Revista de Hematología

Rev Hematol Mex 2011;12(1):28-31

Artículo original

Body mass index as an indicator of prognosis in patients undergoing allogenic hematopoietic stem cell transplantation

Guillermo J Ruiz-Delgado,*,**,*** Julia A Lutz-Presno,*,*** Carlos Alarcón-Urdaneta,*,**,****
Jacqueline Calderón-García*,[1] Guillermo J Ruiz-Argüelles*,**,***

RESUMEN

Entre marzo de 1996 y diciembre de 2010 se hicieron 138 trasplantes de células hematopoyéticas en el Centro de Hematología y Medicina Interna de la Clinica Ruiz de Puebla. Los pacientes se estratificaron de acuerdo con el índice de masa corporal (IMC) previo al trasplante: 17 pacientes tuvieron IMC bajo, 62 IMC normal y 59 IMC alto. La mediana de supervivencia global (SG) fue de 9, 12 y 22 meses respectivamente. Independientemente de otras variables, los pacientes con IMC baja tuvieron una supervivencia menor que la de quienes se encontraron con IMC normal (SG a 58 meses de 24 *versus* 32%), en tanto que los pacientes con sobrepeso tuvieron mejor pronóstico (mediana de SG de 22 meses y SG de 43% a 130 meses). Nuestros hallazgos demuestran una correlación entre el IMC pre-trasplante y la supervivencia post-trasplante y podrían ser de utilidad para definir con más precisión el apoyo nutricional a los pacientes que van a recibir trasplantes de células hematopoyéticas.
Palabras clave: IMC, índice de masa corporal, prognosis, México, obesidad, desnutrición.

ABSTRACT

Between March 1996 and December 2010, a total of 138 patients received an allogeneic stem cell transplantation in the Centro de Hematología y Medicina Interna of the Clinica Ruiz. Patients were stratified according to pretransplantation body mass index (BMI) values: 17 patients had low BMI, 62 had normal BMI and 59 patients had high BMI. Median overall survival (OS) for these three groups were respectively 9, 12 and 22 months. Patients with a low BMI had a lower OS than those with a normal BMI (58-month OS of 24% versus 32%), whereas patients with an increased BMI had a better outcome (median OS of 22 months and 43% OS at 130 months) than those with a normal BMI. Our findings demonstrate a correlation between pretransplantation BMI and posttransplantation survival and should provide insight into how to better manage nutritional support for patients undergoing hematopoietic stem cell transplantation.
Key words: Allografts, BMI, body-mass-index, prognosis, México, obesity, malnutrition

* Centro de Hematología y Medicina Interna. Clínica RUIZ.
** Laboratorios Clínicos de Puebla. Clínica RUIZ
*** Universidad Popular Autónoma del Estado de Puebla
**** Universidad Autónoma de Puebla
[1] Facultad de Medicina. Universidad La Salle. México

Correspondence: Dr. Guillermo J. Ruiz-Argüelles. Centro de Hematología y Medicina Interna 8B Sur 3710. Puebla 72530, México. E-mail: gruiz1@clinicaruiz.com

Este artículo debe citarse como: Ruiz-Delgado GJ, Lutz-Presno JA, Alarcón-Urdaneta C, Calderón-García J, Ruiz-Argüelles GJ. Body mass index as an indicator of prognosis in patients undergoing allogenic hematopoietic stem cell transplantation. Rev Hematol Mex 2011;12(1):28-31.

Both obesity and malnutrition are considered risk factors for complications and increased relapse and nonrelapse mortality in hematopoietic stem cell transplantation (HSCT).[1] An inferior outcome after allogeneic HSCT has been reported in obese adult patients in both allogeneic and autologous HSCT: Overweight individuals seem to develop more complications of graft *versus* host disease and more infections than its normal counterparts.[1] On the other hand, malnutrition has been shown to be a critical prognostic factor in patients with acute lymphoblastic leukemia:[2,3] Undernourished patients relapse more frequently and have worse survival

than well-nourished patients.[2] To elucidate the impact of pretransplantation body mass index (BMI) on clinical outcome, we performed a retrospective cohort study with registration data from the Centro de Hematología y Medicina Interna of the Clínica Ruiz in Puebla, Mexico.

MATERIAL AND METHODS

a) Patients

Data were analysed from all patients who underwent HSCT using the Mexican reduced intensity conditioning schedule in the Centro de Hematología y Medicina Interna de Puebla of the Clinica Ruiz between March 1996 and December 2010. Patients were stratified according to pre-transplantation BMI values: low BMI: BMI < 18.5 kg/m^2, normal BMI: 18.5 - 25 kg/m^2, and high BMI: > 25 kg/m^2.

