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Myelodysplastic Syndromes: Challenges to Improving Patient and Caregiver Satisfaction

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Abstract

The task of improving patient and caregiver satisfaction in the management of myelodysplastic syndromes (MDS) poses many challenges for physicians and patient care teams. Advances in the understanding of MDS biology have resulted in the approval of 3 agents for the treatment of MDS by the US Food and Drug Administration (FDA) in the past decade. However, according to a retrospective physician survey, the majority of recently diagnosed patients with MDS still receive supportive care only. Interestingly, a survey performed in patients with MDS suggests that patient understanding of treatment goals and prognosis is often limited, with a third of patients reporting that prognosis was not discussed with their physician. Efforts to improve patient awareness of their disease severity and establishing clear treatment goals are crucial for setting up an individualized treatment plan and ensuring optimal patient and caregiver satisfaction.

Keywords

Caregiver satisfaction; Myelodysplastic syndromes; Patient satisfaction

Myelodysplastic syndromes (MDS) represent a heterogeneous group of hematologic diseases with various clinical manifestations.[1-3] Because of the complexity and variability of MDS, there are many challenges in terms of patient and caregiver satisfaction, some of which involve our ability as physicians to educate our patients about these disorders, the potential treatment approaches that are available, and expected outcomes for patients with MDS receiving or not receiving active treatment.

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WHAT DO MYELODYSPLASTIC SYNDROMES LOOK LIKE?

The Physician's Perspective

Both the rare incidence of MDS and its many varying presentations and manifestations have made it hard to delineate a clear treatment plan for many patients diagnosed with the disease. Over the past decade, the biology under-pinning MDS has slowly emerged. There are now 3 agents with US Food and Drug Administration (FDA) approval for treatment of patients with MDS: lenalidomide for patients with transfusion-dependent anemia with International Prognostic Scoring System (IPSS)-defined Low- and Intermediate (Int)-1-risk MDS with deletion of the long arm of chromosome 5, or del(5q), with or without other cytogenetic abnormalities; azacitidine for patients with MDS of all French-American-British (FAB) subtypes; and decitabine for patients with MDS of all FAB subtypes and IPSS Int-1–, Int-2-, and High-risk groups. All 3 agents have been shown to reduce red blood cell (RBC) transfusion requirements and improve quality of life in patients with MDS when compared with best supportive care.[4-8] In addition, azacitidine has been shown to significantly prolong overall survival in patients with IPSS Int-2- or High-risk MDS when compared with conventional care regimens in a large randomized phase 3 trial.[7] Despite these advances, there remain many challenges to physicians, their patients, and their patients' caregivers in managing MDS. In 2008, Sekeres and colleagues published the results of a retrospective physician survey comprising data from 6 cross-sectional studies conducted among 101 hematologists and oncologists in 46 states in the United States.[9] Clinical data were collected between June 2005 and January 2007 from 4,514 patients with established or recently diagnosed MDS, with between 614 to 827 patients per study. Despite the inherent biases of the retrospective study design and the fact that participating physicians were likely to be familiar with MDS, these studies present an overview of patient characteristics and therapy habits observed in daily practices of specialists.

Baseline characteristics of the recently diagnosed patients with MDS included in this survey are summarized in Table 1.[9] Most of the recently diagnosed patients had anemia and what was considered mild thrombocytopenia and mild neutropenia.[9] At diagnosis, the likelihood of RBC transfusion dependence was approximately 3 times greater and the likelihood of platelet transfusion dependence was 6 times greater in patients with IPSS-defined higher-risk MDS (Int-2- or High-risk) compared with patients with lower-risk MDS (Low- or Int-1-risk).[9] Interestingly, 42% of patients with higher-risk disease had never needed platelet transfusions; 12% of these patients had also never needed RBC transfusions.[9]

Another surprising finding was that nearly 25% of recently diagnosed patients with MDS had circulating peripheral blasts, a condition that is generally associated with higher-risk MDS subtypes.[1,3,10,11] It is possible that this seemingly high rate may be an overestimation due to the fact that patients with peripheral blasts are more likely to be referred to specialists who are familiar with MDS, such as those who answered the survey. Approximately 10% of patients included in the survey had secondary MDS, which in most cases was subsequent to treatment with chemotherapy. It is plausible that with an increasing number of patients receiving chemotherapy for other malignancies, coupled with an aging population, the incidence of MDS will increase over time.[12]

The approaches to care that were reported were consistent with the finding that ~66% of patients had IPSS-defined lower-risk MDS; most of the recently diagnosed patients received supportive care, including 58% of patients treated with erythropoiesis-stimulating agents (ESAs) and approximately 10% of patients receiving granulocyte or granulocyte/macrophage colony-stimulating agents.[9] Approximately 16% of patients were treated with active therapeutics including azacitidine (16%), lenalidomide (8%), decitabine (2%), and thalidomide (1%).[9] The recommendation to undergo hematopoietic stem cell transplantation (HSCT) was noted in only 4% of patients despite the fact that HSCT is the only potentially curative therapy for patients with MDS.[13] It is suspected that concerns regarding HSCT-related toxicities played a role in the low interest in this treatment modality. Finally, only 1% of patients were treated on clinical trials. As the Sekeres et al.[9] report notes, supportive care with ESAs is still the mainstay of medical intervention for patients with MDS. It appears that advances in the understanding of the biology of MDS and the availability of agents approved to treat patients with MDS have not translated to significant numbers of patients undergoing medical treatment. Would better understanding of the potential impact of disease-targeted therapies by physicians and patients improve these numbers?

