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Bone marrow versus peripheral blood as a graft source for haploidentical donor transplantation in adults using post-transplant cyclophosphamide—A systematic review and meta-analysis

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ABSTRACT

Background: Peripheral-blood (PB) and bone marrow (BM) are both widely used in hematopoietic stem cell transplantation (HSCT). However, it is unclear whether PB or BM produces a more satisfactory outcome in haploidentical HSCT, particularly for patients using post-transplant cyclophosphamide (PTCy), which is the standard therapy. However, to date, no meta-analysis focusing on this issue has been published.
Methods: We systematically searched PubMed, MEDLINE, Web of Science, the Cochrane Library and the ClinicalTrials.gov website for studies regarding the use of BM or PB in haploidentical HSCT for hematological malignancies in adults using PTCy. Data were analyzed using Open Meta-Analyst statistical software.
Results: Fourteen studies were extracted including four comparative retrospective reports and ten single-arm reports, with a total of 1759 patients received PTCy haploidentical HSCT (462 patients received PBSCT, 1297 patients received BMT). The pooled outcomes of comparative retrospective studies showed significantly higher incidence of grade III-IV acute graft-versus-host disease (GVHD) (OR = 1.741, 95%CI 1.032-2.938), incidence of grade II–IV acute GVHD (OR = 1.778, 95%CI 1.314, 2.406) and engraftment rate (OR = 1.843, 95%CI 1.066-3.185) in the PB group. No significant differences were found on the incidence of relapse, 2-year overall survival (OS) and disease-free survival (DFS), acute II–IV GVHD and chronic GVHD between PBSCT or BMT.
Conclusion: The efficacy of PB is not inferior to BM for patients undergoing PTCy haploidentical HSCT with regard to primary outcomes, including OS, DFS, NRM and relapse. However, with regards to convenience and pain relief, PB graft is suitable for haploidentical HSCT, but with a higher risk of acute GVHD.

1. Introduction

Recently, haploidentical hematopoietic stem cell transplantation (HSCT) using high-dose post-transplant cyclophosphamide (PTCy) has gained increasing popularity for its promising results for higher overall survival (OS) with acceptable rates of NRM (non-relapse mortality) and severe graft-versus-host disease (GVHD), as well as other advantages, such as timely donor availability, easy access and cost–effectiveness (Ciurea et al., 2015; Solomon et al., 2015a,b; Wang et al., 2016). Initially, bone marrow (BM) was the only source of stem cells for transplantation. However, as newer transplant protocols have come into clinical practice, peripheral blood (PB) has replaced BM as the predominant source of stem cells for transplantation (Baldomero et al., 2011; Gratwohl et al., 2008).

The harvesting of BM stem cells involves performing an operation that is time-consuming and exposes the donor to the risk of complications. In addition, it is difficult to obtain target CD34+ cells when the weight of the donor and recipient differs greatly. Conversely, PB is more

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convenient to be harvested and contains more CD34+ cells, which provides donor convenience and ensures safety. Moreover, peripheral blood stem cell transplantation (PBSCT) is characterized by faster engraftment, immune reconstitution, lower relapse rate, but an increasing risk of GVHD most likely due to the higher T-cell content of the graft (Anasetti et al., 2012; Nagafuji et al., 2010; Schmitz et al., 2005).In contrast, bone marrow transplantation (BMT) is associated with lower rates of GVHD and transplant-related mortality (TRM) and is accompanied with a higher risk of relapse and longer time to recovery after transplantation (Pulsipher et al., 2013).

To our knowledge, no studies with high methodological quality, such as randomized controlled trials (RCT), have directly evaluated the efficacy of PB and BM in haploidentical HSCT patients using PTCy; however, numerous observational studies are available, and the recommended stem cell sources vary across these studies. Although there have been several meta-analyses examining the prognostic effectiveness of PB and BM as a graft in HSCT involving HLA-matched unrelated donors (MUD) and HLA-matched related donors (MRD), we did not find a meta-analysis that precisely evaluates the efficacy of these two grafts on patients using PTCy with HLA-haploidentical related donors. Furthermore, the conclusions regarding the main outcomes are still controversial in previous meta-analysis.

The objective of this study was to evaluate whether PB or BM is better for patients undergoing haploidentical HSCT using PTCy.

2. Methods

2.1. Search strategy and selection criteria

This meta-analysis was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-analysis statement (PRISMA). Two reviewers independently searched PubMed, Medline, Web of Science, the Cochrane Library and ClinicalTrials.gov website, from database inception to 14 October 2017, with the keywords “hematopoietic stem cell transplantation and cyclophosphamide”. Reference lists of retrieved articles and related reviews were also examined. No restrictions on language or study design were set.

Studies were considered eligible if they were RCTs, prospective cohort studies, or retrospective studies that explored the efficacy of different stem cell sources (BM and PB) in patients suffering from hematological malignancies who were undergoing haploidentical HSCT using PTCy.

