The impact of T-cell depletion techniques on the outcome after haploidentical hematopoietic SCT.

MAREK, A, et al.

Abstract

Several T-cell depletion (TCD) techniques are used for haploidentical hematopoietic SCT (HSCT), but direct comparisons are rare. We therefore studied the effect of in vitro TCD with graft engineering (CD34 selection or CD3/CD19 depletion, 74%) or in vivo TCD using alemtuzumab (26%) on outcome, immune reconstitution and infections after haploidentical HSCT. We performed a retrospective multicenter analysis of 72 haploidentical HSCT in Switzerland. Sixty-seven patients (93%) had neutrophil engraftment. The 1-year OS, TRM and relapse incidence were 48 (36-60)%, 20 (11-33)% and 42 (31-57)%, respectively, without differences among the TCD groups. In vivo TCD caused more profound lymphocyte suppression early after HSCT, whereas immune recovery beyond the second month was comparable between the two groups. Despite anti-infective prophylaxis, most patients experienced post-transplant infectious complications (94%). Patients with in vivo TCD had a higher incidence of CMV reactivations (54% vs 28%, P=0.015), but this did not result in a higher TRM. In conclusion, TCD by graft engineering or alemtuzumab are equally effective for [...]
The impact of T-cell depletion techniques on the outcome after haploidentical hematopoietic SCT

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INTRODUCTION

Haploidentical HSCT has evolved tremendously in the past 20 years and has become a therapeutic option for patients with high-risk hematological diseases lacking conventional donors.1–6 While it is generally accepted that it requires profound T-cell depletion (TCD) because of increased GVHD risk, the best TCD technique is still unknown. In general, TCD techniques can be classified as in vitro if the stem cell manipulation is performed exclusively ex vivo, normally by column adsorption. In contrast, in vivo techniques are based on a partial or complete depletion of donor lymphocytes in the patient after transplanting the stem cell product using ATG or the MoAb alemtuzumab.7–9 With this technique, donor lymphocytes are removed by the host macrophage/monocyte system of the recipient. Very recently, the first protocols for haploidentical HSCT have been introduced without pretransplant TCD using apheresis high-dose CY for TCD and immunosuppression.10

The decision to follow a given protocol largely depends on the experience and the equipment of transplant centers. While in vitro TCD using column adsorption is technically challenging and requires adequate stem cell processing facilities, in vivo TCD is feasible for most transplant centers. As the degree of TCD has a major role in post-transplant immune reconstitution and incidence of GVHD, the choice of a given TCD may have an important impact on the success of the transplant. We therefore analyzed outcome of haploidentical HSCT with regard to TCD, taking the opportunity presented by Swiss transplant centers using different approaches to TCD.

Several T-cell depletion (TCD) techniques are used for haploidentical hematopoietic SCT (HSCT), but direct comparisons are rare. We therefore studied the effect of in vitro TCD with graft engineering (CD34 selection or CD3/CD19 depletion, 74%) or in vivo TCD using alemtuzumab (26%) on outcome, immune reconstitution and infections after haploidentical HSCT. We performed a retrospective multicenter analysis of 72 haploidentical HSCT in Switzerland. Sixty-seven patients (93%) had neutrophil engraftment. The 1-year OS, TRM and relapse incidence were 48 (36–60%), 20 (11–33%) and 42 (31–57%), respectively, without differences among the TCD groups. In vivo TCD caused more profound lymphocyte suppression early after HSCT, whereas immune recovery beyond the second month was comparable between the two groups. Despite anti-infective prophylaxis, most patients experienced post-transplant infectious complications (94%). Patients with in vivo TCD had a higher incidence of CMV reactivations (54% vs 28%, P = 0.015), but this did not result in a higher TRM. In conclusion, TCD by graft engineering or alemtuzumab are equally effective for haploidentical HSCT.

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Keywords: haploidentical transplantation; T-cell depletion; CMV reactivation; immune reconstitution

PATIENTS AND METHODS

Study design

We retrospectively analyzed all haploidentical HSCT performed in Switzerland from 1998 to 2010. The study was performed on behalf of the Swiss Blood Stem Cell Transplantation group (SBST). In Switzerland, allogeneic HSCT are performed in four centers with an approximate total number of 150 transplants per year including pediatric and adult patients.1 Since 1998, a total of 72 patients received a first haploidentical HSCT, all of which were analyzed in this study. All grafts were T-cell-depleted peripheral blood stem cells from a related donor. All patients or their legal representatives gave written informed consent for retrospective data analysis and the local ethics review board approved the study.

