Quality of Life in Patients with Multiple Myeloma: A Qualitative Study

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Abstract

Objective: Multiple myeloma (MM) accounts for approximately 15% of hematological cancers. Although still incurable, the prognosis of MM has much improved within the past two decades due to the use of high-dose chemotherapy (HDT) supported by autologous stem-cell transplantation (ASCT) for eligible patients and a variety of novel agents. How to use and sequence these new potent treatments is a growing challenge. While focus is on efficiency and tolerability, the ultimate goal is the reestablishment and preservation of patients’ quality of life (QoL). This has increased the relevance of examining MM patient’s QoL and experiences as long-term survivors. This qualitative study therefore aimed to gain in-depth knowledge about health related QoL in patients with relapsing-remitting MM (RRMM).

Methods: A literature study identified topics for individual in-depth qualitative interviews with eight Danish myeloma patients, four women and four men. Semi-structured interview guides were applied exploring the participants’ experiences with the course of disease and treatment, its impact on their physical, cognitive and psychosocial QoL and functioning, and if they had unmet care needs. The interviews were transcribed verbatim and analysed using a narrative medical anthropological approach aiming to elicit significant patterns in the patients’ perspectives on the impact of MM on their QoL.

Results: The participants had ambiguous perceptions of MM that was simultaneously seen as life menacing and manageable. Their physical and cognitive functioning was reduced from disease symptoms and treatment-related toxicity. Persistent peripheral neuropathy was considered particularly burdensome. The initial shock of receiving a cancer diagnosis was reduced by reassurance of the high manageable of MM. In the long run, the participants were able to lead ‘fairly normal’ lives but said their QoL was reduced by concerns about underlying disease, relapse and disability. Being able to uphold a social role and meaningful activities was crucial to their QoL. Overall, the participants did not discuss HRQoL issues with their oncologist, however, because the main focus in consultations is on cancer control.

Conclusion: Long-term QoL in patients with MM may be over-estimated. Their disease perspectives and priorities should be explored and taken into account when making treatment decisions. Newly diagnosed patients may have particular needs for emotional support and information about the improved manageable of MM.

Keywords: Multiple myeloma; Haematology; Cancer; Quality of life; Patient needs; Qualitative research

Introduction

Multiple myeloma (MM) is a hematologic cancer arising from the malignant transformation of the immunoglobulin-producing plasma cells of the bone marrow. MM accounts for approximately 15% of hematological cancers-01% of all cancers- and the incidence in Europe is 5.72 per 100,000, corresponding to approximately 27,500 new cases every year [1]. With aging populations in Europe, incidence rates are expected to rise considerably [2].

MM often involves much delayed diagnosis as the symptoms tend to be non-specific and slowly evolving. With a typical age at diagnosis at 65-70 years, general fatigue, weakness and bone pain are often misinterpreted as rheumatic or osteoporotic, for instance [1,3,4]. The four common MM symptoms include elevated calcium, renal failure, anemia and bone lesions (the CRAB criteria). In addition, reduced immune function may lead to frequent and severe infections [5].

Though still incurable, the prognosis of MM has much improved within the past two decades owing to the use of high-dose chemotherapy (HDT) supported by autologous stem-cell transplantation (ASCT) for eligible patients as well as novel agents such as Thalidomide, Bortezomib and Lenalidomide [5,6]. Recently, this positive development is accelerating with the introduction of immunotherapy and targeted agents like histone deacetylase (HDAC) inhibitors, immune checkpoint modulation and proteome recycling pathways [7]. How to use and sequence these new potent treatments is one of the growing challenges. While focus is on efficiency and tolerability, the ultimate goal must always be the reestablishment and preservation of patients’ quality of life (QoL). While induction and consolidation therapy are established treatment periods, the value of continuous treatment and maintenance are not finally determined [8], especially with regard to their influence on QoL. This has increased the relevance of examining the long-term physical and psycho-social QoL of patients with relapsing-remitting myeloma (RRMM). Here we therefore investigate the QoL of patients with relapsed MM in their treatment free period without maintenance.

A literature study showed that physical functioning even in stable RRMM patients’ may be significantly compromised and associated with...
reduced ability to carry out work, domestic chores and leisure activities. Symptoms and treatment-related adverse events have been shown to predominantly lead to fatigue and pain, with peripheral neuropathy (PN) particularly affecting many patients [9,10]. Quantitative assessments have also reported symptoms such as muscle weakness, bone lesions, depression, anxiety, insomnia, anaemia, infections, cognitive and sexual problems [2,10-12]. Factors such as female gender, advanced age, progressive disease and therapy exhaustion may also affect HRQoL in patients with RRMM [13]. It has been argued that symptoms and treatment side effects mainly affect QoL in relation to the impact on patients’ activities and participation, emotional well-being and available support options [4,14]. Symptoms, disease progression or treatment response alone thus does not adequately reflect the overall health related QoL (HRQoL) in patients with MM [10,14]. Using qualitative methods, the present study aimed to examine in depth the patient perspective on RRMM in a Danish setting. The objective was to explore how these patients consider the impact of their symptoms on their QoL.

