CLINICAL SCIENCE

Autologous stem cell transplantation improves quality of life in economically challenged, Brazilian multiple myeloma patients

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OBJECTIVES: 1) To characterize the impact of multiple myeloma on the quality of life of patients treated in two public institutions in São Paulo State, Brazil, using a generic Short Form 36 Health Survey and a questionnaire specific for oncologic patients (QLQ-C30) upon diagnosis, after the clinical treatment, and at day +100 after autologous stem cell transplantation; 2) to evaluate whether autologous stem cell transplantation can improve the quality of life of our economically challenged population aside from providing a clinical benefit and disease control.

METHODS: We evaluated 49 patients with multiple myeloma (a total of 70 interviews) using the two questionnaires. The scores upon diagnosis, post-treatment/pre-autologous stem cell transplantation, and at D+100 were compared using ANOVA (a comparison of the three groups), *post hoc* tests (two-by-two comparisons of the three groups), and paired t-tests (the same case at two different times).

RESULTS : Of the included patients, 87.8% had a family budget under US $600 (economic class C, D, or E) per month. The generic Short Form 36 Health Survey questionnaire demonstrated that *physical function, role-physical,* and *bodily pain* indices were statistically different across all three groups, favoring the D+100 autologous stem cell transplantation group (ANOVA). The questionnaire specific for oncologic patients, the QLQ-C30 questionnaire, confirmed what had been demonstrated by the Short Form 36 Health Survey with respect to *physical function* and *bodily pain,* with improvements in *role functioning, fatigue,* and *lack of appetite* and *constipation*, favoring the D+100 autologous stem cell transplant group (ANOVA). The *post hoc* tests and paired t-tests confirmed a better outcome after autologous stem cell transplantation.

CONCLUSION: The questionnaire specific for cancer patients seems to be more informative than the generic Short Form 36 Health Survey questionnaire and reflects the real benefit of autologous stem cell transplantation in the quality of life of multiple myeloma patients in two public Brazilian institutions that provide assistance for economically challenged patients.

KEYWORDS: Myeloma; Quality of life; SF-36; QLQ-C30; Transplantation.

INTRODUCTION

Multiple myeloma (MM) has a significant impact on a patient's quality of life (QoL) because the patient becomes dependent on others, even for routine activity execution and

personal care.[1] MM treatment includes therapy for the underlying disease and supportive therapy to enhance QoL. The aim of MM treatment is to control the disease, particularly its bone destruction. Healthcare professionals involved in MM treatment must minimize any post-treatment complications and ensure the best possible long-term QoL for each patient. International studies assessing the QoL of patients with MM were validated in developed countries. In Brazilian public hospitals, MM patients have important related social, economic, and emotional difficulties, including the following: a low family budget, unemployment, difficulties in receiving government financial support after diagnosis, a long distance between the home

and the hospital, transportation difficulties for disable patient, the absence of a caregiver, and poor family support related to social problems. Because of these difficulties, we believe that it is important to evaluate whether high-dose chemotherapy followed by autologous hematopoietic stem cell transplantation (ASCT), could improve the QoL of our patients (other than clinical benefits and disease control).

Therefore, the aim of this study was to characterize the impact of MM in the QoL of patients treated in two public institutions in São Paulo State, Brazil, using a generic Short Form 36 Health Survey and a questionnaire specific for oncologic patients (QLQ-C30) upon diagnosis, after the clinical treatment, and at day +100 after ASCT. We also evaluated whether ASCT improves the QoL of our economically challenged population.

