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# Autologous hematopoietic stem cell transplantation with low-intensity conditioning regimens in relapsing remitting multiple sclerosis: clinical outcomes and quality of life

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## Summary

The effect of autologous hematopoietic stem cell transplantation (AHSCT) with low-intensity conditioning regimens, in terms of clinical and patient-reported outcomes, was studied in patients with relapsing-remitting multiple sclerosis (RRMS). In total, 258 RRMS patients were enrolled in a single-center study. The median follow-up duration was 30 months. Low-intensity conditioning regimens (two based on reduced BEAM and one on cyclophosphamide) were applied. Outcomes of AHSCT were evaluated from both the physicians' and patients' perspectives. Reversal of the disability progression, relapse-free survival (RFS), progression-free survival (PFS), as well as changes in quality of life (QoL), and severity of symptoms were analyzed. Transplantation procedure was well tolerated by the patients, and there were no cases of transplantation-related mortality. In addition, no deaths were registered throughout the follow-up period. The vast majority of patients exhibited clinical improvement, or were in stable condition during the entire follow-up period. The estimated proportions of RFS and PFS were 83% and 86%, respectively, at 7 years after AHSCT. No differences in RFS were found between the patients who received reduced BEAM±ATG and high-dose cyclophosphamide+rituximab conditioning regimens. AHSCT resulted in significant and sustained QoL improvement, as well as decrease of symptom burden. The results of our study support feasibility of autologous HSCT with low-intensity conditioning regimens in RRMS. Multicentre cooperative studies should be done to optimize the treatment protocol of mini-AHSCT.

## Keywords

Autologous hematopoietic stem cell transplantation, conditioning regimen, multiple sclerosis, clinical outcomes, quality of life.

## Introduction

Multiple sclerosis (MS) is a severe inflammatory and demyelinating autoimmune disease of the central nervous system (CNS), which affects mainly young people and leads to progressive quality of life (QoL) deterioration due to progressive disability [1, 2]. Relapsing remitting MS (RRMS) evolves into secondary progressive disease in 70-80% of cases during

10-15 years [3, 4]. Hence, this relatively favorable variant of MS seems to be a very difficult condition with high risk of disability. Thus, the goal of treatment is to prevent MS progression and disability, to provide better control of the symptoms and to improve patient's QoL [5]. Conventional DMT (Disease Modifying Therapies) does not provide satisfactory control of MS, due to inability to eradicate self-aggressive T- and B-cell clones. Immunosuppressive treatment including monoclonal antibodies, which are usually used as a second-line therapy, also have only partial beneficial effect [6, 7].

At present, high-dose immunosuppressive therapy with autologous hematopoietic stem cell transplantation (AHSCT) has been used with increasing frequency as a therapeutic option for MS patients [8-14]. The rationale for this method presumes that ablation of the impaired immune system followed by reconstitution of the new immune cell populations may alter the characteristics of the T – and B-cell responses and other immunological properties which can improve clinical course of MS [15, 16]. Previous studies demonstrated that AHSCT was associated with improvement in neurological disability and QoL in RRMS patients [17-21].

At the same time, in spite of promising clinical results, there are still several questions to be clarified before recommending AHSCT as a treatment choice for MS patients, especially for those with relapsing-remitting disease. For example, effectiveness and safety of different conditioning regimens (intermediate and low-intensity) should be analyzed carefully. Several clinical studies have addressed the issue of safety and effectiveness of AHSCT with BEAM as intermediate-intensity conditioning regimen in MS with certain promising results [22-25]. On the other side, it was shown recently, that low-intensity regimens (BEAM-like or Cyclophosphamide based) are associated with similar outcome results and less toxicity profile to compare with more intensive conditioning. Patients' selection for AHSCT is another core issue [26, 27]. Additionally, comprehensive treatment outcomes assessment is very important in all variants of AHSCT [28, 29]. Both disease-free period and improvement of patient's QoL are recognized as important treatment outcomes. Also, one of the key issues is the long-term follow-up and assessment of clinical and patient-reported outcomes [29-31].

Thus, we aimed to evaluate the effect of AHSCT with low-intensity conditioning regimens in patients with RRMS, in terms of clinical and patient-reported outcomes.

