



The impact of divergent forms of social support on health-related quality of life in patients with multiple myeloma and its precursor states

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Abstract

Purpose Multiple myeloma is a largely incurable disease. Patients suffer from the cancer, therapeutic side effects, and often psychological symptoms. Not only multiple myeloma patients but also patients with precursor diseases show high psychological distress. Today, treatment option evaluations are increasingly performed in combination with health-related quality of life (HRQoL) assessments. One factor that is positively associated with HRQoL is social support.

Methods Our recent study used questionnaires (EORTC QLQ-C30, EORTC QLQ-MY20, Illness-specific Social Support Scale) to investigate the influence of positive and negative aspects of social support on HRQoL in patients with multiple myeloma and its precursors.

Results Multiple linear regression analyses with sex, age, treatment line, hemoglobin level, and number of comorbidities as control variables show that positive social support had a significant beneficial association with emotional function ($\beta=0.323$) and social function ($\beta=0.251$). Detrimental interactions had a significant negative association with social function ($\beta=-0.209$) and a significant positive association with side effects of treatment ($\beta=0.266$).

Conclusion Therefore, screening for social support and, if needed, psycho-oncological care can be an important resource and should be implemented in routine care.

Clinical trial registration This study was registered with clinicaltrials.gov (NCT04328038).

Keywords Multiple myeloma · Psychological distress · Health-related quality of life · Social support · Positive support · Detrimental interaction

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Introduction

Multiple myeloma (MM) is, in most patients, an incurable hematological malignancy from the B-cell lineage. The median age of patients at first diagnosis is 69 years (National Cancer Institute). MM is preceded by asymptomatic precursor conditions, including monoclonal gammopathy of undetermined significance (MGUS) and smoldering multiple myeloma (SMM) (Landgren et al. 2009). With the advent of novel therapeutic agents, including proteasome inhibitors (PIs, e.g., bortezomib), immunomodulatory agents (IMiDs, e.g., lenalidomide) and monoclonal antibodies (mAbs, e.g., daratumumab), life expectancy has constantly increased within the past decade. For example, in transplant-ineligible patients with newly diagnosed MM, five-year progression-free survival (PFS) is 52.5%, and the median overall survival (OS) has not been reached applying a therapy consisting of

the anti-CD38 mAb daratumumab, lenalidomide and dexamethasone (Facon et al. 2021). This drives a paradigm shift in the MM landscape, with a need to limit the side effects of the therapy, prevent morbidity and mortality, and increase health-related quality of life (HRQoL). HRQoL in MM is impaired by disease-specific characteristics such as bone pain, anemia, and renal impairment but also psychological distress, e.g., fear of MM relapse, depressive symptoms and anxiety (Maatouk et al. 2019). A previous study showed that not only patients with MM but also patients with precursor diseases (MGUS and SMM) suffered from psychological distress above cutoff scores measured using the National Comprehensive Cancer Network distress thermometer (Maatouk et al. 2019).

As a result, HRQoL and lifestyle considerations have become more important in MM patients (Perrot et al. 2021; Shapiro et al. 2021). More recent trials increasingly include HRQoL as a key outcome (Mohyuddin et al. 2021), and from the patients' perspective, prolonged PFS appears to be a goal equal to high HRQoL (Fleischer et al. 2021). A high HRQoL reflects both a lower symptom burden for patients and lower costs for the healthcare system. It has been shown that the psychological factors of HRQoL are independent prognostic factors for MM (Strasser-Weippl and Ludwig 2008). In patients with various forms of cancer (Manne et al. 2015; Ristevska-Dimitrovska et al. 2015; Wu et al. 2015; Ye et al. 2017) but also in MM patients (Maatouk et al. 2018), HRQoL has been positively influenced by high resilience. One resilience factor that has been associated with HRQoL in MM patients is social support (Hu et al. 2021; Maher & De Vries 2011; Mortensen & Salomo 2016). Social support describes "perceived or objectively existing resources available to a person in his or her social network" (p. 2; Geue et al. 2019). Aside from positive support (PS), e.g., emotional, instrumental, esteem, and tangible support, there are also negative social interactions, i.e., detrimental interactions (DI), including omitting previously promised assistance, making critical remarks, suppressing expressions of emotion, overstepping personal boundaries and not protecting privacy (Lincoln 2000). The influence of DI has thus far only rarely been studied in cancer patients (Sauer et al. 2019), including hematological malignancies (Geue et al. 2019).

