1083-8791/06/1204-0005$32.00/0
doi:10.1016/j.bbmt.2005.11.518

ASBMT American Society for Blood and Marrow Transplantation

Long-Term Survival after Blood and Marrow Transplantation: Comparison with an Age- and Gender-Matched Normative Population

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Received July 15, 2005; accepted November 30, 2005

ABSTRACT

A plateau in long-term survival patterns of patients undergoing blood and marrow transplantation (BMT) from allogeneic donors is apparent, but whether their expected survival ever parallels that of the normative population is unclear. This study attempts to identify a cutoff time for classifying BMT patients as long-term survivors and compares their actual survival with the expected survival of an age- and gender-matched "normal" population. In this study, the records of 1386 patients who underwent allogeneic BMT at Princess Margaret Hospital between 1970 and 2002 were reviewed. Hazard rates (HRs), Kaplan-Meier survival estimates, and loess curves were used to propose a cutoff time classifying patients as long-term survivors. Factors predictive of overall survival and survival for long-term survivors were investigated. Actual survival for these patients was compared with the expected survival of the Canadian "normal" population. A cutoff time of 6 years post-BMT was proposed to define long-term survivors based on loess curves of hazard ratios and yearly survival statistics. The only statistically significant predictor of survival among long-term survivors was having a male donor (HR = 0.39; 95% confidence interval [CI] = 0.17–0.88). Although only 62% of patients survived the first year post-BMT, 98.5% of patients alive after 6 years survived at least another year. Almost 1/3 (31%) of the deaths in long-term survivors resulted from causes unrelated to transplantation or relapse. The observed number of deaths among BMT patients exceeded the expected number from the Canadian population; however, the difference in life expectancy decreased the longer that a patient survived. The 95% CIs for the observed/expected number of deaths cover 1, indicative of no difference, after the tenth year post-BMT. A cutoff of 6 years is proposed to define long-term survivorship after BMT. Life expectancy remained reduced compared with that of the "normal" population; however, this difference decreased the longer that a patient survived. Known risk factors of short-term survival disappeared, with only donor gender predictive of survival among long-term survivors.

KEY WORDS

Allogeneic blood and marrow transplantation • Long-term survival • Normative comparison

INTRODUCTION

Blood and marrow transplantation (BMT) from allogeneic donors has become an established therapeutic option for patients with a variety of otherwise fatal blood disorders. Despite recent improvements in technique, however, the procedure remains associated with considerable transplantation-related risks, as well as failure to control the underlying disease. The contributions to outcome by such risk factors as disease status at BMT, donor match, and graft-versus-host disease (GvHD) to early mortality are well recognized [1-3]; however, whether the influence of these factors remains constant over time or is time-restricted remains unclear. Survival analyses usually focus on risks that determine the probability of early events before stabilization of survival curves. The long-term survival patterns of patients on an apparent plateau are not well established, and whether the mortality rates of long-term survivors ever return to that of the normative population is unclear.

Some of these questions have been addressed by studies on long-term survivors reported to the International Bone Marrow Transplant Registry (IBMTR) and European Bone Marrow Transplant Registry (EBMT). Socie et al. [4] investigated the long-term survival and late deaths after allogeneic BMT of all patients reported to the IBMTR who survived at least 2 years after transplantation. The mortality in these patients was higher than that in the normal population; causes of death were commonly related to relapse or GvHD. A rationale was not provided for the choice of a 2-year cutoff to define long-term survivors, and no indication was given as to whether or not the mortality rate continued to improve over time. Duell et al. [5] reported on the health and functional status of long-term survivors in European BMT patients, choosing 5 years as the cutoff definition for a long-term survivor. Again, no justification was given for this choice of 5 years. Most of the patients were in good health and had returned to full-time work or school. The leading causes of death among these long-term survivors were disease recurrence, chronic GvHD, lung disease, secondary malignancies, and infections secondary to a persisting immune deficiency.

Using a database on 1387 consecutive patients who underwent transplantation at a single center, we explored whether or not the mortality rate of BMT recipients ever returned to equal that of the normal population. To classify patients as long-term survivors, we estimated the time point at which the risk of dying after the transplantation had stabilized. Known predictors of short-term mortality and their effect on survival of long-term survivors were examined. The mortality rate of long-term survivors was then compared with that of the normal age- and gender-adjusted Canadian population.

PATIENTS AND METHODS

Patients

The records of all 1387 patients who received an allogeneic BMT at our institution between 1970 and 2002 were reviewed. One patient refused permission to use his medical record for research purposes; this study includes the records of the remaining 1386 patients.

