

Health-related quality of life in multiple myeloma survivors treated with high dose chemotherapy followed by autologous peripheral blood progenitor cell transplantation: a retrospective analysis

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A pilot study analyses an effect of selected demographic, psychosocial and health aspects on quality of life (QoL) in multiple myeloma survivors treated with high-dose chemotherapy followed by autologous peripheral blood progenitor cell transplantation (PBPCT).

The total number of respondents with multiple myeloma treated with high-dose chemotherapy followed by autologous PBPCT between years 2001-2003 at the Department of Clinical Haematology of the 2nd Department of Internal Medicine of Charles University Hospital and Faculty of Medicine in Hradec Králové, Czech Republic was 32 (18 male, 14 female). The average age of respondents was 60 years old. The Czech version of an international generic European Quality of Life Questionnaire – Version EQ-5D was used. The effect of selected demographics, psychosocial and health aspects on QoL was determined by means of analysis of variance (ANOVA). The QoL questionnaires were evaluated by means of descriptive analysis.

The above-mentioned aspects proved statistically significant dependence of QoL on respondents age and on smoking abuse. EQ-5D score (dimensions of QoL) and EQ-5D VAS (a subjective health condition) significantly decrease with increasing age and with smoking abuse. The effect of other aspects on QoL was not proven as statistically significant. Prevailing complaints in respondents with multiple myeloma were: 1. regular activity with complaints 81,2 % (26/32 respondents), 2. medium serious pain / discomfort 68,8 % (22/32 respondents), 3. movement with complaints 59 % (19/32 respondents), 4. medium serious anxiety / depression 59 % (19/32 respondents). The QoL in patients with multiple myeloma treated with high-dose chemotherapy followed by autologous PBPCT was on low level (mean EQ-5D score was 68,9 %, mean EQ-5D VAS was 66,6 %).

The results had shown that with an increasing age, the QoL of patients with multiple myeloma treated with high-dose chemotherapy followed by autologous PBPCT, declines. The smokers and former smokers have lower QoL than non smokers. The global QoL in all studied patients with multiple myeloma treated with high-dose chemotherapy followed by autologous PBPCT was on low level.

Key words: quality of life, high-dose chemotherapy, autologous peripheral blood progenitor cell transplantation, multiple myeloma.

The haematopoietic stem cell transplantation (HSCT) is a therapeutic method used for biomodulation antitumor therapy of haematological malignancies and of the solid tumors. It is also used for the therapy of non-tumor and hereditary diseases [1]. It is divided into the bone marrow transplanta-

tion (BMT), the transplantation of blood (progenitor) stem cells (PBPCT) and the umbilical cord blood transplantation (UCBT). From a donor's point of view there are three kinds of transplantations: syngenic transplantation (the donor is a monozygotic twin), allogeneic transplantation (HLA from a compatible sibling or parent or HLA from a compatible donor) and autologous transplantation (patient itself is the donor).

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The aim of the HSCT is to replace patient's pathological bone marrow which contains tumorous cells with haematopoietic cells from a healthy donor and to restore haematopoiesis which is damaged by an intensive antitumor therapy. The HSCT influences the further course of disease, and by this the quality of life (QoL) of patients in the same way as other therapeutic methods [2].

The QoL term contains the information on an individual's physical, psychological, social and spiritual condition [2-4]. The QoL evaluation is carried out by means of generic and specific questionnaires [2, 5, 6]. Generic questionnaires generally evaluate a patient's overall condition regardless of his disease. Specific questionnaires are designed for the evaluation of a patient's overall condition in a particular type of disease. Modules are often used with these specific questionnaires. These modules are focused on specific symptoms and complaints in a particular type of disease [2].

The aim of the pilot QoL study was to analyse an effect of selected demographics (age,sex), psychosocial (level of education, marital status, religion) and health (number of associated diseases, smoking abuse and time lapse from autologous PBPCT aspects on QoL in multiple myeloma survivors treated with high-dose chemotherapy followed by autologous PBPCT and to evaluate global QoL in this cohort of patients.

Material and Methods

Study population. All patients scheduled for intensive treatment of multiple myeloma in the Department of Clinical Haematology of the 2nd Department of Internal Medicine of Charles University Hospital and Faculty of Medicine, Hradec Králové, Czech Republic between 1st September 2004 to 31st January 2005 were requested to participate in the QoL study.

