Allogeneic stem cell transplantation for myelodysplastic syndromes with bone marrow fibrosis

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Background
Bone marrow fibrosis in patients with myelodysplastic syndrome is associated with a poor outcome, but whether the outcome after allogeneic stem cell transplantation is related to the degree of bone marrow fibrosis is unknown.

Design and Methods
Patients with myelodysplastic syndrome and known bone marrow histology (n=721) who underwent hematopoietic stem cell transplantation were classified according to the degree of bone marrow fibrosis into those without fibrosis (n=483), those with mild or moderate fibrosis (n=199) and those with severe fibrosis (n=39) and analyzed regarding engraftment, treatment-related mortality, relapse and survival.

Results
The degree of fibrosis was not associated with disease status or abnormal cytogenetics. The cumulative incidence of engraftment achieved at day +30 in non-fibrotic patients was 93% and was significantly lower in those with mild or moderate fibrosis (89%) and severe fibrosis (75%) (P=0.009). Neutrophil engraftment occurred later in patients with mild or moderate fibrosis and severe fibrosis than in patients without fibrosis (median 17 versus 20 versus 16 days, respectively; P=0.002). The cumulative incidence of relapse at 3 years was significantly higher in patients with severe fibrosis than in those with a lesser degree of fibrosis or no fibrosis (47% versus 28% versus 27%, respectively; P=0.04), resulting in comparable 3-year disease-free survival rates in patients without fibrosis and in those with mild or moderate fibrosis (42% versus 38%, respectively) but a lower disease-free survival rate in those with severe fibrosis (18%; P=0.002). Severe fibrosis remained an independent factor for reduced survival (hazard ratio, 1.9; P=0.006).

Conclusions
Among patients with myelodysplastic syndromes, only severe fibrosis affects survival after hematopoietic stem cell transplantation while patients with mild or moderate fibrosis have an outcome comparable to that of patients without bone marrow fibrosis.

Key words: bone marrow fibrosis, allogeneic stem cell transplantation, myelodysplastic syndromes, engraftment.


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Introduction

Myelodysplastic syndromes (MDS) are a heterogeneous group of clonal hematopoietic diseases, for which several scoring systems have been developed to predict prognosis. These scoring systems incorporate information on cytogenetics, number of cytopenias and number of blasts (International Prognostic Scoring System, IPSS), or these variables integrated with transfusion dependency (WHO classification-based Prognostic Scoring System, WPSS). Several studies have shown that other factors, such as bone marrow fibrosis, provide additional information associated with poor outcome in MDS patients.

Allogeneic stem cell transplantation is now more frequently used as a curative treatment approach for MDS. The introduction of so-called dose-reduced conditioning regimens allows transplantation of patients up to the age of 70 years. The major risk factors for outcome after allogeneic stem cell transplantation for MDS are certain cytogenetic characteristics, number of blasts, status of the disease and age of the patient. Information about the impact of bone marrow fibrosis on outcome after allogeneic stem cell transplantation in patients with MDS is only limited. Here we report on 721 MDS patients with known bone marrow fibrosis status, determined by bone marrow histology, who received an allogeneic stem cell transplant and whose data were reported to the European Group for Blood and Marrow Transplantation (EBMT).

Design and Methods

We collected data from 721 patients with MDS and known bone marrow histology at diagnosis who underwent allogeneic stem cell transplantation between 1978 and 2009. The data were extracted from the EBMT registry of patients with MDS or secondary acute myeloid leukemia (sAML). In this study we included only patients diagnosed with MDS. Patients with primary myelofibrosis or overlap syndrome, i.e. with MDS/myeloproliferative syndrome (MPS) were excluded. Out of these 721 patients, 483 were classified as not having fibrosis, 199 were classified as having mild or moderate fibrosis and 39 as having severe fibrosis. The degree of fibrosis was determined by the hematopathologist at each patient’s transplant center. As shown in detail in Table 1 there were no significant differences between the three groups of patients with respect to age, gender, therapy-related MDS/AML, stem cell source, conditioning regimen, donor, disease status, cytogenetics, time from diagnosis to transplant, transplant period and median number of blasts at transplantation. The only difference between the groups was that significantly more patients with mild/moderate fibrosis were positive for cytomegalovirus (P=0.04).