The Patients' Perspective

To better understand the patients' perspective on MDS, a self-directed online survey was conducted over a 2-week period in March 2009.[14] The survey was sponsored by the Aplastic Anemia and MDS International Foundation, and included 358 patients registered with this group across 46 states in the United States. The survey sample population was limited to patients with Internet access who were regular visitors to the noted websites and who had access to websites with patient information on MDS. The median age of survey participants was 65 years, which is younger than the median age of patients with MDS in general (70 years at diagnosis); this suggests that the sample population may not have been fully representative of the general population of patients with MDS.[10,15]

Survey participants reported that they were diagnosed with MDS a median of 3 years prior to the survey, and over half (54%) of them reported an abnormal blood test at a median of 6 years before the survey. This suggests that a majority of patients experienced a 3-year delay between their first abnormal blood test and diagnosis of MDS.[14] Patients reported that their physicians rarely described their disease as "bone marrow cancer" when first explaining their medical condition (only 7%), and more commonly used terms such as "bone marrow disorder" (80%), "anemia" (56%), or "blood disorder" (32%).[14]

When asked about their understanding of their disease, over half of the patients (55%) did not know what their IPSS-defined risk score was and more than a quarter (28%) did not know their disease risk based on cytogenetic analysis. Moreover, a third of patients suggested that prognosis was not discussed with their physician.[14] These figures were considered surprisingly high, especially given that these patients had access to information on MDS.

MDS-associated cytopenias often result in chronic transfusion requirements: 65% of the survey participants had received ≥1 blood transfusion during their disease course.[14] One third (34%) of these patients described blood transfusions as a burden for their family and

two thirds (65%) of the patients would prefer an active drug therapy that allows them to stop or reduce blood transfusion requirements, even if this therapy temporarily impairs their physical well-being.[14]

FDA approval of 3 agents to treat MDS (azacitidine, decitabine, and lenalidomide) has necessitated the development of treatment strategies and goals for patients. Most MDS specialists focus on developing individualized treatment goals, often stratified by the patient's IPSS risk group. For example, often the main goals for patients with IPSS-defined lower-risk disease include efforts to improve bone marrow function, decrease transfusion needs, and decrease the impact of MDS on the patient's quality of life. To best accomplish these goals, a careful monitoring plan should be implemented. The goals for patients with IPSS higher-risk disease might be to stabilize bone marrow function, improve blood cell counts, reduce the risk of progression to acute myeloid leukemia, and attempt to determine how to maximize treatment benefit for the patient. The patient survey found that patient understanding of treatment goals and prognosis was limited.[14] Overall, about a third of patients (37%) believed that their current therapy would increase their chances of survival, whereas another third (36%) were uncertain. Interestingly, 31% of patients who were currently receiving supportive care believed that this "therapy" would increase their chances of survival and did not appear to recognize that supportive care generally aims to improve or maintain quality of life and has a minimal to zero impact on MDS disease biology.

> Only 7% of patients describe MDS as cancer and a third of patients report that prognosis was not discussed with their physician.[14]

OVERCOMING THE CHALLENGES TO PATIENT AND CAREGIVER SATISFACTION

There are many challenges concerning patient and caregiver satisfaction in the management of MDS (Table 2). Physicians caring for patients with MDS must focus on improving patient knowledge of MDS biology and its prognosis, and work to establish goals for any planned supportive or therapeutic approaches. Such discussions are more likely to result in individualized treatment goals and a more realistic appreciation of the potential benefits of the strategy. It is remarkable that a third of patients indicated their disease prognosis was not discussed with their physician.[14]

As noted above, patients report that very few physicians describe MDS as a cancer when first discussing their diagnosis with them. However, when survival for patients with MDS is compared with that of patients diagnosed with lung cancer, outcomes for patients with MDS are worse. Median survival ranges from 0.4 years in patients with IPSS-defined higher-risk MDS to 5.7 years in patients with IPSS-defined lower-risk MDS, compared with 1.2 years (stage IV) to 8 years (stage Ia) in patients with lung cancer.[10,16] Despite the disparity in survival rates between patients with MDS and lung cancer, lung cancer is a disease with great public awareness. Patients should understand the severity of their disease in order to help participate in discussions about the possible treatments available to help reduce disease-related symptoms, prolong survival, and provide possible cure.[5-8,17]