The total number of respondents with multiple myeloma treated with high-dose chemotherapy (single dose of melfalan 200 mg/m² intravenous) followed by autologous PBPCT was 32 (18 male, 14 female). The average age of all respondents was 60 years old (age range 53-67 years old). The number of non-smokers was 15, smokers (number of cigarettes daily was more than 10) was 8 and former smokers (time of abstinence was more than 1 year) was 9. The number of believer respondents was 17 and non-believer respondents was 15. The number of respondents with university education was 5, with secondary education was 12, with apprentice education was 10 and with elementary education was 5. The number of married respondents was 25, divorced respondents was 5 and widows/-er respondents was 2. The number of respondents with 1 associated disease was 12, with 2 associated diseases was 10, with 3 associated diseases was 6 and with more than 3 associated diseases was 4. The number of respondents treated with autologous PBPCT between years 2001 – 2003 shows the Table 1.

The study was approved the Ethics Commission of the Charles University Hospital and Faculty of Medicine, Hradec Králové, Czech Republic.

Table 1. Number of respondents with multiple myeloma treated with high-dose chemotherapy followed by autologous PBPCT between years 2001-2003.

Type of disease	year 2001	year 2002	year 2003	Total number of respondents
Multiple myeloma	10	8	14	32

Table 2. European Quality of Life Questionnaire – EQ-5D Version (dimension of QoL) [2, 7, 22].

Please select one answer which describes your today's health status.

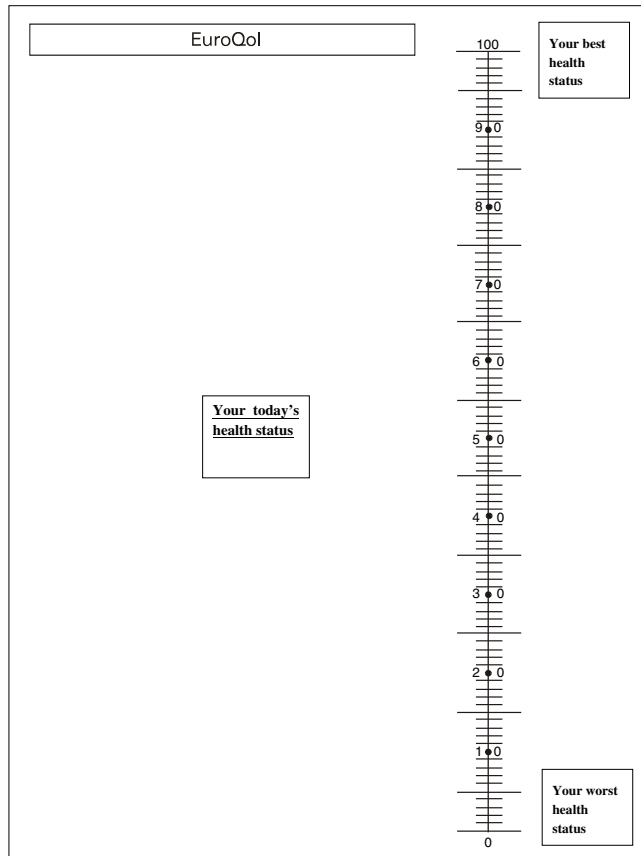
Mobility	<i>none troubles</i>	<input type="checkbox"/>		
	<i>with troubles</i>		<input type="checkbox"/>	
	<i>immobile</i>			<input type="checkbox"/>
Self-care	<i>none troubles</i>	<input type="checkbox"/>		
	<i>with troubles</i>		<input type="checkbox"/>	
	<i>incapable</i>			<input type="checkbox"/>
Usual activities	<i>none troubles</i>	<input type="checkbox"/>		
	<i>with troubles</i>		<input type="checkbox"/>	
	<i>incapable</i>			<input type="checkbox"/>
Pain / discomfort	<i>none</i>	<input type="checkbox"/>		
	<i>weighty</i>		<input type="checkbox"/>	
	<i>extremely</i>			<input type="checkbox"/>
Anxiety / depression	<i>none</i>	<input type="checkbox"/>		
	<i>weighty</i>		<input type="checkbox"/>	
	<i>extremely</i>			<input type="checkbox"/>

