REVIEW ARTICLE

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Geriatric assessment in older patients with a hematologic malignancy: a systematic review

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ABSTRACT

The aim of this systematic review is to give an update of all currently available evidence on the relevance of a geriatric assessment in the treatment of older patients with hematologic malignancies. A systematic search in MEDLINE and EMBASE was performed to find studies in which a geriatric assessment was used to detect impaired geriatric domains or to address the association between geriatric assessment and survival or clinical outcome measures. The literature search included 4,629 reports, of which 54 publications from 44 studies were included. Seventy-three percent of the studies were published in the last 5 years. The median age of the patients was 73 years (range, 58-86) and 71% had a good World Health Organization (WHO) performance status. The median prevalence of geriatric impairments varied between 17% and 68%, even in patients with a good WHO performance status. Polypharmacy, nutritional status and instrumental activities of daily living were most frequently impaired. Whereas several geriatric impairments and frailty (based on a frailty screening tool or summarized geriatric assessment score) were predictive for a shorter overall survival, WHO performance status lost its predictive value in most studies. The association between geriatric impairments and treatment-related toxicity varied, with a trend towards a higher risk of (non-)hematologic toxicity in frail patients. During the follow-up, frailty seemed to be associated with treatment non-completion, especially when patients were malnourished. Patients with a good physical capacity had a shorter stay in hospital and a lower rate of hospitalization. Geriatric assessment, even in patients with a good performance status, can detect impaired geriatric domains and these impairments may be predictive of mortality. Moreover, geriatric impairments suggest a higher risk of treatment-related toxicity, treatment non-completion and use of healthcare services. A geriatric assessment should be considered before starting treatment in older patients with hematologic malignancies.

Introduction

Given the increasing life expectancy and aging of the population, there is a growing number of older patients with cancer, including patients with a hematologic malignancy. Worldwide, hematologic malignancies account for approximately 9% of all cancers and are the fourth most frequently diagnosed cancer.[1] At present, 60% of these patients are older than 65 years and this proportion will increase in the future.[2,3]

Over the last decades, treatment options for hematologic malignancies have progressed. For example, the initial treatment of patients with multiple myeloma changed from cytotoxic chemotherapeutics to better-tolerated agents such as immuno-modulatory drugs or monoclonal antibodies.[4] Moreover, the proportion of older patients with myelodysplastic syndrome or acute myeloid leukemia undergoing hematopoietic stem cell transplantation has increased, partly due to expansion of age limits.[5,6]

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However, it can be difficult to deliver optimal cancer treatment tailored to individual needs of an older patient, particularly as older patients are frequently excluded from clinical trials.[7] Older patients constitute a heterogeneous population due to large differences in comorbidity, functional capacity and psychological and physical reserves. As a result, the benefit of treatment can differ and patients with comorbidity or geriatric impairments are particularly at risk of adverse health outcomes. Choosing the optimal treatment for these patients is a challenge.

It is therefore recommended that the degree of frailty of older patients is assessed.[8] Frailty is a biological syndrome which can exist alongside age, comorbidity or disease characteristics. Over the years, numerous definitions of frailty have been formulated and there is still no consensus on a definition.[9] There are two commonly used approaches to define frailty. The first defines frailty based on phenotypic criteria including reduced grip strength, walking speed, physical capacity, level of energy and weight loss. Patients are considered frail if three or more criteria are present.[10] The second approach proposes a frailty index which is an accumulation of patient's deficits. These deficits consist of physical or cognitive symptoms, functional impairments, abnormal laboratory values and comorbidities.[11,12] In daily practice, frailty is a dynamic state which needs a multidimensional approach and might have various implications in different scenarios.

An appropriate method to assess the level of frailty of older patients is a geriatric assessment.[8,13] This consists of a systematic assessment of an older patient's health status focusing on somatic, psychological, functional and social domains. Different tools can be used to detect geriatric impairments in these domains.[14] Moreover, frailty screening tools were developed in order to identify older patients who require a full geriatric assessment.[15] Nowadays, some form of geriatric assessment is increasingly incorporated in hemato-oncologic care to customize hemato-oncologic treatment.[16]

In 2014, we published a systematic review on the value of performing a geriatric assessment in older patients with a hematologic malignancy, demonstrating that such an assessment can detect multiple health issues and has predictive value for clinical outcome in older patients with a hematologic malignancy.[17] However, evidence was limited, especially regarding clinical outcomes such as treatment-related toxicity, treatment completion or physical functioning after treatment. Since then, many new studies have been published on this subject. The aim of this present systematic review is, therefore, to give an update of all currently available data on the association between geriatric impairments and hematologic cancer-related outcomes.

Methods

Search strategy and article selection

Our aim was to identify studies concerning patients with a hematologic malignancy in which a geriatric assessment was used to detect geriatric impairments or which addressed the association between baseline geriatric assessment and outcome.

Geriatric assessment was defined as an assessment composed of at least two of the following domains: cognitive function, mood, nutritional status, activities of daily living (ADL), instrumental activities of daily living (IADL), polypharmacy (using five or more drugs), objectively measured physical capacity (for instance, gait speed, hand grip strength or balance tests), social support and frailty (assessed with a frailty screening tool or by summarizing the geriatric assessment). As prior medical history/comorbidity and performance status are routine parts of the hematologic work-up, these were not counted as domains of the geriatric assessment for this particular systematic review. The following items were defined as outcomes: prevalence of geriatric impairments, change in oncologic treatment plan, toxicity of chemotherapy, healthcare utilization, physical functioning after treatment, quality of life after treatment and mortality.

The following search was performed on March 4, 2019 and updated on January 20, 2020, in both MEDLINE and EMBASE: ((("Hematologic Neoplasms"[Mesh] OR "Leukemia"[Mesh] OR "Lymphoma"[Mesh] OR "Multiple Myeloma"[Mesh] OR "Myelodysplastic Syndromes"[Mesh] OR leukemia[tiab] OR leukaemia[tiab] OR lymphoma*[tiab] OR hodgkin*[tiab] OR non-hodgkin*[tiab] OR (multiple myeloma[tiab]) OR myelodysplas*[tiab] OR (haematolog* AND malignan*[tiab]) OR (hematolog* AND malignan*[tiab]) OR (myeloid[tiab] OR lymphoid[tiab] AND neoplas*[tiab]) OR myeloproliferative[tiab] OR (plasma cell neoplas*[tiab]) OR plasma cell dyscrasia*[tiab] OR (myeloid[tiab] AND sarcoma*[tiab]) OR waldenstrom[tiab] OR myelofibrosis[tiab] OR mastocystosis[tiab] OR (polycyth* AND vera[tiab]) OR (essential AND thrombocyt*[tiab]))) AND (("frailty"[All Fields] OR "Geriatric Assessment"[Mesh] OR frail*[tiab] OR vulnerabl*[tiab] OR geriatric assessment*[tiab] OR geriatric*[tiab]))

No age or language limitations were applied. All search results until 2013 were reviewed previously by Hamaker *et al.*[17] We therefore limited our search to studies published after January 1, 2013. The titles and abstracts of all studies retrieved by the search were assessed by one reviewer (ES) to determine which warranted further examination.The full texts of all potentially relevant articles were subsequently screened. We excluded studies that did not focus exclusively on hematologic malignancies. Finally, references of included studies were cross-referenced to retrieve any additional relevant citations. Eligible studies from all searches (2013, 2019, 2020) were subsequently combined to form the final study selection.