For these reasons, our current study aimed to investigate, for the first time, the association of positive and negative aspects of social support on the HRQoL of MM patients.

Methods

Study design and procedures

This cross-sectional survey was conducted from July to October 2020 at the National Center for Tumor Diseases

(NCT) in Heidelberg, Germany. Eligible patients with MM and its precursor diseases were approached during their outpatient visits. They were asked to fill out the questionnaire immediately. If this was not possible, the questionnaire was completed at home and returned at the next appointment ($n = 11$, 7.9% of included patients). Patients younger than 18 years and patients who were scheduled for surgery within the next 24 weeks or whose last surgery was less than six weeks prior were excluded from the study.

Ethical considerations

This study was approved by the ethics committee of the University Hospital Heidelberg (application no. S-875/2019). All participants provided written informed consent to participate and were able to withdraw their participation without any disadvantage. This study was conducted in accordance with the Declaration of Helsinki (most recent version; Fortaleza, Brazil, 2013) and registered with clinicaltrials.gov (NCT04328038).

Survey instruments

Health-related quality of life (EORTC QLQ-C30 and EORTC QLQ-MY20). HRQoL was assessed with the 30-item questionnaire of the European Organization for Research (Aaronson et al. 1993) and an additional 20 items for myeloma patients (Cocks et al. 2007). The EORTC QLQ-C30 consists of a global health and HRQoL scale, five functional scales (physical, role, cognitive, emotional, and social), and three symptom scales (fatigue, nausea, and vomiting); dyspnea, appetite loss, sleep disturbance, constipation, diarrhea, and the financial impact of the illness are assessed via one item. The EORTC QLQ-MY20 consists of two functioning scales (body images assessed via one item and future perspective) and two symptom scales (disease symptoms and side effects of treatment). As only 13 patients answered the item on hair loss distress, we excluded this item from the analysis. All scores are transformed to range from 0 to 100; high scores equal high HRQoL (global health scale), high functioning (functional scales), and high symptoms (symptom scales). The questionnaire has been validated in patients with MM (Delforge et al. 2015).

Illness-specific Social Support Scale (ISSS). The subjective perception of PS and DI were surveyed with the short version (Ullrich & Mehnert 2010) of the Illness-specific Social Support Scale (Revenson and Schiaffino 1990). The sum of the two scales PS and DI range from 0 to 16; higher scores indicate higher levels of positive support and detrimental interactions. DI suggests, among other things, overprotectiveness and excessive optimism or pessimism (Ramm & Hasenbring 2003). The German version was validated in a cancer population (Ullrich & Mehnert 2010). Cronbach's

α ranged in our study from 0.70 to 0.82, which indicates acceptable to good internal consistency.

Patient medical and sociodemographic data were assessed from electronic medical records.

Data analysis

All data were coded and analyzed using SPSS®-24 software (IBM Corp 2016) Raw data are displayed as the mean values and SD. The influence of social support (PS and DI) on HRQoL (global health, functioning scales, and symptom scales) was calculated with multiple linear regression analyses with sex, age, treatment line, hemoglobin score (Hb, surveyed on the day of the survey), and number of comorbidities as control variables. Prior to regression analyses, one outlier was removed from the dataset with the help of the Mahalanobis generalized distance ($\alpha = 0.001$). Due to multiple testing of whether social support was related to HRQoL, the significance level was adjusted using the Bonferroni–Holm correction.

Results

Participants

In total, 170 patients with MM or precursor diseases were approached. Ten of these patients met the exclusion criteria. Twenty patients declined participation in this study. Overall, 140 patients were enrolled. A total of 132 questionnaires were returned for a response rate of 94.3%, of which six (4.3%) were excluded due to low data quality. In total, 126 patients (90.0%) were included in the final analysis. A total of 42.5% ($n = 54$) of these patients were female, and the mean age was 64.10 years ($SD = 9.50$; range 38–84). Sociodemographic characteristics are displayed in Table 1.

Disease characteristics and descriptive data

A total of 77.0% of the patients ($n = 97$) were diagnosed with MM, 15.0% with SMM ($n = 19$) and 8.0% with MGUS ($n = 10$). On average, participants were diagnosed four years before the study began (range 0–11). Thirty-five patients were in treatment line 0 (Rajkumar et al. 2015). Further information on disease characteristics is shown in Table 2. Mean values and standard deviation for all subscales of HRQoL and social support are displayed in Table 3.