METHODS

Study design. Between March 2006 to August 2007, we evaluated 49 MM patients who were treated at Disciplina de Hematologia e Hemoterapia, Universidade Federal de São Paulo São Paulo/UNIFESP (a total of 26 patients) and Santa Casa de Misericórdia de São Paulo (a total of 23 patients). We did not include patients with solitary plasmacytoma or monoclonal gammopathy of undetermined significance or patients without a physical/emotional condition for a 30-minute interview. Patients who were more than 70 years old, had chronic renal insufficiency requiring dialysis, congestive cardiac insufficiency, or cardiac amyloidosis did not undergo high-dose chemotherapy followed by ASCT. Written informed consent was obtained from all of the patients, and the study was approved by the ethics committees of these two institutions (CEP no. 0249/06 and CEP no. 374/06, respectively).

Economic class assessment. A questionnaire that defined the economic classes of each of the 49 MM patients was applied using *Brazil's Economic Classification* (www.ibope.com.br). This classification was created in 2000 and considers how many bathrooms, color TVs, radios, cars, vacuum cleaners, washing machines, DVD players, refrigerators, freezers and housemaids are in the patient's household. It also considers the highest education level of any household member (not necessarily the MM patient). The final score classifies the patient within one of seven economic classes (A1/2, B1/2, C, D, or E). Based on the dollar value in 2000, an A1-class patient has a family budget of US $5,000/month, and an E-class patient has a family budget of US $130/month.

Quality-of-life questionnaires. Two quality-of-life instruments were used in this study: the Short Form 36 Health Survey (SF-36)[2] and the European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire-C30 (QLQ-C30).[3] The SF-36 is an internationally validated instrument that can be self-administered or administered over the phone by trained health professionals. It includes a multi-item scale that assesses the following eight health domains: *physical function, role-physical, bodily pain, general health, vitality, social function, role-emotional, and mental health.* The physical and mental components are summaries of the eight domains in the SF-36 questionnaire. These domains have final scores between 0 and 100, where zero corresponds to the worst health state, and 100 corresponds to the best health state.[2] This questionnaire has been adapted and validated in Portuguese since 1999.[2] The EORTC QLQ-C30 questionnaire is an internationally validated instrument in Portuguese (Brazilian) and incorporates nine multi-item scales: five functional scales (*physical, role,*

cognitive, emotional and social); three symptom scales (*fatigue, pain,* and *nausea and vomiting*); and global health and quality-of-life scales (*dyspnea, insomnia, lack of appetite, constipation, diarrhea, and financial difficulty*).[3] These scales have final scores between 0 and 100, where high scores indicate better outcomes for the functional scales and global health and worse outcomes for the symptom and quality-of-life scales. Authorizations for the use of the SF-36 and QLQ-C30 questionnaires (Portuguese [Brazilian] version) were given by Dr. Marcos Bosi Ferraz and Dr. Rozana M. Ciconelli and the EORTC Quality of Life Group, respectively, in May 2006. These questionnaires were administered to patients upon diagnosis, after the clinical treatment (post-treatment/pre-ASCT), and at day +100 after ASCT (D+100 ASCT). Of the 49 patients, 29 were evaluated upon diagnosis, 27 were evaluated post-treatment/pre-ASCT (9 patients were also evaluated at diagnosis), and 14 were evaluated at D+100 ASCT (12 patients were also evaluated post-treatment/pre-ASCT). Thus, the 49 MM patients generated 70 total completed interviews, as depicted in the flow diagram of the study design (Figure 1). All of the interviews were conducted by one of the principal researchers (V.C.S.), and the average time required to complete the questionnaires was approximately 30 minutes (while the patient was waiting for the physician consultation).

Statistical analysis. The sample classification (according to sex, isotype, disease stage, and the International Staging System [ISS]) was expressed as absolute numbers and as relative percentages. Chi-squared tests were used to compare the categorical variables among the groups. The ages were expressed as means $\pm$ standard deviations. For the SF-36 and QLQ-30 questionnaire score analyses, we followed all of the directions provided by each responsible group.[2,4,5] The interviews that were generated by the quality-of-life questionnaires upon diagnosis, post-treatment/pre-ASCT and at D+100 ASCT were compared using ANOVA (for comparisons of the three groups), *post hoc* tests (for two-by-two comparisons of the three groups) and paired t-tests (the same case at two different times). The level of significance for all of the statistical tests was 5%.