Data extraction

For each eligible study, data regarding study design and results were independently extracted by two authors (ES and AV). Extracted items included the type of study, study population (number of patients, median age, malignancy subtype, stage, treatment) and the content of the geriatric assessment. Only validated tools from the geriatric assessment were included. If multiple tools were used to assess one geriatric domain, the result of the most commonly used tool was noted. We registered the prevalence of geriatric impairments, and the reported results on the association between the geriatric assessment and outcome measures. If necessary, study authors were contacted to obtain additional data.

Quality assessment

The methodological quality of each of the studies was assessed independently by two reviewers (ES and AV), using the Newcastle-Ottawa scale adapted to this subject (*Online Supplementary Table S1*).[18] As our main focus was on older patients with hematologic malignancies, we classified studies of patients with a me(di)an age less than 68 years old, or with more than one third of the patients younger than 65 years old, as not being fully representative of our target population. Disagreements among the reviewers were discussed during a consensus meeting and in the case of persisting disagreement, the assistance of a third reviewer (MH) was enlisted.

Data synthesis and analysis

Due to the heterogeneity in the populations of patients and in study designs, with a wide variety in content of geriatric assessments, a meta-analysis was not considered feasible. We therefore summarized the study results to describe our main outcomes of interest.

Results

Study characteristics

The literature search yielded 4,629 citations (832 from MEDLINE and 3,797 from EMBASE), of which 403 were duplicates and 4,184 were excluded for other reasons (*Online Supplementary Figure S1*). This resulted in 42 eligible publications from 34 studies. Cross-referencing yielded four additional publications. Eight publications from the 2014 review by Hamaker *et al.*[17] were also eligible. Thus, we ultimately included 54 publications from 44 studies in this review.[19-72]

The characteristics of these 44 studies are summarized in Table 1. Seventy-three percent were published in the last 5 years. The median sample size of the studies was 100 (range, 25-869), and the me(di)an age of included patients ranged from 58 to 86 years. Eight studies focused on acute myeloid leukemia and/or myelodysplastic syndromes,[19-25,27] two on chronic lymphocytic leukemia,[28,29] 13 on lymphoma,[30-42] seven on multiple myeloma,[42-48] and

Table 1. Characteristics of studies on the association between the geriatric assessment and outcome measures.

Publication		Study population					GA		Outcome measures		
Author	Year	Patient population	Type of malignancy	N. of patients	Me(di)an age*	Treatment	N. of domains assessed	Summarized GA score	Prevalence of geriatric conditions	Survival	Other
Aguiar[19]	2020	65+	MDS	79	77 (70-84)	No disease-modifying therapy	3		+		
Corsetti[20]	2013	65+ or unfit for aggressive CT	AML; RAEB	31	72 (55-84)	CT	2	+	+	+	
Deschler[21]	2013	60+	AML; MDS	195	71 (60-87)	BSC; CT	5		+	+	
Holmes[22]	2014	60+	AML; MDS	50	65 (60-73)	HSCT	8	+	+		
Klepin[23]	2013	60+	AML	74	68 (65-74)	CT	5		+	+	
Klepin[24]	2020	60+	AML (FLT3)	40	68 (61-83)	CT	7		+	+	
Molga[25,26]	2020	65+	AML; MDS	98	77 (66-95)	BSC;CT	7		+	+	Treatment completion
Umit[27]	2018	no age limit	AML	372	63 (19-97)	CT	4		+	+	
Goede[28]	2016	no age limit	CLL	75	75 (48-87)	CT	3		+	+	Toxicity
Molica[29]	2019	65+	CLL	108	71 (65-90)	CT	2	+	+	+	Toxicity
Ribi[30]	2017	no age limit	B-cell lymphoma	41	75 (40-94)	Various	4	+	+	+	
Merli[31]	2020	65+ and unfit	DLBCL	33	82 (68-89)	CT	2		+		
Ong[32]	2019	60+	DLBCL	205	73 (60-97)	CT	2	+	+	+	Health care utilization, toxicity, treatment completion
Spina[33]	2012	70+	DLBCL	100	75 (70-89)	CT	4	+	+	+	Toxicity
Tucci[34]	2009	65+	DLBCL	84	73 (66-89)	CT	1	+	+	+	Toxicity
Tucci[35]	2015	69+	DLBCL	173	77	Various	2	+	+	+	
Aaldriks[36]	2015	70+	NHL	44	78 (70-86)	CT	3		+	+	Treatment completion
Naito[37]	2016	65+	NHL	93	77 (65-90)	Various	5		+	+	Toxicity
Park[38]	2015	65+	NHL	70	74 (65-92)	CT	4		+	+	Treatment completion
Siegel[39]	2006	60+	NHL	25	70 (60-85)	?	3		+		
Soubeyran[40]	2011	70+, unfit for aggressive CT	NHL	32	79 (70-92)	CT	4		+	+	
Winkelmann[41]	2011	18+	NHL	143	63 (18-88)	CT	2		+	+	
Okuyama[42]	2015	65+	Lymphoma; MM	106	74 (65-90)	CT	5	+	+		
Engelhardt[43]	2016	no age limit	MM	125	63 (56-71)	CT	2		+	+	
Gavriatopoulou[44]	2019	80+	MM	110	83 (80-92)	CT	3		+	+	
Palumbo[45]	2015	70+	MM	869	74 (70-78)	CT	2	+	+	+	Toxicity, Treatment completion
Rosko[46]	2019	18+	MM; amyloidosis	100	59 (36-75)	HSCT	6		+		Health care utilization
Wildes[47]	2019	65+	MM	40	71 (66-76)	BSC;HSCT	5		+		
Zhong[48]	2017	no age limit	MM	628	58 (52-66)	CT	2	+	+	+	Toxicity

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Buckstein[49]	2016	65+	Various	445	71 (65-79)	CT	3		+	+	
Deschler[50]	2018	60+	Various	106	66 (60-78)	HSCT	5		+	+	
Derman[51]	2019	60+	Various	192	>67 (60-83)	HSCT	5		+		
Dubruille[52]	2015	65+	Various	90	74 (65-89)	CT	8	+	+	+	
Dumontier[53]	2019	75+	Various	464	80 (76-84)	BSC; CT	3		+	+	Health care utilization
Hamaker[54]	2016	65+	Various	157	78 (67-99)	Various	7	+	+	+	
Huang[55]	2020	50+	Various	148	62 (50-76)	HSCT	6		+	+	Health care utilization, toxicity
Lin[56]	2020	60+	Various	457	66 (60-79)	HSCT	5		+	+	
Liu[57]	2019	75+	Various	448	80 (76-84)	BSC; CT	2	+	+	+	Health care utilization
Muffly[58]	2014	50+	Various	203	58 (54-63)	HSCT	3	+	+	+	
Nawas[59]	2019	50+	Various	184	61 (50-75)	HSCT	5		+	+	Health care utilization, toxicity
Rodrigues[60]	2020	60+	Various	40	68 (60-76)	HSCT	6	+	+		
Rollot-Trad[61]	2008	75+, geriatric department	Various	54	86 (75-99)	Various	4		+	+	
Silay[62]	2015	65+	Various	61	69	?	7		+		Health care utilization
Velghe[63]	2014	70+	Various	50	76 (70-87)	Various	6	+	+		

*Reported as mean (± standard deviation) or median (range or interquartile range). GA: geriatric assessment; MDS: myelodysplastic syndrome; CT: chemotherapy; AML: acute myeloid leukemia; RAEB: refractory anemia with excess of blasts; FLT3: FMS like tyrosine kinase-3; BSC: best supportive care; HSCT: hematopoietic stem cell transplantation; CLL: chronic lymphocytic leukemia; DLBCL: diffuse large B-cell lymphoma; NHL: non-Hodgkin lymphoma; MM: multiple myeloma.