Methods

This study was based on a systematic literature study and individual qualitative interviews with eight patients with RRMM. The interview participants were recruited strategically by MS from the Department of Hematology, Rigs hospitalet, Denmark. Data collection continued until saturation point although an equal number of men and women was required. Eligible patients had received at least one relapse treatment and had been in remission for at least three months at the time of interview. All invited patients agreed to participate. The patients had no significant co-morbidity and represented both sexes to capture any gender differences. The participants received written and oral study information underlining that participation was voluntary, might be interrupted at any time and that all data were treated anonymously following the research ethical standards. All participants gave informed consent and the study did not require ethics committee approval. The qualitative interviews were carried out in participants’ homes or a conference room by GLM in the period of June 2015- March 2016.

The literature study identified relevant topics for an interview guide aiming to explore the QoL impact of MM. Medline, Embase, PsycInfo and Artikelenbasen (for articles in Danish) were searched for literature published 2005-2015 using the key words: ’myelomatosis/multiple myeloma in combination with ’patient’ and ’quality of life/Qol/HRQoL/ functioning’, or psycho-social/burden. The semi-structured interview guide began with questions to the participants’ current and previous partner, family and professional status. The participants then described their experiences with the MM diagnosis and subsequent disease course including periods of relapse, treatment and remission. Questions went on to focus on their physical, cognitive and psychosocial health-related QoL and functioning. Finally, their disease perceptions and hopes for the future were discussed [15] (link to the interview guide).

The interviews were transcribed verbatim and analysed using NVivo (QSR) software and a discourse theoretical approach to the relationship between language and construction of meaning [16]. The participants’ statements were seen as an expression as well as an ongoing construction of the meaning and personal impact of living with MM. This approach is used to analyze a diversity of statements such that clusters of meaning are generated. It involves an exploration of the terminology used to speak about the subject and the ways in which it is related to other issues. Firstly, the data were thus coded into the topics that were raised during the discussions. Secondly, the most important themes within each topic were identified. Finally, the frequency of and connections between topics and themes were analysed. This generated a pattern of the relative meaning that the different topics and themes had for the participants when framing the impact of MM on their physical, emotional and social QoL. All methodological and analytical steps were discussed and alternative interpretations sought with the authors and with an additional anthropologist.

Results

At the time of the interview, the participants were aged between 67-76 years; all were pensioners, and all but a recent widower had a partner, grown children and grandchildren. The participants who were now in remission and without anti-myeloma treatment had previously received various types of MM treatment. Current supportive therapy with analgesics, bisphosphonates and anti-depressants was allowed (Table 1).

The participants were diagnosed with MM after presenting with pain or bone fracture. In some cases, diagnosis took several months of uncertainty with misdiagnosis and various tests before attaining specialist treatment. No participants suspected or had prior knowledge of MM and they were shocked with the diagnosis as the mere concept of cancer suggested a risk of imminent death. The following months, patients and their relatives had been very anxious. Subsequent reassurance depended much on the information they received about MM and management options. Being told that “this is not a disease that you die from, but one that you die with” had been particularly crucial to their coping with MM.

Treatment Experiences

The six participants having received HDT found that this was by far the toughest treatment. All other treatments were described in less disturbing terms. With HDT, some fell sick from the initial treatments; some found the stem cell extraction or holding ice chips in the mouth agonising. HDT was described as a ‘horrible experience’ involving an ‘unsettling feeling that they (the doctors) are killing everything’ leading some patients to briefly consider ‘if this was worth it at all’. In most cases, HDT lead to hair loss, nausea, vomiting and diarrhea for 1 to ½ months. Still, as efficacy ultimately took priority, and because the suffering was limited in time, no participants reclined receiving HDT again, if necessary.

The main treatment side effect was persisting PN experienced in two of three participants having received bortezomib and two in three treated with Thalidomide. These patients suffered from pain, hypoesthesia or paresthesia in their feet. Bortezomib and Thalidomide were therefore the only treatments that four participants rejected receiving again. Excepting those, the participants trusted their oncologists to find the best treatment option when need be and did not request much involvement in treatment decisions. The participants were mostly satisfied with their communication with the oncologist, though some wished they had received psychological support at the time of diagnosis. Many said they still anticipated controls with some apprehension.