RESULTS

There were no statistically significant differences among the three evaluated groups with respect to sex, age, isotype, clinical stage, and ISS (Table 1). With respect to economic class, the following classification was obtained: 4.0% in B1, 8.2% in B2, 63.3% in C, 22.5% in D, and 2.0% in E. According to our classification, 87.8% of the included patients had a familial budget of less than US $600 per month (i.e., economic classes C, D, or E). The generic SF-36 questionnaire demonstrated that *physical function, role-physical,* and *bodily pain* were statistically different across all three groups and favored the D+100 ASCT group (ANOVA; Table 2). The physical component portion of the SF-36 had borderline statistical significance and favored the D+100 ASCT, which corresponds to the *physical function, role-physical,* and *bodily pain* domains. The QLQ-C30 questionnaire confirmed the SF-36 results with respect to *physical function* and *bodily pain* and improved *role functioning, fatigue, the lack of appetite* and *constipation* and usually favored the D+100 ASCT group (ANOVA; Table 3). The significant results obtained using the *post hoc* tests (two-by-two comparisons of the three groups,) are shown in Table 4. The outcomes were better after treatment (including ASCT). Paired t-tests (comparing
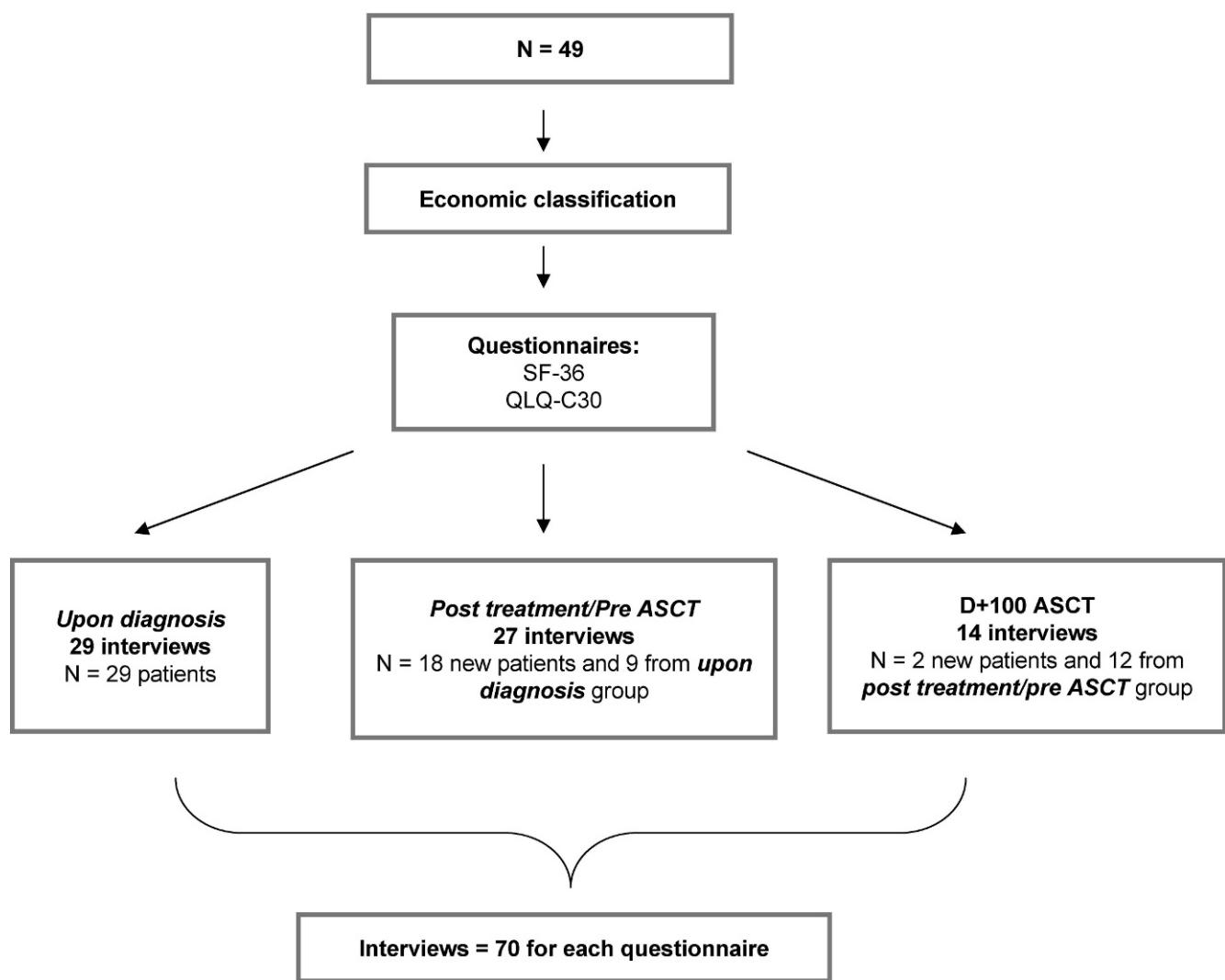
Study Design