Endpoints and definitions

The main endpoints were OS, TRM, incidence and severity of acute and chronic GVHD, the number of bacterial, viral and fungal infections and time to lymphocyte recovery.

Early disease was defined as ALL or AML in first CR or CML in first chronic phase. All other disease stages were classified as advanced disease. Non-malignant disorders were classified as a separate category. Myeloid engraftment was defined as the first of 3 consecutive days with an ANL of 0.5×109/L or higher with evidence of donor hematopoiesis. Absence of engraftment after day 60 was considered as primary graft failure. Secondary graft failure was defined as loss of graft function after initial engraftment. Acute and chronic GVHD was diagnosed and graded according to standard criteria.11,12 TRM was defined as death due to transplant-associated complications without relapse.

Stem cell mobilization

Haploidentical donors were stimulated with 10–12µg/kg G-CSF s.c. for 5 days. G-CSF was administered once or twice daily according to the center’s

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preference. Leukapheresis was performed using a Cobe Spectra cell separator (Cobe Laboratories Inc., Lakewood, CO, USA) for 1–3 days until the pre-specified numbers of CD34 cells was reached. The minimal required number of CD34 cells in all centers was $10^6$/kg body weight.

T-cell depletion

TCD was achieved either by strict in vitro graft engineering or by adding alemtuzumab to the conditioning regimen or to the stem cell bag, leading to a complete or partial in vivo TCD. The selection of the TCD protocol was made by each transplant center based on their infrastructure and clinical experience. Graft engineering consisted in the majority of cases of CD34 selection by ClinMACS (Miltenyi Biotec, Bergisch-Gladbach, Germany) column adsorption. In three pediatric patients, in vitro TCD was performed by CD3/CDC19 depletion as previously published.13 The maximal number of CD3-positive T-cells accepted after in vitro TCD was $10^5$/kg body weight. Alemtuzumab-based TCD was achieved in eight patients by incubating two-thirds of the pooled apheresis product with 20mg alemtuzumab for 30 min on day 1, as previously described.7–9,14 This stem cell product was infused on day 0 without further washing steps (‘Campath in the bag’). One-third of the apheresis product was infused without TCD. In order to enhance the TCD, the washing step after alemtuzumab incubation applied for HLA-identical transplants was omitted; thus, remaining alemtuzumab in the supernatant was infused into the patient at the time of transplantation, leading to a partial in vivo TCD. In eight patients (11%) T-cells were depleted by adding $5 \times 10^7$ apheresis product consisted of $20 \times 10^7$ stem cells to the conditioning regimen on days 4–0 (‘Campath in the patient’) as previously published.7–9 In this protocol the stem cells were infused after ex vivo manipulations, hence a complete in vivo TCD. In three patients with CD34 positive selection alemtuzumab was added to the conditioning regimen of the patient, resulting in an additional in vivo TCD. Therefore, these patients were assigned to the in vivo TCD group. However, excluding these patients did not change the results. For the final analysis, all patients receiving alemtuzumab were pooled and compared with patients receiving strict in vitro TCD.

Conditioning regimens and GVHD prophylaxis

In adult patients, the myeloablative conditioning regimens were as follows: (i) CY and TBI (12.0–13.2Gy) with or without Etoposide (VP16) and antithymocyte globulin (ATG) or (ii) BU with CY or ATG alone or VP16. For pediatric patients, the myeloablative conditioning regimens consisted of (i) CY/TBI +/- ATG and VP16, (ii) BU/CY +/- ATG and VP16, (iii) Fludarabine (Flu), VP16 and TBI +/- ATG or iv) Flu, Melphalan and Thiopeta. Reduced-intensity conditioning consisted of Flu/CY and was only performed in adult patients.

Seventeen patients did not receive GVHD prophylaxis (24%). In the remaining patients, GVHD prophylaxis was administered only short-term and was tapered before day 28 in the absence of active GVHD. The majority of patients received cyclosporine A alone (13%) or in combination with OKT3 (49%) or mycophenolate mofetil alone (11%).

