# Hematopoietic stem cell transplantation: pulmonary function tests and post-transplant mortality*

## Testes de função pulmonar e mortalidade após o transplante de células-tronco hematopoiéticas*

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## Abstract

**Objective:** To determine whether the results of pulmonary function tests carried out in patients subsequently submitted to hematopoietic stem cell transplantation (HSCT) are associated with post-HSCT mortality. **Methods:** This was a prospective study involving patients older than 15 years of age who were submitted to allogenic HSCT between January of 2007 and March of 2008 at the *Hospital das Clínicas da Universidade Federal de Minas Gerais*, located in the city of Belo Horizonte, Brazil. Prior to HSCT, all of the patients underwent spirometry, determination of lung volumes, and determination of DLCO. Those same tests were repeated six months, one year, and two years after HSCT. Kaplan-Meier curves and two-tailed log-rank tests were used for survival analysis. The relative risk (RR) and 95% CI were calculated using the Cox proportional hazards model. The Cox regression model was used in the multivariate analysis. **Results:** The pre-HSCT pulmonary function results were normal in 40 (74.1%) of the 54 patients evaluated, 19 (35.2%) of whom died within the first 100 days after HSCT. By the end of the two-year follow-up period, 23 patients (42.6%) had died, the most common causes of death being septicemia, observed in 11 (47.8%), and septicemia-related respiratory insufficiency, observed in 10 (43.4%). The only variables significantly associated with post-HSCT mortality were alterations in spirometry results prior to HSCT (RR = 3.2; p = 0.016) and unrelated donor (RR = 9.0; p < 0.001). **Conclusions:** Performing spirometry prior to HSCT provides baseline values for future comparisons. Although alterations in spirometry results reveal a higher risk of post-HSCT mortality, such alterations do not contraindicate the procedure.

**Keywords:** Hematopoietic stem cell transplantation/mortality; Respiratory function tests; Donor selection.

## Resumo

**Objetivo:** Verificar se os resultados dos testes de função pulmonar realizados em pacientes submetidos a transplante de células-tronco hematopoiéticas (TCTH) estão associados com a mortalidade após o procedimento. **Métodos:** Estudo prospectivo no qual foram incluídos pacientes maiores de 15 anos submetidos a TCTH alogênico, entre janeiro de 2007 e março de 2008, no Hospital das Clínicas da Universidade Federal de Minas Gerais, em Belo Horizonte (MG), e que realizaram espirometria, medida de volumes pulmonares e medida de DLCO antes do TCTH. Os testes foram repetidos seis meses, um ano e dois anos após TCTH. Para a análise de sobrevida, foram utilizados o método de Kaplan-Meier e testes de log-rank bicaudal. O risco relativo (RR) e IC95% foram calculados por meio do ajuste do modelo de riscos proporcionais de Cox. O modelo de regressão de Cox foi utilizado na análise multivariada. **Resultados:** Dos 54 pacientes incluídos, 40 (74,1%) apresentaram resultados normais de função pulmonar antes do TCTH. Ocorreram 23 óbitos (42,6%) em dois anos após o TCTH, sendo que 19 aconteceram antes de 100 dias. Dos 23 óbitos, 11 (47,8%) foram por septicemia e 10 (43,4%) por insuficiência respiratória aguda associada à septicemia. As únicas variáveis que mostraram associação significativa com mortalidade após TCTH foram alteração na espirometria antes do TCTH (RR = 3,2; p = 0,016) e doador não aparentado (RR = 9,0; p < 0,001). **Conclusões:** A realização da espirometria antes do TCTH fornece valores basais para comparações futuras. Alterações nesses resultados indicam um maior risco de mortalidade após o TCTH, embora esses não contraindicam o procedimento.

**Descritores:** Transplante de células-tronco hematopoéticas/mortalidade; Testes de função respiratória; Seleção do doador.