Statistical Methods

Descriptive statistics, including mean, standard deviation, frequency, and proportions, were used to assess such characteristics as patient age, disease status at time of BMT, donor status, and diagnosis. The database was updated with respect to survival data for all registered patients as of December 31, 2002. All patients known to be alive were censored for survival on that date, and survival estimates were calculated using the Kaplan-Meier method [6]. Hazard rates (HRs) estimating the risk of a patient dying were calculated for time intervals of consistent length post-BMT, and loess smoothers [7] were applied to hazard plots. A loess curve takes a small window of data and plots the average HR in that window; in this study, a window of 45 days was applied. The window is then shifted to encompass the next 45 days, and the average is recalculated and plotted. This is repeated, and the points are connected, forming a curve representing the average HR across time, clearly showing changes in the HR over time.

Multiple plots were constructed using time intervals of different lengths and different loess smoothing parameters. Based on visual inspection of these plots and examination of local extrema in yearly HRs and conditional survival statistics, a cutoff time was proposed such that patients who survived past the cutoff were classified as long-term survivors. Univariate Cox proportional hazards models [8] were used to evaluate whether or not risk factors determined at the time of transplantation that were predictive of survival in the early post-BMT period also contributed to survival of patients defined as long-term survivors.

The survival rate of long-term BMT survivors was compared with that of the Canadian "normal" population. For each year in the period 1970-2002, the total number of patient-years of follow-up of survivors was calculated, grouped by gender and age using PAMCOMP 1.41 [9]. Five-year age intervals (eg, 10–14 years, 15–19 years) were used for the age groupings. The age- and gender-adjusted mortality rate for each year for all Canadians was obtained from Statistics Canada annual reports (catalogue no. 84-209 for the 1991-2002 data and catalogue no. 82-548 for the 1970-1990 data). The number of patient-years was multiplied by the mortality rate for each respective category, yielding the expected number of deaths. The expected number of deaths for each category was summed to obtain an overall expected number of deaths. The observed number of deaths in this patient sample on or before December 31, 2002 was divided by the expected number of deaths to obtain the observed/expected ratio, and exact 95% confidence intervals (CIs) were calculated in PAMCOMP 1.41. All tests were 2-sided, and any P value $\leq .05$ was considered statistically significant. Approval for this retrospective data analysis was obtained from the Princess Margaret Hospital Research Ethics Board.

RESULTS

Descriptive statistics of all patients are summarized in Table 1. The mean patient age at BMT was 38.4 years, and 57% of the study group was male. The majority of patients were diagnosed with either

Table 1. *Descriptive Statistics of BMT Patients*

Variable	All Patients (n = 1386)	Patients Who Survived >6 Years (n = 368)
Mean (SD) age	38.4 (11.8)	34.4 (10.0)
n (%) male	783 (56.5)	206 (56.0)
n (%) with male donor*	747 (54.0)	209 (56.8)
n (%) with a gender matched donor*	768 (55.5)	213 (57.9)
n (%) Diagnosis		
ALL	181 (13.1)	37 (10.1)
AML	397 (28.6)	105 (28.5)
CLL	31 (2.2)	2 (0.5)
CML	428 (30.9)	137 (37.2)
Other	349 (25.2)	87 (23.6)
Donor type		
HLA-identical sibling	1035 (74.7)	313 (85.1)
Syngeneic	24 (1.7)	10 (2.7)
Other related HLA†-matched	23 (1.7)	5 (1.4)
Related 1 Ag mismatched	90 (2.6)	15 (2.2)
Related >= 2 Ag mismatched	4 (0.1)	0 (0)
Unrelated donor HLA-matched	193 (13.9)	25 (6.8)
Unrelated donor HLA-mismatched	17 (1.2)	0 (0)
Status at BMT		
First remission (AML, ALL)	335 (24.2)	100 (27.2)
Other than first remission (AML, ALL)	230 (16.6)	41 (11.1)
First chronic phase (CML)	280 (20.2)	104 (28.3)
Other than first chronic phase (CML)	150 (10.8)	33 (9.0)
Other	13 (0.9)	3 (0.8)
Unknown	378 (27.3)	87 (23.6)
Preparative regimen‡		
CA + CY + TBI	453 (32.7)	180 (48.9)
CY + fTBI	386 (27.8)	49 (13.3)
BU + CY	336 (24.2)	80 (21.7)
Other	211 (15.2)	59 (16.0)
n (%) alive at last follow-up	670 (48.3)	342 (92.9)

*Information on donor gender was unavailable on 2 BMT patients, neither of whom survived >6 years.