15 studies included various hematologic malignancies.[49-63]

The median number of domains addressed in the geriatric assessment was four (range, 2-9). These included ADL in 30 studies (68%), IADL in 37 (84%), cognition in 29 (66%), mood in 24 (55%) and objectively measured physical capacity in 20 studies (46%). Domains less commonly assessed were nutritional status (11 studies; 25%), social support (8 studies; 18%), polypharmacy (13 studies; 30%) and frailty (8 studies assessed with a frailty screening tool and 17 studies by summarizing the geriatric assessment; 18% and 39%, respectively).

The prevalence of geriatric impairments was assessed in all studies (100%). The association between geriatric impairments and mortality was addressed in 33 studies (75%), treatment-related toxicity in ten studies (23%), treatment completion in five (11%) and healthcare utilization in seven studies (16%). No studies assessed the association of geriatric impairments with physical functioning or quality of life after treatment.

Quality assessment

The results of the quality assessment are shown in Figure 1. Detailed results per study are listed in *Online Supplementary Table S1*. The overall quality of the studies was good. Nine studies included a significant proportion of younger patients (i.e. median age less than 68 years old, or more than one third of the patients younger than 65 years old);[22,27,41,43,46,48,50,58,59] these studies were assessed as not being fully representative of the target cohort of the average older patients with a hematologic malignancy. Similarly, eight studies focused on a very specific treatment[20,23,24,31,51,55,56,60] which we considered as not fully representative of our target population. Overall, the duration of follow-up was sufficient but in nine studies the follow-up rate was less than 90%[24,30,46] or the adequacy of follow-up was not reported.[27,32,33,56,57,62] There were no other quality concerns.

Prevalence of geriatric impairments

The prevalence of geriatric impairments is shown in Table 2. The most commonly reported issues were polypharmacy (in a median of 51% of patients; range, 17-80%), risk of malnutrition (median 44%; range, 27-82%) and IADL impairments (median 37%; range, 3-85%). Impaired physical capacity (median 27%; range, 3-80%), ADL impairments (median 18%; range, 4-67%), symptoms of depression (median 25%; range, 10-94%), and cognitive impairment (median 17%; range, 0-44%) were less common. Four studies that addressed social support showed impairment in a median of 20% (range, 7-54%). The median proportion of patients seen as frail based on a frailty screening tool was 68% (range, 25-76%). The median proportion of patients screened as frail based on a summarized geriatric assessment score was 45% (range, 10-88%).

Overall, the median proportion of patients with at least one geriatric impairment was 51% (range, 9-82%). By comparison, the median proportion of patients with a World Health Organization (WHO) performance status of 2 or higher was only 29% (range, 1-91%). Even in studies in which the median age of patients was ≤65 years old, or a small proportion of patients had a poor WHO performance status, geriatric impairments were quite common. For example, in one study, 93% of included patients had a WHO performance status of 0-1; nonetheless, 45% of patients had impairments in IADL, 39% in physical capacity and 25% were frail based on a frailty screening tool (Table 2).[49]

Association between geriatric impairments and mortality

The association of geriatric impairments with mortality was addressed in 33 studies (Table 3). In univariate analysis, 27 out of 29 studies (93%) showed a significant association between at least one geriatric impairment and mortality. The association between a specific geriatric domain and mortality varied between 0 and 74%.

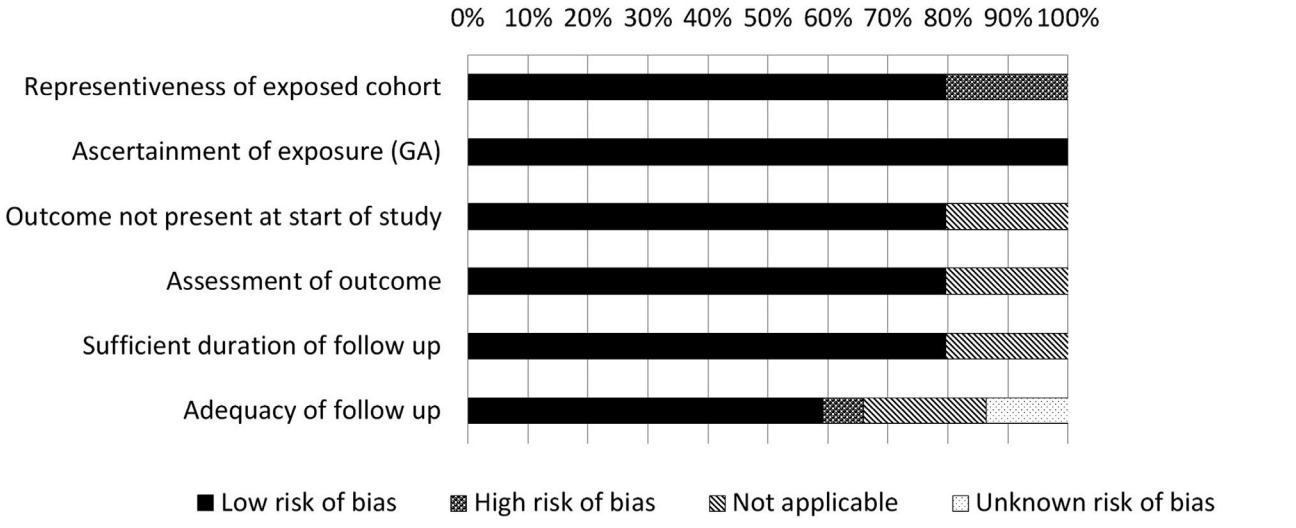

Figure 1. Outcome of the quality assessment. Details are reported in *Online Supplementary Table S1A* (quality assessment questionnaire) and *Online Supplementary Table S1B* (assessment per study).

Polypharmacy was assessed in only two studies and showed no association. For all other geriatric domains except mood, nutritional status and social support, at least 50% of the studies reported a univariate association between impairment and mortality. IADL, ADL, impaired physical capacity and cognition were most frequently associated with mortality (in 74%, 67%, 63% and 55% of the studies, respectively). In multivariable analyses, ADL, IADL, impaired physical capacity and cognition remained associated with mortality (in 40%, 62%, 50% and 50% of the studies, respectively). Moreover, at least 75% of all studies that assessed frailty (with a frailty screening tool or by summarizing the geriatric assessment), demonstrated that this was associated with mortality in multivariable analyses.

Risk factors for mortality commonly used in hemato-oncology such as age, WHO performance status and comorbidity were also associated with mortality in univariate analysis (in 79%, 63% and 64% of the studies, respectively). However, in multivariable analyses, this association was no longer present for WHO performance status; age and comorbidity retained their association with mortality in 43% and 47% of the studies, respectively.