# Patients and methods

All the patients underwent AHSCT in the Transplantation Unit, Department of Haematology and Cellular Therapy, Pirogov National Medical and Surgical Centre (Moscow) from October 2006 to October 2018. The study was conducted according to the principles of Helsinki Declaration, and was approved by the Institute Research Board and local Ethics Committee before initiation. All the patients had given their written informed consent. The patients were eligible if they were >15 years old and met the Poser and McDonald criteria for clinically defined MS [32]. Other criteria for patients' selection included normal mental status and absence of severe concomitant diseases. The vast majority of patients was refractory to 2-4 different lines of conventional treatment including interferons, copaxone, mitoxantrone, cladribine, monoclonal antibodies therapy, azathioprine, intravenous immunoglobulin, glucocorticosteroids etc.

Hematopoietic stem cells were mobilized with granulocyte colony-stimulating factor (G-CSF, 10 μg/kg) during 4-5 days. The mobilized cells were collected by apheresis after 4 days of stimulation until a yield of at least $2.0\times10^6$ CD34+ cells/kg.

Three low-intensity conditioning regimens were applied in the patients. Two regimens were based on reduced BEAM protocol: (1) BM schedule (BCNU 300 mg/m$^2$, Melphalan 100 mg/m$^2$ + horse ATG at the dose of 30 mg/kg on days 1 and 2 for *in vivo* T cell-depletion); (2) BEAM-like regimen (BCNU 300 mg/m$^2$, Etoposide 100 mg/m$^2$, Ara-C 100 mg/m$^2$, Melphalan 100 mg/m$^2$ + horse ATG at the dose of 30 mg/kg on days 1 and 2 for *in vivo* T cell-depletion). The third conditioning regimen included high-dose cyclophosphamide (200 mg/kg) + Rituximab (500 mg/m$^2$) on D+11-12 (one infusion).

G-CSF (5 μg/kg) was administered on D+1 to D+2 until granulocyte recovery. For infection prophylaxis, oral levofloxacin, fluconazole, co-trimoxazole and acyclovir were used.

Toxicity of treatment was evaluated in accordance with National Cancer Institute Common Toxicity Criteria (version 2) [33]. The terms of posttransplant neutrophil engraftment were defined since the first day when absolute neutrophil count was >500 cells/mL. Platelet engraftment was registered since the first day when the platelet count was >20,000 platelets/mL (without platelet transfusions). Transplant-related mortality (TRM) included every death occurring within 100 days of transplantation [34].

The primary end point was disability level defined by the EDSS score [35]. Other studied end-points included safety, relapse-free survival (no acute relapses) and quality of life (QoL) changes. To evaluate clinical outcomes, neurological assessment and MRI scans were performed. Neurological assessment using EDSS was performed at baseline, at discharge, at 3, 6, and 12 months after transplantation, every 6 months thereafter up to 48 months, and, later, at the annual basis. EDSS decrease of 1.0 or more was considered a significant improvement, and an increase of 1.0 or greater was viewed as significant worsening. MRI scans of brain and cervical spinal cord with gadolinium enhancement were performed at baseline, at 3, 6, and 12 months after transplantation, every 6 months up to 48 months, and then at yearly intervals. QoL was assessed using RAND SF-36 [36], common symptoms, by CSP-MS-42 [37]. The SF-36 is generic tool for QoL assessment widely used in patients with chronic diseases, including MS [38, 39]. The Comprehensive Symptom Profile-MS-42 (CSP-MS-42) was developed in 2007 by New Jersey Center for Quality of Life and Health Outcome Research (USA) and Multinational Center for QoL Research (Russia) to assess the severity of 42 symptoms which are common and most disturbing for MS patients. It consists of numerical analogous scales, scored from "0" (no symptom) to "10" (most expressed symptom). The measurements were conducted before AHSCT, at 6 and 12 months after AHSCT, then every 6 months during 2 years after AHSCT and every

12 months after 2 years during 5 years after AHSCT.

For statistical evaluation, paired t-test, Wilcoxon test and ANOVA were used. Progression-free survival (PFS) and relapse-free survival (RFS) after AHSCT were evaluated using Kaplan-Meyer method. To compare survival rates, log-rank criterion and Tarone-Ware criterion were applied. Mc-Nemar's test was used in order to compare the proportions of patients according to symptom prevalence before AHSCT and 12 months following transplant. P values of <0.05 will be used as a cut-off point for statistical significance, and all statistical tests will be two-sided.