†HLA match is defined on the basis of A, B, and DR.

‡CA, cytosine arabinoside 100 mg/m^2/day × 5 days; CY, cyclophosphamide 60 mg/kg/day × 2 days; TBI, total body irradiation 500 cGY/single fraction; fTBI, fractionated total body irradiation at 200 cGy × 6 doses over 3 days; BU, busulfan 4 mg/kg/day × 4 days; AML, acute myelocytic leukemia; ALL, acute lymphocytic leukemia; CML, chronic myelocytic leukemia; CLL, chronic lymphocytic leukemia.

chronic myelocytic leukemia (31%) or acute myelocytic leukemia (29%). Some 54% of the patients had a male donor, 56% were the same gender as their donor, and 75% of the donors were HLA-identical siblings. Based on the institutional policy for patients undergoing transplantation for different diseases and disease states, the majority of patients underwent transplantation using the following preparative regimens: (1) cytosine arabinoside 100 mg/m^2/day × 5 days, cyclophosphamide (CTX) 60 mg/kg/day × 2 days, and total body irradiation (TBI) 500 cGy as a single fraction (n = 453 [32.7%]); (2) CTX 60 mg/kg/day × 2 days (3 days in some cases) and fractionated TBI at 200 cGy × 6 doses over 3 days (n = 386 [27.8%]); and (3) busulfan 4 mg/kg/day × 4 days and CTX 60 mg/kg/day × 2 days (n = 336 [24.2%]). The remaining 211 patients (15.2%) were prepared with various other regimens (not shown). Patients undergoing transplantation after September 10, 1986 received GvHD prophylaxis with cyclosporin and could be treated with ganciclovir for cytomegalovirus (CMV)-related complications. Some 48% of the patients were alive as of December 31, 2002; a total of 368 (27%) patients were known to be alive beyond 6 years after BMT.

Figure 1 depicts a Kaplan-Meier survival plot with 95% CIs for all of the transplantation patients. Numerous patients died shortly after BMT, as indicated by the steep initial slope of the survival curve. With increasing time after transplantation, the survival curve flattened and the probability of patient survival increased, as shown in Table 2, for conditional survival for each year. Some 62% of BMT patients survived at least 365 days, and of those surviving 365 days, 89% survived at least another 365 days. Of the patients who survived 6 years post-BMT, 98.5% survived at least another year.

The HR is defined as the probability that a patient will die shortly after a defined time point given that he or she has survived up to that time. Table 2 gives the HRs of death for the mid point of each year post-BMT. For instance, the probability of a patient dying on day 182 post-BMT given that he or she survived the first 181 days is 0.001293, and the probability of a patient dying on day 548 post-BMT (midpoint of year 1–2) given that he or she survived the first 547 days is 0.000307. Note that the 95% CI for the HR reaches near 0 for the first time in year 6-7 post-BMT.

HRs were estimated for various sequential time intervals, and a loess smoother was used to calculate a weighted average for each time point. This method gives estimated HRs over time. Figure 2 provides a representative graph in which HRs are estimated for 45-day follow-up intervals. Plots using different intervals had similar shapes (data not shown). In Figure 2, the HR was estimated for the 23rd day of each interval, and a loess smoother was applied using the loess functions with a smoothing parameter span of 0.1. As can be seen, the HR dropped to near 0 around 6 years post-BMT and leveled off at around 10 years. The HR 6 years post-BMT was similar for patients undergoing transplantation before (0.0001) and after (0.00006) the availability of cyclosporin and ganciclovir. Thus, 6 years was chosen as the time cutoff point defining long-term survivors.

The effect of selected risk parameters determined at BMT on survival for all patients and for long-term survivors is described in Table 3. Diagnosis, status at BMT, a gender-matched donor, and an HLA-matched donor were all statistically signifi-