Statistical analysis and definitions

Baseline characteristics are shown as median and range values or as proportions. The two groups of TCD were compared using the $\chi^2$, Fisher’s exact or Kruskal–Wallis test for categorical data and the Mann–Whitney U-test for continuous variables. The survival functions were estimated with the method of Kaplan and Meier and compared by log-rank test. Cumulative incidences were calculated using relapse as competing risk for TRM and acute GVHD while death without relapse was used as competing risk for relapse. Cox regression analysis was performed for CMV reactivation and the incidence of acute GVHD, adjusting for the use of ATG, CMV serostatus and the age of the patients. Logistic regression analysis was performed for the overall incidence of post-transplant infections. All reported $P$-values are two-sided, and $P<0.05$ were assumed to be statistically significant. Statistical analyses were performed with SPSS (IBM Corp., Armonk, NY, USA) and NCSS-PASS (NCSS LLC, Kaysville, UT, USA).

RESULTS

Patient characteristics

Table 1 summarizes the baseline characteristics of all haploidentical H SCT recipients. The median age at HSCT was 13 years (range 0–50) with 46 (64%) pediatric patients. The majority of patients received haploidentical H SCT for AML (43%), ALL (39%) or primary immunodeficiencies (10%). Of patients with malignant disease, 19 patients (26%) had an early disease at the time of transplant and 46 (64%) had advanced disease. Fifty-five patients (76%) had received chemotherapy prior to HSCT, nine patients (13%) had received chemotherapy with autologous or allogeneic H SCT and eight patients (11%) did not receive any chemotherapy before haploidentical H SCT. Of the eight patients without previous chemotherapy, seven were transplanted for a primary immunodeficiency and one patient for MDS. Two patients were treated with emergency haploidentical H SCT due to primary graft failure after HLA-identical unrelated H SCT. The majority of patients received myeloablative conditioning with CY/TBI with or without VP16 or ATG (47%) or BU/CY with or without VP16 and ATG (21%).

The reduced-intensity conditioning regimen consisted of Flu/CY in eight adult patients (11%). The remaining patients received different myeloablative conditioning regimens as outlined in the Patients and Methods section (21%).
T-cell depletion

Alemtuzumab-based *in vivo* TCD was performed in 19 (26%) patients and *in vitro* TCD by graft engineering in 53 (74%) patients. There were significant differences between the two groups of TCD. As most children (93%) received haploidentical HSCT with *in vitro* TCD, these patients were significantly younger (median 12 years, range 0–29) than those with *in vivo* TCD (median 23 years, range 0–50, \( P = 0.019 \)). There were fewer patients in the alemtuzumab group that received CY/TBI-based conditioning regimens (21 vs 57%, \( P < 0.001 \)) and all patients receiving reduced-intensity conditioning with Flu/CY were in the alemtuzumab group. Furthermore, more patients with in *vitro* TCD received ATG in the conditioning regimen (P < 0.001), and GVHD prophylaxis including OKT3 was exclusively given in patients with in *vitro* TCD (P < 0.001). Median infused CD34 cell dose per kilogram of the recipient was \( 1.26 \times 10^9 \) (range, 5.9–99.0) without significant differences among groups (\( P = 0.177 \)). The median number of remaining CD3-positive T-cells after *in vitro* TCD was 1.4 \( \times 10^4 \)/kg (range, 0.1–9.6 \( \times 10^4 \)/kg).

Engraftment

Of all 72 patients, 67 (93%) had a sustained neutrophil engraftment after a median of 12 days (range, 0–47). Five patients (7%), all of which occurred in the *in vitro* TCD group. Secondary graft failure occurred in five patients (7%), of which occurred in the *in vitro* TCD group. There was no significant difference in the incidence of primary and secondary graft failure among the groups (\( P = 0.273 \)).

Survival, relapse and TRM

Median follow-up of surviving patients is 23 months (range, 1–137). The 1-year OS of the whole population was 48% (95% CI, 36–60) without significant difference between the groups of TCD (\( P = 0.593 \), Figure 1 and Table 2). The 1-year TRM was 20% (95% CI, 11–33) without differences between the groups of TCD (\( P = 0.460 \)).

The main reasons for TRM were acute respiratory distress syndrome (\( n = 2 \)), sepsis (\( n = 2 \)), toxoplasmosis (\( n = 1 \)), GVHD (\( n = 1 \)) and myelitis (\( n = 1 \)). Finally, the relapse incidence after 1 year was 42% (95% CI, 31–57) without differences between the groups of TCD (\( P = 0.942 \)).

