Acta Haematologica

Patient Reported Outcomes

Acta Haematol
DOI: 10.1159/000547575

Received: February 7, 2025
Accepted: July 12, 2025
Published online: August 20, 2025

Kundalini Yoga for Improving Patient-Reported Outcomes in Patients Diagnosed with Myelodysplastic Syndromes: A Pilot Study

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Keywords
Myelodysplastic syndromes · Yoga · Quality of life · Patient-reported outcomes

Abstract
Introduction: Despite adequate pharmacologic treatment and transfusion support for myelodysplastic syndromes (MDS), there is an ongoing need to explore non-pharmacologic approaches for managing MDS symptom burden. Yoga has proved effective in oncologic patients. The aim of this observational study was to explore the feasibility of an 8-week online Kundalini yoga program, including its impact on symptom burden in MDS patients. ***Methods:*** All patients diagnosed with MDS in our medical center were offered an 8-week online program, in which a 1-h weekly kundalini yoga session was held live via Zoom. All segments included postures in the sitting position, specifically planned for this patient population. Symptom burden was assessed before and after each session and at a later timepoint – 8 weeks post-course completion, using the Edmonton Symptom Self-Assessment Scale – global distress score (ESAS-GDS). ***Results:*** Fourteen patients participated in the program. The median number of sessions per patient was 4. The questionnaires were reasonably easy for the patients to complete. Mean GDSs significantly improved after yoga sessions. Patients consistently endorsed reduced fatigue (78%), increased alertness (65%), increased general well-being (60%), and reduced anxiety (42%) after practicing yoga. Furthermore, symptom burden remained significantly improved 8 weeks after course completion. ***Conclusion:*** This Kundalini yoga program for MDS patients was feasible and resulted in significantly better patient-reported health outcomes, ongoing for at least 8 weeks after the last intervention. Longer follow-up within a longer practice program is planned.

Introduction

Myelodysplastic syndromes (MDS) are a heterogenous group of bone marrow malignancies characterized by abnormal blood cell development, cytopenias, and risk of progression to acute myeloid leukemia [1]. From the initial MDS diagnosis throughout its trajectory, patients' quality of life (QoL) is often deteriorated, sometimes profoundly so. Multiple factors contribute to reduced health-related QoL among these patients, including symptomatic cytopenias, increased health-care facility utilization, emotional distress surrounding the diagnosis [2, 3]. They experience various degrees of fatigue, pain and discomfort, anxiety and depression, and more [4, 5]. In fact, chronic fatigue, characterized by feelings of tiredness, weakness, lethargy, and decreased mental alertness, is consistently reported by MDS

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patients, as the most frequent and debilitating symptom [6, 7].

Edmonton Symptom Assessment System (ESAS) is one of the first quantitative symptom assessment batteries that allows for simple and rapid documentation of multiple patient-reported outcomes (PROs) at the same time [8]. It is a visual analogue scale, using a 10-item rating (0–10, with 10 being the highest degree), which has been previously recommended by the National Comprehensive Cancer Network to assess QoL in all cancer populations [7]. The 10-item scale includes pain, tiredness, nausea, depression, anxiety, drowsiness, appetite, well-being, shortness of breath, and the option of measuring an additional patient-specific symptom. It is a pragmatic easy-to-use PRO measure that takes about 1 min to complete. The ESAS global distress score (GDS) is a pragmatic validated subscale including the first 9 items of the ESAS score.

In MDS, in particular, increasing evidence shows that PROs play a key role in OS prediction in higher risk patients and the incorporation of PROs with traditional disease risk classification strengthens survival prediction [9–12]. There is a clear need to explore alternative approaches, especially given our limited pharmacologic strategies to alleviate symptom burden in this patient population. Yoga has proved an effective method to improve a variety of physical and psychosocial outcomes in cancer patients [13–16]. There is evidence to suggest that yoga can reduce the concentration of cytokines associated with chronic inflammation [17]. However, to the best of our knowledge, the use of yoga in MDS patients has not been reported.