Association of geriatric impairments with treatment-related toxicity

Ten studies assessed geriatric impairments in relation to treatment-related toxicity.[28,29,32-34,37,45,48,55,59] Four out of six studies in which frailty was assessed (based on a summarized geriatric assessment score) reported an association between frailty and treatment-related toxicity.[33,34,45,48] This included hematologic toxicity in one study,[33] non-hematologic toxicity in two studies[45,48] and overall toxicity in one study.[34] One study showed an association specifically between impaired IADL and treatment-related infections in patients with chronic lymphocytic leukemia.[28] In studies in which patients with various hematologic malignancies were included, associations between physical capacity[55] or cognition[59] and treatment-related toxicity were demonstrated. No other associations between frailty (based on a summarized geriatric assessment score) or individual geriatric domains and treatment-related toxicity were found in these ten studies.

Association of geriatric impairments with treatment completion

The association of geriatric impairments with the ability to complete the proposed treatment was studied in five studies.[25,32,36,38,45] Four out of five studies found an association between geriatric impairments and treatment completion. The risk of treatment non-completion was significantly higher in frail patients (based on a summarized geriatric assessment score or frailty screening tool) than in fit patients.[25,36,38,45] Three studies showed a significant association between a specifically geriatric domain and treatment non-completion: in two studies that included patients with non-Hodgkin lymphoma, malnutrition was associated with treatment non-completion.[36,38] Another study, in which patients with acute myeloid leukemia or myelodysplastic syndrome were included, showed an association between impaired IADL, impaired physical capacity or cognitive impairment and treatment non-completion. In this study, no other geriatric impairments or clinical characteristics such as comorbidity or WHO performance status were associated with treatment non-completion.[25]

Association of geriatric impairments with healthcare utilization

The association of geriatric impairments and health care utilization was addressed in seven studies.[32,46,53,55,57,59,62] Six out of these studies showed an association between geriatric impairments and health care utilization. In four studies impaired physical capacity was associated with increased use of health care.[46,55,57,62] In patients with various hematologic malignancies, other geriatric impairments, such as ADL,[62] IADL,[53] cognition[59] and mood[46] were also associated with health care utilization. In one study with patients with diffuse large B-cell lymphoma, no association was found between frailty (assessed by a summarized geriatric assessment score) and unplanned admissions.[32]

Table 2. Comparison of impaired performance status with impairments in geriatric domains.

Author	Year	Type of malignancy	N	Me(di)an age*	Poor PS	ADL	IADL	Cognition	Mood	Physical capacity	Nutritional status	Social support	Poly-pharmacy	Frailty screening tool	Summarised GA score
Aguiar[19]	2020	MDS	76	77 (70-84)	-	-	-	-	-	80 %	-	-	61 %	38 %	-
Corsetti[20]	2013	AML; RAEB	31	72 (55-84)	38 %	17 %	59 %	-	-	-	-	-	-	-	54 %
Deschler[21]	2013	AML; MDS	195	71 (60-87)	47 %	34 %	31 %	9 %	14 %	55 %	-	-	-	-	-
Holmes[22]	2014	AML; MDS	50	65 (60-73)	12 %	16 %		16 %	10 %	18 %	36 %	54 %	> 28 %	-	66 %
Klepin[23]	2013	AML	74	68 (65-74)	22 %	50 %	41 %	29 %	40 %	50 %	-	-	-	-	-
Klepin[24]	2020	AML (FLT3)	40	68 (61-83)	?	?	?	?	?	56 %	-	?	36 %	-	-
Molga[25,26]	2020	AML; MDS	98	77 (66-95)	28 %	29 %	34%	11 %	32 %	31 %	27%	-	-	68%	-
Umit[27]	2018	AML	372	63 (19-97)	91 %	-	80 %	14 %	79 %	-	-	-	-	70 %	-
Goede[28]	2016	CLL	75	75 (48-87)	?	-	19 %	29 %	-	48 %	-	-	-	-	-
Molica[29]	2019	CLL	108	71 (65-90)	?	16 %	19 %	-	-	-	-	-	-	-	10 %
Ribi[30]	2017	B-cell lymphoma	41	75 (40-94)	15 %	-	-	27 %	20 %	-	73 %	7 %	-	-	39 %
Merli[31]	2020	DLBCL	33	85 (68-89)	6 %	18 %	3 %	-	-	-	-	-	-	-	-
Ong[32]	2019	DLBCL	205	73 (60-97)	7 %	7 %	36 %	-	-	-	-	-	-	-	38 %
Spina[33]	2012	DLBCL	100	75 (70-89)	26 %	27 %	31 %	?	?	-	-	-	-	-	13 %
Tucci[34]	2009	DLBCL	84	73 (66-89)	?	12 %	-	-	-	-	-	-	-	-	50 %
Tucci[35]	2015	DLBCL	173	77	?	>4 %; <54 %	>9 %; <54 %	-	-	-	-	-	-	-	38 %
Aaldriks[36]	2015	NHL	44	78 (70-86)	6 %	-	-	5 %	-	-	34 %	-	-	43 %	-
Naito[37]	2016	NHL	93	77 (65-90)	22 %	28 %	27 %	4 %	15 %	-	51 %	-	-	-	-
Park[38]	2015	NHL	70	74 (65-92)	39 %	-	-	37 %	21 %	-	36 %	-	-	47 %	-
Siegel[39]	2006	NHL	25	70 (60-85)	12 %	-	-	0 %	16 %	12 %	-	-	-	-	-
Soubeyran[40]	2011	NHL	32	79 (70-92)	41 %	59 %	81 %	38 %	94 %	-	-	-	-	-	-
Winkelmann[41]	2011	NHL	143	63 (18-88)	16 %	18 %	21 %	-	-	-	-	-	-	-	-
Okuyama[42]	2015	Lymphoma; MM	106	74(65-90)	29 %	33 %	45 %	23 %	30 %	-	-	-	17 %	-	50 %
Engelhardt[43]	2016	MM	125	63 (56-71)	28 %	48 %	85 %	-	-	-	-	-	-	-	-
Gavriatopoulou[44]	2019	MM	110	83 (80-92)	> 60 %	18 %	42 %	-	-	-	-	-	-	73 %	-
Palumbo[45]	2015	MM	869	74 (70-78)	21 %	14 %	18 %	-	-	-	-	-	-	-	30 %
Rosko[46]	2019	MM; amyloidosis	100	59 (36-75)	48 %	?	?	?	19 %	7 %	-	?	-	-	-
Wildes[47]	2019	MM	40	71 (66-76)	40 %	-	63 %	10 %	?	40 %	-	-	77 %	-	-
Zhong[48]	2017	MM	628	58 (52-66)	?	67 %	55 %	-	-	-	-	-	-	-	64 %
Buckstein[49]	2016	Various	445	71 (65-79)	7 %	-	45 %	-	-	39 %	-	-	-	25 %	-
Deschler[50]	2018	Various	106	66 (60-78)	60 %	9 %	31 %	12 %	-	3 %	76 %	-	-	-	-
Derman[51]	2019	Various	192	>67(60-83)	< 50%	-	40 %	7 %	22 %	-	-	?	54 %	-	-
Dubruille[52]	2015	Various	90	74 (65-89)	32 %	11 %	39 %	31 %	25 %	4 %	44 %	-	50 %	72 %	80 %
Dumontier[53]	2019	Various	464	80 (76-84)	?	11%	27%	?	-	-	-	-	-	-	-
Hamaker[54]	2016	Various	157	78 (67-99)	42 %	22 %	47 %	18 %	29 %	30 %	-	20 %	66 %	-	71 %
Huang[55]	2020	Various	148	62 (50-76)	28 %	-	39 %	1 %	44 %	8 %	-	?	50 %	-	-
Lin[56]	2020	Various	457	66 (60-79)	<47 %	4 %	11 %	44 %	18 %	-	-	-	50 %	-	-
Liu[57]	2019	Various	448	80 (76-84)	47 %	-	-	18 %	-	56 %	-	-	-	-	53 %
Muffly[58]	2014	Various	203	58 (54-63)	29 %	7 %	40 %	-	-	24 %	-	-	-	-	25 %
Nawas[59]	2019	Various	184	61 (50-75)	1 %	-	36 %	3 %	35 %	15 %	-	?	-	-	-
Rodrigues[60]	2020	Various	40	68 (60-76)	75 %	-	10 %	21 %	18 %	16 %	43 %	-	80 %	-	19 %
Rollot-Trad[61]	2008	Various	54	86 (75-99)	56 %	39 %	51 %	27 %	-	-	-	-	39 %	-	-
Silay[62]	2015	Various	61	69	?	21 %	26 %	26 %	34 %	16 %	27 %	-	51 %	-	-
Velghe[63]	2014	Various	50	76 (70-87)	?	24 %	38 %	4 %	30 %	-	82 %	-	-	76 %	88 %

