Patient-Reported Outcomes and Assessment of Quality of Life: A Focus on Multiple Myeloma

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Abstract

Patients with multiple myeloma are living longer, yet the chronicity of newer treatment modalities has led to increased symptom burden and a notable effect on quality of life (QOL). The assessment of QOL and evaluation of patient-reported outcomes is an essential element to the care of this population. Patients with MM may experience unwanted side effects or disease-related symptoms that create a burden in everyday living. Subjective patient-reported information has become an important dimension to the overall care and treatment of these patients. Symptoms that negatively affect health-related quality of life (HRQoL) and their impact on future treatments should be assessed using patient-reported tools. Many patients’ treatment decisions are guided by their perception of their HRQoL. It is important for advanced practitioners to explore which factors are most impactful to the patient. Improved understanding of this can further enhance the management of symptoms and adjustments in treatment to avoid further reduction in HRQoL.
different treatments have an impact on HRQoL. Neurologic, hematopoietic, and cardiac side effects are the most common toxicities in patients undergoing prolonged treatment. Because these patients have an extended overall survival, they will frequently discuss HRQoL issues with their providers during follow-up and routine care (Gerecke et al., 2016).

**DISEASE-SPECIFIC SIDE EFFECTS**

Patients with MM may suffer an array of side effects, all potentially impacting HRQoL. Some side effects can include anemia, fatigue, mouth sores, peripheral neuropathy, bone pain, increased risk of infection, fractures, diarrhea, steroid-associated side effects, and deep vein thrombosis. Advanced practitioners must have the ability to assess and manage these potential side effects as patients continue undergoing treatments. Recognizing and treating complications, as well as following regimen protocols and administering preventative medication, are major roles of advanced practitioners.

Gadó & Domján (2013) describe MM as a chronic, incurable disease that may be associated with a reduction in QOL. Pathologic bone fracture, bone pain, fatigue due to anemia and malignant disease itself, and neurologic symptoms that may be associated with hypercalcemia may impact the HRQoL of patients with MM. Many of the therapies for MM are administered via IV injections or infusions and are given frequently, even weekly. Routine laboratory check-ups, repeated blood sample collections that may require painful needlesticks, and bone marrow aspiration and biopsy are frequently required for diagnosis and monitoring of the disease response and recurrence (Gadó & Domján, 2013). All of these procedures have an impact on a patient’s HRQoL. Potential treatment with stem cell transplantation poses considerable effects as well, as does high-dose chemotherapy. In addition, infection, mucusitis, increased use of blood products, and extended or recurrent hospital admissions affect HRQoL (Gadó & Domján, 2013).

Additional side effects may include skeletal disease, myelosuppression, and venous thromboembolic events. To reduce the incidence of skeletal events, bone pain, and hypercalcemia, administering a bone-modifying agent such as pamidronate, zoledronate, clodronate, or denosumab is recommended in combination with systemic treatment (Anderson et al., 2018; Noonan et al., 2017).

Infections are the principal cause of mortality among patients with MM. Patients who present with prolonged neutropenia or recurring bacterial infections can be prescribed granulocyte colony-stimulating factors (G-CSF) and/or intravenous immunoglobulins (Brigle et al., 2017). Patients with MM are also at an increased risk of venous thromboembolism. The risk is comparative to patient-specific factors, including immobility, hyperviscosity, and history of previous venous thrombosis. These risks can increase with the use of immunomodulatory drugs, carfilzomib, or high-dose steroids (Noonan, Rome, Faiman, & Verina, 2017). Prophylactic administration of aspirin or low-molecular heparin depending on the number of risk factors is essential with concurrent treatment (Gerecke et al., 2016).

Supporting patients through side effects to reduce further decline in their HRQoL is important. Encouraging adequate sleep, proper nutrition, increased fluid intake, and moderate activity is essential to maintaining a healthy lifestyle. Medications such as pain medication, antiemetics, or sleep aids, if appropriate, should be utilized.

**EVIDENCE FOR USING QOL TOOLS IN CLINICAL PRACTICE**

As advanced practitioners, there is a need to increase our focus on QOL. Although prolonging survival is typically the main focus and goal of cancer treatment, advanced practitioners need to acknowledge that patients suffer from many disease-related side effects that can further lead to functional impairments (Leppert et al., 2015).

In 2018, the American Society of Clinical Oncology added QOL into their framework for determining the value of treatment regimens (Harrison, 2016). The U.S. Department of Health and Human Services has also put a focus on HRQoL in the study and approval of new anticancer treatment medications (2018). Providers’ understanding that patients will require long-term and possibly multiple treatments, making them susceptible to chronic side effects and treatment-related issues, gives patients the reassurance that providers
consider the impact of treatment on their HRQoL. Many patients feel their quality of life is more important than prolonging their lives. In a sense, health care today has slowed both the aging and dying process (Cavallo, 2014).