Statistical analysis

The characteristics of the patients were expressed as medians and ranges for continuous variables and frequencies for categorical variables. Categorical data were compared by the χ² test, while continuous variables were compared using the Kruskal-Wallis test. Survival curves were either estimated using the Kaplan-Meier method (if no competing risk were involved), and then the significance of the log-rank test was used, or computed in a competing risk framework (to estimate the cumulative incidence of a specific event in the case of competing risks). For multivariate analyses the Cox model was used to estimate hazard ratios and confidence intervals for specific hazards but in the case of competing risks, the curve estimates of

| Table 1. Patients’ characteristics (n=721) according to bone marrow fibrosis. |
|---------------------------------|----------------|----------------|----------------|--------|
| Known fibrosis                  | None (n=483)   | Mild/moderate  | Severe (n=39)  | P value|
| Male                            | 60%            | 57%            | 54%            | 0.7    |
| Female                          | 40%            | 43%            | 46%            |        |
| t-MDS/AML                       | 10%            | 11%            | 15%            | 0.6    |
| Stem cell source                |                |                |                |        |
| bone marrow                     | 36%            | 34%            | 35%            |        |
| peripheral blood                | 62%            | 63%            | 59%            |        |
| cord blood                      | 1%             | 1%             | 3%             | 0.4    |
| bone marrow                     | 1%             | 1%             | 3%             |        |
| + peripheral blood missing      | –              | 1%             | –              |        |
| Conditioning                    |                |                |                |        |
| standard reduced                | 64%            | 70%            | 77%            | 0.12   |
| reduced                         | 36%            | 30%            | 23%            |        |
| TBI-containing regimen          | 44%            | 44%            | 56%            | 0.34   |
| HLA-identical sibling           |                |                |                |        |
| Syngeneic                       | 58%            | 58%            | 59%            |        |
| Matched – other related         | 1%             | 2%             | 0%             |        |
| Matched unrelated               | 29.4%          | 27.5%          | 33%            | 0.07   |
| Mismatched related              | 4%             | 3%             | 3%             |        |
| Mismatched unrelated            | 7%             | 9%             | 5%             |        |
| Related                         | 64%            | 64%            | 62%            |        |
| Unrelated                       | 36%            | 36%            | 38%            | 0.97   |
| Donor sex                       |                |                |                |        |
| male                            | 61%            | 56%            | 56%            |        |
| female                          | 39%            | 44%            | 44%            | 0.4    |
| CMV-positive serostatus of recipient |            |                |                |        |
| Disease status at diagnosis     |                |                |                |        |
| (n=721)                         |                |                |                |        |
| RAR/RARS                        | 36%            | 39%            | 31%            | 0.7    |
| RAEB                            | 43%            | 43%            | 48%            |        |
| RAEB-t                          | 21%            | 18%            | 21%            |        |
| Disease status at transplant (n=685) |            |                |                |        |
| RAR/RARS                        | 28%            | 29%            | 22%            |        |
| RAEB                            | 40%            | 42.5%          | 48%            |        |
| RAEB-t                          | 24%            | 23.5%          | 26%            | 0.8    |
| sAML                            | 8%             | 5%             | 4%             |        |
| Cytogenetics (n=706)            |                |                |                |        |
| normal                          | 43%            | 42%            | 29%            |        |
| abnormal                        | 49%            | 51%            | 58%            | 0.40   |
| not done                        | 8%             | 7%             | 13%            |        |
| Time from diagnosis to SCT      |                |                |                |        |
| <8 months                       | 35%            | 32%            | 31%            |        |
| 6–12 months                     | 33%            | 33%            | 31%            | 0.9    |
| >12 months                      | 32%            | 35%            | 38%            |        |
| IPSS at transplantation (n=294) | n=191          | n=103          |                |        |
| (incl. severe fibrosis)         |                |                |                |        |
| low                             | 8%             | 4%             | 4%             | 0.5    |
| intermediate 1                  | 39%            | 39%            | 39%            |        |
| intermediate 2                  | 24%            | 22%            | 22%            |        |
| high                            | 29%            | 35%            | 35%            |        |
| Median age of recipient (range) | (18–69)        | (18–67)        | (23–70)        | 0.43   |
| Median age of donor (range)     | (1–74)         | (11–69)        | (5–66)         | 0.70   |
| Median number of blasts in bone marrow (range) | n=149          | n=67           | n=9            | 0.35   |
| continued on the next page.     | 10%            | 12%            | 10%            |        |
|                                 | (5–90%)        | (5–80%)        | (6–70%)        |        |
variable (HR, 1.01; \( P = 0.03 \)), bone marrow as the source of stem cells (HR, 1.34; \( P = 0.03 \)). Use of a reduced-intensity conditioning regimen was associated with lower transplant-related mortality (HR 0.64, \( P = 0.006 \)). There was also a significant improvement in transplant-related mortality for patients transplanted in more recent years (\( P = 0.007 \)) (Table 2). In a multivariate analysis the factors significantly related with higher transplant-related mortality were not being in complete remission (HR, 2.05; \( P < 0.001 \)), HLA mismatch (HR, 1.68; \( P = 0.007 \)) and standard conditioning (HR, 1.85; \( P = 0.001 \)) (Table 3).

