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Allogeneic hematopoietic stem cell transplantation in patients 50 years of age and older

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Background and Objectives. The population of elderly patients with hematologic malignancies is increasing and so will the activity of stem cell transplantation (SCT) in this population. The aim of this study was to analyze the toxicity and survival of allogeneic SCT in patients 50 years and older (elderly group), and compare the results with a standard adult population (young group).

Design and Methods. Thirty-two elderly patients (median age 52.5, range 50-59 years) and 97 young patients (median 32, range 20-40) received a myeloablative, allogeneic SCT from HLA-identical siblings at a single institution, and formed the basis of this retrospective study. The majority of transplants in both groups were performed with non-T-cell-depleted bone marrow, conditioned with busulfan + cyclophosphamide and received cyclosporine + methotrexate as graft-versus-host disease (GVHD) prophylaxis. The percentage of high-risk patients was nearly double in the elderly group (41% vs. 23%, $p = 0.06$).

Results. We observed a low incidence of toxicities in the elderly group, including veno-occlusive disease, acute and chronic GVHD, transplant-related mortality, time to engraftment, and relapse incidence, without significant differences compared within the young group. The 3-year survival rates were not statistically different between the elderly and young groups: 51% vs. 55% for all patients; 87% vs. 69% in chronic myeloid leukemia; 79% vs. 62% in standard risk patients and 13% vs. 31% in high risk ones. In multivariate analyses no significant difference in overall survival was found between age groups.

Interpretation and Conclusions. According to our experience, age alone (between 50-59), should not be considered a contraindication to a conventional HLA identical sibling transplant.
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Key words: allogeneic stem cell transplantation; age; elderly; HLA identical sibling; myeloablative conditioning regimen.

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The median age of the patients who receive a stem cell transplantation (SCT) is between 25 and 30 years.[1,2] Nonetheless the majority of patients with hematologic malignancies have a median age well over 50 at diagnosis.[3] Thus, for chronic myeloid leukemia (CML), acute myeloid leukemia (AML), myelodysplastic syndromes (MDS), lymphoma and myeloma there is a gap of nearly 30 years between the median age of diagnosis and the median age at transplantation.[3] For example, the contribution of SCT to the treatment of the whole population of patients with MDS is marginal and will remain so unless the upper age limit of transplantation is raised significantly. If we fix the upper limit for SCT at 40, 50, 60 or 70 years, only 3%, 8%, 16% and 38% of the patients could be transplanted respectively.[4] Consequently, if SCT is restricted to young adults only a minority of the patients will benefit from the procedure. On the other hand, the population of the developed world is getting older and their life expectancy is increasing. People 65 years of age and older, who now account for about 12% of the population, will form 21% of the population by the year 2030.[5] Presently, an otherwise healthy woman of 60 years has a life expectancy of over 83.[6] Therefore, the population of elderly patients with hematologic malignancies is increasing and so will the activity of SCT in this population. More information is needed concerning the outcome of the different types of SCT in elderly patients.

It has been reported that increasing age has a negative impact on allogeneic SCT outcome. Consequently many centers restrict conventional SCT to *young* adults. Improvements in the care and management of SCT patients over the last 20 years has allowed a continuous increase in the age of the patients. The upper age limit of allogeneic SCT has increased over time, and now patients between 40-50 years are generally accepted for HLA-identical sibling SCT. Patients younger than 40 are considered standard young-adults. Nonetheless there is a scarcity of information on the course of SCT for

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patients over 50 years. The aim of this study was to analyze the toxicity of and survival after allogeneic SCT, performed at a single institution, in patients 50 years and older, and compare the results with those in a standard young-adult population.

Design and Methods

Patients

Between January 1990 and March 2000 a total of 294 consecutive patients, conditioned with a myeloablative regimen, received an allogeneic SCT from HLA identical siblings at the Hospital de la Princesa. Two groups of patients were selected from the previous population and formed the basis of this retrospective study. Patients 50 years and older formed the elderly-group, and patients between 20-40 years constituted the young-group. Elderly patients were accepted for SCT if they were in general good condition without organ dysfunction. All patients 50 years and older who fulfilled all the previous conditions were included. In the young group only patients who fulfilled the previous criteria and had CML (in first chronic or accelerated phase), AML or MDS were included to make the comparative group more homogeneous. These 3 types of diseases represented more than 90% of the cases in the elderly-group. Patients were classified into a high-risk group if they had CML in accelerated phase or blastic crisis, leukemia or lymphoma with active disease at transplantation, MDS with ≥ 6% of blast cells in bone marrow, or if they had received a previous SCT. Otherwise they were classified as standard risk. All patients had a minimum follow-up of 1 year, except 2 patients in the young-group who were lost from follow-up at day +61 and +90.