Measurement. The Czech version of an international generic EuroQol EQ-5D Questionnaire was used in the study [2, 7]. This questionnaire evaluates 2 indicators, objective and subjective indicators. The objective indicator includes 5 dimensions of QoL (see Table 2): mobility, self-care, usual activities, pain / discomfort, anxiety / depression. Three kinds of answers which express the degree of complaints are offered to each question (no complaints, mild complaints, severe complaints). Totally 243 (3⁵) combinations of health condition exits. The outcome is EQ-5D score (dimensions of QoL) which has the values from 0 to 1 (0 – the worst health condition, 1 – the best health condition). Subjective indicator includes visual analogous scale (see Table 3) (the value of 100 – the best health condition, the value of 0 – the worst health condition). The respondent marks his subjectively perceived health condition at the thermometer scale. The outcome is EQ-5D VAS (a subjective health condition) which has the values from 0 to 100 [2, 7] (see Table 3).

Procedure. The Euro Qol EQ-5D Questionnaire with a covering letter, in which the whole project was explained, together with a stamped envelope were mailed to a respondents address. The filling in the QoL questionnaire was voluntary and anonymous.

Data collection, statistical methods. The evaluation of QoL questionnaires was carried out by means of descriptive analysis in accordance with European Quality of Life Group Method (7). The independent variables were age, sex, level of educa-

Table 3. European Quality of Life Questionnaire – EQ-5D Version (visual analogue scale) (2, 7, 22).



tion, marital status, number of associated diseases, smoking abuse, religion and time lapse from PBPCT. The dependent variables were EQ-5D score (dimensions of QoL) and EQ-5D VAS (a subjective health condition). The effect of selected aspects on QoL in respondents was evaluated by means of analysis of variance. The value $p < 0,05$ was considered significant. Software StatSoft STATISTICA Base 7.1 for Windows was used for complete evaluating of dates.

Results

The above-mentioned aspects proved statistically significant dependence of QoL (EQ-5D score and EQ-5 VAS) on age (in both cases $p < 0,01$) (see Graph 1) and statistically significant dependence of QoL (EQ-5D score and EQ-5 VAS) on smoking abuse in respondents with multiple myeloma (in both cases $p < 0,05$) (see Graph 2). EQ-5D score (dimensions of QoL) and EQ-5D VAS (a subjective health condition) significantly decrease with increasing age. They are significantly higher QoL (EQ-5D score and EQ-5D VAS) in non-smokers. The effect of other aspects on QoL (EQ-5D score and EQ-5D VAS) was not proven as statistically significant.

Table 4. Comparison of respondents with multiple myeloma treated with high-dose chemotherapy followed by autologous PBPCT according to the level of troubles (n=32).

Dimension of QoL	Level of evaluation	Number of multiple myeloma survivors	
		abs.	rel.
<i>Number of respondents</i>			
Mobility	<i>none troubles</i>	13	41%
	<i>with troubles</i>	19	59%
	<i>immobile</i>	0	
Self-care	<i>none troubles</i>	26	81,2%
	<i>with troubles</i>	6	18,8%
	<i>incapable</i>	0	
Usual activities	<i>none troubles</i>	6	18,8%
	<i>with troubles</i>	26	81,2%
	<i>incapable</i>	0	
Pain / discomfort	<i>none</i>	9	28,1%
	<i>weighty</i>	22	68,8%
	<i>extremely</i>	1	3,1%
Anxiety /depression	<i>none</i>	13	41%
	<i>weighty</i>	19	59%
	<i>extremely</i>	0	
<i>Number of respondents</i>		32	

The global QoL in respondents with multiple myeloma treated with high-dose chemotherapy followed by autologous PBPCT was on low level (mean EQ-5D score was 68,9 %, mean EQ-5D VAS was 66,6 %). Prevailing complaints in respondents with multiple myeloma were: 1. regular activity with complaints 81,2 % (26/32 respondents), 2. medium serious pain/discomfort 68,8 % (22/32 respondents), 3. movement with complaints 59% (19/32 respondents), 4. medium serious anxiety/depression 59 % (19/32 respondents) (see Table 4.)

Discussion

Multiple myeloma is a diffuse neoplasm of bone marrow plasma cells in which the malignant cells mingle with normal haematopoietic cells through-out the red bone marrow (8). Most frequent complications of multiple myeloma are painful pathologic fractures, anaemia, hypercalcaemia, renal failure and recurrent bacterial infections. Obviously, the subjective experience of numerous symptoms caused by these complications reduces the ability of normal functioning and negatively influences patients QoL [8].

