7. Lee SJ, Klein JP, Barrett AJ, Ringden O, Antin JH, Cahn JY, et al. Severity of chronic graft-versus-host disease: association with treatment-related mortality and relapse. Blood 2002;100:406-14.
8. Sullivan Km. Graft-versus-host disease. In: Forman SJ, Blume KG, Thomas ED, editors. Hematopoietic Cell Transplantation. Cambridge, MA: Blackwell Scientific Publications. 1999. p. 515-36.
9. Arora M, Burns LJ, Davies SM, Macmillan ML, Defor TE, Miller WJ, et al. Chronic graft-versus-host disease: a prospective cohort study. Biol Blood Marrow Transplantation 2003; 9:38-45.

Stem Cell Transplantation

Cytomegalovirus infection and chronic graft-versus-host disease are significant predictors of renal failure after allogeneic hematopoietic stem cell transplantation

We investigated the frequencies and predictive factors of prolonged renal failure (PRF) in a retrospective study of 181 consecutive patients undergoing allogeneic hematopoietic stem cell transplantation. Twenty-six patients (23% of long-term survivors) developed PRF. We identified 4 independent prognostic factors; cytomegalovirus infection and chronic graft-versus-host disease appeared as major risk factors for PRF.

haematologica 2005; 90:569-570
(*http://www.haematologica.org/journal/2005/5/.html*)

From 5 to 20% of long-term survivors of allogeneic hematopoietic stem cell transplantation (HSCT) develop late renal failure.[1-5] Predictive factors of renal dysfunction have not been firmly established.[1,6-8] Consecutive patients undergoing allogeneic HSCT in a single institution during ten years were retrospectively studied to determine frequencies and predictive factors of prolonged renal failure (PRF) and chronic renal failure (CRF).

One hundred and eighty-one adult patients, transplanted in the Hematology Unit of Besançon university hospital from January 1990 to December 1999, were included. The most frequent indication for transplantation was acute leukemia, in complete remission in 74% of the cases. All patients were conditioned with a myeloablative regimen, with total body irradiation (TBI) (12 Gy fractionated in 6 doses every 12 hours, with no renal shielding) in 132 cases (Table 1). Graft-versus-host disease (GVHD) prophylaxis comprised cyclosporine (Cs-A) in all but four cases (98%); Cs-A was administered intravenously during the first 3 weeks and adjusted following weekly assays; administration was continued orally at full dose for 3 months and then progressively tapered (10% reduction every week) to be finally stopped 6 months after transplantation in the absence of GVHD. All patients received low-dose heparin to prevent veno-occlusive disease.[9] Creatinine clearance was calculated according to the Cockcroft and Gault formula; PRF was defined by a creatinine clearance remaining under 50 mL/min for at least 6 months, followed by subsequent recovery. CRF was defined by a creatinine clearance remaining under 50 mL/min for at least 12 months without further improvement.

The statistical end-point was PRF; the definitions used for PRF did not allow analyses including observation time or the cumulative incidence and competing risks. By definition analysis was restricted to patients surviving at least 6 months post-transplantation. A logistic regression analysis was chosen to analyze the relation between renal failure and the relevant covariates.

Table 1. Characteristics of the patients and transplants.

Parameter	*Number (%)*
Age (years), Median [Range]	36 [15 - 62]
Sex ratio (Male/Female)	108/73 (60/40)
Diagnosis (pts/%)	
Acute myeloblastic leukemia	50 (28)
Acute lymphoblastic leukemia	43 (24)
Chronic myeloid leukemia	37 (20)
Non-Hodgkin's lymphoma	26 (14)
Myelodysplasia	15 (8)
Myeloma	3 (1.5)
Hodgkin's disease	2 (1)
Other	3 (1.5)
Donor-recipient compatibility (pts/%)	
Identical twins	2 (1)
Related partial match or matched sibling	149 (82)
Unrelated	30 (16)
Conditioning regimen (pts/%)	
Containing TBI*/Containing Cy†	132 (73)/116 (64)
Cy† - TBI*	91 (50)
Bu‡-Cy†/Bu‡-Mel§/Bu‡-Ara-C@	22 (12)/21(12)/34(19)
Other	39 (21)
Previous BMT (pts/%)	28 (15)
Autologous	23 (13)
Allogeneic	5 (3)
Containing TBI	19 (83)
Survival¶	
Median survival time (months)[range]	18 [0.5-128]
5-year survival	42±3%
7-year survival	39±4%