GVHD

Acute GVHD occurred in 25 patients (36%). Most of the patients had grade I (16, 23%) or II (6, 9%) acute GVHD. Three patients had grade III acute GVHD (4%), whereas none had grade IV acute GVHD. The median time to onset of acute grade II–IV GVHD was 19 days (range, 9–79) and cumulative incidence of grade II–IV GVHD at day 100 was 15% (95% CI, 6–27) (Figure 1). Patients with *in vivo* TCD had a higher incidence of grade II–IV GVHD compared with *in vitro* TCD (cumulative incidence at day 100: 31 vs 9%, \( P = 0.045 \)). Multivariate analysis showed an increased hazard ratio, but this did not reach statistical significance (hazard

<table>
<thead>
<tr>
<th>Table 2. Univariate probabilities of transplant outcome</th>
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<tr>
<td><strong>T-cell depletion</strong></td>
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<tr>
<td><strong>In vivo</strong></td>
</tr>
<tr>
<td>Probability (95% CI)</td>
</tr>
<tr>
<td>1 year 12 (3–46)</td>
</tr>
<tr>
<td>2 years 12 (3–46)</td>
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<tr>
<td>3 years 12 (3–46)</td>
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<tr>
<td><strong>In vitro</strong></td>
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<tr>
<td>Probability (95% CI)</td>
</tr>
<tr>
<td>1 year 22 (13–38)</td>
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<tr>
<td>2 years 22 (13–38)</td>
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<td>3 years 22 (13–38)</td>
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</table>

*Cumulative incidence with competing risks analysis. Relapse was used as competing risk for TRM and TRM as competing risk for relapse.

Figure 1. OS, relapse and TRM. The figure displays the (a) OS, (b) relapse, (c) TRM and (d) acute GVHD II–IV. The dashed lines represent the *in vivo* TCD and the solid lines the *in vitro* TCD group.
Lymphocyte recovery
The median lymphocyte count before haploidentical HSCT was 0.605 \times 10^{10}/L (range, 0.002–3.0) (Figure 2). The lowest values were measured 1 month after haploidentical HSCT (0.27 \times 10^{10}/L, range 0–5.292). Six to nine months after HSCT, the total lymphocyte counts reached pretransplant levels and during later follow-up they increased to levels even higher as the pretransplant counts. Patients with \textit{in vivo} TCD had lower lymphocyte counts in the first 2 months after HSCT (first month \( P = 0.001 \), second month \( P = 0.002 \)), whereas the lymphocyte recovery was similar in both groups after the second month. With the exception of NK cells, the lymphocyte subsets showed similar recovery patterns as the total lymphocyte count. NK cells were reduced neither by \textit{in vitro} nor by \textit{in vivo} TCD. There was no difference in the lymphocyte recovery of adult and pediatric patients. However, because of the small groups the comparison between the groups of TCD was performed only in univariate analysis, not taking into consideration potentially influencing factors such as conditioning regimens, concurrent ATG therapy and GVHD prophylaxis.

Infections
All patients received a combination of three drugs as infection prophylaxis depending on the center’s policy (cotrimoxazole/sulfamethoxazole, valacyclovir and fungal prophylaxis with an azole). Patients with long aplasia time or relapsing bacterial infection received also broad-spectrum antibacterial prophylaxis, mostly with levofloxacin. Bacterial, fungal and viral infections were evaluated in the first 24 months after haploidentical HSCT. Despite anti-infective prophylaxis, the vast majority of patients had at least one infection after haploidentical HSCT (94%). Twenty-one patients had one (31%), 20 patients had two (30%), 13 patients had three (19%) and 11 (15%) had four infections with a median number of two infection episodes. The overall incidence of bacterial infections was 56/69 (81%), most frequently due to gram-negative bacteria (26%) and staphylococcal infections (16%). Fungal infections were only counted if they were newly diagnosed after the transplantation and occurred in 22/69 patients (32%). The most frequent fungal infections were pulmonary aspergillosis (15%) and candidiasis (6%), but invasive microbiological diagnostics were only infrequently performed in suspected fungal infections. Viral infections occurred in 45/69 (65%) patients, mostly CMV (35%), herpes (24%) and BK (23%) virus infections. There were no significant differences in the overall incidence of bacterial (82 vs 79%, \( P = 0.772 \)), fungal (34 vs 26%, \( P = 0.541 \)) or viral infections (79 vs 60%, \( P = 0.140 \)) between the \textit{in vitro} and \textit{in vivo} TCD group, respectively. In a multivariate analysis adjusting for age, conditioning with ATG, GVHD prophylaxis, the choice of TCD did not influence the incidence of infections (0.846).

