Exploring Health Behaviors and the Feasibility of a Lifestyle Intervention for Patients with Multiple Myeloma

Allen Hodge (✉ ahodge@mcw.edu)

Medical College of Wisconsin   https://orcid.org/0000-0003-4081-0625

Patricia Sheean

Loyola University Chicago

Paula O'Connor

Loyola University Chicago

Kiley Tyler

Loyola University Chicago

Abigail Kerschner

Medical College of Wisconsin Cancer Center

Alexis Williams

Medical College of Wisconsin Cancer Center

Kathleen Jensik

Medical College of Wisconsin Cancer Center

Alexis Visotcky

Medical College of Wisconsin

Anita D'Souza

Medical College of Wisconsin Cancer Center

Parameswaran Hari

Medical College of Wisconsin Cancer Center

Binod Dhakal

Medical College of Wisconsin Cancer Center

Saurabh Chhabra

Medical College of Wisconsin Cancer Center

Kathryn E. Flynn

Medical College of Wisconsin

Patrick Hagen

Loyola University Chicago Stritch School of Medicine

Melinda Stolley

Medical College of Wisconsin Cancer Center

Research Article

Abstract

Purpose: Multiple Myeloma (MM) is the second most common hematologic malignancy in the U.S., with higher rates observed in older adults and African Americans (AA). Survivors experience fatigue, bone pain, and reduced functioning. The high incidence of obesity among MM survivors may be partly responsible. These factors highlight the value of developing lifestyle interventions to meet the needs of this diverse group. This study aims to inform the development of a lifestyle program tailored to the MM community.

Methods: MM survivors who were ≥100 days post autologous stem cell transplant (ASCT) with a BMI ≥20 kg/m^2 were recruited from two university hospitals, with the goal of obtaining sufficient representation of AA participants. They completed dietary, physical activity, and quality of life (QOL) questionnaires and a qualitative interview.

Results: 72 MM survivors participated (65% white, 35% black). Participants were 62.5±15.8 years of age. 50% were classified as obese and 65% were insufficiently active. Participants reported diets high in added sugars and saturated fats. QOL measures indicated clinically significant challenges in physical and sexual function. Most (87%) were interested in a lifestyle program. Predominant themes regarding survivors' desires for a lifestyle program included social support, guided exercise, meal preparation support, and disease management information.

Conclusion: This study demonstrates the need for and interest in lifestyle change support among a racially diverse sample of MM survivors. Interventions that are group-based, target knowledge gaps, social connections, accountability, and provide structured framework with professional instruction will best address the needs of this survivor population.

Introduction

Multiple Myeloma (MM) is the second most common hematological malignancy in the U.S., with higher rates observed in older adults and African Americans (AA) [1]. Treatment advances, such as autologous stem cell transplant (ASCT) and a growing list of immunomodulatory drugs have drastically improved survival rates. As a result, the disease has largely changed from being an imminently fatal condition to that of a chronic disease, with improvements in average five-year survival rates increasing from 32–56% over the last two decades [2].

Despite improved survival, MM is associated with high morbidity from the disease process, which is then complicated by on-going treatment side-effects. Survivors often experience fatigue, bone pain, sleep problems, and functional decline – all of which can impact physical, emotional, and social health [3]. Many MM survivors also have unfavorable body composition, specifically a high prevalence of obesity and sarcopenia; the latter reflecting a marked loss of skeletal muscle mass and function [4–6]. These body composition phenotypes may contribute to the decreased quality of life (QOL) seen in the MM population. Furthermore, several studies over the past decade have identified obesity as a risk factor both for the transformation of monoclonal gammopathy of undetermined significance (MGUS; MM's precursor disease) to full blown MM and for disease progression of MM itself [5, 7, 8]. Thus, it seems logical that lifestyle interventions aimed at improvements in body composition would reduce disease burden and improve QOL in MM survivors.

A growing body of evidence links positive changes in lifestyle behaviors with improvements in multiple aspects of survivorship [9–11]; however, these data are largely derived from studies involving solid tumors. Few studies have studied exercise among MM patients [12]. Furthermore, studies that have been conducted do not include representative samples [13, 14]. Herein, we report the results of an exploratory study aimed to inform the development of a lifestyle program tailored to meet the needs and desires of the diverse MM survivor community. We hypothesized that MM survivors would have significant symptom burden compared to the general population. We further hypothesized that there would be an interest in a lifestyle intervention program aimed toward improving physical activity and weight loss.