Association of social support with health-related quality of life

Regression analyses with PS and DI as independent variables as well as sex, age, treatment line, Hb levels, and

Table 1 Sociodemographic data ($N = 126$)

	<i>n</i>	%	
Sex			
Male	72	56.7	
Female	54	42.5	
Age	$M = 64.10$	$SD = 9.50$	Range: 38–84
Family status			
Single	5	4.0	
Married/partnership	102	81.0	
Divorced/separated	13	10.2	
Widowed	5	4.0	
Missing	1	0.8	
Education			
No degree	1	0.8	
Secondary school	34	27.0	
Middle School	26	20.6	
High School	14	11.1	
University degree	50	39.7	
Missing	1	0.8	
Employment			
Yes	43	34.1	
No	72	57.1	
Missing	11	8.8	

number of comorbidities as control variables showed a significant relationship with side effects of treatment (EORTC QLQ-MY20), emotional function (EORTC QLQ-C30), and social function (EORTC QLQ-C30). PS had a significant positive association with emotional function ($\beta = 0.323$) and social function ($\beta = 0.251$). DI had a significant negative association with social function ($\beta = -0.209$) and a positive association with side effects of treatment ($\beta = 0.266$). All regression models are found in Table 4.

Discussion

This cross-sectional study examined for the first time the association of the diverging forms of social support (PS and DI) on HRQoL (global health, function scales, and symptom scales) in patients with MM and precursor diseases. Sex, age, treatment line, Hb level, and number of comorbidities were included as control variables. PS had a significant positive association with emotional function and social function. DI had a significant positive association with the side effects of treatment and a significant negative association with social functioning.

The significant association of social support with HRQoL is consistent with previous research regarding patients with other cancers (Mehnert et al. 2010; Sauer et al. 2019; Soares et al. 2013). Previous studies have shown that PS

Table 2 Disease characteristics (N=126)

	<i>n</i>	%	
Diagnosis			
Multiple myeloma	97	77.0	
sMM	19	15.0	
MGUS	10	8.0	
Years since initial diagnosis	M=4		Range: 11–0
Treatment line ^a			
0 (incl. precursor diseases and new diagnosis)	35	27.8	
1	65	51.6	
> 1	26	20.6	
Received treatment			
Chemotherapy	75	59.1	
Radiation	38	29.9	
Immunotherapy	48	37.8	
Autologous stem cell transplantation ^b	68	53.5	
Comorbidity			
Cardiovascular	52	41.3	
Pulmological	58	46.0	
Diabetes	2	1.6	
Other	72	57.1	
Number of comorbidities (categories)			
0	22	17.5	
1	48	38.1	
2	33	26.2	
3	22	17.5	
4	1	0.8	
Osteolyses ^c			
Yes	74	58.7	
No	52	41.3	
Hemoglobin ^d g/dl	M=12.80	SD=1.46	Range: 8.8–16.4

^aBased on Rajkumar et al. (2015)

^bAfter transplantation

^cTaken from the medical documentation (radiology findings/physician 's medical report)

^dSurveyed on the day of the questionnaire assessment

and DI represent distinct constructs and do not belong to the same factor (Sauer et al. 2019). It should be emphasized that our study population reported PS more frequently than DI. This could be related to the higher average age of our study population. A study by Due et al. (1999) found an age difference in the structure and function of social relationships. The authors interpreted the results to reflect that people build social networks over their lifetimes in which PS predominates.

It can be concluded from the results that PS should be increased and DI should be reduced to improve HRQoL. Especially in the period around diagnostics, the PS of cancer patients seems to be of great importance. Studies suggest that PS reduces reoccurrence anxiety (Koch-Gallenkamp et al. 2016) and strengthens patients' sense of coherence (Pasek et al. 2017). Furthermore, it predicts

depression (Akechi et al. 2004; Eom et al. 2013; Hughes et al. 2014), anxiety (Ng et al. 2015), and distress (Akechi et al. 2006). A previous study by our research group (Sauer et al. 2019) showed that patients receive a similar pattern of social support in the year after diagnosis as they did at the time of receiving the diagnosis. The authors suggest that, in particular, patients with low PS or high DI should be identified as early as possible and offered help in the form of psycho-oncological care. Furthermore, other previous studies suggest that social support has an impact on somatic factors such as cancer progression, mortality (Frick et al. 2005), and inflammation levels (Hughes et al. 2014). For this reason, it may be helpful to screen cancer patients for social support as part of the diagnostic process. Patients with low PS and high DI can be offered