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## Introduction

Hematopoietic stem cell transplantation (HSCT), whether allogenic, autologous, or syngeneic, is an important option in the treatment of hematological and oncological diseases, being available at more than 500 facilities distributed throughout 50 countries.[1] Pulmonary complications, which occur in approximately 30-60% of recipients, constitute a major cause of post-HSCT morbidity and mortality. With the advances in prophylaxis and treatment of infectious conditions, the proportion of complications classified as noninfectious pulmonary complications (NIPCs) has increased significantly.[2] Early diagnosis and treatment of such complications can change the prognosis of HSCT recipients.[3-7]

The pulmonary function tests (PFTs) used in the assessment and follow-up of patients submitted to HSCT include measurement of lung volumes, spirometry, and measurement of DLCO.[2,8-10] Although PFTs are internationally adopted for pre- and post-HSCT assessment, their true usefulness and the ideal interval between HSCT and PFTs remain debatable.[6,11] The current recommendation is that PFTs be performed prior to HSCT and one year after HSCT.[8] Some authors suggest that PFTs should be performed more frequently in the first two years after HSCT, especially in patients with chronic graft-versus-host disease (GVHD).[9-11] It is believed that performing PFTs more frequently after HSCT would not only allow the identification of NIPCs but could enable early preventive and therapeutic interventions in at-risk patients.[8,12]

The objective of the present study was to prospectively investigate whether the PFT results obtained prior to and after HSCT are associated with post-transplant mortality and post-transplant NIPCs, as well as to determine whether abnormal PFT results obtained prior to HSCT are associated with changes in the management of HSCT.

## Methods

The study sample included patients older than 15 years of age who underwent allogenic HSCT between January of 2007 and March of 2008 at the *Hospital das Clínicas da Universidade Federal de Minas Gerais*(HC-UFMG, Federal University of Minas Gerais *Hospital das Clínicas*), located in the city of Belo Horizonte, Brazil. Prior to HSCT, all of the patients underwent spirometry, measurement of lung volumes, and measurement of DLCO. Patients submitted to autologous transplantation were excluded, as were those aged 15 years or younger and those who, prior to HSCT, underwent spirometry only.

The variables studied were as follows: type of hemato-oncological disease that led to transplantation; chemotherapy received; sources of hematopoietic stem cells used; donor status (related or unrelated); pre-HSCT conditioning regimen; pharmacological prophylaxis used for GVHD; smoking status; lung diseases; and death. The occurrence of acute or chronic GVHD was established on the basis of the clinical, histological, and biochemical criteria devised by Sullivan.[13] For the purpose of the present study, reports or descriptions of any kind of pulmonary infection, prior to or after HSCT, were not considered lung disease. The major NIPCs investigated after HSCT were as follows: bronchiolitis obliterans; bronchiolitis obliterans organizing pneumonia (BOOP); recent airflow obstruction; pulmonary fibrosis; and diffuse alveolar hemorrhage. Clinical, radiological, and functional criteria were applied in order to identify those complications.[2,14] None of the patients underwent lung biopsy for the diagnosis of such complications.

Through June of 2009, all PFTs were performed with the use of a Collins GSII system (Collins, Braintree, MA, USA). Between July of 2009 and February of 2010, a Collins CPL system was used in accordance with the Brazilian Thoracic Association guidelines.[15] The following variables were measured by spirometry: VC; FVC; $FEV_1$; $FEF_{25-75\%}$; the $FEV_1$/FVC ratio; and the $FEF_{25-75\%}$/FVC ratio. The predicted reference values used were those published by Pereira et al. for the Brazilian population aged between 25 and 78 years, for males, and between 20 and 74 years, for females.[15] The values devised by Mallozi were used for males between 15 and 24 years of age and for females between 15 and 19 years of age.[16] The multiple-breath helium dilution method was used for measuring absolute lung volumes, and the following variables were obtained: TLC; RV; and the RV/TLC ratio. The reference values were those devised by Crapo for patients younger than 20 years of age[17] and those devised by Neder et al. for patients

older than 20 years of age.[18] The single-breath hold technique (10-s breath hold) was used for the DLCO test. Values of DLCO were corrected for hemoglobin concentration. In accordance with Gaensler & Smith,[19] DLCO was considered reduced when it was below 75% of the predicted value.