Methods

Study design and participants

This cross-sectional, mixed methods study was designed to: 1) obtain general information about AA and non-Hispanic white MM survivors in two large urban areas of the Midwest (Milwaukee and Chicago), and 2) identify optimal methodologies to capture specific topic areas of interest, perhaps unique to population group or geographic areas. By design, most assessment tools and data points across the two sites were identical; however, differences were permitted due to varying resources and to allow within and across site comparisons. Participants were recruited from two university hospitals with active stem cell transplant programs, reflecting cities with diverse patient populations. Patients were recruited from hospital oncology clinics, through recruitment letters and/or phone calls using contact information provided by medical oncologists (July, 2019 – July, 2020). We intentionally sought representation of AA participants since MM impacts this population disproportionately and a racially diverse perspective on intervention needs and interests would be critical to informing future studies. Thus, recruitment aimed to achieve 50% AA representation. Ethical approval was granted from the respective institutions prior to study initiation.

Eligible participants were required to be 18 years of age or older, at least 100 days post-ASCT, with a BMI $\geq$20 kg/m^2, a performance status of ECOG 0-1 or Karnofsky >70, and life expectancy of at least 6 months. Prior to recruitment, participant eligibility was ascertained via the electronic health record or clearance from medical oncologists verifying clinical stability and appropriateness of inclusion.

Study procedures

Once deemed eligible, participants scheduled a time to complete informed consent, questionnaires, and a qualitative interview conducted either in-person or over the phone. For feasibility purposes, body composition and physical performance were only collected at the Chicago site. At this site, the in-person visit was scheduled no more than 30 days after initial study eligibility and entailed ~90 minutes to complete questionnaires and/or physical measures. In March 2020, all in-person methodologies were stopped due to the impact of COVID19. Thereafter, recruitment and consent were conducted over the phone and data collection was restricted to phone or mailed questionnaires. Participants received a $20 gift card for their participation.

Demographics and Medical Information

Demographic data included age, gender, race/ethnicity, marital status, employment status, annual household income, household size, and education. Clinical data on co-morbid conditions and treatments were collected. Height and weight were measured and used to classify normal weight, overweight, and obese, based on calculated BMI.

Body composition and physical performance (Chicago only)

Body composition was non-invasively measured using dual energy x-ray absorptiometry (DXA). A certified radiation technologist performed and analyzed participants using a Discovery W (Hologic Inc.) device, which was calibrated daily with manufacturer's phantom. Applying the methods of Kaul et al. [15], android fat was automatically defined and measurements of abdominal and visceral fat were obtained from the android region. Sarcopenia was explored using appendicular skeletal mass (ASM)/ height^2 using the cut-points of Baumgartner et al. [16] (7.26 for men and 5.45 for women). Cardiorespiratory fitness was assessed using a sub-maximum 6-minute walk test on an indoor track. Total distance was recorded and used to determine fitness level. Upper body muscle strength was measured using Jamar Hand Dynamometer following standard procedures [17]. Measures were obtained twice for each participant's non-dominant and dominant hands. Scores of the dominant hand were averaged and the cut-point of <27 kg and <20 kg for men and women, respectively, were used to define compromised functioning [18]. Lower body muscle strength was measured by quantifying the number of 'Chairs Stands' in 30 seconds; <5 rises in 15 seconds was used to indicate compromised strength.

Dietary intake

Two different dietary screeners were used to assess ease and comparability of results across sites. Both allowed for the evaluation of general trends in intake with minimal burden. Participants at the Milwaukee site completed the validated Block Fat/Sugar/Fruit/Vegetable Screener [19]. This tool takes ~20 min to complete and queries about usual consumption and portion sizes of 55 food items. Participants at the Chicago site completed the Block Fruit/Vegetable/Fiber Screener [20]; a 10-item on-line

fruit, vegetable and fiber screener that ranks individuals with regard to their usual intake of fruits and vegetables [21]. Estimates of total fat, saturated fat, added sugars, fruit, vegetables, and/or dietary fiber were generated.

Physical activity

The Godin Leisure Physical Activity Index asks about time spent engaged in light, moderate, and strenuous activities over the past 7-day period [22]. Results are used to classify participants as sufficiently active (meets current physical activity guidelines of 150 mins of moderate activity or 75 mins of vigorous activity per week) or insufficiently active. Because current cancer survivorship guidelines recommend a minimum of twice weekly resistance exercise training (RET) [23], participants were also asked: 1) if they engage in RET and 2) if yes, how many times per week.