Table 3 Mean and standard deviation for EORTC QLQ-30, EORTC QLQ-MY20, and SSUK-8

	<i>N</i>	<i>M</i>	<i>SD</i>
EORTC QLQ-C30			
Global health/HRQoL	125	62.80	22.24
Physical Function	126	77.59	23.16
Role function	126	69.18	31.49
Emotional function	126	60.54	25.84
Cognitive function	126	75.79	25.53
Social function	125	64.80	31.55
Fatigue	126	43.30	28.43
Nausea/vomiting	125	6.53	13.86
Pain	126	35.58	31.29
Dyspnea	124	29.03	34.26
Insomnia	125	38.67	34.24
Appetite loss	126	13.76	26.42
Constipation	125	14.93	26.93
Diarrhea	126	19.05	30.24
Financial problems	125	17.33	29.81
EORTC QLQ-MY20			
Disease symptoms	125	27.62	22.33
Side effects of treatment	125	27.07	19.02
Body image	124	81.18	31.01
Future perspective	125	47.91	30.01
ISSS			
PS	118	13.40	3.16
DI	118	4.45	3.59

support services to reinforce the positive aspects of social support and thus serve as an important resource. Interventions can include examining (e.g., with the CCAT-PF; Siminoff et al. 2008) and training communication patterns in couples and families (Zaider et al. 2017) or finding a better way to deal with DI. It should be considered that patients with MM are mostly elderly people. In contrast to younger people, they tend to be less oriented to the outer world and the future but more focused on internal processes and the present (Blank & Bellizzi 2008). On the one hand, this means that elderly people more often deal

pragmatically with interpersonal conflicts, but on the other hand, it also implies that they tend to have fewer social contacts than younger people (Due et al. 1999). For this reason, interventions should pay attention to older people who do not have family (anymore) or who are only poorly socially integrated. Regular contacts (with psycho-oncological or social work interventions) can also provide basic stabilizing social support (Abbey et al. 1985). This topic has become particularly important in the current COVID-19 pandemic, as older people with preexisting illnesses were required to limit their contact with others.

Strengths and limitations

To the best of our knowledge, this is the first study to investigate the association of social support (PS and DI) and HRQoL in MM patients. The strengths of this study are the subdivision of positive and negative aspects of social support as well as the differentially assessed control variables. Nevertheless, the limitations of the study should also be described: The study participants were patients in outpatient treatment. Thus, this is a patient group with comparatively mild symptoms and, in part, without treatment histories. For this reason, the study results cannot be generalized to patients in inpatient treatment. The results refer to cross-sectional data. For this reason, the relationship between social support and HRQoL must be interpreted with caution. The potential impact of social support on HRQoL needs to be replicated in future studies with a longitudinal design.

In summary, social support has a significant association with different domains of HRQoL in MM patients. Based on previous research, it can be assumed that social support can also influence the course of the disease. Screening for social support as part of the diagnostic process, followed by psycho-oncological care if needed, can help promote PS as well as better management of DI. Especially for patients who are not well-integrated socially, low-threshold regular contacts (e.g., by a psycho-oncologist or social worker) can be a stabilizing intervention. In the future, the influence of social support on the HRQoL of MM patients should also be investigated in longitudinal studies. This would provide important information over the course of the disease.