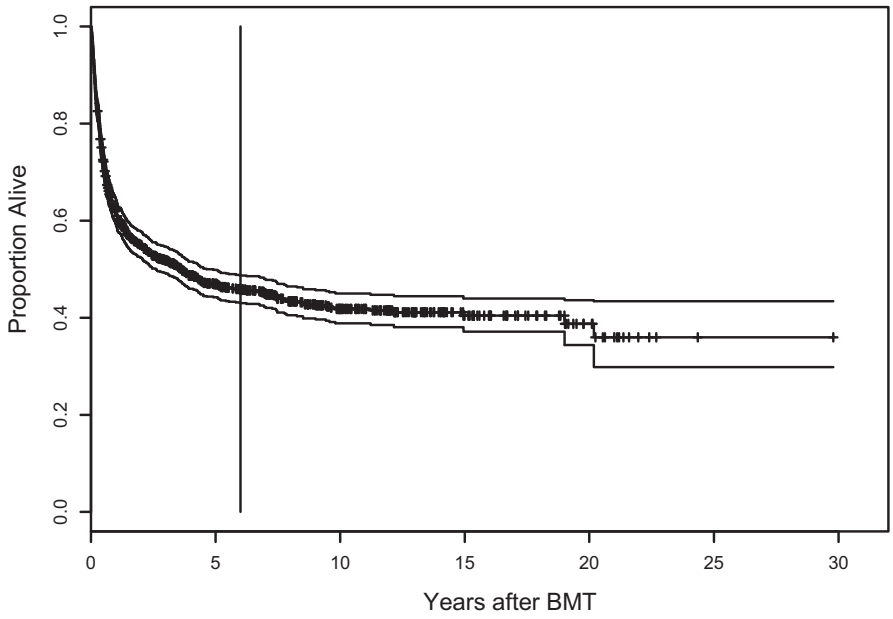

Figure 1. Overall survival with 95% CIs of all 1386 patients undergoing transplantation between 1970 and 2002.

cant predictors of overall survival. Only donor gender was a statistically significant predictor of long-term survival beyond 6 years. Having a male donor decreased the HR rate by an estimated 0.39 times (95% CI = 0.17–0.88) for these patients. Sixteen of the 143 long-term BMT survivors who had a female donor are known to have died, compared with 9 of the 198 long-term BMT survivors who had a male donor. All 41 patients with AML or acute lymphocytic leukemia experiencing more than 1 remission, as well as both chronic lymphocytic leukemia patients, who survived 6 years were alive at last follow-up; thus, no proportional hazards estimate could be made for these variables. The choice of the preparative regimen had no impact on the survival of patients living beyond 6 years (P = .27; Figure 3).

To compare the mortality rate of long-term survivors with that of the Canadian normal population, the number of patient-years of follow-up at least 6 years post-BMT was calculated. There were 26 long-term survivors who died in 2092.49 patient-years. The expected number of deaths in the same follow-up period is 4.6855, resulting in an estimated observed/expected ratio of 5.55 (95% CI = 3.62–8.13). Table 4 gives the observed/expected ratios by year post-BMT, and Figure 4 displays this information visually. This plot shows the mortality rate and respective 95% CI for BMT patients by year after

Table 2. *Survival Statistics by Year of Follow-Up*

Days	Years	Patients Alive at Year Start	Number of Deaths (716)	Number Censored (670)	Estimated HR at the Middle Time ($\times 10^{-4}$) (95% CI)	Overall Survival (95% CI)	One-Year Conditional Survival (95% CI)
0-365	0-1	1386	517	75	12.93 (11.85, 14.02)	61.8 (59.2, 64.4)	61.8 (59.2, 64.4)
366-730	1-2	794	82	43	3.07 (2.41, 3.73)	55.3 (52.6, 58.0)	89.4 (87.3, 91.6)
731-1095	2-3	669	36	46	1.57 (1.06, 2.08)	52.2 (49.5, 54.9)	94.4 (92.7, 96.2)
1096-1460	3-4	587	31	72	1.59 (1.03, 2.14)	49.2 (46.5, 52.0)	94.3 (92.4, 96.3)
1461-1825	4-5	484	15	52	0.91 (0.45, 1.37)	47.7 (44.9, 50.4)	96.8 (95.2, 98.4)
1826-2190	5-6	417	9	40	0.63 (0.22, 1.04)	46.6 (43.8, 49.4)	97.7 (96.3, 99.2)
2191-2555	6-7	368	5	45	0.40 (0.05, 0.75)	45.9 (43.1, 48.7)	98.5 (97.2, 99.8)
2556-2920	7-8	318	9	32	0.83 (0.29, 1.37)	44.5 (41.6, 47.4)	97.0 (95.1, 98.9)
2921-3285	8-9	277	3	34	0.32 (0.00, 0.68)	44.0 (41.1, 46.9)	98.9 (97.6, 100.0)
3286-3650	9-10	240	4	31	0.49 (0.01, 0.98)	43.2 (40.3, 46.2)	98.2 (96.5, 100.0)
3651-4015	10-11	205	0	34	0.00 (—, —)	43.2 (40.3, 46.2)	100.0 (—, —)
4016-4380	11-12	171	1	27	0.17 (0.00, 0.52)	43.0 (40.0, 45.9)	99.4 (98.2, 100.0)
4381-4745	12-13	143	1	24	0.21 (0.00, 0.62)	42.7 (39.6, 45.7)	99.3 (97.9, 100.0)
4746-5110	13-14	118	0	19	0.00 (—, —)	42.7 (39.6, 45.7)	100.0 (—, —)
5111-5475	14-15	99	1	21	0.31 (0.00, 0.92)	42.1 (39.0, 45.3)	98.7 (96.3, 100.0)
5476-	15-	77	2	75	—	—	—