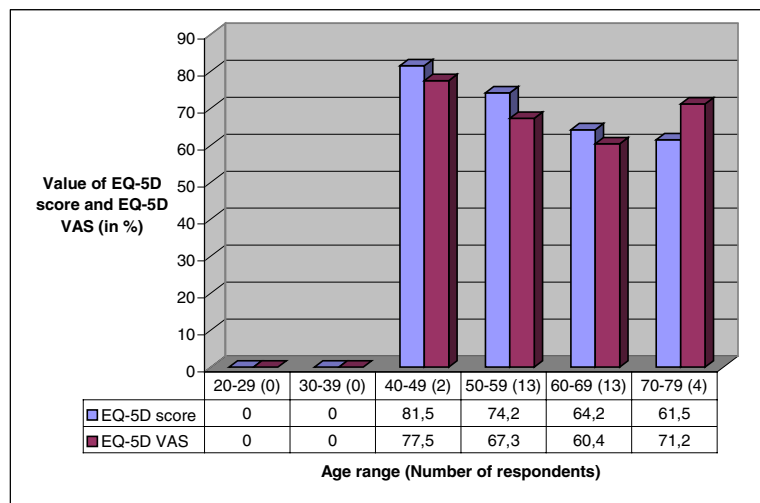
In our pilot QoL study, we found three main outcomes in subjective well-being patients who were able to high-dose chemotherapy followed by autologous PBPCT.

First, our results had shown that a lower QoL correlates with increasing age of patients who underwent the autologous PBPCT. We think that with increasing age a number of associated diseases can occur and these diseases reduce the patients QoL. Also, we think that in patients with increasing number of associated diseases there is a lower overall physical condition and this means the lower QoL. De Souza [9],

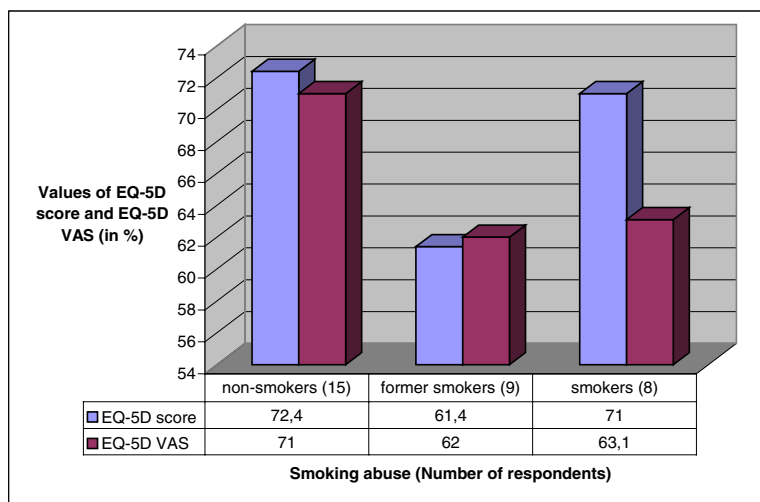
Heinonen [10, 11], Chiodi [12], Wang [13], Wong [14], Andrykowski [15] and Zittoun [16] discovered a similar trend in their studies. De Souza [9] points out in his longitudinal study conducted in the group of 26 patients. Also, this author [9] further explained his statements by the fact that with increasing age a number of associated diseases can occur. These diseases reduce the QoL [9]. Zittoun [16] discovered another interesting piece of information in his transversal study conducted in the group of 179 patients with haematological malignancy who underwent the HSCT. He points out that increasing overall fatigue and emotional complaints which decrease the QoL correlate with increasing age [16]. So [17] also discovered an interesting piece of information in his transversal study conducted in the group of 157 patients with haematological malignancy who underwent the BMT. He proved a high degree of overall fatigue in patients over the age of 50 with associated diseases [17]. Another author who agrees with Zittoun's [16] and So's [17] opinions is Saleh [18]. He conducted a transversal study in the group of 41 patients who underwent the BMT. This author [18] points out that in patients with increasing number of associated diseases there is a lower overall physical condition and this means the lower QoL.