On the basis of spirometry results, absolute lung volume values and DLCO values, abnormal pulmonary function was classified as follows[15]: obstructive lung disease; restrictive lung disease; mixed obstructive and restrictive lung disease; increased RV and increased RV/TLC; and reduced DLCO. Subsequently, the patients were divided into two groups on the basis of abnormal results: those with abnormal spirometry results, abnormal absolute lung volumes, and abnormal DLCO; and those with abnormal spirometry results only.

Descriptive statistics are expressed as frequencies and percentages. The first step was to compare the different variables by univariate analysis, with the use of the Kaplan-Meier method and two-tailed log-rank tests.[20] The relative risk (RR) and 95% CI were quantified with the Cox proportional hazards model. The second step was to use the Cox regression model for determining which variables were independently associated with mortality.[21] Covariates with a p value < 0.25 (log-rank test) in the univariate analysis were included in the initial model. Covariates that, in isolation, had a p value $p < 0.05$ were retained for the next step. The same criterion was used in several analyses until only variables with a p value $p < 0.05$ remained, indicating that those variables showed independent association and statistical significance. All analyses were performed with the programs R (R Development Core Team) and Epi Info, both of which are in the public domain.

The study was approved by the UFMG Research Ethics Committee (Ruling no. ETIC 244/06 of September 22, 2006), and all participating patients gave written informed consent.

## Results

Between January of 2007 and December of 2008, 91 patients were submitted to HSCT at the HC-UFMG. Of those 91 patients, 37 were excluded: 18 because the HSCT was autologous; 10 because they were younger than 15 years of age; and 9 because, prior to HSCT, they underwent spirometry only. Therefore, the initial sample consisted of 54 patients, whose clinical characteristics are summarized in Table 1. There was a high proportion of male patients (59%), of patients who had been previously diagnosed with chronic myeloid leukemia or had received other diagnoses (68%), and of nonsmokers (87%). Only 1 patient was found to have pre-existing lung disease, and 7 (15%) developed an NIPC after HSCT. Of the 54 patients submitted to HSCT, 18 (33%) had acute GVHD. Among the 35 patients in whom it was possible to investigate chronic GVHD (19 of the 54 patients died within the first 100 days after HSCT), the condition was found to be present in 14 (40%). The most commonly used conditioning regimen was busulfan + cyclophosphamide (in 72%), and the most commonly used GVHD prophylaxis was cyclosporine + methotrexate (in 65%). The most common source of stem cells for HSCT was the bone marrow (in 57%), and 91% of those cases involved unrelated donors. In the study sample, 4 patients developed an NIPC within the first six months after HSCT (2 had diffuse alveolar hemorrhage, 1 had BOOP, and 1 had recent airflow obstruction). Of those 4, only the patient who had developed recent airflow obstruction survived. At six months after HSCT, 3 patients (6%) developed airflow obstruction. However, by the end of the two-year follow-up period, no new events had occurred. Of the 4 patients who developed recent airflow obstruction, 2 improved during the follow-up period.

The mean age of the patients was 31.6 years, and the mean time from diagnosis to transplantation was 14.6 months. Table 2 lists the values for the functional parameters, expressed as means and standard deviations. The baseline pulmonary function values were comparable to those of the general population.