*Reported as mean (± standard deviation) or median (range or interquartile range)? Although geriatric condition was assessed, the proportion of patients with geriatric impairments could not be extracted from the published data. PS: World Health Organization performance status; ADL: activities of daily living; IADL: instrumental activities of daily living; GA: geriatric assessment; MDS: myelodysplastic syndrome; AML: acute myeloid leukemia; RAEB: refractory anemia with excess of blasts; FLT3: FMS-like tyrosine kinase-3; CLL: chronic lymphocytic leukemia; DLBCL: diffuse large B-cell lymphoma; NHL: non-Hodgkin lymphoma; MM: multiple myeloma.

Discussion

This systematic review of 44 studies shows that impairment in geriatric domains is common among older patients with a hematologic malignancy, even in those with a good performance status. The most relevant impairment is frailty (assessed with a frailty screening tool or by summarizing the geriatric assessment), which showed an association with mortality, treatment-related toxicity and treatment non-completion. Other relevant geriatric impairments were IADL functioning, nutritional status and polypharmacy. Impaired physical capacity was mainly associated with healthcare utilization.

These data should, however, be interpreted with care. The included studies are heterogeneous in study population, design, treatment regimens, content of geriatric assessment and reported outcomes. Various hematologic malignancies can have very different disease courses and

Table 3. The association of geriatric assessment, age, performance status, and comorbidity with mortality.

Publication Author	Year	Number of patients	Type of malignancy	Results of univariate and multivariate analysis												
				Age	PS	Comorbidity	ADL	IADL	Cognition	Mood	Physical capacity	Nutritional status	Social support	Polypharmacy	Frailty screening tool	Summarized GA score
Corsetti[20]	2011	31	AML; RAEB					-								-
Deschler[21]	2013	195	AML; MDS	- -	+ +	+ +	+ +	- -	- -	-	- -					
Klepin[23]	2013	74	AML	- -	- -	- -	- -	- -	+ +	- -	+ +					
Klepin[24]	2020	40	AML (FLT3)		-	-	-	-	-	-	-		-	-		
Molga[25]	2020	98	AML; MDS		- -	+ +	+ +	+ +	- -	- -	- -	- -				
Umit[27]	2018	372	AML	+	+										+	
Goede[28]	2016	75	CLL	- -		-		-	- -		- -					
Molica[29]	2019	108	CLL	+ +	+	+ +	+ +	+								+ +
Ribi[30]	2017	41	B-cell lymphoma			-			-	-		+	-			+
Ong[32]	2019	205	DLBCL													+ +
Spina[33]	2012	100	DLBCL				- -	- -								+ +
Tucci[34]	2009	84	DLBCL													+
Tucci[35]	2015	173	DLBCL	+		+	+	+								+ +
Aaldriks[36]	2015	44	NHL									-			+ +	
Naito[37]	2016	93	NHL	-	-	+ +	-	+	+ +	-		-				
Park[38]	2015	70	NHL		- -				-	-		+ +			-	
Soubeyran[40]	2011	32	NHL				+	+	+	+						
Winkelmann[41]	2011	143	NHL	- -	- -	- -	- -	+ +								
Engelhardt[43]	2016	125	MM	+		+ +									+ +	
Gavriatopoulou[44]	2019	110	MM												- -	
Palumbo[45]	2015	869	MM	+ +		- -	+ +	+ +								
Zhong[48]	2017	628	MM	- -		- -	- -	- -								-
Buckstein[49]	2016	445	Various	+	+	+ +		+			+				+ +	
Deschler[50]	2018	106	Various	+ +	+ +	-		-			+	-				
Dubruille[52]	2015	90	Various	+ +	- -	-			+ +		-	-		-	-	-
Dumontier[53]	2019	452	Various	- -		- -	- -	+ +								
Hamaker[54]	2016	157	Various	- -	- -	- -										+ +
Huang[55]	2020	148	Various		-			+ +	-							
Lin[56]	2020	457	Various	+	+ +	- -		+ +								
Liu[57]	2019	448	Various	+ +					+ +		+ +					
Muffly[58]	2014	203	Various	+ +	-	+ +	-	+ +			+ +					
Nawas[59]	2019	184	Various		- -			+ +					+			
Rollot-Trad[61]	2008	54	Various	- -	- -		- -	- -	- -							
Proportion of studies with a significant association in univariate analysis				79 %	63 %	64 %	67 %	74 %	55 %	14 %	63 %	33 %	33 %	0 %	71 %	67 %
Proportion of studies with a significant association in multivariate analysis				43 %	27 %	47 %	40 %	62 %	50 %	0 %	50 %	50 %	NA	NA	75 %	100 %

+: association in univariate analysis; -: no association in univariate analysis; ++: association in multivariate analysis; - -: no association in multivariate analysis; NA: not applicable. PS: World Health Organization performance status; ADL: activities of daily living; IADL: instrumental activities of daily living; GA: geriatric assessment; AML: acute myeloid leukemia; RAEB: refractory anemia with excess of blasts; MDS: myelodysplastic syndrome; FLT3: FMS-like tyrosine kinase-3; CLL: chronic lymphocytic leukemia; DLBCL: diffuse large B-cell lymphoma; NHL: non-Hodgkin lymphoma; MM: multiple myeloma.

require very different intensities of treatment; geriatric impairments that were associated with outcome in one setting may not retain their predictive value in another disease entity. In addition, the content of geriatric assessments, including the definition of frailty (assessed by summarizing the geriatric assessment), was not consistent. Moreover, geriatric impairments were mainly assessed with screening tools (for example, the Mini-Mental State Examination for cognition), and it should be realized that the ensuing results are not the same as an actual diagnosis made by a comprehensive geriatric assessment. Given this heterogeneity, a meta-analysis or a meaningful subgroup analysis (for example, by type of malignancy) could not be performed; and interpretation and extrapolation of results should be done with caution. Another limitation of this review is the procedure used to select the literature. We decided to select only those studies for which a full text is available and which performed a geriatric assessment with validated tools covering at least two geriatric domains. Studies which focused on a single impairment and its relation to outcome were not included, meaning some information on individual associations may have been missed.