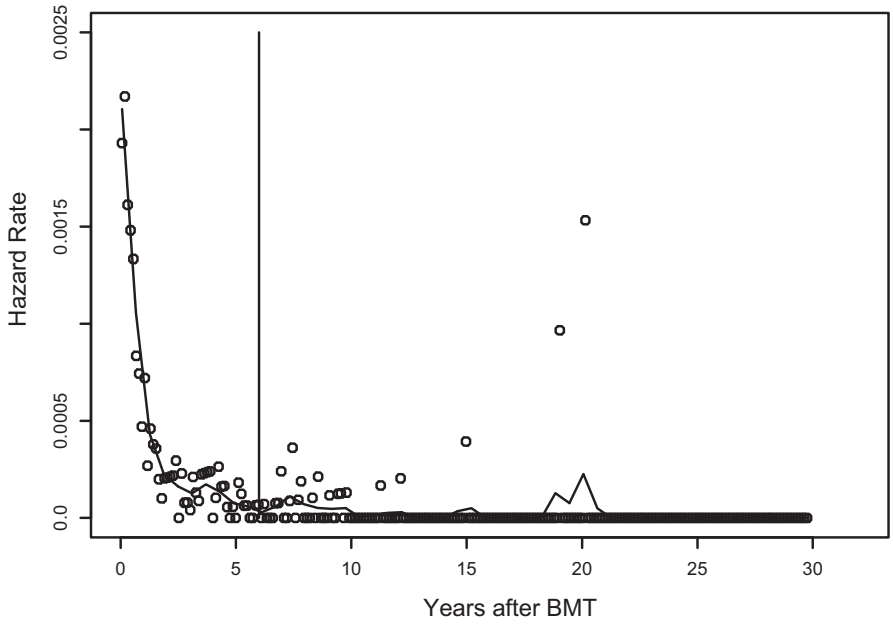

Figure 2. Loess curve of HRs divided by consecutive 45-day intervals after transplantation.

transplantation compared with the Canadian age- and gender-adjusted normal population, indicated by the horizontal line. The horizontal line represents an observed/expected ratio of 1 consistent with the point at which there is no increased mortality risk. The ratio exceeds 1 for each year post-BMT, indicating that the observed number of deaths in this population is significantly greater than expected for the normal population. The 95% CIs calculated for the observed/expected mortality for each year after the 10th year post-BMT included the ratio of 1, suggesting that the observed mortality rate is not significantly different from that expected. The confidence interval is wide for these estimates based on <2 deaths per year.

Table 3. *Univariate Predictors of Long-Term Conditional Survival*

Variable	Hazard Ratio (95% CI)	
	All Patients	Patients Surviving 6 + Years
Age (/10 years)	1.05 (0.98, 1.12)	1.02 (0.67, 1.55)
Male	0.91 (0.79, 1.06)	0.97 (0.45, 2.10)
Male donor	1.00 (0.86, 1.16)	0.39 (0.17, 0.88)
Donor gender match	0.85 (0.73, 0.98)	1.04 (0.48, 2.27)
Diagnosis		
ALL	1.33 (1.08, 1.63)	0.28 (0.04, 2.06)
AML	1.17 (1.00, 1.37)	0.88 (0.37, 2.11)
CLL	1.12 (0.68, 1.84)	Insufficient Data
CML	0.72 (0.61, 0.85)	1.32 (0.60, 2.87)
Other	1.01 (0.85, 1.20)	1.34 (0.56, 3.19)
HLA-identical sibling	0.55 (0.47, 0.64)	1.71 (0.40, 7.27)
Status at BMT		
First remission (AML, ALL)	0.83 (0.70, 0.99)	1.07 (0.47, 2.46)
Other than first remission (AML, ALL)	1.85 (1.56, 2.21)	Insufficient Data
First chronic phase (CML)	0.46 (0.37, 0.57)	0.79 (0.32, 1.97)
Other than first chronic phase (CML)	1.63 (1.32, 2.01)	2.65 (1.00, 7.04)
Other	1.05 (0.89, 1.24)	1.27 (0.53, 3.03)

ALL, acute lymphocytic leukemia; AML, acute myelocytic leukemia; CLL, chronic lymphocytic leukemia; CML, chronic myelocytic leukemia.