# Results

## General characteristics

A total of 258 patients with RRMS were enrolled in the study. Mean age was 36.5 years old; male/female ratio, 73/185. Median EDSS value before transplantation was 2.0 (range 1.5-6.5). Mean duration of the disease was 4.9 years (median 3.0, range 0.5-24). Patients' characteristics are shown in Table 1.

**Table 1. Characteristics of the patients with multiple sclerosis**

| Clinical/demographic parameters | n/% |
|---|---|
| **Gender:** | |
| Males | 73/28,3 |
| Females | 185/71.7 |
| **Age, years:** | |
| 15-25 | 39/15.1 |
| 26-35 | 87/33.7 |
| 36-45 | 79/30.6 |
| 46-70 | 53/20.6 |
| **EDSS:** | |
| EDSS <4 | 211/81.8 |
| EDSS 4-6 | 46/17.8 |
| EDSS =6.5 | 1/0.4 |
| **Disease duration, years:** | |
| <5 years | 143/55.4 |
| ≥5 years | 94/36.5 |
| ND | 21/8.1 |

***Abbreviations:*** *EDSS, Expanded Disability Status Scale score; ND, no data.*

## Safety

The procedure of autologous HSCT was well tolerated by the patients. There were no cases of transplantation-related mortality. Mobilization was successful in all cases with median number of $2.1\times10^6$/kg (range 2-$10.9\times10^6$/kg) collected CD34+cells; no major clinical adverse events were observed during this phase.

The mean time of neutropenia (grade 4) was 8.0 days. The mean time of thrombocytopenia (grade 3-4) was 7.0 days. Neutrophil engraftment was registered on D+8- D+11. No differences in hematological toxicity between the three conditioning regimens were found (P>0.05).

Common adverse effects after AHSCT were as follows: hepatic toxicity (grade 2 and 3) – 20.5%; mucositis (grade 2), 1.6%; temporary neurological worsening, 6.4%; neutropenic fever, 27%; local infection, 6.2%; anemia (grade 3), 1.9%; allergic reactions, 2.3%. No differences in toxicity were observed among the patients who received different conditioning regimens. No deaths were registered throughout the entire follow-up period.

## Clinical outcomes

Median follow-up after AHSCT was 30 months (3.7-110.9). The vast majority of patients (99%) responded to treatment. The decrease of EDSS score from median 2.0 to 1.5 was observed at 12 months after AHSCT, and it remained at this level during the follow-up of more than 60 months (Fig. 1). The EDSS score improved significantly for the entire group (P <0.001) at all the time intervals, as compared with baseline. EDSS changes in patients with RRMS prior to and at different time-points after AHSCT are presented in Table 2. The proportion of patients with change of >1.0 in EDSS score was 36% (86 patients) with index of improvement at 12 months, and 0.4% (1 patient) with an index of the disease progression. At 2 years post-transplant, 47 (32%) patients showed improvement, 1 patient (0.7%) became worse, and others presented with stable disease. At 3 years posttransplant, improvement was observed in 23 (25%) patients, worsening – in 1 (1.1%) patient, the others were in stable clinical state. At 4 years posttransplant, the majority (83.1%) of patients were stable, there was no further worsening, and 10 patients (16.9%) exhibited improvement. Hence, the vast majority of patients was stable during the continuous follow-up; clinical deterioration took place in 6% of patients.