Methods

The Israeli MDS group initiated a yoga program, consisting of 8 1-h sessions, in which 9 Israeli medical centers participated. The classes were held by certified Kundalini yoga teachers, who delivered a mild-medium intensity program combining deep breathing exercises, structured movements, and mantras. All segments included postures in the sitting position and were specifically planned for this patient population. Each medical center hosted its own course. All MDS patients were invited to take part in the program, regardless of disease risk or performance status. Overall, a total of 140 patients in 9 centers participated in at least one in-person yoga class. All participants, regardless of performance status, were able to engage and complete most exercises throughout the class. Many of the patients were able to return to following classes. There was no formal recording of these data, so we do not have the exact numbers. Built upon the feasibility seen in the in-person class, we initiated an online live program, within an observational study, presented herein.

All MDS patients, at our medical center, were offered an 8-week yoga online program, in which a 1-h weekly live session was held via Zoom. The teacher was attuned to participants' comments and questions throughout the session. The symptom burden was assessed using the ESAS-GDS scale.

Patients who participated in the online class filled out the questionnaire before and after each meeting. If needed, a study coordinator assisted them over the phone. Importantly, all patients were seen regularly in clinic, including regular blood work, and received best supportive care, i.e., RBC transfusions for a hemoglobin threshold below 80 g/L (or higher thresholds if clinically indicated), iron chelation was given to patients with iron overload, etc. We also recorded comorbidities and cardiac function in each participant. Notably, since the participants were their own controls, and the questionnaires were filled out within 1 h of each other (before and after yoga class), we do not expect individual differences in clinical characteristics to significantly confound the measured effect. In addition, all patients completed the questionnaire once more, 8 weeks after the last yoga session they had attended. At that timepoint, hemoglobin level and other changes in their medical status were recorded, as well.

The before and after GDS of each patient was compared as matched data using the paired sample t test. A value of $p < 0.05$ was defined as statistically significant. Statistical analysis was performed using SPSS software version 29 (IBM SPSS statistics for Windows, version 29, Armonk, NY, USA).

Results

Fourteen patients participated in this single-center online 8-weekly live yoga sessions via Zoom. All attended at least one prior in-person session. Median age of the participants was 75 years (range, 63–95), 78% were males, 64% had low-risk disease (defined as Revised International Prognostic Scoring System [IPSS-R] score ≤3.5), and 36% were transfusion dependent; in all high transfusion burden according to IWG 2018 [18], 43% were on active treatment during the yoga intervention with hypomethylating agents (Table 1). All patients filled out the questionnaires before and after each session. Altogether, 62 before and after ESAS-GDS questionnaires were filled out. Most patients were able to complete the whole 60-min session and participated in subsequent sessions, as well. Median number of sessions per patient was 4 (range, 1–8). The most common barrier to full participation was concomitant clinic appointments. Another barrier was technical difficulties with the Zoom session.

Table 1. Baseline demographic and clinical characteristics

Demographic and clinical characteristics	Total (N = 14)
Age, years	
Median (range)	75 (63–95)
Gender	
M	11 (78%)
F	3 (22%)
ECOG categories	
0	1 (7%)
1	5 (36%)
2	6 (43%)
3	2 (14%)
TD	
TI	9 (69%)
TD (low/high transfusion burden according to IWG 2018)	5 (0/5) (36%)
Charlson comorbidity ≥3	
No	11 (79%)
Yes	3 (21%)
IPSS-R risk category	
Low	9 (64%)
High	5 (36%)
Cytogenetics	
Very good	0 (0%)
Good	8 (56%)
Intermediate	2 (14%)
Poor	2 (14%)
Very poor	1 (7%)
Blasts, %	
Median (range)	4 (0–14)
WHO 2022 subtype	
5q	1 (7%)
SF3B1	1 (7%)
biTP53	0 (0%)
MDS-LB	6 (43%)
MDS-IB1	4 (28%)
MDS-IB2	2 (14%)
Hypomethylating agent use at any time	
No	8 (57%)
Yes	6 (43%)

IPSS-R, Revised International Prognostic Scoring System; MDS, myelodysplastic syndrome; IB, increased blast; LB, low blast; TD, transfusion dependent; TI, transfusion independent; WHO, World Health Organization.