Figure 5 shows the survival curves for patients undergoing transplantation in different time periods. A statistically significant ($P < .001$) difference in survival can be seen between patients treated before September 10, 1986 and those treated after that date. The long-term survival of those patients undergoing transplantation after September 10, 1986 shows a pattern similar to that of the entire cohort (data not shown); however, the data have not matured sufficiently to allow us to draw definite conclusions about this subset of patients. Only 298 patients (9 of whom later died) underwent transplantation after September 10, 1986 and had more than 6 years of follow-up, and no patient died with more than 10 years of follow-up. Before year 10, the observed number of deaths was greater than expected for this cohort.

Impact of Causes of Death

Causes of death were grouped broadly as transplantation-related (TRM), associated with recurrence of the underlying disease (relapse), or other causes. Early TRM contributed predominantly to the very early mortality after BMT, with 310 of 517 (60%) deaths in the first year attributed to TRM. Between the end of the first year and the beginning of the sixth year, death was most frequently attributed to relapse, occurring in 73 of 173 (42%) deaths. Of the 26 patients who died after the sixth year, 10 died due to late

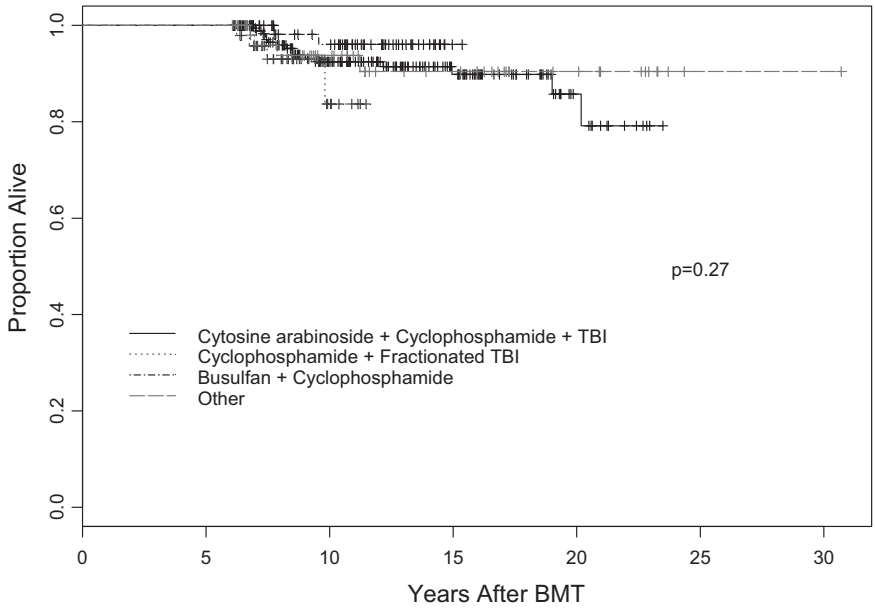

Figure 3. Overall survival of patients alive at 6 years after transplantation by preparative regimen.

BMT complications, including chronic GvHD(6 patients; 23%), respiratory failure (3 patients; 13%), and late graft failure (1 patient; 4%). Other causes of death in this group were relapse (8 patients; 31%), secondary malignancy (7 patients; 27%), and myocardial infarction (1 patient; 4%).

DISCUSSION

We have described a study evaluating the short-term and long-term outcomes of BMT allograft recipients who underwent transplantation in a single center. Follow-up of all but 1 of 1387 patients who underwent transplantation in 1970–2002 was available, thus precluding any influence of selection bias. There is a considerable risk of patients dying shortly after allogeneic BMT, as indicated by the procedure's 2-year survival rate of approximately 55%. The risk of death decreases as patients survive longer after transplantation.