2.2. Quality assessment and data extraction

Two authors worked independently on quality assessment. Comparisons between retrospective studies were assessed using the Newcastle-Ottawa Scale. Potential scores ranged from 0 to 10, with higher scores indicating higher quality. Single-arm studies were assessed using the Newcastle-Ottawa Scale modified for cohort studies without controls, as previously used by Lopez-Olivoa (Wells et al., 2017; Lopez-Olivo et al., 2013). Potential scores ranged from 0 to 6, with higher scores indicating higher quality. The following components were assessed: selection, which includes the representativeness of the exposed cohort; ascertainment of exposure; demonstration that the outcome of interest was not present at the start of the study; and outcome, which consists of an assessment of outcome, followed-up long enough for outcomes to occur, and adequacy of the follow-up of cohorts.

Two independent authors extracted the data. If disagreements occurred, an adjudicator was consulted. We used a standardized extraction form to extract information about the publication year, name of the authors, number of patients, the prophylaxis of GVHD, the conditioning regimen in each study, engraftment, OS, DFS, acute/chronic GVHD, relapse and NRM.

2.3. Data analysis and statistical methods

All analyses were performed using the Open Meta-Analyst software (Tufts Medical Center, Boston, MA, USA). We conducted separate analyses for retrospective reports comparing the treatment outcomes of BMT and PBSCT directly and most single-arm retrospective studies studying the treatment outcomes of PBSCT or BMT. Dichotomous data obtained from each study were expressed as proportions. The heterogeneity of the research results was determined by the calculation of aI^2statistic and p-value. If the 95% confidence interval (CI) of outcomes among different graft-source groups did not overlap, then we concluded that the outcomes were statistically significant.

3. Results

3.1. Search results

We initially identified 10,708 potentially relevant papers from the electronic databases. After excluding 7125 duplicates, a careful review of the abstracts and full texts indicated that 14 studies met the inclusion criteria, including four retrospective reports that directly compared the treatment outcomes of BMT and PBSCT and ten reports that were mostly single-arm retrospective studies only examining the treatment outcomes of PBSCT or BMT. The detailed process of study selection and identification is depicted in Fig. 1.

The 14 studies examined included a total of 1759 patients who received haploidentical HSCT using PTCy; 462 patients received PBSCT, and 1297 patients received BMT. Demographics, conditioning regimens and prophylaxis of GVHD of the 14 studies are summarized in Table 1.

3.2. Quality assessment

The results of risk of bias for each adult study are shown in Table 1. All studies had a score > 5, which indicates a relatively high research quality. The subjects included were representative, and ascertainment of exposure was confirmed by secure record. Outcome assessment was based on pharmacy and medical records, and the follow-up period was sufficient for outcomes to occur.

3.3. Overall and disease-free survival

Thirteen studies (Bashey et al., 2017; O’Donnell et al., 2016; Cieri et al., 2015; Sugita et al., 2015; Solomon et al., 2015a,b; Gaballa et al., 2016a,b; Raj et al., 2014; Munchel et al., 2011; Ciurea et al., 2012; Gaballa et al., 2016a,b; McCurdy et al., 2017; Raiola et al., 2014) including three comparative retrospective reports and ten single-arm reports reported the 2-year OS between the two target groups involving a total of 1759 patients with hematologic malignancies (Figs. 2 and 3). No significant difference was found in OS between the two groups, neither in the comparative retrospective studies nor single-arm studies. The pooled OR for the 2-year OS of the comparative retrospective studies was 0.916 (95%CI, 0.466-1.799). The pooled OS of single-arm BM and PB studies were 0.543 (95%CI, 0.453-0.632) and 0.591 (95%CI, 0.470-0.713), respectively.

Twelve studies (Bashey et al., 2017; Bradstock et al., 2015; O’Donnell et al., 2016; Cieri et al., 2015; Sugita et al., 2015; Solomon et al., 2015a,b; Raj et al., 2014; Munchel et al., 2011; Ciurea et al., 2012; Gaballa et al., 2016a,b; McCurdy et al., 2017; Raiola et al., 2014) reported data on the 2-year DFS involving a total of 1709 patients. Based on the data given, no evidence supported that transplantation with BM improved 2-year DFS compared to transplantation with PB. The pooled OR for 2-year DFS for the comparative retrospective studies was 1.723 (95% CI, 0.896-3.312, Supplementary material Fig. A1). The pooled incidence of DFS (Supplementary material Fig. A2) in single-arm BMT and PBSCT studies were 0.438 (95%CI, 0.354-0.522) and 0.519 (95%CI, 0.373-0.666), respectively.

