Med Rep. 2009; 8(6):325–30. [PubMed: 19904073]
59. Sprod LK, Mohile SG, Demark-Wahnefried W, Janelsins MC, Peppone LJ, Morrow GR, et al. Exercise and Cancer Treatment Symptoms in 408 Newly Diagnosed Older Cancer Patients. Journal of geriatric oncology. 2012; 3(2):90–7. [PubMed: 22712028]
60. Battaglini CL, Hackney AC, Garcia R, Groff D, Evans E, Shea T. The effects of an exercise program in leukemia patients. Integrative cancer therapies. 2009; 8(2):130–8. [PubMed: 19679621]
61. Bryant AL, Deal AM, Battaglini CL, Phillips B, Pergolotti, Coffman EM, Foster M, Wood WA, Bailey C, Hackney AC, Mayer DK, Muss H, Reeve BB. The Effects of Exercise on Patient-Reported Outcomes and Performance-Based Physical Function in Adults with Acute Leukemia undergoing Induction Therapy. ntegrative Cancer Therapies. 2017
62. Chang PH, Lai YH, Shun SC, Lin LY, Chen ML, Yang Y, et al. Effects of a walking intervention on fatigue-related experiences of hospitalized acute myelogenous leukemia patients undergoing chemotherapy: a randomized controlled trial. Journal of pain and symptom management. 2008; 35(5):524–34. [PubMed: 18280104]
63. Jarden M, Møller T, Kjeldsen L, Birgens H, Christensen JF, Christensen KB, et al. Patient Activation through Counseling and Exercise–Acute Leukemia (PACE-AL)–a randomized controlled trial. BMC cancer. 2013; 13(1):446. [PubMed: 24083543]
64. Chang P-H, Lai Y-H, Shun S-C, Lin L-Y, Chen M-L, Yang Y, et al. Effects of a walking intervention on fatigue-related experiences of hospitalized acute myelogenous leukemia patients undergoing chemotherapy: a randomized controlled trial. Journal of pain and symptom management. 2008; 35(5):524–34. [PubMed: 18280104]
65. Rogers BB. Advances in the management of acute myeloid leukemia in older adult patients. Oncology nursing forum. 2010; 37(3)
66. El-Jawahri AR, Abel GA, Steensma DP, LeBlanc TW, Fathi AT, Graubert TA, et al. Health care utilization and end-of-life care for older patients with acute myeloid leukemia. Cancer. 2015; 121(16):2840–8. [PubMed: 25926135]
67. Nazha A, Khoury JD, Verstovsek S, Daver N. Second line therapies in polycythemia vera: What is the optimal strategy after hydroxyurea failure? Critical Reviews in Oncology/Hematology. 2016
68. Taylor LK, et al. Potential prevention of small for gestational age in Australia: a population-based linkage study. BMC pregnancy and childbirth. 2013; 13(1):210. [PubMed: 24246011]
69. Puchalski CM, et al. Spirituality and health: the development of a field. Academic Medicine. 2014; 89(1):10–6. [PubMed: 24280839]
70. Ghodraty-Jabloo V, et al. Keep your mind off negative things: coping with long-term effects of acute myeloid leukemia (AML). Supportive Care in Cancer. 2016:2035–45. [PubMed: 26542270]
71. Amadori S. Treating older patients with AML. Leukemia supplements. 2012; 1(Suppl 2):S16–7. [PubMed: 27175234]
72. Burnett AK, Milligan D, Prentice AG, Goldstone AH, McMullin MF, Hills RK, et al. A comparison of low-dose cytarabine and hydroxyurea with or without all-trans retinoic acid for acute myeloid leukemia and high-risk myelodysplastic syndrome in patients not considered fit for intensive treatment. Cancer. 2007; 109(6):1114–24. [PubMed: 17315155]
73. Estey E. Acute myeloid leukemia and myelodysplastic syndromes in older patients. Journal of Clinical Oncology. 2007; 25(14):1908–15. [PubMed: 17488990]
74. Hamaker ME, Stauder R, van Munster BC. Exclusion of older patients from ongoing clinical trials for hematological malignancies: an evaluation of the National Institutes of Health Clinical Trial Registry. Oncologist. 2014; 19(10):1069–75. [PubMed: 25170014]

75. Shenoy P, Harugeri A. Elderly patients' participation in clinical trials. Perspectives in clinical research. 2015; 6(4):184–9. [PubMed: 26623388]

76. S, A. Elderly Representation in Clinical Trials: Not a Gray Area. InVentiv Health; 2014. Available from: InVentivHealthclinical.com

77. Siu LL. Clinical trials in the elderly--a concept comes of age. N Engl J Med. 2007; 356(15):1575–6. [PubMed: 17429089]

Table 1

Comprehensive Geriatric Assessment

Domain	Tests
Functional Status	Activities of Daily Living, Instrumental Activities of Daily Living Performance Status using ECOG and KPS Falls—Timed Up and Go
Comorbidity	Older American Resources and Services
Cognition	Blessed Orientation-Memory Concentration test
Psychologic	Hospital Anxiety and Depression Scale
Social Functioning	Medical Outcomes Survey (MOS) Social Activity Limitations
Social Support	MOS Support Survey: Emotional/Information and Tangible Susbscales
Nutrition	Body Mass Index, weight loss, mini-nutritional assessment

Table 2

AML Exercise Studies (n=6)

Author/Year	Design	Sample Size	Aerobic Exercise	Intensity & Measurement	Outcomes
Chang et al, 2008 (62)	RCT	22	Walking in hallway	12 min, 5 times/week	Lower levels of Anxiety, Depression Higher QOL, Emotional well-being
Battaglini et al, 2009 (60)	non-RCT	10	2 sessions (AM & PM) 5–10 min cycle/tread mill 5–15 min resistance 5–10 min core	3–4 times/week for 3–5 weeks	Lower levels of Fatigue, Anxiety, Depression, Higher QOL
Klepin et al, 2011 (5)	non-RCT	24	5–15 min walking 15 min strength & flexibility 5–15 min walking	3 times/week for 4 weeks offered Intensity: Mild (walking)	Lower level of Depression
Alibhai et al, 2012 (47)	non-RCT	35	10–40 min walk or bike 10–25 min resistance 5–10 min flexibility	4–5 times/week during induction treatment Intensity: Light to moderate	Lower Levels of Fatigue, Anxiety, Depression, Higher QOL
Jarden et al, 2013 (63)	non-RCT	17	Stationary cycling Dynamic and resistance training Relaxation training Walk program with step counter Health counseling	6 week exercise program 20 min/session with or without rest intervals, 3 days/week 20 min/session, 3 days/week 20 min/session, 3 days/week 1 day/week	Higher levels of Mental health, Vitality Lower level of Symptom burden and Symptom interference Higher QOL
Bryant et al, 2017 (61)	RCT	17	2 sessions (AM & PM) 5–10 min cycle/tread mill 5–15 min resistance 5–10 min core	4 times/week for 4–6 weeks	Lower levels of Fatigue, Anxiety, Depression, Sleep Disturbance, Improved Cognition Higher QOL