The present study was undertaken to determine whether long-term survivors of BMT could ever expect a mortality rate comparable to that of the normal population. Six years was chosen as the cutoff time for classifying patients as long-term survivors. This was based on a detailed analysis that estimated HRs over time. The mortality rate remained relatively constant for patients once they survived 6 years after BMT, and approximately 30% of all deaths were attributable to causes other than relapse or treatment. Variables known to predict short-term survival did not predict survival after 6 years. Thus, patients who are at greater

Table 4. *Mortality Statistics by Year of Follow-Up*

Days After BMT	Year After BMT	Patients Alive at Year Start	Deaths Prior to 12/31/2002	Patient-Years of Follow-Up	Expected Number of Deaths	Observed/Expected Number of Deaths (95% CI)
0-365	0-1	1386	517	1012.57	2.2196	232.92 (213.28, 253.90)
365-730	1-2	794	82	719.79	1.5763	52.02 (41.37, 64.57)
730-1095	2-3	669	36	622.77	1.4016	25.68 (17.99, 35.56)
1095-1460	3-4	587	31	534.89	1.2109	25.60 (17.39, 36.34)
1460-1825	4-5	484	15	450.44	1.0107	14.84 (8.31, 24.48)
1825-2190	5-6	417	9	389.60	0.8747	10.29 (4.70, 19.53)
2190-2555	6-7	368	5	345.99	0.7645	6.54 (2.12, 15.26)
2555-2920	7-8	318	9	297.06	0.6397	14.07 (6.43, 26.71)
2920-3285	8-9	277	3	258.56	0.5734	5.23 (1.08, 15.29)
3285-3650	9-10	240	4	224.42	0.5168	7.74 (2.11, 19.82)
3650-4015	10-11	205	0	187.85	0.4267	—
4015-4380	11-12	171	1	157.59	0.3495	2.86 (0.07, 15.94)
4380-4745	12-13	143	1	130.51	0.2969	3.37 (0.09, 18.77)
4745-5110	13-14	118	0	107.88	0.2270	—
5110-5475	14-15	99	1	88.86	0.1937	5.16 (0.13, 28.76)
5475-	15-	77	2	293.77	0.6973	2.87 (0.34, 10.36)

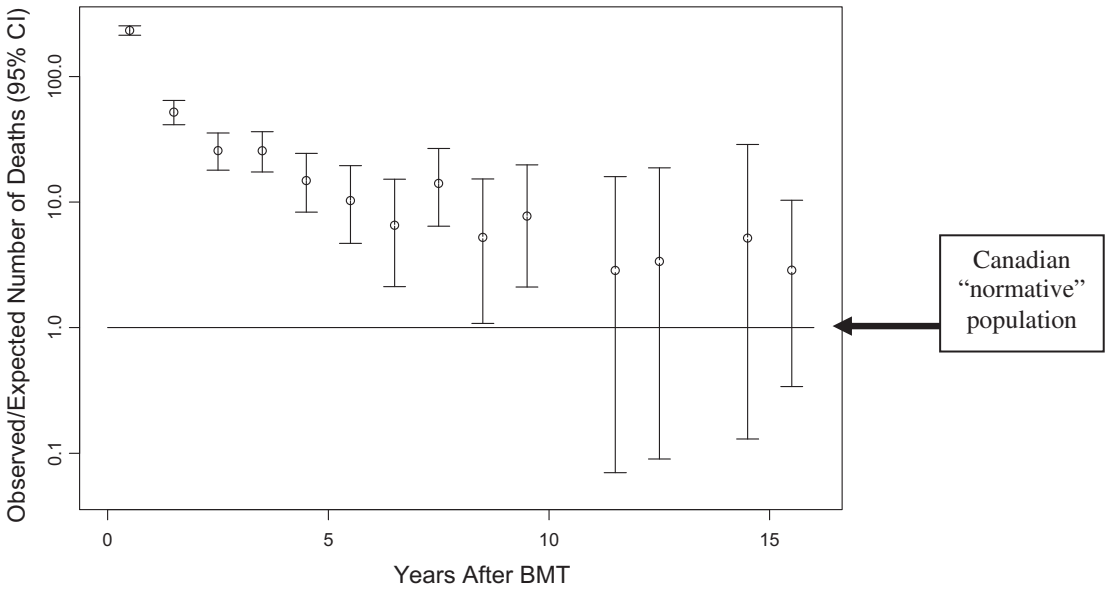

Figure 4. The ratio of observed versus expected numbers of deaths of allograft recipients per year after transplantation, along with their respective 95% CIs. The horizontal line represents the expected number of deaths of the age- and gender-adjusted Canadian "normal" population.

risk of dying immediately after BMT do not appear to be at any greater risk once they become long-term survivors. Donor gender was the only statistically significant predictor of long-term survival; this finding is consistent with the observation by Socie et al. [4] that male recipients of BMT from a female donor were at significantly ($P < .001$) higher risk of death more than 2 years after the transplantation.

