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Cardiac involvement and treatment-related mortality after non-myeloablative haemopoietic stem-cell transplantation with unselected autologous peripheral blood for patients with systemic sclerosis: a retrospective analysis.

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Abstract

BACKGROUND: Autologous haemopoietic stem-cell transplantation (HSCT) benefits patients with systemic sclerosis but has been associated with significant treatment-related mortality and failure to improve diffusion capacity of carbon monoxide (DLCO). We aimed to assess efficacy of HSCT and use of rigorous cardiac screening in this group.

METHODS: We assessed patients with diffuse systemic sclerosis or limited systemic sclerosis and interstitial lung disease who were treated with HSCT as part of a study or on a compassionate basis at Northwestern University (Chicago, IL, USA) or the University of São Paulo (Ribeirão Preto, Brazil). Unselected peripheral blood stem cells were harvested with cyclophosphamide (2 g/m(2)) and filgrastim. The transplant regimen was a non-myeloablative regimen of cyclophosphamide (200 mg/kg) and rabbit anti-thymocyte globulin (rATG; 4·5-6·5 mg/kg). We followed patients up to 5 years for overall survival, relapse-free survival, modified Rodnan skin score, and pulmonary function tests.

FINDINGS: Five (6%) of 90 patients died from treatment-related causes. Despite standard guidelines that recommend echocardiogram for screening before transplantation, four treatment-related deaths occurred because of cardiovascular complications (one constrictive pericarditis, two right heart failures without underlying infection, and one heart failure during mobilisation), and one death was secondary to sepsis without documented underlying heart disease. Kaplan-Meier analysis showed survival was 78% at 5 years (after eight relapse-related deaths) and relapse-free survival was 70% at 5 years. Compared with baseline, we noted improvements after HSCT in modified Rodnan skin scores at 1 year (58 patients; p<0·0001), 2 years (42 patients; p<0·0001), and 3 years (27 patients; p<0·0001) and forced vital capacity at 1 year (58 patients; p=0·009), 2 years (40 patients; p=0·02), and 3 years (28 patients; p=0·004), but total lung capacity and DLCO were not improved significantly after HSCT. Overall mean DLCO was significantly improved in patients with normal baseline echocardiograms (p=0·005) or electrocardiographs (p=0·05).

INTERPRETATION: Autologous HSCT with a non-myeloablative regimen of cyclophosphamide and rATG with a non-selected autograft results in sustained

improvement in skin thickness and forced vital capacity. DLCO is affected by baseline cardiac function. Guidelines for cardiac screening of patients with systemic sclerosis to assess treatment-related risk from pulmonary artery hypertension, primary cardiac involvement, or pericardial disease should be reconsidered and updated.

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Comment in

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