The median GDS significantly improved after yoga practice. The median GDS at baseline was 21 (IQR, 11–30) and after 1 h of yoga practice – 18.5 (IQR, 9–26) (Fig. 1).

The mean GDS at baseline was 23.8 and after 1 h of yoga practice 21.7. Paired sample T test was performed: mean difference was 2.01; 95% confidence intervals, 0.3–3.9, $p = 0.023$.

Comparing the assessment before and after each session, GDS decreased 39 times, increased 14 times, and did not change 9 times. Twelve patients (85%) reported an improvement in symptom burden in a median of 3 sessions per patient.

Twelve patients completed the GDS questionnaire 8 weeks after the last yoga session. Median GDS remained significantly improved (compared with the

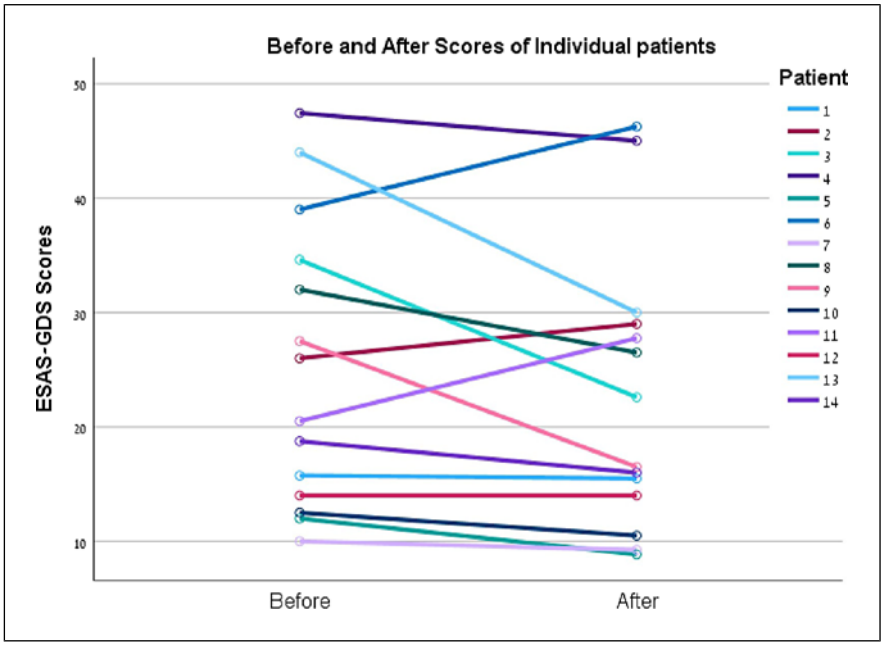

Fig. 1. Before and after ESAS-GDS cumulative scores for each individual patient.

initial GDS before the yoga intervention). Of note, no other major differences in external factors (such as acute illness, recent hospitalization, HB level, and other laboratory values at the first and last timepoints, changes in treatment) that could explain this finding were recorded in this time frame for all 12 patients.

The symptoms reported as most debilitating were fatigue (93%), daytime somnolence (91%), decreased general well-being (84%), and anxiety (81%). Those were also the most frequently reported physical benefits after each yoga intervention. Overall, patients endorsed reduced fatigue (78%), increased alertness (65%), increased general well-being (60%), and reduced anxiety (42%).

Discussion

In this small interventional study, patients with MDS participated in a Kundalini yoga program, specifically designed for this population, incorporating physical postures, breathing exercises, and meditation. The practice proved to be feasible and effective.

Yoga, a thousand-year-old Indian tradition, is increasingly used by cancer patients to improve their well-being [19]. Kundalini yoga and meditation techniques have been traditionally used in depression, fatigue, and anxiety states [20, 21]. We found tremendous value in the cooperation between medical staff and yoga teachers, who worked together to build practical and engaging sequences, which proved to overcome potential barriers specific to this patient population. Plus, unlike other programs, where the focus is on the physical postures, our sequences put equal emphasis on breathing and meditation mantras, which were performed mostly concomitantly with the physical postures. The fact that the sessions were being held live enabled the teacher to communicate personally with the participants during the session.