Figure 1 - A flow diagram of the study design. ASCT - autologous stem cell transplantation.

the same case at two different times) demonstrated improvements in *fatigue* ($p = 0.036$) and global health ($p = 0.045$) after clinical treatment compared to the time of diagnosis (as determined by the QLQ-C30). This finding confirms the *post hoc* results. Paired t-tests demonstrated improvements in *physical function* ($p = 0.022$) and *role-emotional* ($p = 0.043$) when the patients at the end of their clinical treatments were compared to the patients at D+100 ASCT using the SF-36 questionnaire. The QLQ-C30 detected significant improvements in the global health ($p = 0.034$) and social characteristics ($p = 0.044$) when the same patients in the two aforementioned situations were compared.

DISCUSSION

In this study, we characterized the impact of MM on the QoL of patients treated in two public institutions in São Paulo State, Brazil, using a generic (SF-36) questionnaire and a questionnaire specific for oncologic patients (QLQ-C30) upon diagnosis, after clinical treatment and at day +100 after

ASCT. The SF-36 is an internationally validated instrument that can be self-administered or given over the phone. This questionnaire has been adapted and validated in Portuguese since 1999.[2] We found only one previous report that described the use of the SF-36 questionnaire in MM patients to compare QoL pre- and post-kyphoplasty.[6] Recently, the EORTC validated a disease-specific questionnaire module (QLQ-MY20) for patients with MM. The study was performed through the EORTC Quality of Life Group using clinical trials in seven countries. The social support scale was removed in the final analysis because it did not discriminate between the groups in this population.[7] The differences observed when comparing the MM patients upon diagnosis and at D+100 ASCT were already present in one recent QoL study from the University of Arkansas for Medical Sciences, Little Rock, that used other indices.[8]

However, in Brazilian public hospitals, the economic situation of MM patients is completely different from that of developed countries, where all of the questionnaires were designed. The majority of patients in this study are in

Table 1 - The clinical and laboratory characteristics of the 49 MM patients (upon diagnosis, post-treatment/pre-ASCT, and D+100 ASCT). Total of 70 interviews.