Patient quote 1: Quality of life impact of peripheral neuropathy

“Physical and cognitive quality of life effects in multiple myeloma” Five participants said they had become prone to infections; some had been hospitalized several times with pneumonia. Four participants had PN; one suffered from cramps and six from pain in the joints.
or bone-mainly in their back or shoulders-leading sometimes to sleep disturbances. All participants had lost some mobility, physical strength and stamina reducing their ability to work, do house work and exercise, in particular. Some had recovered from severe loss of physical functioning following fractures or HDT with very negative impact on their QoL. The participants explained that this was mainly due to the fact that they attached identity, self-esteem and meaning to being active and able to use their craftsmanship around the house or to help out family members (males), caring for grandchildren or being fit and attractive (women).

Six participants felt their cognitive functioning had decreased with loss of short-term memory and concentration in particular. Only one found this reduced her daily functioning, though, and many were unsure if their reduced physical or cognitive abilities were due to MM, treatment or ageing.

**Patient quote 2: Physical functioning bring meaning to patients’ lives**

“Psycho-social quality of life impact of multiple myeloma” In two of three participants who had retired due to MM, this had been a difficult change of everyday life. After the initial crisis, most said they had led ‘fairly normal’ lives outside of treatment, however. Today, the participants said the disease was not constantly worrying but that they always had ‘an underlying consciousness of it’. Some said they had become emotionally vulnerable and that spouts of pain, for instance, might lead to worries about it being a symptom of ‘something dangerous’, i.e. relapsing disease. Still, when relapses had indeed occurred, most said they had had no premonition and reacted with renewed anxiety—i.e. relapsing disease. Still, when relapses had indeed occurred, most

**Table 1: Participant characteristics.**

| Participant | Male (M) | Female (F) | Age at time of interview (years) | Personal status at diagnosis | Professional status at diagnosis | Year of diagnosis | MM treatments | Current IMWG status |
|-------------|---------|------------|-------------------------------|-----------------------------|-------------------------------|------------------|---------------|-------------------|
| M1          | 73      | Married 2 children 5 grand children | Self-employed | 2007 | 1 Line 2007 CyDex induction with stem cell harvested and HD-treatment 2 Line 2009 local irradiation 3 line 2012 VCD induction and HD treatment 4 line 2013 Rd | CR since Nov. 2014 |
| M2          | 76      | Widowed 2 children 5 grand children | Retired | 2011 | 5 line 2012 MPT 6 line 2013 Bendal-VD 7 line 2014 Rd | VGPR since Okt. 2015 |
| M3          | 63      | Divorced 2 children (1 deceased) 1 grand child | Employed | 2008 | 8 line 2008 CyDex induction + harvest + HD-mel 2009 9 line 2013 local irradiation | CR since Nov. 2013 |
| M4          | 73      | Married 2 children 1 grand child | Self-employed | 2005 | 1 line 2005 VAD induction + harvest + HD-Mel 2 line 2009 Td induction + HD-mel II | VGPR since Okt. 2010 |
| F1          | 67      | Married 2 children 5 grand children | Retired | 2007 | 1. line 2007/8 VAD induction + harvest + HD-Mel 2 line 2013 VCD x 3 induction and HD mel II 3. line 2015 Rdx 3 + dax | VGPR since June 2015 |
| F2          | 67      | Married 2 children 4 grand children | Employed | 2007 | 1. line 2007 CyDex induction + harvest + HD-Mel II 2. line 2010 Td + HD-Mel III 3. line 2010 local irradiation 4. line 2014/15 Td + HD-Mel IV 5. line 2015 local irradiation | PR since May 2015 |
| F3          | 67      | Married 3 children (1 deceased) 1 grand daughter | Employed | 2003 | 1. line 2003 VAD/Cy-Dex induction + harvest + HD-Mel I x 2 2. line 2015 V-MPdx 7 3. line 2015 local irradiation | PR since July 2015 |
| F4          | 74      | Co-habiting partner 2 children 1 grand child | Retired | 2011 | 1. line 2012 MPT × 8 2. line 2014 local irradiation 3. line 2015 Rd × 7 | VGPR since Okt. 2015 |