Quality of life has become an important endpoint in recent, randomized clinical trials (Roussel et al., 2020; Schjesvold et al., 2020). Gadó & Domján (2013) state that studies that have demonstrated a reduction in HRQoL in patients with MM have determined that HRQoL assessment should become part of routine clinical care. Clinical trials should include HRQoL as a study endpoint as well be considered as a potential primary endpoint for future studies. Improved QOL in patients with MM has demonstrated improved prognostic significance, thus making HRQoL assessment an essential element of patient care. Evaluating HRQoL creates a meaningful influence on both the patient’s and caregiver’s overall well-being and has been noted to improve the process of adapting to having a disease (Leppert, Gottwald, & Forycka, 2015).

Obtaining HRQoL assessments is critical to capture health aspects that matter to patients and go beyond just the prolongation of life (Leleu et al., 2017). Unfortunately, there are no standard guidelines or recommendations for monitoring patient-related outcomes and HRQoL assessments in clinical trials (LeBlanc, Hirschey, Leak Bryant, LeBlanc, & Smith, 2019). Despite this, appreciation of which factors are most important to the individual patient will assist in finding the right treatment for the patient while attempting to alleviate worrisome side effects.

Reduction in a patient’s HRQoL may be the reason for treatment discontinuation and consequently disease progression, particularly when physiologic or psychologic side effects are inappropriately managed (Amgen, 2015; Faiman, 2016; Faiman, 2017; King & Faiman, 2017). It is important for advanced practitioners to explore which factors impact the patient most. A deeper understanding of this can improve the management of symptoms and adjustments in treatment, therefore avoiding a larger reduction in HRQoL. Quality of life is not simply defined, and its meaning will differ for everyone. Identifying patients who may require additional care or support should focus on patient-reported outcomes, including side effects and symptom burden, as part of routine practice (Ramsenthaler et al., 2016).

Patients with chronic illness such as MM experience many emotions throughout their treatment course. Because of the many advancements in treatment options, there has been an increase in disease-free periods when dealing with malignancies. This is where the evaluation of HRQoL becomes significant in clinical practice. Lingering effects of therapy may persist even if patients are not currently on treatment for their illness. Advanced practitioners have a responsibility to determine what is important to the individual patient. Patients will confide in us, explain what they are feeling, and express their frustration if we show more understanding and empathy.

The fundamental reason for using QOL measures in daily practice is to make sure that treatment plans focus on the person rather than the disease itself (Higginson & Carr, 2001). This idea goes back to Florence Nightingale, as she was one of the first clinicians to assert the notion of considering the effects and consequences of routine care when evaluating treatments (Higginson & Carr, 2001). Quality of life measurement in clinical practice is essential for prioritizing problems, understanding what matters to the patient, and assessing changes the patient is experiencing. In all stages, whether reviewing current care, monitoring for improvement in disease, or noting progression of disease, QOL assessment is warranted. King, King, and White (2017) state that there is a benefit to using self-reported tools and patient-reported outcomes in assessing HRQoL to better understand how the treatment and/or disease impacts the patient. They also mention there is expanding evidence favoring the use of patient-reported outcomes specifically in the clinical care of the MM patient. The inclusion of HRQoL measurement into patient care plans will also determine future needs and outcomes.

Measuring QOL begins with using a reliable and valid tool. The tool chosen must be reflective of the patient population and appropriate for use in clinical practice. Specifically, it needs to be able to measure what a provider is seeking to evaluate. It needs to be consistent and reliable. The results need to be able to be appropriately interpreted by
the providers. HRQoL is described as a complex process, and the evaluation is critically dependent upon which tool is utilized for analysis (Kvam & Waage, 2015).

**COMMON TOOLS USED TO ASSESS QOL**

Numerous questionnaires have been developed to assess QOL in clinical practice (Table 1). Some are very broad, and some are specific to one disease or symptom. The European Organization for Research and Treatment of Cancer (EORTC) QLQ-C30 is a questionnaire developed to assess the QOL of patients with cancer. EORTC-QLQ-C30 is the most widely used instrument in cancer questionnaires approved for use in the analysis of the cancer population (Kontodimopoulos, Ntinoulis, & Niakas, 2011). Consistency, reliability, and validity in measuring the health-related status of cancer patients were demonstrated with this tool. The EORTC-QLQ-C30 survey is designed with multi-item modules and single-item measures. Included in this are functional scales (physical, role, cognitive, emotional, and social), symptom scales (fatigue, pain, nausea and vomiting), and a global health status/QOL scale. Single items are also assessed to evaluate other symptoms described by patients, including shortness of breath, loss of appetite changes, difficulty sleeping, changes in bowel patterns, and financial burden of being affected by illness. A briefer variety of the EORTC scale that is adapted for palliative care is the EORTC QLQ-C15-PAL.