Transplantation procedure

The same conditioning regimens, graft-versus-host disease (GVHD) and anti-infective prophylaxis policies were applied to both groups. Patients were cared for in private rooms with HEPA-filtered air, with no antibacterial or absorbable antifungal prophylaxis. Standard hand-washing techniques and masks were used. All patients received prophylaxis against *Pneumocystis carinii* with trimethoprim/sulfamethoxazole. No prophylactic ganciclovir or gammaglobulins were used. All CMV seropositive patients (or seronegative with a seropositive donor) received high dose prophylactic intravenous acyclovir (500 mg/m^2 three times daily) starting five days before transplantation until 28 days after SCT.

The majority of the patients were conditioned with oral busulfan (16 mg/kg over 4 days) plus i.v. cyclophosphamide (120 mg/kg over 2 days) or CY-TBI (cyclophosphamide 60 mg/kg/day × 2 days plus 1200 cGy of fractionated total body irradiation, with the lungs shielded at 900 cGy). Only 2 patients received a graft T-cell-depleted by CD34$^+$ positive selection. Bone marrow was the source of stem cells for all except 7 patients who received peripheral blood progenitor cells (PBPC) from donors treated with granulocyte colony-stimulating factor (G-CSF). The reasons for the use of PBPC instead of bone marrow were: 2 donors positive for hepatitis B surface antigen (HBsAg) and 1 donor hepatitis C virus positive (to avoid homologous transfusion in the bone marrow harvest); 1 old donor (73 years) with heart disease and a pacemaker; 1 significant weight discrepancy between patient and donor; 2 patients included in a protocol of CD34 positive selection. Most patients received cyclosporine plus a short course of methotrexate (15 mg/m^2 on day +1, and 10 mg/m^2 on days +3, +6, and +11 post-SCT) for GVHD prophylaxis. The day of leukocyte engraftment was defined as the first day on which the absolute neutrophil count was ≥ 0.5×10^9/L. Patients who died in aplasia before 21 days had elapsed from their transplant were considered unevaluable for engraftment. Patients were considered evaluable for acute GVHD if they survived at least 10 days after the transplant.

Patients were considered evaluable for chronic GVHD if they survived at least 100 days after the SCT or survived less than 100 days but had already developed chronic GVHD.

Statistical analysis

Comparisons between baseline characteristics of the patients and outcomes of the elderly-group vs. the young-group were performed using Student's t test, the χ^2 test or Fisher's exact test when indicated. Survival curves and actuarial rates were generated using the Kaplan-Meier method. Differences in actuarial probability of survival and relapse between subgroups were analyzed with the log-rank test. Patients who died before day +31 without relapse were considered unevaluable for the analysis of probability of relapse.

A proportional hazards Cox regression model was used to assess the independent effect of several variables on survival. These variables included age group (young vs. elderly), underlying disease (CML vs. AML plus MDS), risk group (low vs. high), source of stem cells (blood vs. bone marrow), patient CMV seropositivity (positive vs. negative), acute GVHD (grade II-IV vs. 0-I), chronic GVHD (none vs. limited/exten-

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sive), transplant year (1995-2000 vs. 1990-1994), and conditioning regimen (with TBI vs. non-TBI). A significance level of 0.05 was used for all the analyses. All *p* values are two sided and confidence intervals (CI) refer to 95% boundaries. Statistical analyses were performed using the SPSS program.