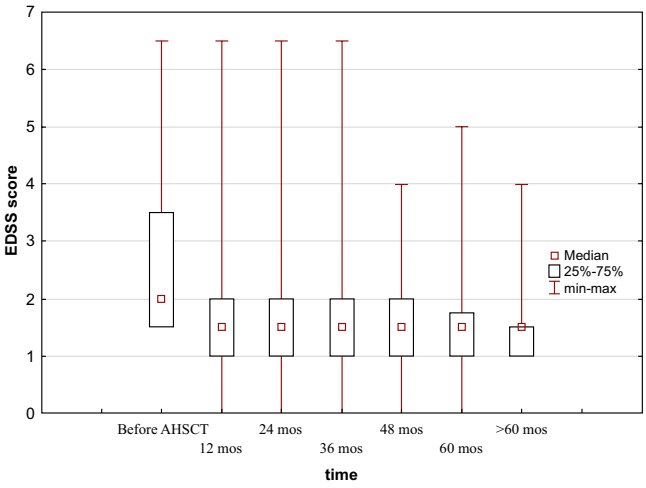


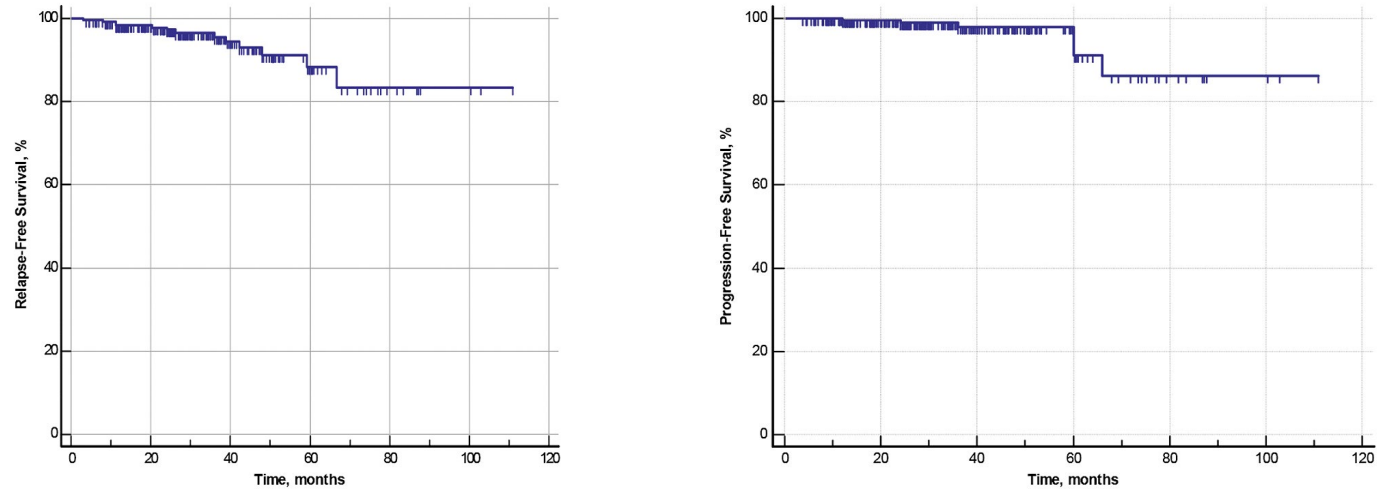

**Figure 1. EDSS medians in patients with RRMS before and at different time-points after AHSCT**

After AHSCT, the vast majority of patients with RRMS were relapse-free (245 out of 258). The mean term until relapse was 30.4 months (95% CI 18.24-42.52). Estimated relapse-free survival (RFS) at the median follow-up of 29.5 months was 95% (95% CI: 92.3-97.7) (Fig. 2A).

Estimated RFS at the follow-up of 36 months was 95.6% (95% CI: 92.4-98.8), at the follow-up of 60 months, 88.2% (95% CI: 80.2-96.2); at the follow-up of 84 months, 83.3%

**Table 2. EDSS changes in patients with RRMS before and at different time-points after AHSCT**

| EDSS | Observation terms | | | | | | |
|---|---|---|---|---|---|---|---|
| | Before AHSCT | 12 mo | 24 mo | 36 mo | 48 mo | 60 mo | >60 mo |
| *N* | 258 | 237 | 145 | 92 | 59 | 32 | 16 |
| Median (interquartile range) | 2.0 (1.5-3.5) | 1.5 (1.0-2.0) | 1.5 (1.0-2.0) | 1.5 (1.0-2.0) | 1.5 (1.0-2.0) | 1.5 (1.0-0.75) | 1.5 (1.0-1.5) |
| Mean, (SD) | 2.6 (1.2) | 1.68 (1.15) | 1.60 (1.04) | 1.75 (1.01) | 1.60 (0.69) | 1.64 (0.94) | 1.50 (0.73) |
| 95% CI | 2.4-2.7 | 1.53-1.82 | 1.43-1.78 | 1.54-1.95 | 1.42-1.78 | 1.30-1.98 | 1.11-1.89 |
| Type of EDSS changes, *n* (%) | | | | | | | |
| Stabilization (change≤0,5 score) | | 150 (63.3) | 97 (66.9) | 68 (73.9) | 49 (83.1) | 24 (75.0) | 14 (87.4) |
| Improvement (≥1 score) | | 86 (36.3) | 47 (32.4) | 23 (25.0) | 10 (16.9) | 6 (18.8) | 1 (6.3) |
| Worsening (≥1 score) | | 1 (0.4) | 1 (0.7) | 1 (1.1) | - | 2 (6.2) | 1 (6.3) |