CMV reactivation
Forty-four donor–recipient pairs had a positive CMV serostatus prior to HSCT. Twenty-five patients experienced a CMV reactivation defined by an increase in the CMV–PCR or the pp65 CMV Ag after HSCT and the cumulative incidence at day 100 was 35% (95% CI, 24–46%). None of the patients experienced CMV disease.

Figure 2. Recovery of lymphocytes and lymphocyte subsets. The figure displays the recovery of the total lymphocyte count and the lymphocyte subsets (CD3, CD4, CD8, CD19 and NK). The open bars represent patients with \textit{in vivo} TCD and the gray bars patients with \textit{in vitro} TCD. The bars show means \( \pm \) s.e.m. The total lymphocyte counts and the lymphocyte subsets were evaluable in 58 (81%) and 30 (42%) patients, respectively.
Alemtuzumab in the bag to the TCD technique. Both, addition of alemtuzumab to the conditioning regimen and to the stem cell bag resulted in a higher incidence as compared with CD34 selection.

Figure 3. CMV reactivations after haploidentical HSCT. The figure displays the cumulative incidence of CMV reactivation according to the TCD technique. Both, addition of alemtuzumab to the conditioning regimen and to the stem cell bag resulted in a higher incidence as compared with CD34 selection.

Table 3. Cox regression analysis of CMV incidence

<table>
<thead>
<tr>
<th></th>
<th>Hazard ratio 95%-CI</th>
<th>P-value</th>
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<tr>
<td>A: T-cell depletion</td>
<td></td>
<td></td>
</tr>
<tr>
<td>In vitro</td>
<td>1.0</td>
<td>0.025</td>
</tr>
<tr>
<td>In vivo</td>
<td>3.2 (1.2–9.0)</td>
<td></td>
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<tr>
<td>CMV serostatus</td>
<td></td>
<td></td>
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<tr>
<td>Neg/Neg</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>12.2 (1.6–92.2)</td>
<td></td>
</tr>
<tr>
<td>Conditioning</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No ATG</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>ATG</td>
<td>0.5 (0.1–1.7)</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adults</td>
<td>1.0</td>
<td>0.219</td>
</tr>
<tr>
<td>Pediatrics</td>
<td>0.6 (0.2–1.4)</td>
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| B: T-cell depletion         |                     |         |
| CD34 selection with OKT3*  | 0.9 (0.2–4.9)       | 0.936   |
| CD34 selection without OKT3| 3.3 (1.1–9.3)       | 0.027   |
| Alemtuzumab                |                     |         |
| Neg/Neg                    | 1.0                 | 0.025   |
| Other                      | 15.1 (2.0–114.2)    | 0.008   |
| Conditioning               |                     |         |
| No ATG                     | 1.0                 |         |
| ATG                        | 0.6 (0.2–2.0)       | 0.367   |
| Age                        |                     |         |
| Adults                     | 1.0                 | 0.333   |
| Pediatrics                 | 0.6 (0.2–2.0)       |         |

*Short-term post-transplant OKT3 as GVHD prophylaxis.

The median time to CMV reactivation was 27 days (range, 1–127). Patients with in vivo TCD had significantly more often CMV reactivations (54%; 95% CI, 31–77%) as compared with those with in vitro TCD (28%; 95% CI, 16–41%; P = 0.0015; Figure 3). There was no difference in the incidence of CMV reactivations between patients receiving alemtuzumab in the bag or in the conditioning regimen. In Cox regression analysis adjusting to the CMV serostatus, CMV reactivation remained independently associated with in vivo TCD (HR, 3.2; P = 0.025, Table 3A). Moreover, we further divided the group of in vitro TCD in patients with or without post-transplant GVHD prophylaxis with short-term OKT3. As shown in Table 3B, the addition of post-transplant OKT3 did not increase the risk of CMV reactivation, whereas it remained elevated in patients with in vivo TCD (HR 3.3, P = 0.027).

DISCUSSION

In this study we have demonstrated that in vitro TCD with CD34 selection and in vivo TCD with alemtuzumab for haploidentical hematopoietic stem cell transplantations show comparable results with regard to OS, TRM, relapse incidence, acute and chronic GVHD, and post-transplant lymphocyte recovery. In contrast, in vivo TCD was significantly associated with a higher incidence of CMV reactivations.