Results

Patients' characteristics

The principal characteristics of both groups are given in Table 1. Thirty-two patients were 50 and over (elderly-group), and 97 between 20-40 years (young-group). In the elderly group, 23 patients were 50-54 years old and 9 were 55 or older. There were no differences in distribution of sex, conditioning regimens or number of cells infused. There was, of course, a significant difference in the age of the patients, and also in the donors' age which was strongly correlated with the patients' age (Pearson's correlation=0.795, $p = 0.01$). Sixteen donors were 50 years and older (of these, 14 were donors for elderly patients). CML accounted for 50% of all cases in both groups. The distribution of the rest of the underlying diseases was significantly different in the two groups, with equal proportions of AML and MDS in the elderly group but more AML in the young-group. There were nearly double the number of high-risk patients in the elderly group. A higher proportion of elderly patients received PBPC instead of bone marrow (19% vs. 1%). Three patients did not receive GVHD prophylaxis, as they were transplanted from an identical twin. More elderly patients were CMV seropositive prior to SCT.

Engraftment, veno-occlusive disease and graft-versus-host disease

Leukocyte engraftment occurred in all except one case in each group (these patients died in aplasia on day +22 and +25 post-transplant) with no significant difference in the time to obtain more than 0.5×10^9/L PMN. Hepatic veno-occlusive disease (VOD) occurred more frequently in the young group, although the difference was not statistically significant. All the 4 fatal cases of VOD occurred in the young group. The rates of GVHD in the elderly-group were low and similar to those in the young-group, including acute GVHD grades II-IV and extensive chronic GVHD (Table 2).

Transplant-related mortality, relapse and survival

Overall there were 55 deaths (14 in the elderly-group and 41 in the young-group) (Table 3). Global mortality and cause of death [transplant-related

Table 1. Patients' characteristics.

	Elderly group	*Young group*	*p*
Nº of patients	32	97	
Age* Patients	52.5 (50-59)	30.3 (20-40)	<0.001
Donors	50 (38-73)	32 (8-58)	<0.001
Sex (Male/Female)	14/18	52/45	NS
Underlying disease			
CML/AML/MDS	16 (50%)/6/7 (CML: 13 CP, 2AP, 1 BC)	50 (51%)/41/6 (CML: 43 CP, 7AP)	0.007
NHL/MM/SAA#	1/1/1	0	
Risk groups (as defined in the text)			0.06
High	13 (41%)	22 (23%)	
Active leukemia or lymphoma	4	10	
CML-accelerated phase	2	7	
Second SCT@	2	1	
MDS ≥ 6% blast at SCT	5	4	
Low	19	75	
CMV seropositive			
Patients	29 (91%)	63 (65%)	0.02
Donors	26 (81%)	64 (66%)	NS
Conditioning			NS
CY-TBI/BUCY	4/25	18/78	
CY-TLI/other‡	1/2	0/1	
Source of stem cells			
Bone marrow/blood	26/6	96/1	0.001
Cell dose* ($\times10^8$/kg)#	3.6 (2.7-4.6)	3.6 (1.9-6.6)	NS
GVHD prophylaxis			0.034
CsA+MTX	24 (75%)	92 (90%)	
CsP±prednisone	6	7	
No prophylaxis	2	1	
Follow-up, years*	2.8 (1-8)	4.1 (1-10.4)	0.06

**Median (range); #NHL: non-Hodgkin's lymphoma; MM: multiple myeloma; SAA: severe aplastic anemia; ‡other conditionings: BUCY + etoposide; CBV (cyclophosphamide + BCNU + etoposide); cyclophosphamide + BCNU + Ara-C. CY-TLI for the SAA; #cell dose: only for bone marrow transplant @Second SCT: 1 MM and 1 CML in blast crisis in the elderly-group and 1 CML in accelerated phase in the young-group. NS: not significant.*

Table 2. Engraftment and GVHD.

	Elderly group	*Young group*	*p*
WBC engraftment	31/32	91/92	NS
Unevaluable (death <21 days)	0/32	5/97	
Days* to PMN ≥ 0.5×10^9/L	20 (10-29)	21 (11-55)	NS
VOD	3 (9%)	19 (20%)	NS
Fatal	0	4	
Acute GVHD II-IV	7/32 (22%)	24/95 (25%)	NS
Chronic GVHD	14/29 (48%)	37/82 (45%)	NS
Limited	7 (24%)	19 (23%)	
Extensive	7 (24%)	18 (22%)	

**Median (range); VOD: hepatic veno-occlusive disease. NS: not significant.*

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Table 3. Mortality, survival and relapse.