**Relapse**

The cumulative incidence of relapse for the study population at 5 years was 29% (95% CI, 25-33%). Factors significantly related to a higher incidence of relapse were severe bone marrow fibrosis (HR, 2.33; \( P < 0.005 \)), abnormal cytogenetics (HR, 1.73; \( P < 0.001 \)), donor’s age as a continuous variable (HR, 1.01; \( P = 0.02 \)), number of blasts at the time of transplantation (HR, 1.02; \( P = 0.003 \)), T-cell depletion in vivo and ex vivo (HR, 1.61; \( P = 0.05 \)), and disease status (refractory anemia with excess blasts [RAEB]; HR, 1.61; RAEB in transformation [RAEB-t]; HR, 2.08; sAML: HR, 2.17; \( P = 0.006 \)). Furthermore, there was a trend for higher relapse incidence among patients who received reduced-intensity conditioning (HR, 1.29; \( P = 0.09 \)) and for those for whom the source of stem cells was peripheral blood (HR, 1.31; \( P = 0.08 \)) (Table 2). In a multivariate analysis the following factors remained significant: advanced disease status, defined as RAEB, RAEB-t or sAML (HR = 0.004), abnormal cytogenetics (HR, 1.96; \( P < 0.0001 \)) and donor’s age (HR, 1.02; \( P = 0.02 \)) (Table 3).

**Disease-free survival**

The 3-year estimated disease-free survival for the study population was 40% (95% CI, 36-44%). In a univariate analysis the following factors were significantly associated with poor disease-free survival: not being in complete remission at the time of transplantation (HR, 1.52; \( P = 0.001 \)), high blast percentage at transplantation (HR, 1.02; \( P < 0.001 \)), abnormal cytogenetics (HR, 1.44; \( P = 0.001 \)) and bone marrow fibrosis (mild/moderate: HR, 1.13; severe: HR, 1.38; \( P = 0.005 \)). Furthermore, there was a trend for reduced disease-free survival according to disease stage (RAEB: HR, 1.45; RAEB-t: HR, 1.44; sAML: HR, 1.51; \( P = 0.06 \)) and HLA-mismatched transplantation (HR, 1.51; \( P = 0.07 \)) (Table 2). In a multivariate analysis, disease stage \( (P = 0.004) \), severe fibrosis (HR, 1.75; \( P = 0.02 \)), abnormal cytogenetics (HR, 1.32; \( P = 0.02 \)) and not being in complete remission before transplantation (HR, 1.85; \( P < 0.001 \)) remained statistically significant (Table 3).

**Overall survival**

The 3-year estimated overall survival for the study population was 45% (95% CI, 41-49%). Disease stage (RAEB: HR, 1.54; RAEB-t: HR, 1.51; sAML: HR, 1.30; \( P = 0.03 \)) not being in complete remission at transplantation (HR, 1.57; \( P = 0.001 \)), abnormal cytogenetics (HR, 1.53; \( P = 0.01 \)), HLA-mismatch (HR, 1.50; \( P = 0.007 \)), blast percentage at transplantation (HR, 1.01; \( P = 0.001 \)) and bone marrow fibrosis (mild/moderate: HR, 1.13; severe: HR, 1.94; \( P = 0.002 \)) were significant factors in the univariate analysis (Table 2). In a multivariate analysis disease status \( (P = 0.005) \), severe fibrosis (HR, 1.90; \( P = 0.006 \)), not being in complete remission at transplantation (HR, 1.82; \( P < 0.001 \)) and HLA-mismatch (HR, 1.89; \( P = 0.006 \)) not being in complete remission at transplantation (HR, 1.82; \( P < 0.001 \)) remained statistically significant (Table 3).
(HR, 1.48; P=0.02) remained independent factors associated with poor survival (Table 3).