Parameters	Upon diagnosis	Post-treatment/ Pre-ASCT	D+100 ASCT	Total	p-value
Sex					0.965
Female	15 (21.4%)	13 (18.6%)	7 (10%)	35 (50%)	
Male	14 (20%)	14 (20%)	7 (10%)	35 (50%)	
Age (years)	55.4 ± 13.3	53.9 ± 9.8	54.1 ± 7.8		0.856
Isotype					0.717
IgG	20 (28.6%)	21 (30%)	9 (12.9%)	50 (71.5%)	
IgA	5 (7.1%)	2 (2.9%)	1 (1.4%)	8 (11.4%)	
IgM	0 (0%)	1 (1.4%)	1 (1.4%)	2 (2.8%)	
Light chain	3 (4.3%)	1 (1.4%)	2 (2.9%)	6 (8.6%)	
Non-secretor	1 (1.4%)	2 (2.9%)	1 (1.4%)	4 (5.7%)	
Stage					0.583
IA	2 (2.9%)	1 (1.4%)	0 (0%)	3 (4.3%)	
IIA	1 (1.4%)	1 (1.4%)	0 (0%)	2 (2.8%)	
IIIA	18 (25.7%)	19 (27.1%)	13 (18.6%)	50 (71.4%)	
IIIB	8 (11.5%)	6 (8.6%)	1 (1.4%)	15 (21.5%)	
ISS					0.593
1	10 (14.3%)	11 (15.7%)	5 (7.1%)	26 (37.1%)	
2	9 (12.9%)	8 (11.4%)	7 (10%)	24 (34.3%)	
3	10 (14.3%)	8 (11.4%)	2 (2.9%)	20 (28.6%)	

ASCT - autologous stem cell transplantation.
The ages are expressed as means ± standard deviations.
The p-values were calculated using a chi-squared test (for the categorical variables) or ANOVA (for age).

economic class C, which means that 87.8% of the included patients have a family budget of less than US $600/month (i.e., economic class C, D, or E). Therefore, it is important to apply such questionnaires in underdeveloped countries to ensure that ASCT is a good option for their incurable disease in this population. The QLQ-MY20 was not validated in Portuguese (Brazilian) when the questionnaires were applied and, therefore, was not used in our study. Although the questionnaires are designed to be self-completed, in this study the questionnaires were given during interviews performed by a principal researcher. The questionnaires were conducted in an interview because most of the patients were considered to be functionally illiterate and/or could not complete the forms alone. Others could read but were unable to understand what needed to be answered. We believe that administering the questionnaire by the same person provides more uniform results.

One criticism of this study design is that the patient groups were not the same at the three time-points that were investigated. This could limit the power of the observation; however, the paired t-test results from both questionnaires showed improvements in the patients' QoL.

In conclusion, this study supports the use of the EORTC QLQ-C30 as part of routine clinical care in MM patients in developing countries. Our results also suggest that the questionnaire for cancer patients, QLQ-C30, seems to be more informative than the generic questionnaire, SF-36.

Table 3 - Analysis of variance (ANOVA) comparing the three groups according to the QLQ-C30 questionnaire.

Scale	Upon diagnosis, Mean (± SD)	Post-treatment/ Pre-ASCT, Mean (± SD)	D+100 ASCT, Mean (± SD)	p-value
Global health	64 (± 24)	70 (± 22)	71 (± 16)	0.455
Functional scale				
Physical	43 (± 34)	59 (± 24)	71 (± 20)	**0.01**
Role	39 (± 40)	72 (± 34)	83 (± 29)	**0.001**
Emotional	64 (± 27)	70 (± 28)	77 (± 34)	0.391
Cognitive	65 (± 30)	76 (± 23)	69 (± 24)	0.339
Social	62 (± 31)	71 (± 35)	82 (± 32)	0.186
Symptom scale				
Fatigue	53 (± 31)	27 (± 24)	21 (± 24)	**0.001**
Nausea	14 (± 25)	5 (± 12)	7 (± 22)	0.289
Pain	58 (± 34)	31 (± 27)	34 (± 27)	0.002
Quality of life scale				
Dyspnea	15 (± 27)	5 (± 18)	7 (± 19)	0.239
Insomnia	43 (± 31)	26 (± 32)	21 (± 38)	0.061
Lack of appetite	34 (± 47)	11 (± 24)	14 (± 31)	**0.046**
Constipation	36 (± 43)	9 (± 20)	7 (± 14)	**0.002**
Diarrhea	2 (± 12)	0	9 (± 20)	0.059
Financial difficulties	53 (± 41)	30 (± 40)	31 (± 38)	0.071

The p-values were calculated using an ANOVA.
QoL: Quality-of-life.
ASCT- autologous stem cell transplant.