Despite these limitations, this review provides a thorough update and overview of all currently available evidence on the relevance of a geriatric assessment for older patients with a hematologic malignancy. At the time of the previous systematic review, by Hamaker *et al.*,[17] the evidence was limited because of a lack of published studies. In the last 5 years, the number of publications concerning the association of geriatric assessment with outcomes in patients with hematologic malignancies has increased greatly, enabling a useful update on the available data.

Performing a geriatric assessment could have an additive value to clinical judgment, treatment allocation and the implementation of non-oncological interventions.

In daily practice, oncologists are able to detect obviously frail patients by clinical judgment. However, estimating the reserve capacity and resilience of the remaining older patients by clinical judgment is difficult, as demonstrated by the discrepancy between performance status and geriatric assessment. In addition, it can be challenging to distinguish whether the detected vulnerabilities are disease-related or patient-related. This may require a more thorough evaluation of the patient's overall health status, including consultation of a geriatrician.

The impact of performing a geriatric assessment on treatment allocation has already been demonstrated in older patients with solid malignancies.[73,74] In a systematic review, the oncological treatment plan was altered in 28% of patients after geriatric assessment, primarily resulting in a less intensive treatment option. This review showed that using a geriatric assessment to guide treatment decisions appeared to have a positive effect on clinical outcome, resulting in less treatment-related toxicity, fewer complications, and increased treatment completion.[75] For example, in patients with cognitive impairments, treatment decisions should be made with great care because of the higher risk of chemotherapy-related progression of cognitive dysfunction, treatment non-compliance and death.[52,71]

In order to tailor cancer treatment to individual needs, it could be interesting to incorporate patient-reported outcome measures (PROMS) into the treatment decision-making process. PROMS, such as physical functioning and quality of life during and after treatment, were hardly assessed in the studies included in this review, despite quality of life being of primary importance to many older patients.[76] It is, therefore, highly relevant that future studies address the association between geriatric impairments and PROMS.[77]

In addition to clinical judgment and treatment allocation, a geriatric assessment can be used to introduce non-oncological interventions before and during treatment in the hope of improving the patient's health status, resilience and treatment tolerance. However, evidence concerning the effectiveness of such non-oncological interventions is limited. Previous research suggests that perhaps physiotherapy[78,79] as well as nutritional counseling[80-82] can improve survival, physical functioning and quality of life. Non-oncological interventions in older patients undergoing chemotherapy can improve treatment completion and treatment modifications.[83] The process by which a patient's condition can be enhanced before starting treatment is called prehabilitation. Although results of the first studies assessing the effectiveness of prehabilitation in patients with solid malignancies are promising,[84,85] the level of evidence is weak, making it too early to draw definitive conclusions. Currently, according to clinicaltrials.gov (searched February 5, 2020), there are 29 ongoing trials in which the effect of non-oncological interventions on clinical outcome measures in older cancer patients is being assessed; six out of these 29 trials focus on hematologic malignancies.[86] Based on these numbers, further data will follow in the coming years.

In conclusion, this review demonstrates the relevance of performing a geriatric assessment in older patients with a hematologic malignancy. Although the results should be interpreted and extrapolated carefully, our review shows that even in patients with a good performance status, a geriatric assessment can detect geriatric impairments that might be predictive of mortality. Moreover, geriatric impairments seem to be associated with a higher risk of treatment-related toxicity, treatment non-completion and utilization of healthcare services. Future research is needed to extend these findings with a focus on reserve capacity, resilience, quality of life and the effectiveness of non-oncological interventions.

References

1. Smith A, Howell D, Patmore R, Jack A, Roman E. Incidence of haematological malignancy by sub-type: a report from the Haematological Malignancy Research Network. Br J Cancer. 2011;105(11):1684-1692.
2. National Cancer Institute. Cancer Stat Facts [Internet]. [cited 2019 Jul 21]. Available from: https://seer.cancer.gov
3. Bron D, Ades L, Fulop T, Goede V, Stauder R. Aging and blood disorders: new perspectives, new challenges. Haematologica. 2015;100(4):415-417.
4. Warren JL, Harlan LC, Stevens J, Little RF, Abel GA. Multiple myeloma treatment transformed: a population-based study of changes in initial management approaches in the United States. J Clin Oncol. 2013;31(16):1984-1989.
5. Abel GA, Koreth J. Optimal positioning of hematopoietic stem cell transplantation for older patients with myelodysplastic syndromes. Curr Opin Hematol. 2013;20(2):150-156.