Quality of life (QOL), symptom burden and social support

Symptom burden and functioning were measured using the Patient-Reported Outcomes Measurement Information System (PROMIS) [24]. The PROMIS-29 profile assesses seven health domains (Physical Function, Anxiety, Depression, Fatigue, Sleep Disturbance, Ability to Participate in Social Roles and Activities, Pain Interference). To further assess social relationships, PROMIS short forms measuring social isolation, companionship, and various domains of support, such as informational and emotional support, were also administered. Short forms measuring self-efficacy in managing symptoms, cognitive function, and sexual function were administered given these are frequent concerns in the MM population [3].

Qualitative Data

Using open-ended questions in interviews (Milwaukee) and written prompts (Chicago) on the survey, information regarding (1) post diagnosis changes in health behaviors, (2) post diagnosis changes in general health, (3) unmet needs, and (4) interests related to a lifestyle intervention were gathered.

Statistical analysis

Data analyses were performed for quantitative and qualitative data. For quantitative data, categorical data were described using percentages, while continuous data were presented using means and standard deviations. PROMIS scores were reported on the T-distribution, which has been normalized to the U.S. population, so that 50 corresponds to the U.S. average with a standard deviation of 10. Higher scores represent more of that domain. Based on recent work by Jensen et al., a 3-point difference in T-score was considered clinically significant between our study population compared to the U.S. population not affected by cancer [25]. Qualitative data from interviews relied on thematic coding. Several authors independently reviewed participant responses to open-ended questions to identify key topics areas and codes within each topic area. Subsequently, coders met to group codes into themes and to resolve discrepancies. Quantitative and qualitative data was stratified to examine racial, gender, and site differences.

Results

Study participants

At the Milwaukee site, 95 MM survivors met eligibility criteria; 47 did not respond to recruitment efforts, 11 declined due to scheduling conflicts and/or lack of interest, and 37 enrolled. At the Chicago site, 53 MM survivors met eligibility criteria, 9 did not respond to recruitment efforts, 9 declined due to lack of interest, and 35 enrolled. Between the two recruitment sites, 72 MM survivors participated (65% white, 35% black, 56% male, 44% female). Participants were 62.5 ± 15.8 years of age. The majority were married or living with a partner, retired, and earning $40,000 to $79,999 annually. Most had graduated from college or had advanced degrees. Common comorbidities included arthritis, hypertension, hyperlipidemia, and chronic kidney disease.

Table 1
Characteristics of Multiple Myeloma cancer survivor participants

Variable	Overall N (%) = 72	Milwaukee Site n (%) = 37	Chicago Site n (%) = 35
Race			
Black or African American	25 (34.7)	17 (45.9)	8 (22.9)
White	47 (65.3)	20 (54.1)	27 (77.1)
Gender			
Female	32 (44.4)	20 (54.1)	12 (34.3)
Male	40 (55.6)	17 (45.9)	23 (65.7)
Variable	Overall Mean (SD) or N (%)	Milwaukee Site Mean (SD) or n (%)	Chicago Site Mean (SD) or n (%)
Age	62.5 (15.8)	60.4 (19.8)	64.7 (9.8)
Body Mass Index (BMI)	30.6 (5.4)	29.8 (5.8)	31.4 (4.9)
% normal weight	13 (18.1)	9 (24.3)	4 (11.4)
% overweight	23 (31.9)	11 (29.7)	12 (34.3)
% obese	36 (50.0)	17 (45.9)	19 (54.3)
Marital Status			
Single	7 (10.0)	3 (8.6)	4 (11.4)
Married or living with partner	52 (74.3)	26 (74.3)	26 (74.3)
Divorced or separated	6 (7.6)	3 (8.6)	3 (8.6)
Widowed	5 (7.1)	3 (8.6)	2 (5.7)
Missing	2	2	0
Education			
Some high school	2 (2.8)	1 (2.7)	1 (2.9)
High school graduate or GED	16 (22.5)	8 (21.6)	8 (23.5)
Associate degree or 2-year certificate	7 (9.9)	3 (8.1)	4 (11.8)
College graduate	31 (43.7)	17 (45.9)	14 (41.2)
Graduate or professional degree	13 (18.3)	6 (16.2)	7 (20.6)
Other	2 (2.8)	2 (5.4)	0 (0.0)
Missing	1	0	1
Income			
Less than $20,000	5 (7.6)	4 (12.5)	1 (2.9)
$20,000-$39,999	7 (10.6)	4 (12.5)	3 (8.8)
$40,000-$59,999	16 (24.2)	9 (28.1)	7 (20.6)
$60,000-$79,999	12 (18.2)	7 (21.9)	5 (14.7)
$80,000 or more	26 (39.4)	8 (25.0)	18 (52.9)