A B

**Figure 2. Relapse-free (a) and progression free (b) survival Kaplan-Meyer curves in RRMS patients after AHSCT**

(95% CI: 71.3-95.3). Estimated progression-free survival (PFS) at the follow-up of 36 months was 98% (95% CI: 95.6-100.0), at the follow-up of 60 months, 91.2% (95% CI: 81.9-100.0), at the follow-up of 84 months, 86.2% (95% CI: 73.1-99.3), as seen from Fig. 2B.

Separate analysis of RFS probability in the groups of patients with different conditioning regimen was also performed. Comparison was made between the conditioning regimens based on BEAM-like and Cyclophosphamide+Rituximab protocols. Previously, it was shown that the outcomes for mini-BEAM and BM were similar [24]. Thus, the BEAM-like group included mini-BEAM and BM conditioning regimens. No differences in RFS were found between patients who received BEAM-like and these who received high-dose cyclophosphamide+Rituximab (log-rank, P=0.92), as shown in Fig. 3.

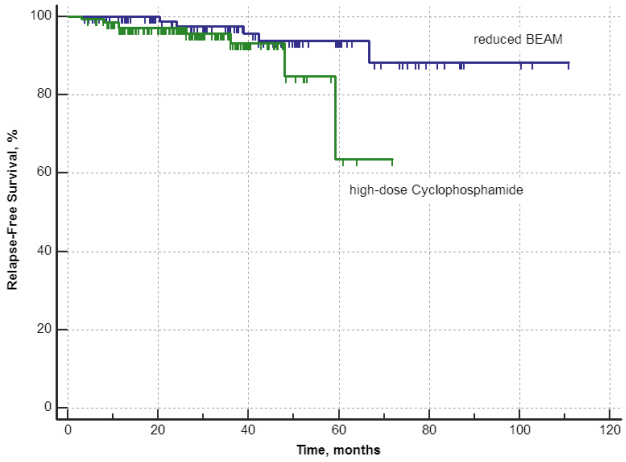



**Figure 3. Relapse-free survival Kaplan-Meyer curves for patients who received BEAM-like *vs* who received high-dose Cyclophosphamide+Rituximab**

**Table 3. Quality of life mean values in RRMS patients at baseline and 12 months after AHSCT**

| SF-36 scales | Baseline (n=78) | | 12 after AHSCT (n=78) | | *p** |
|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | |
| PF | 72.50 | 24.03 | 84.05 | 21.76 | <0.001 |
| RPF | 52.63 | 42.74 | 73.08 | 38.17 | 0.001 |
| BP | 70.13 | 23.06 | 76.76 | 24.49 | 0.004 |
| GH | 58.24 | 20.81 | 72.09 | 18.29 | <0.001 |
| V | 51.69 | 23.01 | 66.86 | 22.38 | <0.001 |
| SF | 68.02 | 25.12 | 81.41 | 24.40 | <0.001 |
| REF | 68.44 | 38.32 | 81.62 | 33.83 | 0.011 |
| MH | 67.81 | 18.28 | 76.01 | 16.59 | <0.001 |
| IQoLI | 0.405 | 0.214 | 0.584 | 0.262 | <0.001 |

***Notes:*** **Wilcoxon test*

***Abbreviations:*** *RRMS, relapsing-remitting multiple sclerosis; AHSCT, autologous hematopoietic stem cell transplantation; SD, standard deviation; PF, physical functioning; RPF, Role physical functioning; BP, Bodily pain; GH, General health; V, Vitality; SF, Social functioning; REF, Role emotional functioning; MH, Mental health; IQoLI, Integral QoL Index.*