Results according to grade of bone marrow fibrosis
The cumulative incidence of engraftment achieved at day +30 in patients without fibrosis was 93% and was significantly lower in those with mild/moderate (69%) or severe (75%) bone marrow fibrosis (P=0.009). Furthermore, in those patients who engrafted successfully, the median time to leukocyte engraftment (white cell count > 1x10^9/L) was 16 days in patients with no fibrosis, 17 days in patients with mild/moderate fibrosis and 20

<table>
<thead>
<tr>
<th>Table 2. Univariate analysis of relapse and therapy-related mortality (TRM), overall survival (OS) and disease-free survival (DFS).</th>
</tr>
</thead>
<tbody>
<tr>
<td>Relapse (n=543)</td>
</tr>
<tr>
<td>-----------------</td>
</tr>
<tr>
<td>Reduced intensity conditioning</td>
</tr>
<tr>
<td>Abnormal cytogenetics</td>
</tr>
<tr>
<td>Donor age</td>
</tr>
<tr>
<td>Bone marrow fibrosis</td>
</tr>
<tr>
<td>none</td>
</tr>
<tr>
<td>mild/moderate</td>
</tr>
<tr>
<td>severe</td>
</tr>
<tr>
<td>Blasts (in bone marrow)</td>
</tr>
<tr>
<td>Not in complete remission</td>
</tr>
<tr>
<td>Disease</td>
</tr>
<tr>
<td>RA/RAES</td>
</tr>
<tr>
<td>RAEB</td>
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<tr>
<td>RAEB-t</td>
</tr>
<tr>
<td>sAML</td>
</tr>
<tr>
<td>other/unknown</td>
</tr>
<tr>
<td>HLA mismatch</td>
</tr>
<tr>
<td>Stem cell source: PB</td>
</tr>
<tr>
<td>SCT in year</td>
</tr>
<tr>
<td>&gt;2001</td>
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<tr>
<td>1998–2001</td>
</tr>
<tr>
<td>1998</td>
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<tr>
<td>&lt;1998</td>
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<tr>
<td>T-cell depletion</td>
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<tr>
<td>no</td>
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<tr>
<td>in vivo</td>
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<tr>
<td>ex vivo</td>
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<tr>
<td>in vivo + ex vivo</td>
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<table>
<thead>
<tr>
<th>Table 3. Significant factors in multivariate analysis for relapse, transplant-related mortality (TRM), disease-free survival (DFS), and overall survival (OS).</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disease status</td>
</tr>
<tr>
<td>-----------------</td>
</tr>
<tr>
<td>RA/RAES</td>
</tr>
<tr>
<td>RAEB</td>
</tr>
<tr>
<td>RAEB-t</td>
</tr>
<tr>
<td>sAML</td>
</tr>
<tr>
<td>other/unknown</td>
</tr>
<tr>
<td>Abnormal cytogenetics</td>
</tr>
<tr>
<td>Not CR prior to SCT</td>
</tr>
<tr>
<td>HLA mismatch</td>
</tr>
<tr>
<td>Standard conditioning</td>
</tr>
<tr>
<td>Age of donor</td>
</tr>
<tr>
<td>Bone marrow fibrosis</td>
</tr>
<tr>
<td>none</td>
</tr>
<tr>
<td>mild/moderate</td>
</tr>
</tbody>
</table>

RA: refractory anemia; RARS: refractory anemia with ringed sideroblasts; SCT: stem cell transplantation; PB: peripheral blood.

RA: refractory anemia; RARS: refractory anemia with ringed sideroblasts; CR: complete remission; SCT: stem cell transplantation.
days in patients with severe fibrosis ($P=0.002$) (Figure 1). There were no significant differences in acute and chronic graft-versus-host disease between the three groups. The incidence of relapse at 5 years was significantly higher in the group with severe fibrosis than in those with mild/moderate or no fibrosis (47% versus 27% versus 28%, respectively; $P=0.04$), resulting in a significantly lower disease-free survival at 5 years (18% versus 38% versus 42%; $P=0.002$) and, likewise, a significantly lower overall survival at 3 years (21% versus 40% versus 49%; $P=0.002$) (Table 4).