Variable	Overall N (%) = 72	Milwaukee Site n (%) = 37	Chicago Site n (%) = 35
Missing	6	5	1
Employment			
Employed (full-time or part-time)	20 (27.8)	7 (18.9)	13 (37.2)
Out of Work	1 (1.4)	0 (0.0)	1 (2.9)
Retired	41 (56.9)	21 (56.8)	20 (57.1)
Disabled	7 (9.7)	6 (16.2)	1 (2.9)
Homemaker	1 (1.4)	1 (2.7)	0 (0.0)
Other	2 (2.8)	2 (5.4)	0 (0.0)
Missing	1 (1.4)	0 (0.0)	1 (2.9)
Comorbidities			
Asthma	12 (16.7)	5 (13.5)	7 (20.0)
Diabetes	8 (11.1)	4 (10.8)	4 (11.4)
High Blood Pressure	31 (43.1)	16 (43.2)	15 (42.9)
High Cholesterol	23 (31.9)	9 (24.3)	14 (40.0)
Kidney Disease	13 (18.3)	8 (22.2)	5 (14.3)
Arthritis	35 (48.6)	16 (43.2)	19 (54.3)

Quantitative data

Mean BMI was 30.6 ± 5.4; 32% were classified as overweight and 50% as obese (Table 1). 35% reported physical activity levels considered sufficiently active (minimum of 150 min of moderate or 75 min of vigorous activity weekly) and 34% met the recommended twice weekly resistance exercise training guidelines (Table 2). The majority (65%) were insufficiently active. For dietary patterns, participants reported diets high in added sugars, saturated fats, total fat. Protein, fiber, fruits, and vegetables were low. Furthermore, AA participants reported a statistically significant lower fiber intake compared to white participants.

Table 2
Physical activity patterns

Variable	Overall N (%) = 72	Milwaukee Site n (%) = 37	Chicago Site n (%) = 35
Insufficiently active	44 (64.7)	21 (56.8)	23 (74.2)
Sufficiently active	24 (35.3)	16 (43.2)	8 (25.8)
Resistance exercise 2x weekly or more	23 (33.8)	14 (37.8)	9 (29.0)

Biometrics

In total, 13 individuals at the Chicago site completed the physical measures prior to COVID lockdown. Using DXA output, median percent body fat was 30.4% (28.0% -35.9% IQR), and no participants were classified as sarcopenic. However, 50% and 40% of participants scored below age and sex-adjusted norms for chair stands and handgrip strength, respectively, indicating some degree of impaired muscle strength. The median meters walked in 6-min was 565 (529– 587 m IQR).

PROMIS (QOL)

PROMIS QOL measures indicated clinically significant challenges in physical function and sexual function domains. Pain interference was also an area of concern but fell short of being clinically significant. When compared to the U.S. norms for the general population, survivors felt less depressed, had greater companionship, and were better supported. Ability to participate socially was higher at the Chicago site. Women reported having greater companionship and support in the informational, emotional, instrumental domains compared to men.

Table 3
PROMIS quality of life domains of Multiple Myeloma survivor participants

Domain	Overall T score (SD)	Milwaukee Site T score (SD)	Chicago Site T score (SD)	P Value
Physical Function	45.39 (8.70)	43.85 (9.49)	47.29 (7.33)	0.109
Depression	45.95 (8.00)	47.09 (8.85)	44.55 (6.70)	0.200
Anxiety	48.70 (9.37)	50.61 (9.76)	46.33 (8.42)	0.062
Fatigue	51.11 (8.16)	52.61 (8.53)	49.25 (7.41)	0.094
Sleep disturbance	50.66 (7.23)	49.17 (8.23)	52.51 (5.33)	0.059
Pain interference	52.56 (9.58)	52.85 (10.77)	52.21 (8.08)	0.788
Ability to participate socially	51.64 (8.42)	48.89 (8.48)	54.94 (7.17)	0.003
Social isolation		42.04 (9.43)	Not measured	
Companionship		54.07 (8.91)	Not measured	
Informational support		56.76 (11.27)	Not measured	
Emotional support		55.21 (10.53)	Not measured	
Instrumental support		59.36 (8.53)	Not measured	
Cognitive function		51.58 (9.41)	Not measured	
Self-efficacy managing symptoms		51.89 (8.20)	Not measured	
Interest in sexual activity		36.28 (12.38)	Not measured	
Satisfaction with sex life		47.12 (9.74)	Not measured	
Orgasm pleasure		43.98 (8.69)	Not measured	
Erectile function		40.68 (8.89)	Not measured	
Vaginal discomfort		53.10 (9.94)	Not measured	
Note: U.S. population mean = 50, SD 10; difference of +/- 3 points considered clinically meaningful				