**Table 4. Mean values for QoL indexes in RRMS patients at baseline and in long-term follow-up after AHSCT**

| SF-36 scales | Baseline (n=41) | | Long-term follow-up after AHSCT (n=41) | | *p** |
|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | |
| PF | 64.79 | 25.22 | 89.11 | 15.54 | <0.001 |
| RPF | 33.13 | 36.42 | 85.00 | 29.31 | <0.001 |
| BP | 69.45 | 22.21 | 82.33 | 18.82 | 0.004 |
| GH | 52.12 | 20.96 | 68.00 | 19.23 | <0.001* |
| V | 44.63 | 21.50 | 65.75 | 19.86 | <0.001* |
| SF | 62.19 | 23.08 | 88.13 | 15.49 | <0.001 |
| REF | 63.33 | 39.08 | 89.17 | 27.62 | 0.001 |
| MH | 65.65 | 19.99 | 78.80 | 15.08 | 0.001 |
| IQoLI | 0.321 | 0.178 | 0.633 | 0.208 | <0.001* |

***Notes:*** **Wilcoxon test (t-test for GH, V and IQoLI scales)*

***Abbreviations:*** *RRMS, relapsing-remitting multiple sclerosis; AHSCT, autologous hematopoietic stem cell transplantation; PF, physical functioning; RPF, Role physical functioning; BP, Bodily pain; GH, General health; V, Vitality; SF, Social functioning; REF, Roleemotional functioning; MH, Mental health; IQoLI, Integral QoL Index.*

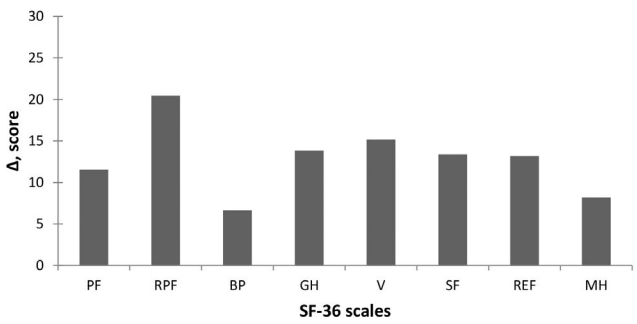



**Figure 4. QoL changes in RRMS patients at 12 months after AHSCT as compared to baseline (before ASCT)**

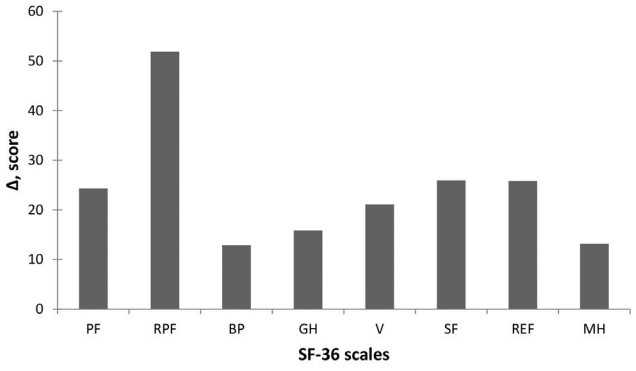



**Figure 5. QoL changes in RRMS patients at long-term follow-up after AHSCT as compared to baseline (before ASCT)**

## Patient-reported outcomes

Mean QoL values in RRMS patients before AHSCT and 12 months after AHSCT (n=78) are presented in Table 3. QoL changes (Δ) of scores according to all the SF-36 scales in 12 mo after AHSCT were compared to the baseline levels (Fig. 4).

We have also performed analysis of QoL changes at long-term follow-up after AHSCT (≥18 months) as compared to baseline values (n=41). Median follow-up was 22.9 months (interquartile range: 16.8-35.7 mo; mean±SD, 23.9±5.05 mo;95% CI: 22.3 to 25.5 mo). The mean QoL values in RRMS patients before AHSCT and in the course of long-term follow-up after AHSCT are presented in Table 4. QoL changes (Δ) of scores for all SF-36 scales over long-term follow-up after AHSCT were compared to baseline scores (Fig. 5).