6. McClune BL, Weisdorf DJ, Pedersen TL, et al. Effect of age on outcome of reduced-intensity hematopoietic cell transplantation for older patients with acute myeloid leukemia in first complete remission or with myelodysplastic syndrome. J Clin Oncol. 2010;28(11):1878-1867.
7. 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):1069-1075.
8. Extermann M, Aapro M, Bernabei R, et al. Use of comprehensive geriatric assessment in older cancer patients: recommendations from the task force on CGA of the International Society of Geriatric Oncology (SIOG). Crit Rev Oncol Hematol. 2005;55(3):241-225.
9. Gobbens RJ, Luijkx KG, Wijnen-Sponselee MT, Schols JM. Toward a conceptual definition of frail community dwelling older people. Nurs Outlook. 2010;58(2):76-86.
10. Fried LP, Tangen CM, Walston J, et al. Frailty in older adults: evidence for a phenotype. J Gerontol A Biol Sci Med Sci. 2001;56(3):146-156.
11. Mitnitski AB, Mogilner AJ, Rockwood K. Accumulation of deficits as a proxy measure of aging. ScientificWorldJournal. 2001;8(1):323-336.
12. Rockwood K, Song X, MacKnight C, et al. A global clinical measure of fitness and frailty in elderly people. CMAJ. 2005;173(5):489-495.
13. Mohile SG, Dale W, Somerfield MR, et al. Practical assessment and management of vulnerabilities in older patients receiving chemotherapy: ASCO guideline for geriatric oncology. J Clin Oncol. 2018;36(22):2326-2347.
14. Wildiers H, Heeren P, Puts M, et al. International society of geriatric oncology consensus on geriatric assessment in older patients with cancer. J Clin Oncol. 2014;32(24):2595-2601.
15. van Walree IC, Scheepers E, van Huis-Tanja LH, et al. A systematic review on the association of the G8 with geriatric assessment, prognosis and course of treatment in older patients with cancer. J Geriatr Oncol. 2019;10(6):847-858.
16. Goede V, Stauder R. Multidisciplinary care in the hematology clinic: implementation of geriatric oncology. J Geriatr Oncol. 2019;10(3):497-503.
17. Hamaker ME, Prins MC, Stauder R. The relevance of a geriatric assessment for elderly patients with a haematological malignancy - a systematic review. Leuk Res. 2014;(38):275-283.
18. Wells GA, Shea B, O'Connell D, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. Ottawa Hospital Research Institute, 2012.
19. Aguiar APN, Mendonça P da S, Ribeiro-Júnior HL, et al. Myelodysplastic syndromes: an analysis of non-hematological prognostic factors and its relationship to age. J Geriatr Oncol. 2020;(11):125-127.
20. Corsetti MT, Salvi F, Perticone S, et al. Hematologic improvement and response in elderly AML/RAEB patients treated with valproic acid and low-dose Ara-C. Leuk Res. 2011;35(8):991-997.
21. Deschler B, Ihorst G, Platzbecker U, 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):208-216.
22. Holmes H, Des Bordes JKA, Kebriaei P, et al. Optimal screening for geriatric assessment in older allogeneic hematopoietic cell transplantation candidates. J Geriatr Oncol. 2014;5(4):422-430.
23. 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.
24. Klepin HD, Ritchie E, Major-Elechi B, et al. Geriatric assessment among older adults receiving intensive therapy for acute myeloid leukemia: report of CALGB 361006 (Alliance). J Geriatr Oncol. 2020;(11):107-113.
25. Molga A, Wall M, Chhetri R, et al. Comprehensive geriatric assessment predicts azacitidine treatment duration and survival in older patients with myelodysplastic syndromes. J Geriatr Oncol. 2020;(11):114-120.
26. Molga A, Wall M, Wee LYA, et al. Screening for deficits using the G8 and VES-13 in older patients with myelodysplastic syndromes. J Geriatr Oncol. 2020;(11):128-130.
27. Umit EG, Baysal M, Demir AM. Frailty in patients with acute myeloid leukaemia, conceptual misapprehension of chronological age. Eur J Cancer Care (Engl). 2018;27(2):e12810.
28. Goede V, Bahlo J, Chataline V, et al. Evaluation of geriatric assessment in patients with chronic lymphocytic leukemia: results of the CLL9 trial of the German CLL study group. Leuk Lymphoma. 2016;57(4):789-796.
29. Molica S, Giannarelli D, Levato L, et al. A simple score based on geriatric assessment predicts survival in elderly newly diagnosed chronic lymphocytic leukemia patients. Leuk Lymphoma. 2019;60(3):845-847.
30. Ribi K, Rondeau S, Hitz F, et al. Cancer-specific geriatric assessment and quality of life: important factors in caring for older patients with aggressive B-cell lymphoma. Support Care Cancer. 2017;25(9):2833-2842.
31. Merli F, Cavallo F, Salvi F, et al. Obinutuzumab and miniCHOP for unfit patients with diffuse large B-cell lymphoma. A phase II study by Fondazione Italiana Linfomi. J Geriatr Oncol. 2020;(11):37-40.
32. Ong DM, Ashby M, Grigg A, et al. Comprehensive geriatric assessment is useful in an elderly Australian population with diffuse large B-cell lymphoma receiving rituximab-chemotherapy combinations. Br J Haematol. 2019;(187):73-81.
33. Spina M, Balzarotti M, Uziel L, et al. Modulated chemotherapy according to modified comprehensive geriatric assessment in 100 consecutive elderly patients with diffuse large B-cell lymphoma. Oncologist. 2012;17(6):838-846.
34. Tucci A, Ferrari S, Bottelli C, Borlenghi E, Drera M, Rossi G. A comprehensive geriatric assessment is more effective than clinical judgment to identify elderly diffuse large cell lymphoma patients who benefit from aggressive therapy. Cancer. 2009;115(19):4547-4553.
35. Tucci A, Martelli M, Rigacci L, et al. Comprehensive geriatric assessment is an essential tool to support treatment decisions in elderly patients with diffuse large B-cell lymphoma: a prospective multicenter evaluation in 173 patients by the Lymphoma Italian Foundation (FIL). Leuk Lymphoma. 2015;56(4):921-926.
36. Aaldriks A, Giltay E, Nortier J, et al. Prognostic significance of geriatric assessment in combination with laboratory parameters in elderly patients with aggressive non-Hodgkin lymphoma. Leuk Lymphoma. 2015;56(4):927-935.
37. Naito Y, Sasaki H, Takamatsu Y, Kiyomi F, Tamura K. Retrospective analysis of treatment outcomes and geriatric assessment in elderly malignant lymphoma patients. J Clin Exp Hematop. 2016;56(1):43-49.
38. Park S, Hong J, Hwang I, et al. Comprehensive geriatric assessment in elderly patients with newly diagnosed aggressive non-Hodgkin lymphoma treated with multi-agent chemotherapy. J Geriatr Oncol. 2015;6(6):470-478.
39. Siegel AB, Lachs M, Coleman M, Leonard JP. Lymphoma in elderly patients: novel functional assessment techniques provide better discrimination among patients than traditional performance status measures. Clin Lymphoma Myeloma. 2006;7(1):65-69.
40. Soubeyran P, Khaled H, MacKenzie M, et al. Diffuse large B-cell and peripheral T-cell non-Hodgkin's lymphoma in the frail elderly. A phase II EORTC trial with a progressive and cautious treatment emphasizing geriatric assessment. J Geriatr Oncol. 2011;2(1):36-44.
41. Winkelmann N, Petersen I, Kiehntopf M, Fricke HJ, Hochhaus A, Wedding U. Results of comprehensive geriatric assessment effect survival in patients with malignant lymphoma. J Cancer Res Clin Oncol. 2011;137(4):733-738.
42. Okuyama T, Sugano K, Iida S, Ishida T, Kusumoto S, Akechi T. Screening performance for frailty among older patients with cancer: a cross-sectional observational study of two approaches. J Natl Compr Cancer Netw. 2015;13(12):1525-1531.
43. Engelhardt M, Dold SM, Ihorst G, et al. Geriatric assessment in multiple myeloma patients: Validation of the International Myeloma Working Group (IMWG) score and comparison with ther common comorbidity scores. Haematologica. 2016;101(9):1110-1119.
44. Gavriatopoulou M, Fotiou D, Koloventzou U, et al. Vulnerability variables among octogenerian myeloma patients: a single-center analysis of 110 patients. Leuk Lymphoma. 2019;60(3):619-628.
45. Palumbo A, Bringhen S, Mateos MV, et al. Geriatric assessment predicts survival and toxicities in elderly myeloma patients: an International Myeloma Working Group report. Blood. 2015;125(13):2068-2074.
46. Rosko AE, Huang Y, Benson DM, et al. Use of a comprehensive frailty assessment to predict morbidity in patients with multiple myeloma undergoing transplant. J Geriatr Oncol. 2019;10(3):479-85.