Qualitative data
Qualitative data was summarized into three primary themes:

Changes and challenges with health behaviors (diet, physical activity, etc.) post-diagnosis

Lifestyle impact post-diagnosis was a shared theme among respondents. Common issues include low physical functioning, symptom burden (sleep problems, pain, fatigue), fear, anxiety, impaired cognition, and a reduction in social activity. While some participants reported worse lifestyle habits secondary to complications from MM, many attempted self-directed lifestyle changes

with the goal of improving QOL and regaining physical function. The majority of efforts focused on improving exercise habits and eating healthier (i.e., reducing sugar and alcohol intake).

Another theme was the lack of direction/lifestyle support post-diagnosis. Only 17% of participants were aware of the American Cancer Society's nutrition and physical activity guidelines and 56% reported no one from their oncology team had discussed lifestyle recommendations with them since transplant. Those who did have lifestyle discussions felt "it was too long ago" and that they "did not remember any of the specific recommendations".

Unmet survivorship needs

Discussions of unmet needs centered on living with MM and the need for a "well-rounded program that addresses all the issues of cancer survivors". Specific requests were noted for support groups and opportunities to connect with other survivors. For many survivors, the social aspect of the program was considered critical to keep them engaged with behavioral change and to build accountability. Furthermore, participants acknowledged the value of addressing healthy eating and exercise, relating they would like professional assistance to make changes tailored to their needs and abilities. There were specific requests for access to dieticians to advise on healthy eating. Instructor support to guide physical activity was also requested given a general lack of knowledge and fear of injury during exercise. The latter being especially prominent among women.

Interest in lifestyle program intervention and suggested format and content

There was considerable interest in a dual component diet and exercise program with 87% of participants reporting they would join or consider joining such a program. Reasons for joining included the desire to incorporate healthy diet and exercise habits into daily routines while simultaneously building connections with other survivors. The majority of those not interested were already engaged in other support programs.

Related to the intervention structure and content, survivors expressed interest in learning practical information (e.g., "how many calories to eat", "how much red meat is too much") to facilitate behavioral change. The majority preferred having in-person group sessions to build a sense of comradery and accountability, although some expressed interest in an individualized, home-based program. Participants envisioned the exercise component to be led by an older instructor who could relate to an aging population and provide guidance on how to exercise safely. Preferred exercise modalities were aerobics, weight training, and yoga. Dietary components included cooking classes, healthy recipes that are affordable and convenient, and access to a dietitian to inform development of meal plans.

Additional desired components included sessions on MM disease information where participants could have their questions answered by health care providers. Furthermore, participants were open to using technology-based tools such as activity monitors and text messages for motivation and reminders.

In terms of location, participants preferred the program to be based at a community fitness center (e.g., YMCA) or at a medical facility. Regarding timing, the morning or early afternoon was favored by those who identified as retired or disabled. However, participants who were still employed preferred the evening. Overall, participants felt that a program like this would be feasible and should be held at least weekly to produce long-term behavior change and meaningful impact.

Discussion

The benefits of nutrition and physical activity interventions on QOL and body composition in patients living with cancer is gaining recognition. However, the MM population has been understudied in this field due to concerns of fractures and pain. Contrary to this belief, a limited number of studies have demonstrated personalized exercise programs are not only safe but also improve QOL in MM survivors, particularly related to fatigue and weakness [12, 13]. Considering the benefits of exercise and the potential contribution of adverse body composition on MM survivorship, the present study was designed to inform the development of a lifestyle intervention tailored to the needs of the diverse MM population, making it one of the first to do so.