Prevalence of the most common symptoms by CSP-MS42 in RRMS patients at 12 mo after ASCT against appropriate baseline values is shown in Fig. 6. Before AHSCT, the ten most common symptoms were present in more than half of the patients. Such symptoms as constant tiredness feeling, early exhaustion after physical activity, decreased energy, fatigue, heaviness in legs, loss of balance, lack of working coordination, difficulty walking and poor tolerance of hot water were reported by the vast majority of patients. As seen from the Fig. 6, their prevalence decreased 12 months post-transplant. The number of patients who experienced these symptoms except of *heaviness in legs* was significantly less after AHSCT as compared with baseline prevalence ($P<0.05$). The severity of all these symptoms also decreased after AHSCT ($P<0.05$).

AHSCT was accompanied by a significant improvement in patient's QoL and decrease of symptom burden. Improved QoL was preserved during the entire period of follow-up. AHSCT is beneficial in unfavorable group of MS patients, those with progressive MS, with high disability and long lasting disease.

# Discussion

We have analyzed a cohort of 258 patients with RRMS undergoing AHSCT, with a median follow-up of 30 months. Low-intensity conditioning regimens based on BEAM and cyclophosphamide were applied. Outcomes of AHSCT were evaluated both from physician's and patient's perspective. Transplantation procedure was well tolerated by the patients. There were no cases of transplantation-related mortality. In our cohort, the vast majority of patients responded to treatment and exhibited clinical improvement, or were stable during the entire period of follow-up. Significant decrease of EDSS score was observed after transplantation; the EDSS score improved (decreased by ≥1.0 point), with 32% and 17% of patients demonstrating improvement at 2 years and 4 years, respectively. In our cohort, relapse-free survival and progression-free survival at 7-year follow-up were 83% and 86%, respectively. These results are in line with previously published data by R. Burt [18, 19].

Moreover, AHSCT was accompanied by significant improvement in patient's QoL. The analysis of QoL demonstrated benefits of AHSCT with low-intensity conditioning regimens in this patient population. QoL is an important outcome of MS treatment and its assessment provides the patient's perspective on the overall effect of treatment and allows evaluating patient benefits. Our results definitely show that AHSCT resulted in significant and sustained improvement of patient's QoL. Also, prevalence and severity of common symptoms of MS decreased after transplantation. Thus, noticeble decrease of symptom burden after AHSCT was demonstrated.

For the first time to our knowledge, we report the AHSCT outcomes in MS patients after different low-intensity conditioning regimens and long-term follow-up. We did not find any differences in RFS between the patients who received