In our respondents with multiple myeloma treated with high-dose chemotherapy followed by autologous PBPC we proved lower QoL in smokers in comparison with non-smokers or former smokers. Chang [19] found an opposite trend in his longitudinal follow-up of patients with chronic myeloid leukaemia following allogeneic HSCT, in whose an effect of alcohol and smoking abuse on QoL was observed. The group consisted of 114 patients. The author did not prove in his study the effect of alcohol and smoking abuse on QoL in this group of patients [19]. Slovacek [2] in previous study was not able to prove the effect of smoking abuse on QoL in respondents after HSCT in his cross-sectional study conducted in the group of 71 patients after HSCT.

Also, we found out a low global QoL in respondents with multiple myeloma treated with high-dose chemotherapy followed by autologous PBPC. The mean value of EQ-5D score (dimension of QoL) was 68,9 % and the mean value of EQ-5D VAS (subjective health condition) was 66,6 %. Prevailing complaints in respondents were: 1. regular activity with complaints 81,2 % (26/32 respondents), 2. medium serious pain / discomfort 68,8 % (22/32 respondents), 3. movement with complaints 59 % (19/32 respondents), 4. medium serious anxiety / depression 59 % (19/32 respondents). Poulos [20] revealed a similar trend in his descriptive study of the year



Graph 1. Dependence of EQ-5D score and EQ-5D VAS on individual age groups in multiple myeloma survivors treated with high-dose chemotherapy followed by autologous PBPC between years 2001 – 2003 (n=32, p<0,01).



Graph 2. Dependence of EQ-5D score and EQ-5D VAS on smoking abuse in multiple myeloma survivors treated with high-dose chemotherapy followed by autologous PBPC between years 2001 – 2003 (n=32, p<0,01).

2001 in the group of patients with multiple myeloma which comprised 346 patients. The author observed an effect of pain and mood disturbances on QoL in these patients. The study results prove that 29% of patients with multiple myeloma feel a pain of moderate up to strong intensity. Furthermore, the study indicates a significant association between an intensity of pain and a mood disturbance. Moreover, a tumorous pain and mood disturbances are found significant predictors of QoL in this group of patients [20].

In conclusion, we are informed, that our pilot study together with the study of the Czech Myeloma Society of the

year 2002, which evaluated QoL and a tolerance of sustained therapy in patients with multiple myeloma, is one of few Czech studies related with QoL in haematooncological patients. Our study reveals global QoL in patients with multiple myeloma treated with high-dose chemotherapy followed by autologous PBPCT.

In the future, we would like to continue this study and carry on a prospective study which would longitudinally evaluate health-related quality of life (HRQoL) in addition to stage of multiple myeloma, to clinical prognostic factors (plasmatic cells infiltration of bone marrow, index of apoptosis, labeling index, serum concentration of lactatedehydrogenase, serum concentration of thymidinekinase, serum concentration of beta2-microglobulin, value of hemoglobin, marker of bone resorption and marker of bone proliferation i.e.), global supportive care and to present and extent of ossification.

We are also aware of the fact that our study can be limited by a few other factors:

1. The study deals only with the effect of selected aspects on the global QoL. We could add a few other aspects. But we decided for presented aspects only, because patients were able and willing to provide this information in retrospectively and anonymously carried out study.
2. In study we used only generic European Quality of Life Questionnaire – EQ-5D for evaluation of global QoL in our patients. We decided for its evaluation because our patients were able and willing to complete only this questionnaire. Our patients emphasized that this questionnaire was very intelligible and especially brief. We could use originaly Czech version of FACT–G Questionnaire or EORTC QLQ-C30 Questionnaire, but our patients were negative for complete one of this questionnaires. The patients emphasized that this questionnaires is very comprehensive and time consuming.
3. The relatively small group of all our patients underwent autologous PBPCT.

It is common in the clinical practice to evaluate a patient's health condition and the success of the treatment based only on one type of markers, the most often by means of somatic, laboratory or detecting markers [2]. But the trend in modern clinical medicine is to evaluate a patient's health condition in a more complex way, using even other aspects. The QoL means more dimensional evaluation of number of life aspects [2]. Different aspects can be affected in a different way in a different phase of the disease and its treatment. That is why this information enriches our knowledge concerning patient's needs and it can significantly contribute to the medical treatment improvement. It can also help us to reveal the mechanisms which modify the origin and the course of disease [2, 21–23].

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