47. Wildes TM, Tuchman SA, Klepin HD, et al. Geriatric assessment in older adults with multiple myeloma. J Am Geriatr Soc. 2019;67(5):987-991.
48. Zhong YP, Zhang YZ, Liao AJ, Li SX, Tian C, Lu J. Geriatric assessment to predict survival and risk of serious adverse events in elderly newly diagnosed multiple myeloma patients: A multicenter study in China. Chin Med J (Engl). 2017;130(2):130-134.
49. Buckstein R, Wells RA, Zhu N, et al. Patient-related factors independently impact overall survival in patients with myelodysplastic syndromes: an MDS-CAN prospective study. Br J Haematol. 2016;174(1):88-101.
50. 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 article. Bone Marrow Transplant. 2018;53(5):565-575.
51. 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.
52. Dubruille S, Libert Y, Roos M, et al. Identification of clinical parameters predictive of one-year survival using two geriatric tools in clinically fit older patients with hematological malignancies: major impact of cognition. J Geriatr Oncol. 2015;6(5):362-369.
53. DuMontier C, Liu MA, Murillo A, et al. Function, survival, and care utilization among older adults with hematologic malignancies. J Am Geriatr Soc. 2019;(67):889-897.
54. Hamaker ME, Augschoell J, Stauder R. Clinical judgement and geriatric assessment for predicting prognosis and chemotherapy completion in older patients with a hematological malignancy. Leuk Lymphoma. 2016;57(11):2560-2567.
55. Huang LW, Sheng Y, Andreadis C, et al. Functional status as measured by geriatric assessment predicts inferior survival in older allogeneic hematopoietic cell transplantation recipients: functional status predicts post-alloHCT survival. Biol Blood Marrow Transplant. 2020;(26):189-196.
56. Lin RJ, Elko TA, Devlin SM, et al. Impact of geriatric vulnerabilities on allogeneic hematopoietic cell transplantation outcomes in older patients with hematologic malignancies. Bone Marrow Transplant. 2020;(55):157-164.
57. Liu MA, DuMontier C, Murillo A, et al. Gait speed, grip strength, and clinical outcomes in older patients with hematologic malignancies. Blood. 2019;134(4):374-382.
58. 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.
59. Nawas MT, Andreadis C, Martin TG, et al. Limitation in patient-reported function Is associated with inferior survival in older adults undergoing autologous hematopoietic cell transplantation. Biol Blood Marrow Transplant. 2019;25(6):1218-1224.
60. Rodrigues M, de Souza PMR, de Oliveira Muniz Koch L, Hamerschlak N. The use of comprehensive geriatric assessment in older patients before allologeneic hematopoietic stem cell transplantation: a cross-sectional study. J Geriatr Oncol. 2020;(11):100-106.
61. Rollot-Trad F, Lahjibi H, Lazarovici C, Bauer C, Saint-Jean O, Gisselbrecht M. Haematological malignancies in older adults: experience in a geriatric acute care department. Rev Med Interne. 2008;29(7):541-549.
62. Silay K, Akinci S, Silay YS, et al. Hospitalization risk according to geriatric assessment and laboratory parameters in elderly hematologic cancer patients. Asian Pacific J Cancer Prev. 2015;16(2):1783-1786.
63. Velghe A, Petrovic M, De Buyser S, Demuynck R, Noens L. Validation of the G8 screening tool in older patients with aggressive haematological malignancies. Eur J Oncol Nurs. 2014;18(6):645-648.
64. Klepin HD, Geiger AM, Tooze JA, et al. The feasibility of inpatient geriatric assessment for older adults receiving induction chemotherapy for acute myelogenous leukemia. J Am Geriatr Soc. 2011;59(10):1837-1846.
65. Klepin HD, Tooze JA, Pardee TS, et al. Effect of intensive chemotherapy on physical, cognitive, and emotional health of older adults with acute myeloid leukemia. J Am Geriatr Soc. 2016;64(10):1988-1995.
66. Isaacs A, Fiala M, Tuchman S, Wildes TM. A comparison of three different approaches to defining frailty in older patients with multiple myeloma. J Geriatr Oncol. 2020;11(2):311-315.
67. Hamaker ME, Mitrovic M, Stauder R. The G8 screening tool detects relevant geriatric impairments and predicts survival in elderly patients with a haematological malignancy. Ann Hematol. 2014;93(6):1031-1040.
68. Hofer F, Koinig KA, Nagl L, Borjan B, Stauder R. Fatigue at baseline is associated with geriatric impairments and represents an adverse prognostic factor in older patients with a hematological malignancy. Ann Hematol. 2018;97(11):2235-2243.
69. Lin RJ, Shahrokni A, Dahi PB, et al. Pretransplant comprehensive geriatric assessment in hematopoietic cell transplantation: a single center experience. Bone Marrow Transplant. 2018;53:1184-1187.
70. Lin RJ, Dahi PB, Shahrokni A, et al. Feasibility of a patient-reported, electronic geriatric assessment tool in hematopoietic cell transplantation–a single institution pilot study. Leuk Lymphoma. 2019;60(13):3308-3311.
71. Hshieh TT, Jung WF, Grande LJ, et al. Prevalence of cognitive impairment and association with survival among older patients with hematologic cancers. JAMA Oncol. 2018;4(5):686-693.
72. Muffly LS, Boulukos M, Swanson K, et al. Pilot study of comprehensive geriatric assessment (CGA) in allogeneic transplant: CGA captures a high prevalence of vulnerabilities in older transplant recipients. Biol Blood Marrow Transplant. 2013;19(3):429-434.
73. Corre R, Greillier L, Le Caër H, et al. Use of a comprehensive geriatric assessment for the management of elderly patients with advanced non-small cell lung cancer: the phase III randomized ESOGIA-GFPC-GECP 08-02 study. J Clin Oncol. 2016;34(13):1476-1483.
74. Kirkhus L, Benth JŠ, Rostoft S, et al. Geriatric assessment is superior to oncologists' clinical judgement in identifying frailty. Br J Cancer. 2017;117(4):470-477.
75. Hamaker ME, te Molder M, Thielen N, van Munster BC, Schiphorst AH, van Huis LH. The effect of a geriatric evaluation on treatment decisions and outcome for older cancer patients – a systematic review. J Geriatr Oncol. 2018;9(5):430-440.
76. Van Leeuwen KM, Van Loon MS, Van Nes FA, et al. What does quality of life mean to older adults? A thematic synthesis. PLoS One. 2019;14(3):1-39.
77. Stauder R, Lambert J, Desruol-Allardin S, et al. Patient-reported outcome measures in studies of myelodysplastic syndromes and acute myeloid leukemia: literature review and landscape analysis. Eur J Haematol. 2020 Jan 27. [Epub ahead of print]
78. Meneses-Echávez JF, González-Jiménez E, Ramírez-Vélez R. Supervised exercise reduces cancer-related fatigue: a systematic review. J Physiother. 2015;61(1):3-9.
79. Buffart LM, Kalter J, Sweegers MG, et al. Effects and moderators of exercise on quality of life and physical function in patients with cancer: an individual patient data meta-analysis of 34 RCTs. Cancer Treat Rev. 2017;52:91-104.
80. Baldwin C, Spiro A, Ahern R, Emery PW. Oral nutritional interventions in malnourished patients with cancer: a systematic review and meta-analysis. J Natl Cancer Inst. 2012;104(5):371-385.
81. Schuetz P, Fehr R, Baechli V, et al. Individualised nutritional support in medical inpatients at nutritional risk: a randomised clinical trial. Lancet. 2019;393(10188):2312-2321.
82. Caillet P, Liuu E, Raynaud Simon A, et al. Association between cachexia, chemotherapy and outcomes in older cancer patients: a systematic review. Clin Nutr. 2017;36:1473-1482.
83. Kalsi T, Babic-Illman G, Ross PJ, et al. The impact of comprehensive geriatric assessment interventions on tolerance to chemotherapy in older people. Br J Cancer. 2015;112(9):1435-1444.
84. Bruns ERJ, van den Heuvel B, Buskens CJ, et al. The effects of physical prehabilitation in elderly patients undergoing colorectal surgery: a systematic review. Color Dis. 2016;18(8):267-277.
85. Driessen EJ, Peeters ME, Bongers BC, et al. Effects of prehabilitation and rehabilitation including a home-based component on physical fitness, adherence, treatment tolerance, and recovery in patients with non-small cell lung cancer: a systematic review. Crit Rev Oncol Hematol. 2017;114:63-76.
86. ClinicalTrials.gov. U.S. National Library of Medicine [Internet]. [cited 2020 Feb 5]. Available from: https://clinicaltrials.gov/