**TBI: total body irradiation; †Cy: cyclophosphamide; ‡Bu: busulfan; §Mel: melphalan; @Ara-C: cytarabine; ¶The occurrence of acute renal failure or PRF had no significant impact on survival after HSCT.*

Seventy-nine patients (44%) were long-term survivors with a median follow-up of 52 months (12-128) post-transplantation; 124 patients (68%) developed acute renal failure. PRF was diagnosed in 26 patients (23% of those surviving more than 6 months); 5 of them recovered a normal creatinine clearance after 6 months of renal insufficiency. Ten patients, 38% of the patients with PRF and 11% of those surviving more than one year, still had altered renal function at that time and were classified as having CRF. No patient developed CRF without previous acute renal failure or PRF. One patient with CRF still required dialysis 5 years after HSCT. A few factors had a significant impact on PRF in univariate analysis: male sex, response status after transplantation, the number of days of Cs-A exposure and the presence of chronic GVHD, hypertension or

Table 2. Logistic regression analysis of factors influencing prolonged renal failure.

Parameter	*Odds-ratio*	*CI [95%]*	*p value*
Lowest creatinine clearance (during the first 6 months)	0.49	[0.32 – 0.74]	0.001
Chronic GVHD*	5.58	[1.90 – 16.40]	0.01
CMV Infection†	3.29	[1.13 – 9.59]	0.03
Total duration of cyclosporine therapy (days)	1.1	[1.02 – 1.20]	0.05

**GVHD: graft-versus-host disease; †CMV: cytomegalovirus.*

cytomegalovirus (CMV) infection. Except hypertension, observed in 58% of PRF patients versus 38% of patients with normal renal function (p=0.04), no specific data focusing on renal function, such as urinalyses, were available. When entered into the logistic regression model, 4 variables with an unfavorable impact remained statistically significant: chronic GVHD, CMV infection, Cs-A exposure and the lowest creatinine clearance during initial hospital stay (Table 2). Analyses of prognostic factors for CRF were inappropriate because of the low number of patients. Nevertheless, TBI seemed to play a negative role, 90% of the CRF patients having received TBI versus only 55% of patients with preserved renal function (p=0.05).

Our study focused on late renal failure and identified chronic GVHD and CMV infection as crucial events influencing the risk of PRF.[10] This concept of PRF is described for one of the first times: the late normalization of renal function in a subset of patients could be explained by the same mechanisms as those observed after malignant hypertension[5] or the progressive withdrawal of nephrotoxic drugs. TBI did not have a significant impact on PRF but the use of irradiation affected the incidence of CRF, confirming the late impact of radiation therapy on the kidneys.[6,7] The long-term nephrotoxicity of Cs-A does not seem to be linked to chronic GVHD; these 2 factors were independent in the multivariate analysis. The high incidence of PRF among patients with chronic GVHD is in favor of specific renal impairment even if confounding factors cannot be excluded.[5] The CMV status of the donor and the recipient had a clear influence on survival after allogeneic HSCT.[4] We identified CMV infection as a strong independent risk-factor for the occurrence of PRF. Drugs used for CMV treatment are nephrotoxic in high concentrations and the correlation between CMV infection and PRF may also be due to this treatment.

The interweaving between CMV infection, GVHD and the prolonged use of Cs-A prevent us from drawing definitive conclusions. Examining the effect of early renal injury we found that a decrease of 10 mL/min in creatinine clearance during the first 3 months post-transplant was associated with a 2-fold higher risk of developing PRF, but late recovery of renal function can occur.