Although the mortality rate of BMT patients stabilizes around 6 years after BMT, the rate remains higher than that of the Canadian normal population. There is considerable variability in the observed/expected rate, but the 95% CI includes a ratio of 1, indicating equality, for the first time in the 10th year post-BMT.

Management of patients with prophylactic cyclosporine and the therapeutic use of ganciclovir appear to be significant predictors of overall survival; patients who underwent transplantation before September 10, 1986 have a worse outcome than those who did so after this date. The observed number of deaths among long-term survivors undergoing transplantation after September 10, 1986 remains greater than expected; however, the numerical value for this subset of pa-

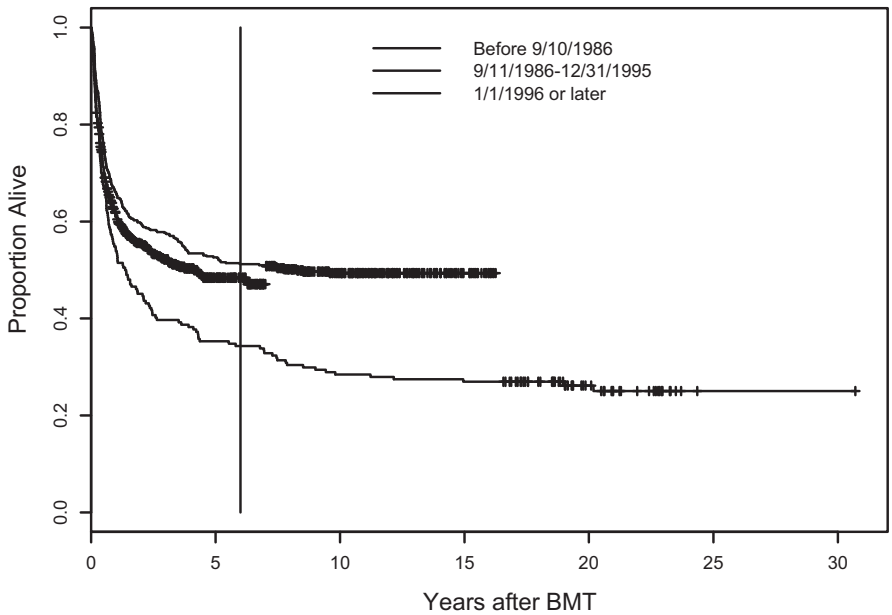

Figure 5. Overall survival of patients undergoing transplantation for 3 different time intervals.

tients is closer to 1 than for all patients. The number of patient-years of follow-up is insufficient for a detailed analysis on this subset of patients at this time.

All patients in this cohort underwent BMT at the same institution. Generalizations of the survival pattern to other institutions may not be appropriate. The comparison group for expected number of deaths was the entire Canadian population, despite the fact that most patients were residents of a single Canadian province (Ontario). This choice was made because there were residents of other provinces in the database as well and because age- and gender-specific mortality rates were publicly available only at a national level, not at a provincial level. Finally, all patients were censored at December 31, 2002 unless death was noted. This was due to the completeness of the database and the belief that all patient deaths would be recorded promptly. More than 1 year passed between censoring date and data extraction, however; thus, although it is possible that some patients died before the censoring date and were not recorded, it is believed to be highly unlikely.

Frequently, patients who undergo BMT question whether their life expectancy ever becomes equivalent to that of the normal population and whether the risk factors at the time of BMT remain risk factors after becoming a long-term survivor. This study is the first to attempt to quantify when a BMT patient can be classified as a long-term survivor and to attempt to answer these questions. Apparently, a BMT patient can be considered a long-term survivor after having lived 6 years post-BMT. The risk of death appears to level off at this time, and when death does occur, it is more likely attributable to causes not considered related to BMT. Although the life expectancy of BMT patients appears to remain lower than that of the normal population, the difference appears to decrease with increasing survival time. The currently available data suggest that this remains true even for patients who received GvHD prophylaxis with cyclosporine and had ganciclovir available, although stating a definite conclusion will require longer follow-up. The difference between transplantation patients and the normal population is apparently even smaller in the most recent BMT patient cohort. Known risk factors for short-term survival appear to disappear over time, with only donor gender appearing to predict survival among long-term survivors.

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