Table 3 shows the most common lung diseases, as determined on the basis of spirometry results, lung volume values, and DLCO values. As can be seen, 22.2% of the patients had significantly abnormal pre-HSCT PFT results. Increased RV and an increased RV/TLC ratio did not correlate with obstructive lung disease prior to or after HSCT. Only 1 patient with pre-HSCT airflow obstruction survived to the end of the two-year post-transplantation follow-up period. Of the 5 patients who were

**Table 1 -** Clinical and demographic characteristics of the patients submitted to hematopoietic stem cell transplantation.

| Characteristic | Patients | |
|---|---|---|
| | n | % |
| Gender | | |
| Male | 32 | 59.3 |
| Female | 22 | 40.7 |
| Hematological disease | | |
| Chronic myeloid leukemia or other diagnoses[a] | 37 | 68.5 |
| Aplastic anemia | 17 | 31.5 |
| Recurrence | | |
| Yes | 4 | 7.4 |
| No | 50 | 92.6 |
| Smoking | | |
| Yes | 7 | 13.0 |
| No | 47 | 87.0 |
| Pre-existing lung disease | | |
| Yes | 1 | 1.9 |
| No | 53 | 98.1 |
| Conditioning regimen | | |
| Alemtuzumab | 15 | 27.8 |
| Busulfan + cyclophosphamide | 39 | 72.2 |
| Source of cells | | |
| Bone marrow | 31 | 57.4 |
| Stem cells | 22 | 40.7 |
| Cord | 1 | 1.9 |
| Donor status | | |
| Related | 49 | 90.7 |
| Unrelated | 5 | 9.3 |
| Chemotherapy | | |
| Yes | 29 | 53.7 |
| No | 25 | 46.3 |
| GVHD prophylaxis | | |
| Yes | 35 | 64.8 |
| No | 19 | 35.2 |
| Acute GVHD | | |
| Yes | 18 | 33.3 |
| No | 36 | 66.7 |
| Chronic GVHD[b] | | |
| Yes | 14 | 40.0 |
| No | 21 | 60.0 |
| Noninfectious pulmonary complications | | |
| Yes | 7 | 15.0 |
| No | 47 | 85.0 |
| Onset of noninfectious pulmonary complications | | |
| Within the first 100 days after transplantation (DAH) | 2 | 4.3 |
| At 100 days after transplantation (BOOP, AFO) | 2 | 4.3 |
| At six months after transplantation (AFO) | 1 | 2.1 |
| At one year after transplantation (AFO) | 2 | 4.3 |
| At two years after transplantation | 0 | 0.0 |
| No complications | 47 | 85.0 |
| Death | | |
| Yes | 23 | 42.6 |
| No | 31 | 57.4 |

GVHD: graft-versus-host disease; DAH: diffuse alveolar hemorrhage; BOOP: bronchiolitis obliterans organizing pneumonia; and AFO: airflow obstruction. [a]Acute lymphocytic leukemia, myelodysplasia, Hodgkin's lymphoma, and non-Hodgkin's lymphoma. [b]A total of 35 patients were assessed for this characteristic, since 19 died within the first 100 days after transplantation.

**Table 2 -** Pulmonary function test results prior to hematopoietic stem cell transplantation (n = 54).[a]

| Parameter | Results expressed as absolute values | Results expressed as % of predicted |
|---|---|---|
| VC, L | 4.0 ± 1.0 | 99.1 ± 14.5 |
| FVC, L | 4.0 ± 1.0 | 98.6 ± 14.4 |
| $FEV_1$, L | 3.4 ± 0.8 | 99.7 ± 14.5 |
| $FEF_{25-75\%}$, L | 4.0 ± 1.1 | 103.0 ± 30.9 |
| $FEV_1$/FVC | 86.6 ± 6.4 | 99.6 ± 6.7 |
| $FEF_{25-75\%}$/FVC | 103.4 ± 32.7 | 104.9 ± 32.5 |
| TLC, L | 5.4 ± 1.4 | 96.4 ± 14.4 |
| RV, L | 1.4 ± 0.5 | 90.1 ± 24.6 |
| DLCO, mL • $min^{-1}$ • $mmHg^{-1}$ | 90.7 ± 11.7 | 94.7 ± 11.7 |

[a]Values expressed as mean ± SD.

found to have recent airflow obstruction, 3 were submitted to a specific therapeutic intervention. Of those 3 patients, the one who had developed BOOP died, and the other 2 improved as a result of the treatment. All patients with reduced VC also had reduced TLC. Of the survivors, 7 did not undergo pulmonary function tests at the end of the two-year follow-up period.