Eric Deconinck,# Marc Kribs,° Jean-Michel Rebibou,°# CE Bulabois,@ Didier Ducloux,°# Jean-Yves Cahn@*

**Hématologie, CHRU Jean Minjoz, Besançon; °Néphrologie, CHRU St Jacques, Besançon; #Inserm, U645, Besançon; Univ Besançon, Besançon; EFS, BFC, Besançon, France; @Oncologie & Hématologie, CHRU Hôpital Nord Michallon, Grenoble, France*

Funding: this work was supported in part by grants from "La ligue départementale contre le cancer, comités du Doubs, de la Haute-Saône, du Jura et du territoire de Belfort".

Key words: kidney failure, allogeneic hematopoietic stem cell transplantation, transplant complications, radiation injuries, late effects.

Correspondence: Jean-Yves Cahn, Département d'Oncologie & d'Hématologie, Hôpital Nord Michallon, Centre Hospitalo-Universitaire, Grenoble Cedex 9, France. Phone: international +33.4-.76765590. Fax: international +33.4. 76765661. E-mail: jean-yves.cahn@ujf-grenoble.fr

References

1. Cohen EP. Renal failure after bone-marrow transplantation. Lancet 2001;357:6-7.
2. Deconinck E, Cahn JY. Renal toxicity after bone marrow transplantation. Int J Radiat Oncol Biol Phys 2004;58:661-2.
3. Vincent F, Costa M, Rondeau E. Chronic renal failure: a non-malignant late effect of allogeneic stem cell transplantation. Blood 2003;102:2695.
4. Socié G, Tichelli A, (EBMT). Renal and other rare late complications following allogeneic stem cell transplantation. Blood 2003;102:2695-6.
5. El-Seisi S, Gupta R, Clase CM, Forrest DL, Milandinovic M, Couban S. Renal pathology at autopsy in patients who died after hematopoietic stem cell transplantation. Biol Blood Marrow Transplant 2003;9:683-8.
6. Miralbell R, Sancho G, Bieri S, Carrio II, Helg C, Brunet S, et al. Renal insufficiency in patients with hematologic malignancies undergoing total body irradiation and bone marrow transplantation: a prospective assessment. Int J Radiat Oncol Biol Phys 2004;58:809-16.
7. Leblond V, Sutton L, Jacquiaud C, Item C, Sadoun R, Jaudon MC, et al. Evaluation of renal function in 60 long-term survivors of bone marrow transplantation. J Am Soc Nephrol 1995;6:1661-5.
8. Parikh CR, McSweeney PA, Korular D, Ecder T, Merouani A, Taylor J, et al. Renal dysfunction in allogeneic hematopoietic cell transplantation. Kidney Int 2002;62:566-73.
9. Cahn JY, Flesch M, Brion A, Deconinck E, Leconte Des Floris MF, Voillat L, et al. Prevention of veno-occlusive disease of the liver after bone marrow transplantation: heparin or no heparin? Blood 1992;80:2149-50.
10. Gerstenkorn C, Robertson H, Bell A, Shenton B, Talbot D. CMV infection as a contributory factor for renal allograft injury and loss. Transplant Proc 2001;33:2461-2.

Stem Cell Transplantation

A psychosocial assessment interview of candidates for hematopoietic stem cell transplantation

There is evidence that psychosocial issues are associated with poorer compliance and higher mortality in the post-transplant period. Thus, psychosocial assessment of candidates for transplantation is an important way of detecting early those patients who are susceptible to developing psychiatric symptoms and psychosocial difficulties during treatment. We developed a psychosocial structured interview to assess candidates for hematopoietic stem cell transplantation. The interview is a short and comprehensible instrument, requiring an average of 50 minutes to be completed.

haematologica 2005; 90:570-572
(http://www.haematologica.org/journal/2005/4/570.html)

Hematopoietic stem cell transplantation (HSCT) is a