b) Allo-HSCT

The "Mexican method" of RIC was used in all patients.[4] A Karnofsky score of 100% was required to conduct the allograft. In all instances, the donor was a sibling with compatible (5/6) or identical (6/6) HLA. The study protocol was approved by the Institutional Review Board and the Ethics Committee of the institution. Written consent was obtained from all patients. Subcutaneous G-CSF (10 µg/kg/day) was given to the sibling donors on days -5 to +2, and one to three aphaeresis procedures were planned for days 0, +1 and +2 by means of a Haemonetics V-50 PLUS machine (Haemonetics Corporation, Braintree, MA), a Baxter C-3000 PLUS machine (Baxter Healthcare, Deerfield, IL), an AMICUS (Baxter Healthcare, Deerfield, IL) or a COBE-Spectra (Gambro, Lakewood, CO) using the Spin-Nebraska protocol.[4] The endpoint of collection was the processing of 5000-7000 ml of blood/m^2 in each aphaeresis procedure, providing a total amount of at least 2 x 10^6 viable CD34$^+$ cells/kg of the weight of the recipient. The Mexican method of non-ablative conditioning used in this study consisted of the following:[20] oral busulphan, 4 mg/kg, given on days -6 and -5; I.V. cyclophosphamide, 350 mg/m^2, on days -4, -3 and -2; and I.V. fludarabine, 30 mg/m^2, on days -4, -3 and -2. In 5 patients with very severe aplastic anaemia, busulphan was not used, and the cyclophosphamide dose was doubled on days -4 through -1; oral cyclosporin A (CyA) was administered at 5 mg/kg starting on day –1. In all the patients I.V. methotrexate (5 mg/m^2) was given on days +1, +3, +5 and +11, CyA was continued through day 180, with adjustments made to obtain serum CyA levels of 150–275 ng/mL, and then tapered over 30-60 days. If GVHD was present, CyA was tapered over a longer period. Ondansetron (1 mg I.V. every hour for 4 h after I.V. chemotherapy), an oral quinolone, and an azole were used in all patients until granulocyte counts were greater than 500 x 10^6/L for 3 consecutive days. The PBSC aphaeresis products were infused on days 0 to +1. The total counts of white blood cells, mononuclear cells (MNCs) and CD34$^+$ cells were enumerated by flow cytometry[5] with an EPICS Elite ESP machine (Coulter Electronics, Hialeah, FL), using the anti-CD34 monoclonal antibody HPCA-2 (Becton Dickinson, San José, CA). No purging procedures were performed. Engraftment was defined as an absolute neutrophil count of >0.5 x 10^9/L for at least 3 consecutive days, and platelet engraftment was defined as occurring on the first of 7 consecutive days with a platelet count of >20 x 10^9/L, without a platelet transfusion. Graft failure was defined as the failure to reach an absolute granulocyte count of >0.5 x 10^9/L on day +30. Chimerism was assessed in cases involving a sex mismatch with a fluorescent *in situ* hybridisation technique to mark the X and Y chromosomes.[6] In cases with an ABO mismatch, a flow cytometry-based approach was used, whereas polymorphic markers (STRs)[7] were analysed in the absence of any mismatch.

c) Statistics

The primary objective of the analysis was to assess the survival after the HSCT. Overall survival (OS) was calculated from the day of HSCT until the day of death or the last follow-up and was estimated according to the Kaplan-Meier method[8] using the log-rank chi-square test.

RESULTS

a) Patients

Between March 1996 and December 2010, a total of 138 patients received an allogeneic HSCT and were included in the study, all of them with a Karnofsky performance index of 100%. Details regarding age, gender, donor type, donor and recipient genders, and diagnosis are listed in Table 1. Patients were stratified according to pretransplantation BMI values (*vide supra*): 17 patients had low BMI, 62 had normal BMI and 59 patients has high BMI.

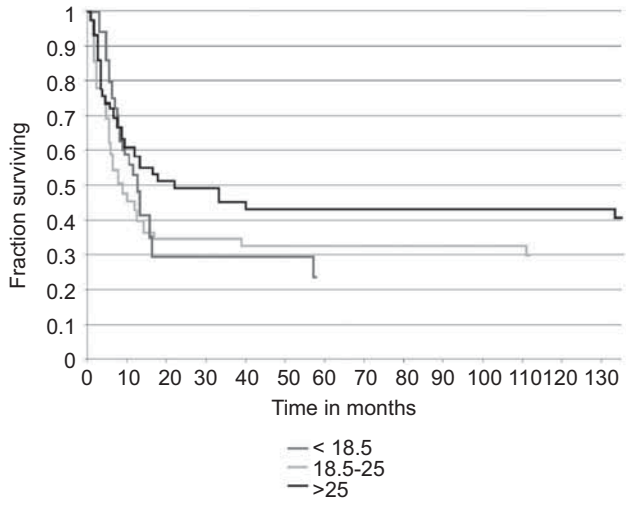

Figure 1. Overall survival of the patients which were allografted, classified according to the body mass index: 17 patients with low BMI (<18.5 kg/m^2), 62 with normal BMI (18.5 – 25 kg/m^2) and 59 with high BMI (>25 kg/m^2)

b) Allografts

All patients received peripheral blood stem cells allografts. Most of the grafts (67%) were 6/6 matches. Engraftment occurred in all patients. Chimerism studies were performed in all patients using the techniques previously described. Evidence of chimerism was found in all the allografted individuals.

c) Survival

Patients with low, normal or high BI had different median OS: 9, 12 and 22 months respectively ($p < 0.01$). Patients with a low BMI had a lower OS than those with a normal BMI (58-month OS of 24% versus 32%). Patients with an increased BMI had a better outcome (median OS of 22 months and 43% OS at 130 months) than those with a normal BMI (110-month OS of 32%).