Table 4 Regression analyses

Outcome variable	<i>N</i>	Predictors	β	<i>p</i>	R^2	<i>p</i>	<i>p</i> value Bonferroni–Holm correction
EORTC QLQ-MY20: side effects of treatment	117	Sex	− 0.126	0.158	0.219	$F(7,109)=4.360$	< 0.001
		Age	− 0.074	0.407			
		Treatment line	0.272	0.003			
		Hb	− 0.036	0.689			
		No. comorbidities	0.112	0.198			
		ISSS_PS	− 0.017	0.849			
		ISSS_DI	0.266	0.004			
EORTC QLQ-C30: emotional function	117	Sex	− 0.025	0.781	0.179	$F(7,109)=3.388$	0.003
		Age	0.160	0.082			
		Treatment line	− 0.106	0.258			
		Hb	0.091	0.326			
		No. comorbidities	− 0.010	0.908			
		ISSS_PS	0.323	< 0.001			
		ISSS_DI	− 0.174	0.062			
EORTC QLQ-C30: social function	116	Sex	− 0.030	0.743	0.163	$F(7,108)=3.015$	0.006
		Age	0.165	0.075			
		Treatment line	− 0.079	0.407			
		Hb ^a	0.053	0.568			
		No. comorbidities	− 0.143	0.115			
		ISSS_PS	0.251	0.007			
		ISSS_DI	− 0.209	0.027			
EORTC QLQ-C30: cognitive function	117	Sex	0.126	0.176	0.155	$F(7,109)=2.864$	0.009
		Age	0.075	0.417			
		Treatment line	− 0.187	0.050			
		Hb	0.055	0.556			
		No. comorbidities	− 0.054	0.552			
		ISSS_PS	0.222	0.016			
		ISSS_DI	− 0.121	0.200			
EORTC QLQ-C30: role function	117	Sex	− 0.033	0.725	0.154	$F(7,109)=8.829$	0.010
		Age	0.081	0.385			
		Treatment line	− 0.086	0.366			
		Hb	0.146	0.122			
		No. comorbidities	− 0.167	0.065			
		ISSS_PS	0.227	0.014			
		ISSS_DI	− 0.156	0.099			
EORTC QLQ-C30: global health/HRQoL	116	Sex	− 0.052	0.576	0.149	$F(7,108)=2.707$	0.013
		Age	− 0.022	0.813			
		Treatment line	− 0.129	0.180			
		Hb	0.207	0.030			
		No. comorbidities	− 0.033	0.715			
		ISSS_PS	0.174	0.059			
		ISSS_DI	− 0.177	0.063			

Table 4 (continued)

Outcome variable	<i>N</i>	Predictors	β	<i>p</i>	R^2	<i>p</i>	<i>p</i> value Bonferroni–Holm correction	
EORTC QLQ-C30: physical function	117	Sex	0.098	0.297				
		Age	−0.076	0.416				
		Treatment line	−0.101	0.295	0.135	$F(7,109)=2.420$	0.024	0.096
		Hb	0.088	0.356				
		No. comorbidities	−0.155	0.091				
		ISSS_PS	0.208	0.025				
		ISSS_DI	−0.040	0.671				
EORTC QLQ-MY20: disease symptoms	117	Sex	−0.226	0.018	0.130	$F(7,109)=2.320$	0.030	0.096
		Age	−0.012	0.899				
		Treatment line	0.113	0.241				
		Hb	−0.055	0.566				
		No. comorbidities	0.037	0.685				
		ISSS_PS	−0.041	0.660				
		ISSS_DI	0.196	0.042				
EORTC QLQ-MY20: body image	117	Sex	0.104	0.276	0.105	$F(7,109)=1.830$	0.089	0.178
		Age	0.247	0.011				
		Treatment line	−0.105	0.284				
		Hb	−0.064	0.507				
		No. comorbidities	−0.149	0.110				
		ISSS_PS	0.102	0.276				
		ISSS_DI	−0.053	0.581				
EORTC QLQ-MY20: future perspective	117	Sex	−0.043	0.652	0.086	$F(7,109)=1.473$	0.184	0.184
		Age	0.114	0.236				
		Treatment line	−0.136	0.168				
		Hb	0.158	0.107				
		No. comorbidities	−0.091	0.332				
		ISSS_PS	0.046	0.626				
		ISSS_DI	−0.096	0.325				

^ag/dl, surveyed on the day of the questionnaire assessment; low/weak variance explanation: $R^2=0.02$, medium/moderate variance explanation: $R^2=0.13$, high/strong variance explanation: $R^2=0.26$, (Cohen 1988)

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Author contributions AG: conducted the data analyses, contributed to interpreting the results and wrote the manuscript. RK: contributed to the study design, collected the data, extracted the data, and contributed to the writing of the manuscript. EKM: recruited patients and contributed to writing the manuscript. HG: conceived and designed the study, recruited patients and revised the manuscript. JW: conceived and designed the study and revised the manuscript. AF: contributed to interpreting the results and writing the manuscript. LR: contributed to interpreting the results and writing the manuscript. UD: designed the study and revised the manuscript. IM conceived and designed the study,

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Data availability The datasets generated and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Declarations

Conflict of interest EKM reports a Consulting or Advisory Role, Honoraria, Research Funding, and Travel Accommodations and Expenses from Bristol Myers Squibb/Celgene, GlaxoSmithKline, Janssen-Cilag, and Takeda.

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