	Elderly group	*Young group*	*p*
Global mortality#	44% (14)	42% (41)	NS
TRM#	22% (7)	27% (26)	NS
Early TRM (<100 days)	9% (3)	14% (14)	NS
Leukemic related#	22% (7)	15% (15)	NS
Survival*			
Global	51.3% (31-71.6)	55.1% (44.3-65.8)	NS
CML	87% (69.7-100)	68.9% (55.2-82.4)	NS
Standard-risk	79% (60-97.2)	62% (50.3-73.3)	NS
High-risk	25.6% (0-52.7)	31% (9.3-52.9)	NS
MDS+AML	23% (0-46)	40% (25-55.4)	NS
Relapse*	36.7% (14-59.5)	30.6% (19.4-41.5)	NS

*Values in parentheses are numbers of events; *Kaplan-Meier estimations at 3 years (95% CI); NS: not significant.*

Table 4. Multivariate analysis of overall survival.

	RR (95% CI)	*p*	*Favorable*
Age group (young vs. elderly)	0.99 (0.36-2.72)	0.978	NS
Underlying disease (CML vs. AML + MDS)	0.23 (0.09-0.59)	0.002	CML
Risk groups (high vs. low)	2.46 (1.05-5.79)	0.038	Low
Patient CMV seropositivity (negative vs. positive)	1.30 (0.54-3.12)	0.551	NS
Conditioning (non-TBI vs. TBI)	0.89 (0.35-2.29)	0.816	NS
Source of stem cells (bone marrow vs. blood)	0.11 (0.03 –0.465)	0.002	Bone marrow
Acute GVHD (0-I vs. II-IV)	0.36 (0.15 –0.89)	0.027	Grade 0-I
Chronic GVHD			
Extensive vs. No	0.67 (0.41-1.69)	0.429	NS
Limited vs. No	0.34 (0.09-1.29)	0.114	NS
Year of transplant (1990-1994 vs. 1995-2000)	1.48 (0.61-3.59)	0.384	NS

NS: not significant.

mortality (TRM) vs. leukemic] were not different between the two groups. The early-TRM (death before day +100 post-transplant) was low in the elderly group (9%) with no difference compared to that in the young-group (14%). The 1-month post-transplant mortality was low and similar in both groups: 1 case in the elderly group (3%) and 7 patients in the young-group (7%). The mortality of the patients with acute GVHD was high and similar in both groups (62.5% vs. 65% for elderly and young patients, respectively). CMV disease incidence was not significantly different in the two groups. It occurred in 3 elderly patients (two died of CMV pneumonitis), and in 6 young patients. Four out of 6 patients of the elderly group and the patient in the young group transplanted with PBPC died (two from transplant-related causes and 3 due to relapse). In the elderly group, all the 4 cases conditioned with TBI died (3 due to leukemic relapse and 1 from TRM) compared with 10 out of 28 conditioned without TBI. All elderly patients who received TBI belonged to the high-risk group. The Kaplan-Meier survival estimation at 3 years for patients who received TBI or non-TBI conditioning regimens, were: 0% vs 64% ($p = 0.034$) in the elderly group and 49% vs 58% ($p = 0.52$) in the young groups.

No significant differences in the 3-year overall survival and relapse rates were observed in elderly patients compared within young patients, as shown in Table 3 and Figures 1 and 2. The overall survival was around 50% in both groups and the relapse rate around 30%. The survival for CML (Figure 2) and standard risk patients was particularly good in the elderly-group. For CML in chronic phase, only 1 out 13 elderly patients died, giving a survival at 3 years of 92%. The overall survival for patients 55 years and older compared to that of patients 50-54 years was not significantly different either (55% vs. 63%) although the numbers were quite small.

Multivariate analyses (Table 4) showed significantly better survival in patients with CML, low risk diseases, no acute GVHD and those transplanted with bone marrow as the source of stem cells. Few patients, only 7, were transplanted with PBPC. No significant difference in overall survival was found between age groups. A multivariate analysis performed adding 41 patients aged 41-49 years (intermediate age group), who fulfilled the same inclusion criteria used for the young-group, showed similar results (*data no shown*) when compared with the analysis of the two original groups (elderly and young).