Table 2 - Analysis of variance (ANOVA) comparing the three groups according to the SF-36 questionnaire.

Domains	Upon diagnosis, Mean (± SD)	Post-treatment/ Pre-ASCT, Mean (± SD)	D+100 ASCT, Mean (± SD)	p-value
Physical function	33 (± 33)	44 (± 27)	60 (± 25)	**0.026**
Role-physical	31 (± 36)	47 (± 28)	56 (± 29)	**0.041**
Bodily pain	36 (± 26)	53 (± 23)	55 (± 28)	**0.025**
General health	60 (± 22)	66 (± 14)	60 (± 14)	0.388
Vitality	58 (± 23)	63 (± 17)	68 (± 24)	0.364
Social function	45 (± 38)	54 (± 31)	68 (± 25)	0.094
Role-emotional	49 (± 39)	58 (± 24)	69 (± 33)	0.158
Mental health	64 (± 23)	73 (± 19)	74 (± 21)	0.194
Physical component	33 (± 11)	37 (± 8)	40 (± 7)	0.053
Mental component	47 (± 13)	49 (± 8)	51 (± 11)	0.362

The p-values were calculated using an ANOVA.
ASCT - autologous stem cell transplantation.

Table 4 - *Post hoc* tests comparing the three groups (two by two).

POST HOC Test	Group	*p*-value
Physical function (SF-36)	Upon diagnosis D+100 ASCT [†]	**0.02**
Physical (QLQ-C30)	Upon diagnosis D+100 ASCT [†]	**0.011**
Role (QLQ-C30)	Upon diagnosis Post-treatment/Pre-ASCT [†]	**0.003**
Role (QLQ-C30)	Upon diagnosis D+100 ASCT [†]	**0.001**
Fatigue (QLQ-C30)	Upon diagnosis Post-treatment/Pre-ASCT [†]	**0.003**
Fatigue (QLQ-C30)	Upon diagnosis D+100 ASCT [†]	**0.002**
Pain (QLQ-C30)	Upon diagnosis Post-treatment/Pre-ASCT [†]	**0.003**
Pain (QLQ-C30)	Upon diagnosis D+100 ASCT [†]	**0.042**
Lack of appetite (QLQ-C30)	Upon diagnosis Post-treatment/Pre-ASCT [†]	**0.05**
Constipation (QLQ-C30)	Upon diagnosis Post-treatment/Pre-ASCT [†]	**0.005**
Constipation (QLQ-C30)	Upon diagnosis D+100 ASCT [†]	**0.016**

ASCT - autologous stem cell transplantation.
[†]The group with the superior outcome.

Additionally, the QLQ-C30 reflects the benefits of ASCT for the QoL of MM patients from two public Brazilian institutions that provide assistance for economically challenged patients.

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AUTHOR CONTRIBUTIONS

Etto LY was responsible for the draft of the manuscript, analysis and interpretation of the data. Morelli VM was responsible for the draft of the manuscript, analysis and interpretation of the data, and approval of the final version of the manuscript. Silva VC: collected the data. Hungria VTM and Durie B were responsible for the critical revision of the manuscript regarding important intellectual content. Ciconelli R was responsible for the design of the study, analysis and interpretation of the data. Almeida MSS, Oliveira JSR, Barros JC collected the data. Colleoni GWB conceived and designed the study, drafted the article, analyzed and interpreted the data, critically revised the article for important intellectual content, and gave final approval of the version of the article that was submitted.

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