Of the 54 patients evaluated, 23 (42.6%) died, the most common causes of death being septicemia, in 11 (47.8%), septicemia-related acute respiratory failure, in 10 (43.4%), and liver failure related to kidney failure, in 2 (8.8%). The 100-day survival rate was 65%, whereas the two-year survival rate was 57%.

Table 4 shows the result of the univariate analysis (log-rank test or Cox model) comparing variables between the patients who died and those who did not.

Table 5 shows the final multivariate regression model. The variable *pre-existing lung disease* was excluded from this analysis because of its low frequency in the sample (only in 1 patient). In this model, the variables statistically related to death were unrelated donor (RR = 9.9; $p < 0.001$) and abnormal spirometry results (RR = 3.2; $p = 0.016$). In the final model, mortality was not found to be associated with the combination of abnormal spirometry results, abnormal lung volume values, and abnormal DLCO values.

## Discussion

The main results of the present study show that patients with impaired pulmonary function, as assessed by spirometry, and an unrelated donor were the most likely to die after HSCT. However, abnormal spirometry results do not contraindicate the procedure.

**Table 3 -** Lung diseases and abnormal DLCO in the patients submitted to hematopoietic stem cell transplantation, over time.

| Type of lung disease/ abnormal DLCO | Status | Prior to transplantation | | At 100 days after transplantation | | At six months after transplantation | | At one year after transplantation | | At two years after transplantation | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | n | % | n | % | n | % | n | % | n | % |
| Obstructive | Yes | 5 | 9.3 | 3 | 8.8 | 2 | 7.4 | 3 | 10.7 | 2 | 9.5 |
| | No | 49 | 90.7 | 31 | 91.2 | 25 | 92.6 | 25 | 89.3 | 19 | 90.5 |
| Restrictive | Yes | 5 | 9.3 | 3 | 8.8 | 3 | 11.1 | 2 | 7.1 | 2 | 9.5 |
| | No | 49 | 90.7 | 31 | 91.2 | 24 | 88.9 | 26 | 92.9 | 19 | 90.5 |
| Mixed obstructive and restrictive | Yes | 0 | 0.0 | 0 | 0.0 | 1 | 3.7 | 1 | 3.6 | 1 | 4.8 |
| | No | 54 | 100.0 | 34 | 100.0 | 26 | 96.3 | 27 | 96.4 | 20 | 95.2 |
| ↑RV and ↑RV/TLC | Yes | 4 | 7.4 | 4 | 11.8 | 2 | 7.4 | 2 | 7.1 | 4 | 19.0 |
| | No | 50 | 92.6 | 30 | 88.2 | 25 | 92.6 | 26 | 92.9 | 17 | 81.0 |
| ↓DLCO | Yes | 2 | 3.7 | 5 | 14.7 | 2 | 7.4 | 0 | 0.0 | 2 | 9.5 |
| | No | 52 | 96.3 | 29 | 85.3 | 25 | 92.6 | 28 | 100.0 | 19 | 90.5 |

↑: increased; ↓: reduced.