Discussion

In this study 32 patients (Table 4) aged 50 years and older (elderly-group) were compared with a group of 92 young adults (aged 20-40), all conditioned with a myeloablative regimen and transplanted from HLA identical siblings at a single institution. As far as we know, this is the largest single-center series of allogeneic SCT in patients 50 years and over published by a European team. No significant differences were found in the main transplant outcomes including engraftment, GVHD, transplant-related mortality, relapse rate, and overall survival.

Increasing age in adult allogeneic transplant recipients has been associated with a higher morbidity and TRM than those in younger patients (mainly due to an increase in GVHD and interstitial

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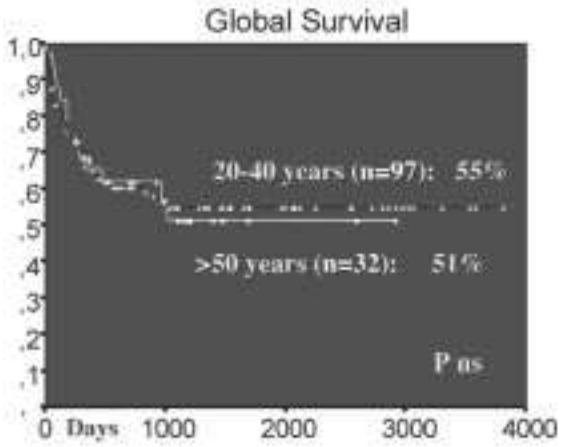

Figure 1. Kaplan-Meier estimate of overall survival of elderly and young groups. Differences between groups were not significant.

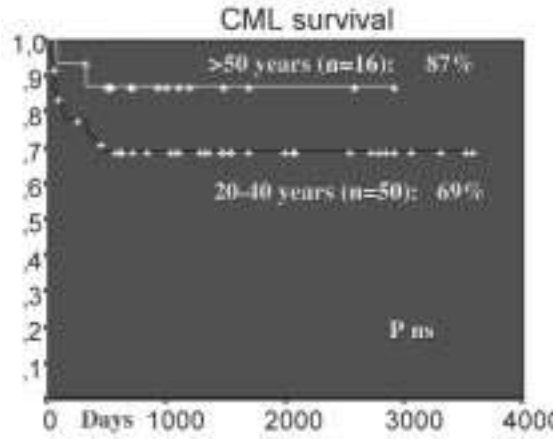

Figure 2. Kaplan-Meier estimate of overall survival for chronic myeloid leukemia (CML) patients by age group. Differences between groups were not significant.

pneumonitis), resulting in a lower survival in some[7,8] but not in all old studies.[9,10] Given this higher TRM, new SCT modalities have been proposed in old patients, such as reduced-intensity conditioning transplants (*minitransplants*). Interestingly, increasing age has not been related to an increase in the relapse rate in any of the studies that compare older vs. younger adult recipients of allogeneic SCT[10-16] or autologous SCT.[17-22] Nonetheless, most of the studies that analyze the impact of age have compared children with adults. If we study age in this way it does have an adverse impact in SCT. The question we tried to study is different: whether patients in their fifties had a worse course than young adults, that is patients aged 20-40.

The reasons for studying this particular population (≥ 50 years) were two. Firstly, there is a large elderly population (≥ 50 years) with hematologic malignancies; this population is going to increase significantly in the future, so the treatment of the elderly with SCT will be more frequent in day-to-day practice. Secondly, there is a scarcity of information on the course of SCT in patients over 50 years old. In studies published before 1990 there were no more than 20 patients older than 50 years.[7-11,23] In the last 10 years, several studies, involving more than 230 patients aged 50 years and older, analyzed the impact of age in adult allogeneic related SCT[12-16] or explored the utility of SCT in elderly patients.[24,25]

Successful conventional allogeneic SCT has been performed in patients up to 66 years old.[24] There are other studies that have analyzed the impact of age in unrelated or mismatched related SCT which are not commented on here, as our series includes only related donors.