The Functional Assessment of Cancer Therapy—General (FACT-G) is another example of a discrete questionnaire for patients with malignancies. Furthermore, there are detailed modules for different malignancies, all of which are guided by

| Questionnaires That Assess Quality of Life in Clinical Practice | Description |
|---------------------------------------------------------------|-------------|
| **FACT-G (Functional Assessment of Cancer Therapy: General)** | Self-administered, approximately 5 min to complete |
| | 27 items, 5 domains |
| | Based on a 5-point numeric ranking scale (0 = not at all; 1 = a little bit; 2 = somewhat; 3 = quite a bit; and 4 = very much) |
| **EORTC QLQ-C30 (European Organization for Research and Treatment of Cancer—Quality of Life)** | Most widely used instrument in cancer care |
| | Uses functional and symptom scales |
| | Uses a 4-point rating system |
| | 30 questions and takes approximately 10-15 min to complete |
| **RSCL (Rotterdam Symptom Checklist)** | Self-administered with 39 items |
| | Patients are asked to indicate the degree to which they have been concerned by the indicated symptoms in the past week |
| | Uses a 4-point Likert-type scale (not at all, a little, quite a bit, and very much) |
| | Evaluates physical symptoms, psychological symptoms, and activities of daily living |
| | Takes approximately 8 min to complete |
| **ESAS (Edmonton Symptom Assessment System)** | Visual analog scale |
| | Ranges from 0 (absent) to 10 (worst possible severity), with 9 items |
| | Self-administered, but if this is not possible, can be completed with assistance, or administered by a caregiver/health professional |
| **HADS (Hospital Anxiety and Depression Scale)** | Self-reported and self-administered questionnaire that measures depression and generalized anxiety |
| | 4-point Likert scale; response options vary |
| **POMS (Profile of Mood States)** | Uses a 5-point Likert scale; response options are not at all, a little, moderately, quite a lot, and extremely |
| | Self-administered questionnaire |
| | Takes approximately 5-10 min to complete |
| | Extensive testing, used widely in multiple areas |
| **VAS-C (Visual Analogue Scale—Cancer)** | Psychometric measuring instrument |
| | Self-administered |
| | Easy and quick to administer |
scoring manuals and specific guidelines, making for detailed assessments of QOL that are disease specific and reliable. In oncology, some other common tools include the Visual Analogue Scale—Cancer (VAS-C), Profile of Mood States (POMS), and the Rotterdam Symptom Checklist (RSCL). Other general tools used frequently include the Short Form 36 (SF-36), a patient self-reported scale, the Edmonton Symptom Assessment System (ESAS), and the Hospital Anxiety and Depression Scale (HADS).

The FACT-G scale was originated to measure QOL in cancer patients undergoing treatment. It includes subscales to evaluate overall well-being. The four subscales include physical, social/family, emotional well-being, and overall functional well-being. Clinicians using the FACT-G scale can produce a total score and four subscale scores with scale and distributions that are specific to the sample (Yost et al., 2012).

The RSCL tool is used to evaluate symptoms and questions involving patients’ daily activities. It includes both psychological and physical factors (Leppert et al., 2015). Irritability, mood, nervousness, tension, anxiety, difficulty concentrating, and distress about the future are dimensions that are assessed. It is a valid tool in assessing the many domains that affect QOL in a patient. These domains include psychological, professional, social, and physical areas that may compromise QOL (Leppert et al., 2015).

The ESAS tool is comprised of visual analogue scales, which evaluate discomfort, activity, emotional state, insomnia, appetite, general well-being, and difficulty breathing or shortness of breath. It also allows for a patient to explain any additional symptoms they may be experiencing. This, too, is an accepted tool with proper validity and reliability (Leppert et al., 2015).

IMPLEMENTING QOL TOOLS INTO PRACTICE

In a review of studies that have implemented tools to evaluate QOL in clinical practice, it is suggested that these tools have the potential to improve communication between the provider and the patient and may also improve care. However, these tools are not being widely used enough (King et al., 2016). Quality of life tools enable advanced practitioners to be able to better discuss sensitive issues that may be important to the patient, both medical and emotional matters (Kvam & Waage, 2015). There has been widespread belief among health-care specialists that these tools have a beneficial role to play in improving clinical practice (King et al., 2016). Evaluating QOL gives advanced practitioners the ability to obtain important information from patients. In doing so, physical symptoms, psychological, social, and spiritual dimensions are also assessed (Leppert et al., 2015). Instruments utilized should be easy to understand and consider the clinical staging of the patient. They should be easily included in daily clinical practice. Quality of life assessment is a substantial element in clinical trials and a source of growth in oncology treatment and the symptom management of malignancies. An important goal in cancer care is the improvement and maintenance of the highest HRQoL possible, especially in those patients who suffer advanced, ongoing disease. (Leppert et al., 2015).