**Table 4 -** Results of the univariate analysis of the patients submitted to hematopoietic stem cell transplantation, by outcome (death vs. non-death).

| Variable | Patients, n | | Statistical result | p |
|---|---|---|---|---|
| | Death | Non-death | | |
| Gender | | | | |
| Male | 15 | 17 | 1.1 | 0.285* |
| Female | 8 | 14 | | |
| Hematological disease | | | | |
| Chronic myeloid leukemia or other diagnoses[a] | 19 | 18 | 3.3 | 0.697* |
| Aplastic anemia | 4 | 13 | | |
| Preexisting lung disease | | | | |
| Yes | 1 | 0 | 2.4 | 0.126* |
| No | 22 | 31 | | |
| Conditioning regimen | | | | |
| With alemtuzumab | 17 | 22 | 0.1 | 0.789* |
| Without alemtuzumab | 6 | 9 | | |
| Source of cells | | | | |
| Bone marrow | 11 | 20 | 1.1 | 0.291* |
| Stem cells | 11 | 11 | | |
| Donor status | | | | |
| Related | 18 | 31 | 26.6 | < 0.001* |
| Unrelated | 5 | 0 | | |
| Chemotherapy | | | | |
| Yes | 9 | 16 | 0.5 | 0.467* |
| No | 14 | 15 | | |
| Prophylaxis | | | | |
| Cyclosporine + methotrexate | 18 | 17 | 2.5 | 0.117* |
| Cyclosporine | 5 | 14 | | |
| Acute graft-versus-host disease | | | | |
| Yes | 9 | 9 | 0.1 | 0.772* |
| No | 14 | 22 | | |
| Abnormal pulmonary function | | | | |
| All tests | | | | |
| Yes | 9 | 5 | 4.0 | 0.044* |
| No | 14 | 26 | | |
| Spirometry alone | | | | |
| Yes | 8 | 2 | 9.6 | 0.001* |
| No | 15 | 29 | | |
| Age, years | 31 | 23 | - | 0.356** |

[a]Acute lymphocytic leukemia, myelodysplasia, Hodgkin's lymphoma, and non-Hodgkin's lymphoma. *Log-rank test. **Cox model.

In the pre- and post-HSCT assessment, PFTs play an important role, being universally recommended. Although there are many studies on this subject in the literature, questions remain about the true usefulness of PFTs.[10] There has been only one retrospective study conducted in Brazil, undertaken at a major center for HSCT, in which spirometry alone was used in the pre- and post-HSCT assessment of pulmonary function.[5]

One relevant aspect of the present study was that spirometry results were evaluated together with lung volume values and DLCO values. This was due to the fact that these variables represent different markers of the physiological status of such patients. Spirometry measures the volume of air inhaled and exhaled, as well as respiratory flows.[15] Although the causes of an obstructive pattern on PFTs are limited

**Table 5 -** Results of the final model of the analysis of the patients submitted to hematopoietic stem cell transplantation, adjusted for mortality.

| Variable | Final model | Relative risk | 95% CI | p |
|---|---|---|---|---|
| Donor status | Unrelated | 9.9 | 2.9-33.5 | < 0.001 |
| Abnormal spirometry results | Yes | 3.2 | 1.2-7.3 | 0.016 |

to the airway, bronchiolitis obliterans being the pulmonary complication with the worst prognosis, a restrictive pattern can be secondary to parenchymal and nonparenchymal pulmonary involvement.[9] Thoracic irradiation, pulmonary toxicity of chemotherapy, infections, idiopathic pneumonitis, and GVHD are the factors most commonly associated with restrictive lung disease after HSCT.[9] The DLCO test measures the diffusion of gases from the alveoli into the interior of red blood cells; DLCO can be affected by a number of factors, such as alveolar-capillary membrane thickening, hemoglobin levels, and factors associated with restrictive lung disease.[9,15]

The results of the present study show that most of our patients (78%) had normal pre-HSCT PFT results (absolute lung volumes, spirometry, and DLCO) prior to HSCT, and that even those who had abnormal pre-HSCT PFT results underwent the procedure.