The analysis of "before" and "after" ESAS-GDS surveys highlighted the beneficial effect of this personalized practice on patients' symptom burden. Unsurprisingly, the most devastating reported symptoms were fatigue, daytime somnolence, decreased general well-being, and anxiety. Those were also the most likely to improve after each yoga intervention. Indeed, despite the physical intensity of the sessions, upon completion, patients noticed reduced fatigue and anxiety together with increased alertness and general well-being. In this challenging patient population, elderly persons with numerous comorbidities, and reduced performance status, this is a valuable milestone. The fact that the improvement was maintained even 8 weeks after the sessions had been completed suggests there is an ongoing benefit, lasting beyond the immediate intervention itself. We find this a particularly noteworthy finding, which deserves further follow-up in larger future studies. It is unknown whether some of the patients participated in further yoga classes independently or practiced yoga moves on their own during this time frame.

Once again, the ESAS survey proved to be a practical and easy-to-use PRO measure. This tool has the potential to contribute to an improved diagnostic process for MDS and other cancers, may enhance survival prediction, and serves to implement palliative care strategies more accurately to improve patient care.

Notably, a higher GDS is associated with decreased overall survival in patients with metastatic cancers [22] and in those with acute leukemias [23]. Furthermore, as shown in a recent meta-analysis, PROs provide independent prognostic information for overall survival across cancer populations and disease stages [24]. For instance, in patients with advanced solid malignancies, regular symptom reporting with automated clinician e-mail alerts resulted in better health-related QoL, fewer ER visits, fewer hospitalizations, a longer duration of palliative chemotherapy, and superior quality-adjusted survival [25]. Indeed, good symptom surveying and management in oncology is associated with improved patient and family QoL, greater treatment compliance, and may even offer survival advantages [26].

Hence, regular PRO measuring in this patient population along with constant attempts to improve patients' symptoms, both pharmacologically and non-pharmacologically, holds promise for improving QoL and survival. Our study has several limitations, namely, a small sample size and lack of a longer follow-up. While this is a pilot study, the small sample size ($n = 14$) and predominance of male, low-risk patients limit generalizability. Moreover, the lack of a control group limits the ability to distinguish true intervention effects from potential placebo responses or regression to the mean. We did not account specifically for individual clinical variables, such as hemoglobin level. However, as mentioned previously, all patients were followed closely and received ongoing supportive care. In the future, we plan to have a multicenter patient enrollment with predefined serial symptom assessment at different timepoints as well as biological correlates of inflammation. Another noteworthy point is that although it was felt that the reported difference was clinically meaningful for the patients, the minimal clinically important difference for the ESAS-GDS in patients with MDS has not been specifically established. Further research is needed to establish MDS-specific minimal clinically important difference values for the ESAS-GDS. Additional consideration should be given to patients' access to computers, as well as the provision of technical support for those interested in the program but less familiar with technology. Overall, we found Kundalini yoga to be a useful non-pharmacologic tool that could be added in the future, to other interventions, designed to improve our patients' well-being and functionality.

Conclusions

This Kundalini yoga program for MDS patients was found feasible and improved patient-reported health outcomes: subjective physical health (e.g., fatigue), psychological health (e.g., depression, anxiety), and general health (e.g., general well-being, sleep). The improvement was seen at later follow-up as well, suggesting an ongoing benefit, beyond immediate intervention. Furthermore, once again, ESAS-GDS proves to be an accessible and useful tool for QoL assessment.

Statement of Ethics

This study protocol was reviewed and approved by the Ethics Committee by the Sheba Medical Center committee, Approval No. 1908-15-SMC. Written informed consent was obtained from all participants to participate in the study.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Funding Sources

No funding was received for this study.

Author Contributions

Irina Amitai and Drorit Merkel contributed to conceptualization, formal analysis, and methodology. Yoav Amitai performed the statistical analysis and created the figure. Irina Amitai wrote the original draft. Abraham Avigdor and Ronit Marcus contributed equally to the acquisition, analysis, or interpretation of data for this work. All authors contributed equally to data curation, investigation, resources, validation, and writing of the manuscript in terms of review and editing; critically reviewed the work; approved the final version to be published; and had access to and verified the underlying data.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

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