**Results according to the International Prognostic Scoring System score and fibrosis**

To evaluate the impact of fibrosis and the IPSS score, we correlated fibrosis and IPSS score in 294 patients for whom the IPSS score at transplantation was known. The degree of fibrosis was well balanced in patients with all IPSS scores (*data not shown*). The estimated 3-year overall survival rates for patients with intermediate-1-risk MDS with and without fibrosis were 49% and 52%, respectively ($P=0.6$). The estimated 3-year overall survival rates for patients with intermediate-2-risk MDS with and without bone marrow fibrosis were 42% and 48%, respectively ($P=0.6$), and those for high-risk patients also did not differ significantly between patients with (22%) and without bone marrow fibrosis (33%, $P=0.4$).

**Discussion**

Here we analyzed the impact of bone marrow fibrosis on outcome after allogeneic stem cell transplantation in MDS patients reported to the EBMT registry. We included only patients diagnosed with MDS, while those with primary myelofibrosis or overlap syndrome (MDS/MPS) were excluded from this analysis. The prognostic impact of bone marrow fibrosis in MDS patients has come into focus and several studies have confirmed a negative impact of fibrosis on survival\textsuperscript{3-7} with some authors suggesting that MDS with fibrosis could be considered as a distinct entity.\textsuperscript{3-11} Although bone marrow fibrosis is not included in the current prognostic risk scores such as the International Prognostic Scoring System (IPSS), it is known that bone marrow fibrosis is an important risk factor for treatment-related mortality (TRM) and relapse.

**Table 4. Results of stem cell transplantation in MDS patients without bone marrow fibrosis, with mild or moderate fibrosis and with severe fibrosis.**

<table>
<thead>
<tr>
<th>Fibrosis</th>
<th>None</th>
<th>Mild/ moderate</th>
<th>Severe</th>
<th>$P$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cumulative incidence of engraftment at day +30</td>
<td>93% (91-95)</td>
<td>89% (85-93)</td>
<td>75% (61-89)</td>
<td>0.009</td>
</tr>
<tr>
<td>Median days to leukocyte engraftment (&gt;1.0×10⁹/L)</td>
<td>16 (1-69)</td>
<td>17 (7-47)</td>
<td>20 (11-34)</td>
<td>0.002</td>
</tr>
<tr>
<td>Acute GVHD grade II - IV</td>
<td>31%</td>
<td>35%</td>
<td>31%</td>
<td>0.49</td>
</tr>
<tr>
<td>Chronic GVHD n = 450</td>
<td>45%</td>
<td>35%</td>
<td>56%</td>
<td>0.13</td>
</tr>
<tr>
<td>1-year therapy-related mortality</td>
<td>26% (22-30)</td>
<td>30% (24-36)</td>
<td>31% (17-45)</td>
<td>0.34</td>
</tr>
<tr>
<td>3-year cumulative incidence of relapse</td>
<td>28% (24-32)</td>
<td>27% (21-33)</td>
<td>47 (29-65)</td>
<td>0.04</td>
</tr>
<tr>
<td>3-year disease-free survival</td>
<td>42% (36-48)</td>
<td>38% (30-46)</td>
<td>18% (4-32)</td>
<td>0.002</td>
</tr>
<tr>
<td>3-year overall survival</td>
<td>49% (43-55)</td>
<td>40% (32-48)</td>
<td>21% (7-35)</td>
<td>0.002</td>
</tr>
</tbody>
</table>

GVHD: Graft-versus-host disease, in brackets: 95% confidence interval.

Figure 1. Cumulative incidence of (A) engraftment, (B) treatment-related mortality (TRM), and (C) relapse according bone marrow fibrosis grading.
IPSS1 and WPSS, some investigators recommend more aggressive treatment for patients with bone marrow fibrosis than either the IPSS or WPSS score would dictate. When we analyzed the outcome of patients according to IPSS and whether or not they had bone marrow fibrosis, we found no significant differences in overall survival. Given the low number of patients with severe fibrosis this group of patients could not be analyzed separately regarding IPSS score. The prognostic impact of bone marrow fibrosis in MDS patients who underwent allogeneic stem cell transplantation has not been studied in detail. In one study no differences in overall survival, relapse-free survival and non-relapse mortality were found between patients with or without bone marrow fibrosis. However, when patients with intermediate-2-risk or high-risk MDS were studied separately, the presence of bone marrow fibrosis was associated with a negative impact on outcome. In our study, based on a large cohort of patients, we found that while patients with mild or moderate bone marrow fibrosis had a similar outcome to those without bone marrow fibrosis after allogeneic stem cell transplantation, patients with severe bone marrow fibrosis had a significantly worse survival. Our results are consistent with reports indicating a lower engraftment rate as well as delayed leukocyte engraftment for patients with increased bone marrow fibrosis, although they contrast with those of other investigators who did not find a difference in engraftment for patients with bone marrow fibrosis. In this EBM T study the difficulties in engraftment resulted only in a trend to a higher treatment-related mortality. Notably, bone marrow fibrosis did not influence the incidence of acute or chronic graft-versus-host disease. Regarding relapse incidence we observed a significantly higher risk of relapse in the group with severe fibrosis, but only in univariate analysis. In multivariate analysis for relapse and treatment-related mortality, fibrosis was not a significant independent risk factor. However, in a multivariate analysis for disease-free and overall survival severe fibrosis remained a significant independent risk factor.