IMWG: International Myeloma Working Group; CR: Negative immunofixation on the serum and urine and disappearance of any soft tissue plasma cytomas and <5% plasma cells in bone marrow; VGPR: Serum and urine M-protein detectable by immunofixation but not on electrophoresis or ≥50% reduction in serum M-protein plus urine M-protein level < 100 mg/24 h; PR: ≥50% reduction of serum M-protein and reduction in 24 hours urinary M-protein by ≥50% or to <200 mg/24 h if the serum and urine M-protein are unmeasurable, 5a ≥50% decrease in the difference between involved and uninvolved FLC levels is required in place of the M-protein criteria If serum and urine M-protein are not measurable, ≥50% reduction in plasma cells is required in place of M-protein, provided baseline bone marrow plasma cell percentage was ≥30%. In addition to the above listed criteria, if present at base; CyDex: cyclophosphamide/dexamethasone; HDT: High-Dose Chemotherapy (with ASCT); ASCT: Autologous Stem-Cell Transplantation; VCD: Bortezomib/Cyclophosphamide/Dexamethasone; Rd: Lenalidomide/Dexamethasone; Mel: Melphalan; MPT: Melphalan/Prednisone/Thalidomide; Bendal-VD/BVD: Bendamustine/Bortezomib/Dexamethasone; VAD: Vincristine/Doxorubicin/Dexamethasone; Td: Thalidomide/dexamethasone

Table 1: Participant characteristics.
upholding an important social and familial role was crucial to their QoL.

Discussion

The MM diagnosis came as a shock to the participants who had no prior knowledge about this disease. Early information about the promising treatment options was crucial to reduce their anxiety. Today, all stressed that MM ‘is not a disease you die from but one that you die with’. In our analysis, this is a core phrase for understanding the ambiguous patient perspective on MM: any cancer is instinctively considered critical, but—to the surprise of many—the tolerable symptom burden and medical manageability enables patients to lead ‘fairly normal lives’ albeit with some reduced physical and cognitive functioning.

While HDT was indeed very challenging [4], only PN was described as persistently reducing the QoL of some patients. Aside from PN, MM was considered a ‘strange disease that you cannot feel when outside of treatment’, i.e. a potentially deadly disease without major symptoms in periods of remission. The patients had faith in the treatment options but from fear of relapse, they continuously felt uneasy with controls and potential symptoms. Though not a source of constant worries, the uncanny consciousness of underlying disease lead to emotional vulnerability, changed body image as well as to positive life priorities. As others have argued, living with RRMM involves an ever-shifting perspective between illness and wellness that sustains a state of uncertainty [17].

Our study suggests that upholding one’s social role and keeping active were crucial to coping with MM and preserving normality which was decisive to the patients’ QoL. Fear of disability had thus largely replaced the initial fear of dying. We therefore agree that the distress of symptoms is linked to the contexts in which they challenge patients’ relations and activities [4,9]. In our study, the women particularly tried to spare their loved ones from worries which may explain why female patients may suffer more from disturbed role, isolation and emotional aspects [2].

Yet it is a limitation of our study that it may be biased by the majority of participants stating to have supporting partners and relatives and thus may not adequately reflect the experiences of low-functioning patients and those lacking supports. Selecting eligible participants may have implied a bias towards well-spoken patients with good physician rapport. Recall-bias may also involve an under-communication of the ambiguous patient perspective on MM: any cancer is instinctively considered critical, but—to the surprise of many—the tolerable symptom burden and medical manageability enables patients to lead ‘fairly normal lives’ albeit with some reduced physical and cognitive functioning. The MM diagnosis came as a shock to the participants who had no prior knowledge about this disease. Early information about the promising treatment options was crucial to reduce their anxiety. Today, all stressed that MM ‘is not a disease you die from but one that you die with’. In our analysis, this is a core phrase for understanding the ambiguous patient perspective on MM: any cancer is instinctively considered critical, but—to the surprise of many—the tolerable symptom burden and medical manageability enables patients to lead ‘fairly normal lives’ albeit with some reduced physical and cognitive functioning.

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Our qualitative approach provided explanations of how and why symptoms affect the roles, relations and activities that patients find meaningful and crucial to their QoL. This study confirms the existence of an unmet need for emotional support and information, particularly at the time of diagnosis [2,18]. It also suggests a continued need for communication, not only about test results and treatment options, but also addressing patients’ emotional concerns e.g. worries about role functioning and disability. Also, prophylactic treatment against infections should be considered as infections jeopardise patients’ health and may trigger anxiety. Finally, the negative QoL impact of PN should be taken into consideration when making treatment decisions.

An increased integration of QoL measurement in clinical trials has also been suggested to focus more on patient-welfare as well as survival [19,20]. Our study confirms that patients do not always report HRQoL problems, mainly because the main focus in consultations is on the cancer control and management. This may contribute to physicians overestimating HRQoL in patients with MM [9]. Clinicians and patients have also been shown to have different treatment priorities with respect to improving life expectancy and QoL and that discordance may exist between their respective perceptions of symptoms and side effects [3]. Overall, and especially in the context of new MM treatments, patients’ HRQoL and preferences should be increasingly considered in treatment choices.

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