Several recent studies found similar outcomes in elderly patients compared within young adults, as seen in our study. The largest multicenter series, reported by the IBMTR,[12] included 80 patients 50 years and older (Table 5). The incidence of leukemia-free survival, GVHD and relapse were comparable among the four age cohorts studied (30-39, 40-44, 45-49, and 50-62 years). Only patients with advanced leukemia aged 45 years and older had a slightly higher risk of TRM and poor survival. These results indicate that patients with leukemia who are 40 and older have transplant outcomes similar to those patients aged 30 through 39 years. Du *et al.*[16] reported the largest single center series of conventional allogeneic SCT in patients older than 50 years (Table 5). They compared 59 patients >50 years with 377 younger adults (18-50 years). TRM, relapse and overall survival at 2 years were not significantly different between elderly and young patients. Only the 1-month post-transplant mortality was significantly higher in the >50-year old group when compared with the 18-39-year old subgroup (15% vs. 5%). We did not observe a higher 1-month post-transplant mortality as was observed in the study by Du *et al.*[16] In a EBMT study focusing on CML, which include related and unrelated transplants, compared with pediatric patients (< 20 years), adult patients (≥ 20 years) had a higher TRM, lower survival and a similar relapse rate, but no significant differences were seen when comparing older adults (≥ 40 years) with younger adults (aged 20-40).[15]

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Table 5. Allogeneic SCT in elderly patients from related donors. Recent studies.

Type study	*Ringden Multicentric (IBMTR)*	*Cahn Multicentric (EBMT)*	*Du Unicentric*	*Rapoport* Unicentric*	*Present series Unicentric*
Diseases included	CML,AML,ALL	CR1:AML, ALL	Several	CML,AML,ALL	Several
Age groups, no. of patients					
>50 years	80	??	59	9	32
40-50 years	818	41-56 years: 192	124	21	0
Younger (age)	1,282 (30-39)	1,119 (16-40)	253 (18-39)	62 (1-39)º	97 (20-40)
Engraftment[&]	NE	NE	No dif.	NE	No dif.
Acute GVHD[&]	No dif.	NE	No dif.	No dif.	No dif.
Chronic GVHD [&]	No dif.	NE	No dif.	No dif.	No dif.
TRM [&]	Higher ADvL	Higher in AML	No dif.[#]	No dif.	No dif.
Relapse[&]	No dif.	No dif.	No dif.	No dif.	No dif.
Survival[&]	Poor in ADvL	No dif.	No dif.	No dif.	No dif.

*CML: chronic myeloid leukemia; ALL: acute lymphoblastic leukemia; AML: acute myeloblastic leukemia; AdvL: advanced leukemia; [#]global TRM was no different; only the 1-month post-transplant mortality was significantly higher in the >50 years group when compared with the <40 years group; *some transplants were done from unrelated donors or related mismatched donors; [&]compares elderly patients vs young adults. NE: no specified. No dif: no difference. ºIn the Rapoport study the young control population included some children (ages 1-39 years); Cahn et al. (1997): The TRM was significantly higher only in older patients (>45 years) with AML (41% vs 29% at 5 years); Ringden et al. (1993): Leukemia-free survival at 2 years in early and intermediate leukemia was not significantly different among age groups. In advanced leukemia, patients ≥ 45 years did particularly poorly, although the probability of survival was not calculated.*

The number and outcome of patients 50 years and older was not commented on. The Seattle group published the study of conventional allogeneic SCT at the highest median age.[24] They studied 50 patients with myelodysplastic syndromes (MDS) who were 55 to 66 years of age (median 58.8). The Kaplan-Meier survival at 3 years was 45%, and non-relapse mortality at 2 years was 39%. The non-relapse morbidity and mortality were similar to those observed by the same team in younger patients with MDS. Very good results have been reported in elderly CML patients, like those from the Seattle team.[25] They reported 33 patients 50 years of age and older with a survival at 3 years of more than 80%, similar to our findings.

No difference between time to engraftment or VOD incidence in elderly patients and young adults undergoing allogeneic SCT was seen in our study or in others. Only in one study, on autologous BMT, did more patients aged 50 years and older die of VOD than younger patients.[18]

We found similar incidences of acute and chronic GVHD in elderly patients and young patients. The relation between age and risk of acute GVHD is complex and controversial,[26] and generally age has not been associated with an increased risk of acute GVHD.[12,13,16,27-29] In any case, the age gradient is modest and the relationship is biased.[26] The increase in the incidence occurs early (around 20 years) after which the incidence of GVHD remains fairly stable. Advanced age has been associated with an increased risk of dying of acute GVHD in some studies[26,30] but not in our study or other studies.[13,28]

In our study older patients tended to have older donors. There was a strong correlation between donors' and patients' age (r=0.795) as has been reported previously in related SCT,[31] but not in unrelated SCT.[1] We had 16 donors aged 50 years and older (of these, 14 were donors to elderly patients). Bone marrow harvest has been reported to be safe in donors of advanced age.[32,33] Most allogeneic SCT in patients older than 50 years have been done using bone marrow as the source of stem cells. As the rate and time to engraftment is not different in older adults compared to in young adults, and given the higher risk of GVHD associated with PBPC,[34] PBPC is not *a priori* a better stem cell source than bone marrow for these patients.