Haploidentical allogeneic HSCT offers an important treatment modality for patients without conventional stem cell donors. Over the years, a wealth of studies has led to a variety of different transplantation techniques with regard to patient selection, TCD, conditioning regimens, stem cell numbers as well as many other factors, and its complexity has been highlighted by a number of recent reviews.2–6,10,13,15,16 In reality, however, transplant centers generally choose one transplant technique according to the feasibility in their institution and continue with this technique with slight modifications. Nevertheless, although direct comparisons of different TCD are sparse, studies in haploidentical HSCT generally consider them as comparable.

Here, we studied the effect of different TCD methods on the outcome and immune reconstitution after HSCT. As patients were treated in four centers each using a different approach to haploidentical HSCT, the study population is rather heterogeneous. This constitutes a weakness of the current study, but it also reflects the reality of case mixes in most transplant centers. Reassuringly, however, the most important quality control measures of allogeneic HSCT such as TRM and neutrophil engraftment did not differ among centers and patient groups irrespective of the different conditioning regimens and transplant techniques applied. The TRM was 20% after 1 year without differences between pediatric and adult patients and between the transplant centers being in line with other studies.1,17–21 In the published patient series, TRM at 1 year ranged from 17–37%, whereas a recent large multicenter showed slightly higher TRM incidences depending on the donor and the disease.1,12,22 Likewise, the primary neutrophil engraftment rate was in the range of other studies.8,14,23,24 While patients with non-myeloablative conditioning had a faster engraftment, there was no difference between the groups of TCD.

The effect of in vivo TCD has been studied in a number of publications investigating HLA-identical or -mismatched HSCT from unrelated donors. Whereas intense TCD of the graft has enabled better prevention of acute GVHD, the severe, long-lasting immunodeficiency was responsible for very high morbidity and mortality.25,26 However, a recent retrospective study of the CIBMTR comparing TCD with immunosuppressive therapy in patients with HLA-matched HSCT showed that rigorous TCD reduced GVHD with similar incidences of relapse and a comparable disease-free survival.27 Moreover, partial TCD using ATG or alemtuzumab is frequently used as GVHD prophylaxis in patients with HLA-identical unrelated or HLA-mismatched donors.28–30

The feasibility of TCD with alemtuzumab in haploidentical HSCT has been demonstrated in several studies showing comparable results to in vitro TCD.7,8 However, only few studies compared TCD strategies in this setting. The Tuebingen group studied the effect of different in vitro graft manipulations.1,21 Stem cell selection with MoAb against CD34 or CD133, or T/B-cell depletion with CD3/CD19 depletion resulted in a similar neutrophil engraftment and immune reconstitution, whereas CD3/CD19 depletion had slightly higher incidences of grade II acute GVHD. There are no studies comparing alemtuzumab-based TCD with in vitro TCD.
Delayed immune reconstitution and infectious complications remain outstanding issues for haploidentical HSCT and are important causes for TRM. We investigated the immune reconstitution following in vivo or in vitro TCD by measuring the total lymphocyte counts as well as the lymphocyte subsets regularly after HSCT. Both TCD techniques resulted in a profound depletion of the total lymphocytes and all lymphocyte subsets with the exception of NK cells. In vivo TCD resulted in slightly lower lymphocytes in the first 2 months after HSCT, but the lymphocyte recovery starting 3 months after HSCT was comparable and the pretransplant level was reached with both techniques 6–9 months after HSCT. Other studies have demonstrated comparable results for haploidentical HSCT, whereas the recovery starts slightly earlier after T-replete HSCT.13,17,32–34

Irrespective of the lymphocyte counts, patients after haploidentical HSCT face a substantial risk for post-transplant infections. In the current study, 94% of all patients had one or several post-transplant infections. The overall incidence of infections did not differ between the two TCD regimens, but the incidence of CMV reactions was elevated in the in vivo TCD group. Thus, alemtuzumab represents an important risk factor for CMV reactivation in patients receiving haploidentical HSCT, which has been observed in other patients with or without allogeneic HSCT.30,35,36

In conclusion, TCD by graft engineering or alemtuzumab seem to be equally effective for haploidentical HSCT. This is reassuring as it offers the possibility that transplant centers can choose the TCD according the equipment and local feasibility. However, these data need to be confirmed in larger, more homogeneous populations.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

ACKNOWLEDGEMENTS

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REFERENCES