Some authors interpret bone marrow fibrosis in MDS patients as a more malignant subtype of MDS and found some correlation with multilineage dysplasia or excess of blasts, but in our population of patients mild/moderate and severe bone marrow fibrosis were seen in all categories and disease stages of MDS, and were not associated with other known risk factors such as disease status, abnormal cytogenetics, age or number of blasts. The comparable interval between diagnosis and transplantation of about 8 months further suggests that MDS patients with bone marrow fibrosis are not in a more advanced stage. The observed risk factors for relapse such as age, disease status and abnormal cytogenetics, as well as the risk factors for overall survival, such as disease status, not being in complete remission at transplantation and HLA-mismatch, show that this study population was not a selected cohort and represented a common MDS population.

The pathogenesis of fibrosis in MDS patients is unclear. The bone marrow fibrosis may lead to cytopenia and marrow insufficiency. It remains to be determined whether overproduction of cytokines, such as platelet-derived growth factor-α or -β, transforming growth factor-β1 or basic fibroblast growth factor by malignant or inflammatory cells, is involved, as it is in other diseases. Also, while MDS with bone marrow fibrosis can share some features with primary myelofibrosis, cytogenetic features and molecular markers differ substantially between the two diseases. Buesche found dyserythropoiesis and greater than 50% micromegakaryocytes with a hypolobulated round nucleus exclusively in MDS patients, while more than 10% giant megakaryocytes were found in 100% of the patients with primary myelofibrosis and in only 6% of the MDS-fibrosis patients. Furthermore, splenomegaly, leukocytosis and thrombocytosis were more common in primary myelofibrosis while thrombocytopenia and anemia were more often seen in MDS-fibrosis patients. In the same trial the investigators observed a correlation between bone marrow fibrosis and multilineage dysplasia, severe thrombocytopenia, a higher probability of clonal karyotype abnormalities and a higher percentage of blasts in peripheral blood and a shorter survival of MDS fibrosis patient. The prognostic significance was independent of the IPSS. In a similar study Della Porta detected moderate to severe bone marrow fibrosis in 17% of the MDS patients and fibrosis was associated with multilineage dysplasia, poor-risk cytogenetic abnormalities and high transfusion requirement. Those patients had a poor outcome irrespectively of the presence of an excess
of blasts. Since our study is a retrospective registry study and no central review was performed to confirm the diagnosis of MDS, it cannot be excluded that some cases were misdiagnosed as MDS and should have been classified as MPS or MDS/MPS overlap syndrome. Unfortunately, data about spleen size or molecular markers such as the JAK2 mutation are only available for a small minority of the patients, but some indirect facts support the belief that the study population was a MDS population. First, the time from diagnosis to transplantation was only 8 months, which is substantially shorter than that observed in patients with myelofibrosis. Furthermore, the survival of myelofibrosis patients with usually severe fibrosis is reported to be about 50% after allogeneic stem cell transplantation, and substantially better than the observed 18% disease-free survival in patients with severe bone marrow fibrosis in the current study. We conclude that bone marrow fibrosis in MDS patients influences engraftment after allogeneic stem cell transplantation but that only severe bone marrow fibrosis affects survival because of a higher risk of relapse, while MDS patients with mild or moderate bone marrow fibrosis have an outcome comparable to that of MDS patients without bone marrow fibrosis.

Authorship and Disclosures

The information provided by the authors about contributions from persons listed as authors and in acknowledgments is available with the full text of this paper at www.haematologica.org. Financial and other disclosures provided by the authors using the ICMJE (www.icmje.org) Uniform Format for Disclosure of Competing Interests are also available at www.haematologica.org.

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