CMV seropositivity increases with age as seen in our study and in others.[1,35,36] This carries a higher risk of CMV reactivation,[28] so CMV should be closely monitored in elderly patients. Moreover CMV seropositivity was found to be an independent risk factor for an increase in GVHD incidence and TRM in other studies.[36,37] This must also be taken into account when SCT results in elderly patients are analyzed. The negative impact of age on TRM could also be related to other factors such as CMV seropositivity.

Other studies have suggested that T-cell-depleted BMT may be necessary to obtain good survival rates for patients older than 40 years.[11] Our experience and that of others[13,16] suggest that this is not necessarily the case.

The majority (80%) of the elderly patients in our study were conditioned with busulfan plus

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cyclophosphamide. The most appropriate conditioning regimen for elderly patients is not known. The use of TBI in some recent studies in elderly patients has been low (0-13-20%)[13,16] and tends to be lower than in younger patients.[12] No obvious advantage was seen in our study or in others for the use of TBI. In fact in one study, patients 55 years and older treated with TBI-based regimens showed a significantly lower survival than that of younger patients.[17] In elderly patients, survival has been reported to be higher among patients conditioned with a regimen that incorporates administration of plasma-level-targeted busulfan.[24] It seems that exclusive chemotherapy regimens, mainly Bu-Cy, are well tolerated in older adults.

One of the criticisms that can be made of this and other studies that evaluated SCT results in elderly patients is the selection bias. It is possible that the older patients included in these studies were a selected group and therefore not representative of the whole elderly population of the same age. Although the authors of different publications[12,13] perceived no obvious bias it is probable that this bias does nevertheless occur in practice. Probably all adult patients who received a SCT are in some way a selected population. It is possible that older patients are selected more rigorously than younger patients are. Nonetheless, if an elderly patient (age 50-59) is in good general condition, the results of these studies show that the transplant outcome is no worse than that obtained in young adults, particularly if the patient has standard or intermediate risk disease.

In conclusion, in our study no significant differences were found in GVHD incidence, TRM, relapse rate, and survival between elderly patients (aged 50-59) and young adults (aged 20-40). Survival in the elderly is probably more related to the prognosis of the underlying disease than to the age. Age alone (between 50-59) should not be an absolute barrier to conventional allogeneic SCT from an identical sibling donor.

Contributions and Acknowledgments

RC and AA were the main investigators. They designed the study, collected part of the data, did the statistical analysis and interpreted the results. RC wrote the manuscript. JLL and RA critically revised the manuscript. EG, GRM and CSR collaborated in collecting the data. RC, JLS, RA, VGS and AF were responsible for the clinical care of the patients. JMFR contributed to the design of clinical protocols and as the Senior Author is cited last. The criteria for the order in which the names of the authors appear are based on the contributions to the design, development of the study, analysis and interpretation of the data.

Disclosures

Conflict of interest: none.

Redundant publications: no substantial overlapping with previous papers.

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Peer Review Outcomes

Manuscript processing

This manuscript was peer-reviewed by two external referees and by Professor Mario Cazzola, Editor-in-Chief. The final decision to accept this paper for publication was taken jointly by Prof. Cazzola and the Editors. Manuscript received March 5, 2002; accepted July 16, 2002.

What is already known on this topic

It is generally believed that increasing age in adult allogeneic stem cell transplant recipients is associated with higher morbidity and mortality.

What this study adds

This study shows no significant difference in transplant related morbidity and mortality between elderly patients (aged 55-59) and young adults (aged 20-40) receiving allogeneic stem cell transplantation at a single institution.

Potential implications for clinical practice

These findings suggest that age alone (between 50 and 59) should not be an absolute contraindication to conventional allogeneic stem cell transplantation from an identical sibling donor.

Mario Cazzola, Editor-in-Chief

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