This study's findings highlight the QOL challenges MM survivors face post-diagnosis and the obstacles they encounter while learning to live with the disease. Using a combination of PROMIS measures and free responses, we learned our MM survivor

population has numerous limitations. Decreased physical function, fatigue, sleep problems, and sexual dysfunction are just some examples. Given these constraints on daily life, it is understandable that some survivors perceive a decline in their lifestyle habits. However, to our surprise, results support many participants making self-directed attempts to improve QOL and regain physical function through healthy eating, and to a lesser extent, increased physical activity. Despite these attempts, MM survivors were found to have suboptimal dietary patterns (high intakes of sugar and fat, low intakes of fiber, fruits, and vegetables). Furthermore, only 35% were sufficiently active. Both factors likely contribute to the high prevalence of overweight and obesity seen in our sample; 82% of our participants were overweight or obese, which was markedly higher than the national average of 69% for cancer survivors [26].

Current cancer models propose that obesity promotes MM development in those with MGUS and furthers progression in those with MM through dysregulation of insulin, sex hormones, and inflammatory cytokines [27]. Furthermore, a recent study by Fairfield et al. [28] demonstrates a bidirectional interaction between bone marrow adipocytes and MM cells and proposed targeting of bone marrow adipose cells as a novel therapeutic target. Thus, it is crucial that obesity be addressed when considering MM survivorship.

One possible explanation for the high prevalence of overweight and obesity among our sample is lack of guided lifestyle change. Many participants reported attempting self-directed lifestyle changes, however, knowledge was a stated barrier. Interest in receiving specific instructions and guidance by professionals was common in our sample and likely stems from a lack of discussions regarding healthy lifestyles with their medical team. Examples of expressed knowledge gaps included how to conduct exercises, how to avoid injury, and how to determine what foods are healthy. Lack of motivation and desire for support and accountability were also related. Our participants were looking for programs that would provide structure and oversight, keep them engaged and allow them to establish relationships with other survivors. As a solution, we propose the implementation of a lifestyle intervention program for MM survivors targeting both physical exercise and healthy eating. This program should be tailored to addressing the needs and preferences of the MM community to motivate initiation and maintenance of positive behavioral change in a group setting. Ultimately, the goal of the program would be to help survivors achieve a QOL worthy of being described as "thriving, not surviving".

Our study is not without its limitations. First, to be approached for the study, patients were required to appear clinical stable; thus, an inherent selection bias is present. As a result, our findings may not be generalizable to the entire MM community; however, we purposefully recruited participants who were capable of and appropriate for participating in lifestyle programs. Soliciting feedback from patients at the end of life is not practical, as these patients are not appropriate or intended targets of our work. Second, while all study measures were validated, many surveys relied on self-report data (e.g., dietary screeners, physical activity measures). In this circumstance, more comprehensive quantitative data would be more informative. Given our funding restrictions and the confines of COVID19, these opportunities were diminished. Finally, our goal was to recruit a racially diverse patient population. Additional efforts will be needed going forward to achieve our 50% goal.

Conclusion

Given the rising incidence rates of MM among the aging U.S. population and the efficacy of modern therapies, this survivor population is rapidly growing. Unfortunately, these survivors experience comorbidities and QOL challenges. Thus, it is imperative that survivorship programming be implemented to proactively address these concerns. Here we propose the development of a program tailored to the MM community. Interventions that are group-based, target knowledge gaps, social connections, accountability, and provide a structured framework with professional instruction will best address the needs of this survivor population.

Declarations

Funding

Competing Interests

The authors have no relevant financial or non-financial interests to disclose.

Availability of Data and Material

All primary data is under full control and is available for review upon request.

Code Availability

Not applicable.

Author Contributions

All authors contributed to the study conception, design and/or funding acquisition. Material preparation, data collection and analysis were specifically performed by Allen Hodge, Patricia Sheean, Paula O'Connor, Kiley Tyler, Abby Kerschner, Alexis Williams, Kathleen Jensik, Alexis Visotcky, and Melinda Stolley. The first draft of the manuscript was written by Allen Hodge, Patricia Sheean, Abby Kerschner, and Melinda Stolley. All authors read and approved the final manuscript.

Ethics Approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study was approved by the Bioethics Committee of the Medical College of Wisconsin and Loyola University Chicago.

Consent to Participate

Informed consent was obtained from all individual participants included in the study.

Consent to Publish

Not applicable.

Acknowledgement

Sincere gratitude to the participating patients.

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