The incorporation of HRQoL tools in cancer care can serve many purposes in clinical practice: understanding the patient’s overall state, screening for emerging disease, assessing needs, setting treatment goals, monitoring response to therapy and disease progression, improving provider-patient communication, and standardizing interactions between patients and providers (Bjordal, 2004). Implementing policy change and further research to promote awareness of tools with training on the use and interpretation are all important to create clinical practice guidelines (King et al., 2016).

A simple way to begin implementation into practice would be to first determine what tool is best for the individual practice. Then, having an advanced practitioner review it as part of the patient’s care plan will prompt the discussion on what is impacting HRQoL for that patient. This will lead to a more impactful patient-provider experience, a more focused discussion, and better identification of the patient’s difficulties and needs.

EXAMPLE OF EVALUATION OF QOL IN CLINICAL PRACTICE

Fragola (2018) sought to investigate factors that affected HRQoL in patients with MM, as well
as providers’ knowledge and perceptions of the importance of QOL in clinical practice. A non-interventional approach was taken. The sample included 20 providers within two office outpatient settings in which a pre-test, educational intervention, and post-test were performed. Patient data were collected from 21 adult patients with MM. A 4-week time frame was allotted to gather patient information, verbally present the patient data to providers, and administer the post-test. The EORTC-QLQ-C30 questionnaire (version 3), as well as the EORTC-QLQ-MY20 MM-specific supplemental scale were used to obtain patient data responses. The tool used for providers to assess their perception of the importance of QOL in clinical practice and the basis for the pre- and post-test questionnaires were found in an open-access article by Bossola and colleagues (2010).

An evaluation of patient scales revealed that patients suffered side effects that influenced their HRQoL. Nausea, vomiting, appetite loss, constipation, and effects on cognition were commonly reported. There was a significant difference using a Wilcoxon signed-rank test with cognition between gender (Fragola, 2018). The Wilcoxon test is a nonparametric statistical test that compares two paired groups. The test calculates the difference between each set of pairs and analyzes these differences (Investopedia, 2020). Males experienced more severe cognitive disruption than females. Once patient data was evaluated, it was noted that their QOL was indeed affected by ongoing treatment and disease-related side effects.

Quality of life was determined to influence diagnostic strategies within this evaluation. After evaluating the symptoms that most impacted patients, it was then explained to providers within the practice setting. Findings based on that data allowed Fragola (2018) to educate the providers on the importance of developing an assessment tool that can be utilized in clinical practice. Ninety percent of providers sampled subsequently indicated they would likely utilize a QOL tool in practice, as opposed to 30% prior to the presentation of patient data. The clinical practice was receptive to these findings, and a practice tool is currently being implemented into the clinical setting.

Results from the information presented by Fragola (2018) suggested that the importance of HRQoL was better perceived after review of the patient data scales. Providers need an accurate understanding of this, as treatment of many malignancies is ongoing, and determining what matters most to the patient will ultimately lead to better continuity of care. Notable findings suggested that a QOL tool is useful in the treatment and care of patients with MM. The study also validated that HRQoL is indeed affected by the many treatment modalities used to treat this disease. The results exposed the importance of providers having knowledge and an understanding of how QOL is affected, as well as the positive impact this understanding will have on the patient’s overall treatment plan.

**RECOMMENDATIONS FOR FUTURE RESEARCH**

There is a need for research focused on the correlation between HRQoL and improved prognosis of patients. The application of research findings should then be utilized to further develop and encourage QOL tools into the assessment and care of patients with chronic illness. There is no doubt that HRQoL adds an important element to the traditional endpoints in clinical trials, and these measures should be incorporated within future studies (Kvam & Waage, 2015).

Few studies focus on the assessment of the provider’s knowledge of or attitudes towards HRQoL, or how providers would accept implementing QOL measures into practice. What is known is that inquiring about both a patient’s psychosocial and physical issues are related to increased overall satisfaction as well as improved health outcomes (Bossola et al., 2010). Bossola and colleagues (2010) noted that over 80% of physician participants would like to incorporate QOL into clinical practice, but only a small portion (one third) understood what QOL measures were.

**CONCLUSION**

Evaluating HRQoL and patient-reported outcomes is an essential element of patient care. It has been shown to have a positive impact on both the patient’s and the caregiver’s overall well-being, as well as improve the process of adapting to having a disease. It is a privilege for advanced practitioners to assist patients through what is often the most
difficult time in their lives as they deal with their chronic disease. We do this day by day, and we impact patients more than we know. Therefore, it is essential to incorporate the assessment of HRQoL for comprehensive care. Regardless of the specific disease or prognosis, HRQoL should be evaluated when the illness is diagnosed, throughout treatment, during follow-up, and at the end of life as we offer our support to patients and their families throughout the entire course of illness.

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