Post-HSCT mortality showed significant associations with abnormal pre-HSCT spirometry results and with unrelated donor. It should be highlighted that there were 19 deaths within the first 100 days after HSCT, a fact that prevented the investigation of a possible association between abnormal PFT results after HSCT and mortality. The investigation of the causes of death after HSCT revealed that mortality was associated with infection in 47.8% of cases, as well as with acute respiratory failure and infection in 43.4%. It is known that mortality can range from 10-40% within the first 100 days after HSCT, and this rate is associated with receptor-related factors, such as age and underlying disease, as well as with the conditioning regimen, with procedure-related factors, such as GVHD, and with immunodeficiency and infection.[1,2] Despite the advances in prophylaxis and treatment of infectious complications, the incidence of infection remains high at our facility and contributed significantly to mortality, which, according to the literature, is close to 80% in patients who develop severe respiratory failure and require mechanical ventilation.[2] It is possible that, even without differentiating lung diseases, abnormal spirometry results reveal a higher risk of post-HSCT mortality, and this should be considered in the pre-operative assessment of patients with such results. Contrary to expectation, when evaluating abnormal spirometry results together with abnormal lung volume values and abnormal DLCO values, we found no significant association with mortality. The pre-HSCT incidence of reduced DLCO was very low in the study population, and the sample size might have contributed to this result. The data obtained in the present study are in accordance with those obtained by Parimon et al., who also showed that pre-HSCT abnormal pulmonary function is significantly associated with post-HSCT risk of respiratory failure and of mortality. That study developed a risk score and found that lower $FEV_1$ and DLCO values and respiratory failure are associated with higher post-HSCT mortality.[22]

The higher mortality rate observed in recipients from unrelated donors was also reported by Patriarca et al.,[23] who found a significant association between mortality and unrelated donor ($p = 0.04$). The degree of relatedness and the HLA match between donor and receptor play an important role in immune reconstitution after transplantation. Therefore, recipients of grafts from unrelated or HLA-unmatched donors, or a combination of the two, require stricter control of rejection mechanisms, which might be associated with immunodeficiency states and higher mortality.[24]

The incidence of NIPCs in our study was 15% in two years, highlighting the fact that 15% of the patients died within the first 100 days after HSCT and therefore did not complete the PFTs. These data are in accordance with the 10-20% rates of NIPC incidence previously reported for patients submitted to HSCT.[23,25] In the present

study, it was not possible to investigate the association between NIPCs and abnormal PFT results because of the low occurrence of NIPCs at the time points assessed. In the literature, there are studies describing an association between NIPCs and abnormal pulmonary function. Two groups of authors retrospectively found that obstructive lung disease is associated with NIPCs after HSCT.[25,26] Chien et al., in a study of 915 patients, showed that a decrease of 5% in $FEV_1$ at 100 days after transplantation is associated with airflow obstruction at one year after transplantation (RR = 2.6; 95% CI: 2.1-3.1) but not with mortality.[27]

In the present study, unlike what is described in the literature, the PFTs were performed at relatively short time intervals, in the first year after HSCT, at an accredited laboratory, by a single professional, and in accordance with internationally accepted guidelines, thereby reducing the chance of methodological variations in the tests. In addition, we used the reference equations that best correlate with the different age groups and genders. These premises were emphasized by Chien et al. in their review of PFTs in HSCT.[10] Age and losses due to death within the first 100 days after transplantation significantly reduced the number of patients in our final sample. The increase in the number of autologous HSCTs, rather than in the number of allogenic HSCTs, in the two years when the patients were included also contributed to the smaller final sample size, in addition to complicating comparisons with most other studies, which were retrospective and included recipients of autologous or allogenic transplantation.

Despite the aforementioned restrictions, the results of the present study suggest that performing pre-HSCT spirometry is important because it provides baseline values for future comparisons. In addition, abnormal spirometry values reveal a higher risk of post-HSCT mortality, although such values do not contraindicate the procedure. Given that spirometry is inexpensive and relatively easy to perform, compared with measurement of absolute lung volumes and measurement of DLCO, which are not readily available at most health care facilities in Brazil, it seems reasonable that spirometry alone should be used in pre-HSCT PFTs, the more complex tests being reserved for selected cases. Ruling out NIPCs should be a priority in the assessment of patients with respiratory symptoms after HSCT.

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