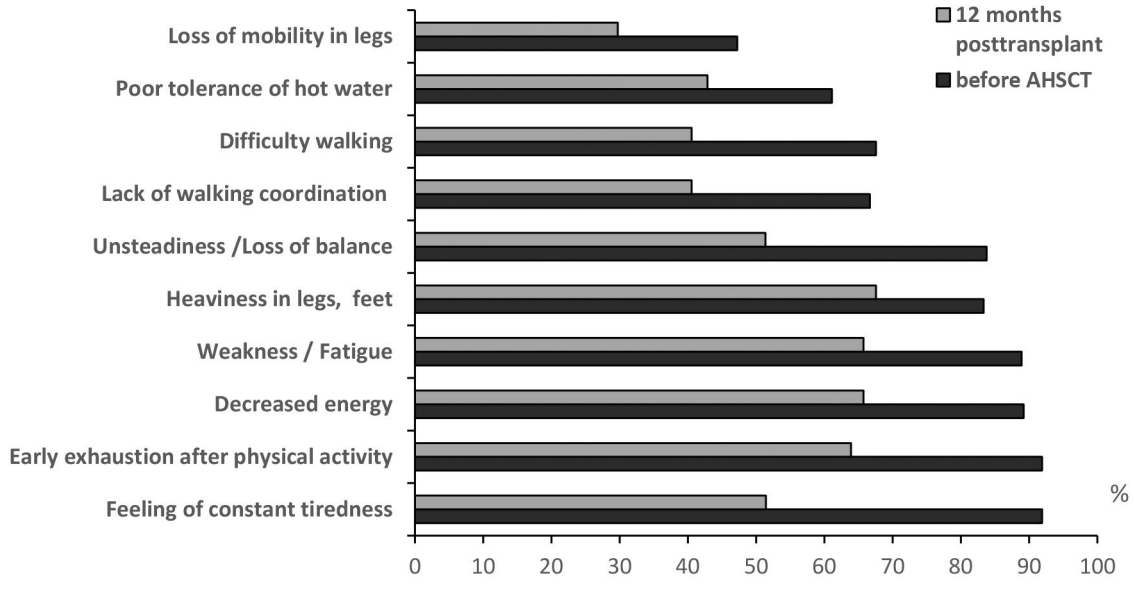



**Figure 6. Prevalence of common MS symptoms before and at 12 months posttransplant**

BM/BEAM-like+ATG, and those who received high-dose cyclophosphamide+Rituximab. These data are in line with the results we have published previously [29]. Our study also demonstrated that RFS did not differ between various age groups, and between the groups with different duration of the disease.

On the contrary, disability status was an important factor influencing the outcomes of transplantation: RFS was dramatically better in patients with EDSS<4 as compared to patients with EDSS=4-6.5. This finding supports the idea that AHSCT is beneficial for patients with highly active relapsing-remitting MS and moderate disability.

This study has several important limitations. Firstly, the study was conducted at a single academic institution, which may introduce some bias. However, all patients had clinical continuity and were monitored for in terms of relapses or need for additional treatment. Secondly, a large number of patients were treated on a compassionate basis rather than within a study protocol. Thirdly, a long-term follow-up (i.e, for ≥4 years) was not available for a substantial proportion of patients. Fourth, this was an observational cohort lacking a control group. Therefore, any inferences about causal effects of AHSCT can't be made.

Thus, the risk/benefit ratio of AHSCT with low-intensity conditioning regimens in our population of RRMS patients is rather favorable. The consistency of our clinical and QoL results, together with persistent improvement suggest clinical efficacy of AHSCT strategy in RRMS patients. In general, the results of our study support the feasibility of AHSCT with low-intensity conditioning in RRMS patients. To optimize the mentioned treatment protocols of AHSCT in RRMS, multicenter cooperative studies are necessary in future.

## Conflicts of interest

None reported.

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# Аутологичная трансплантация гемопоэтических стволовых клеток с режимом сниженной интенсивности при ремиттирующем рассеянном склерозе: клиническая эффективность и качество жизни

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## Резюме

Высокодозная иммуносупрессивная терапия с аутологичной трансплантацией гемопоэтических стволовых клеток (ВИСТ+ТГСК) – новый эффективный метод лечения рассеянного склероза (РС). В данной публикации представлены результаты комплексной оценки клинической эффективности и оценок, данных пациентом, у больных с ремиттирующим вариантом течения РС до и в разные сроки после ВИСТ+ТГСК с использованием режимов кондиционирования сниженной интенсивности (две программы на основе BEAM и одна на основе циклофосфамида). В исследование включены 258 пациентов, средний возраст – 36,5 лет, мужчины/женщины – 71/185. Медиана индекса инвалидизации по шкале EDSS до трансплантации – 2,0 балла. Средняя длительность периода наблюдения составила 4,9 года. Для оценки клинической эффективности использовались динамика индекс EDSS и данные МРТ. Также проводился анализ безрецидивной выживаемости и выживаемости без прогрессирования заболевания. Для оценки качества жизни использовали общий опросник RAND SF-36 и опросник оценки симптомов CSP-MS-42. Процедура мобилизации и трансплантации хорошо переносилась больными. Безрецидивная выживаемость и выживаемость без прогрессирования заболевания составила 83% и 86%, соответственно, в течение 7 лет после ТГСК.

В результате исследования не было выявлено различий в эффективности и токсичности при применении режимов кондиционирования сниженной интенсивности на основе BEAM с АТГ и циклофосфамида с ритуксимабом. После ТГСК отмечено значительное улучшение параметров качества жизни и снижение выраженности симптомов у подавляющего большинства пациентов. Таким образом, с помощью оценки клинического ответа и параметров качества жизни, продемонстрирована высокая эффективность и безопасность режимов кондиционирования сниженной интенсивности у пациентов с ремиттирующим РС.

## Ключевые слова

Аутологичная трансплантация гемопоэтических стволовых клеток, режим кондиционирования, рассеянный склероз, клинический ответ, качество жизни.