DISCUSSION

Both obesity and malnutrition have been considered as adverse prognostic factors in patients undergoing HSCT.[1, 9-11] Obesity is associated with an increased risk of hyperglycemia, which can lead to an inferior outcome after allogeneic HSCT (9-10). On the other hand, malnutrition has been reported to be associated with an increased risk of early death after allogeneic HSCT.[10,11] We[2,3] and others[3,12] have previously shown that a low BMI is associated with a worse outcome and diminished OS in patients with acute leukemia treated with combined chemotherapy.

In this study, a BMI below 18.5 kg/m^2 was associated with a worse prognosis after allogeneic HSCT (58-month OS of 24%); however, the difference in survival was not statistically significant when compared with that observed in well nourished individuals. On the other hand, an increased BMI (> 25 kg/m^2) was not associated with a worse outcome; by the contrary, an increased BMI was associated with a better long-term post-allograft outcome (130-month OS of 43%), this information being consonant with the recent observation which indicates that obesity does not preclude safe and effective allogeneic HSCT.[13]

Our findings demonstrate a correlation between pretransplantation BMI and posttransplantation survival. Although BMI depends strongly on multiple factors, the effect of both malnutrition and obesity on clinical outcome should be evaluated in a prospective study. There is currently no agreement regarding a suitable target range of pretransplantation BMI for clinical management. These results should provide insight into how to better manage nutritional support for patients undergoing HSCT.

REFERENCES

1. Fuji S, Kim SW, Yoshimura K, Akiyama H, Okamoto S, Sao H, Takita J, Kobayashi N, Mori S. Japan Marrow Donor Program.: Possible association between obesity and posttransplantation complications including infectious diseases and acute graft-versus-host disease. Biol Blood Marrow Transplant 2009;15:73-82.
2. Lobato-Mendizábal E, Ruiz-Argüelles GJ, Marín-López A.: Leukaemia and nutrition I. Malnutrition is an adverse prognostic factor in the outcome of treatment of patients with standard-risk acute lymphoblastic leukaemia. Leuk Res 1989;13:899-906.
3. Lobato-Mendizábal E, López-Martínez B, Ruiz-Argüelles GJ. A critical review of the prognostic value of the nutritional status at diagnosis in the outcome of therapy of children with acute lymphoblastic leukemia. Rev Invest Clín Méx 2003; 55:31-35.
4. Gómez-Almaguer D, Ruiz-Argüelles GJ, Ruiz-Argüelles A, González-Llano O, Cantú OE, Hernández NE.: Hematopoietic stem cell allografts using a non-myeloablative conditioning regimen can be safely performed on an outpatient basis. Bone Marrow Transpl 2000;25:131-133.
5. Ruiz-Argüelles A, Orfao A.: Caracterización y evaluación de células totipotenciales en sangre periférica y médula ósea. In Ruiz-Argüelles GJ, San-Miguel JF (editors): Actualización en Leucemias. México: Médica Panamericana, 1996;p:79-82.
6. Pinkel D, Straume T, Gray JW. Cytogenetic analysis using quantitative, high sensitivity fluorescence hybridization. Proc Natl Acad Sci USA 1996;83:2934-2938.
7. Yam P, Petz L, Knowlton R, et al. Use of DNA restriction fragment length polymorphisms to document marrow engraftment

and mixed hematopoietic chimerism following bone marrow transplantation. Transplantation 1987;43:399-407.
8. Kaplan EL, Meier P. Nonparametric estimations from incomplete observations. J Am Stat Assoc 1958;53:457-463.
9. Navarro WH, Loberiza FR, Bajorunaite R, van Besien K, Vose JM, Lazarus HM, Rizzo D. Effect of body mass index on mortality of patients with lymphoma undergoing autologous hematopoetic stem cell transplantation. Biol Blood Marrow Transplant 2006;152:541-551.
10. Deeg HJ, Seidel K, Bruemmer B, et al. Impact of patient weight on non-relapse mortality after marrow transplantation. Bone Marrow Transplant 1995;15:461-468.
11. Le Blanc K, Ringden O, Remberger A. A low body mass index is correlated with poor survival after allogeneic stem cell transplantation. Haematologica 2003;88:1044-1052.
12. Viana MB, Murao M, Ramos G, et al. Malnutrition as a prognostic factor in lymphoblastic leukemia: a multivariate analysis. Arch Dis Child 1994;71:304-310.
13. Navarro WH, Agovi MA, Logan BR, Bolwell BJ, et al. Obesity does not preclude safe and effective myeloablative hematopoietic cell transplantation (HCT) for acute myelogenous leukemia (AML) in adults. Biol Blood Marrow Transplant 2010;16:1442-1450.