The IPSS, which was introduced in 1997, remains the most widely used tool to help determine MDS prognosis.[10] However, this system was developed before the approval of any drugs to treat MDS. More recent studies have worked to improve the prognostic information provided by the IPSS. The World Health Organization (WHO)-based Prognostic Scoring System (WPSS), a time-dependent model, considers transfusion dependency in addition to WHO MDS subtype and IPSS karyotype.[18] Other models aim to identify patients with lower-risk disease who may benefit from early initiation of therapy rather than simply using supportive care,[19] or continue to refine the IPSS by including duration of MDS and the number of prior therapies as part of the prognostic score.[20] Finally, MDS subtypes that were excluded from the IPSS, such as proliferative-type chronic myelomonocytic leukemia (i.e., patients with white blood cell counts >12,000 cells/mL)[21] and therapy-related MDS,[22] now have tools to help offer prognosis to patients with these forms of the disease. Again, the importance of improving patients' understanding of their disease and setting realistic expectations of supportive care and treatments cannot be underestimated.

The focus on the physician–patient relationship must recognize the many important roles that various caregivers and other health professionals play in the support of patients with MDS. Many patients face years of being under direct medical care, which includes frequent clinic visits and routine blood testing to monitor blood counts.[23] Other patients pursue treatments that involve supportive care and/or active therapy. All of these options are made easier with social support. Academic centers often can provide multidisciplinary teams of allied health professionals that include nurses, nurse practitioners, social workers, nutritionists, physical therapists, and other specialists to help manage the diverse aspects of a condition. Such patient-centered management teams not only assist patients and their families or caregivers in negotiating week-to-week care routines, but are invaluable in physicians' efforts to provide end-of-life care for patients with progressive disease.

> Multidisciplinary teams, including oncologists, primary care physicians, nurses, social workers, and other specialists, can optimize education, support, and care for patients with MDS. Ultimately, this will lead to improved patient and caregiver satisfaction.

SUMMARY

Physicians and their patient care teams face many challenges when working to improve patient and caregiver satisfaction. In addition to the rigors of medical care required to keep patients with MDS healthy and active, physicians must continually work to provide information to patients and their families or caregivers in order to enhance their understanding of the expected disease evolution, the potential goals that various treatment approaches may achieve, and a realistic appreciation of the expected outcomes from the different treatments. Improving communication between physicians and patients may also result in more patients exploring not only potentially curative treatment approaches, such as HSCT, but clinical trials as well. By recognizing and addressing these challenges we expect to improve patient and caregiver satisfaction, and ultimately improve the care for patients with MDS.

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Table 1

Patient Baseline Characteristics at Diagnosis

Characteristic	Patients with Recently Diagnosed MDS (N = 670)
Male (%)	55
Median age at diagnosis (yrs)	71
IPSS Int-2–risk/High-risk (%)	29
Secondary MDS (%)	10
Prior chemotherapy, radiotherapy, or both	90
Patients with circulating blasts (%) (95% CI)	
1%–5% blasts in peripheral blood	16 (13-19)
≥5% blasts in peripheral blood	10 (8-12)
Median hemoglobin (g/dL) (IQR)	9.1 (8-10)
Median platelet count ($\times 10^9$/L) (IQR)	100 (56-151)
Median absolute neutrophil count ($\times 10^9$/L) (IQR)	1.8 (1.1-2.8)
RBC transfusion-dependent (%)	
IPSS Low-risk/Int-1–risk	22
IPSS Int-2–risk/High-risk	68
Platelet transfusion-dependent (%)	
IPSS Low-/Int-1–risk	6
IPSS Int-2–risk/High-risk	33

CI = confidence interval; Int = intermediate; IPSS = International Prognostic Scoring System; IQR = interquartile range; MDS = myelodysplastic syndromes; RBC = red blood cell.

Adapted from *J Natl Cancer Inst.*[9]

Table 2

Overcoming Key Challenges to Patient and Caregiver Satisfaction

Key Challenges	Optimizing Patient and Caregiver Satisfaction
Many patients have an inadequate understanding of the severity of MDS and their individual risk group and prognosis	Physicians should focus on improving patient knowledge of the biology of MDS, its general prognosis, and details of their individual risk factors
	Physicians and their allied healthcare teams must work to facilitate patient participation in discussions on disease management
Many patients have a limited understanding of treatment goals and unrealistic expectations of the intervention	Physicians must recognize the importance of providing information on the various treatment approaches and agents available to treat MDS
	Efforts to establish the realistic expectations of each treatment plan is crucial
Many patients face years of being under direct medical care, which includes frequent office visits, routine blood draws to monitor counts, supportive care, and active treatment	Multidisciplinary teams can optimize MDS patient education, support and care, and thus improve patient and caregiver satisfaction

MDS = myelodysplastic syndromes.