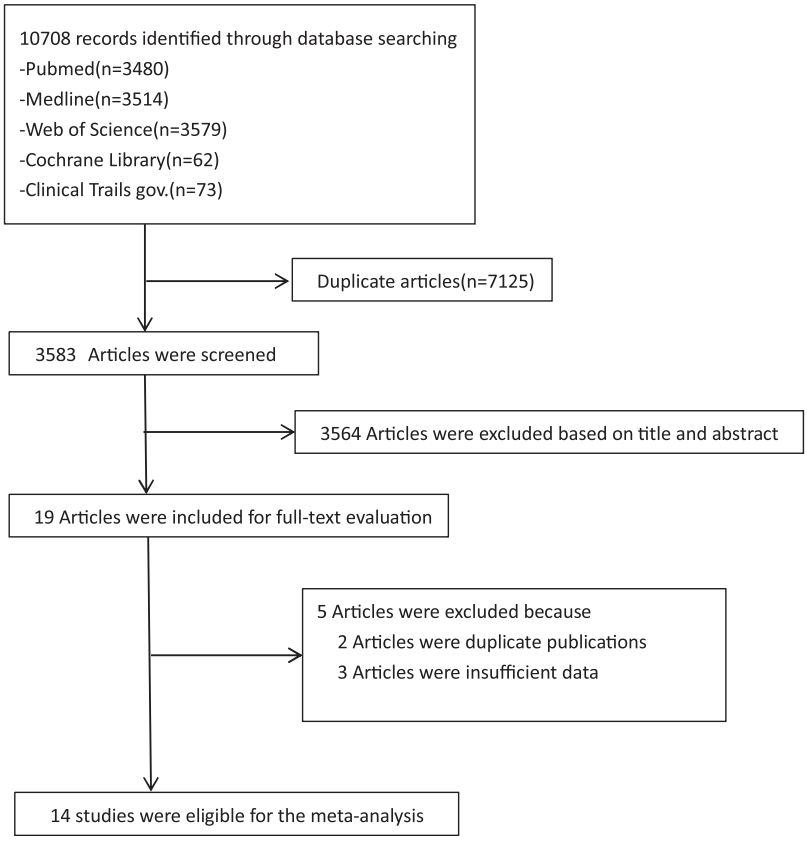

Fig. 1. Flow diagram of the study selection procedure. The detailed process of study.

3.4. Relapse incidence

Data were available for seven out of 14 studies (Solomon et al., 2015a,b; Gaballa et al., 2016a,b; Raj et al., 2014; Munchel et al., 2011; Gaballa et al., 2016a,b; McCurdy et al., 2017; Raiola et al., 2014), and 1656 patients were analyzed. No significant difference was found between BM and PB regarding the incidence of relapse. The pooled OR was 0.532(95% CI, 0.181-1.563, Fig. 4). The pooled incidence of relapse (Fig. 5) of the single-arm BMT and PBSCT studies were 0.404 (95%CI, 0.287-0.521) and 0.243 (95%CI, 0.171-0.315), respectively.

3.5. Non-relapse mortality

Twelve studies (Bashey et al., 2017; Castagna et al., 2014; O'Donnell et al., 2016; Cieri et al., 2015; Sugita et al., 2015; Gaballa et al., 2016a,b; Raj et al., 2014; Munchel et al., 2011; Ciurea et al., 2012; Gaballa et al., 2016a,b; Raiola et al., 2014) reported data on the NRM involving a total of 1425 patients. No significant difference was found in the NRM between the two groups. The pooled OR of NRM in comparative retrospective studies was 0.972 (95% CI, 0.490-1.930, Supplementary material Fig. A3). The pooled incidence of NRM (Supplementary material Fig. A4) in the single-arm BM and PB studies were 0.279 (95%CI, 0.070-0.488) and 0.136 (95%CI, 0.037-0.236), respectively.

3.6. Chronic GVHD

Eleven studies (Bashey et al., 2017; Bradstock et al., 2015; O'Donnell et al., 2016; Ciurea et al., 2012; Gaballa et al., 2016a,b; Munchel et al., 2011; Raiola et al., 2014; Cieri et al., 2015; Raj et al., 2014; Solomon et al., 2015a,b; Sugita et al., 2015) reported data on chronic GVHD involving a total of 1337 patients. No significant difference was found in chronic GVHD between the two groups. The pooled OR of chronic GVHD in comparative retrospective studies was 1.332 (95% CI, 0.497-3.569, Fig. 6). The pooled chronic GVHD (Fig. 7) of single-arm BM and PB studies were 0.131 (95%CI, 0.091-0.172) and 0.260 (95%CI, 0.108-0.412), respectively.

3.7. Acute GVHD

Thirteen (Bashey et al., 2017; Bradstock et al., 2015; Castagna et al., 2014; Ciurea et al., 2012; Gaballa et al., 2016a,b; Munchel et al., 2011; O'Donnell et al., 2016; Raiola et al., 2014; Cieri et al., 2015; Gaballa et al., 2016a,b; Raj et al., 2014; Solomon et al., 2015a,b; Sugita et al., 2015) studies reported data on the grade II–IV acute GVHD involving a total of 1456 patients. The pooled OR of grade II–IV acute GVHD from comparative retrospective studies showed a significantly higher incidence of grade II–IV acute GVHD in the PB group (OR = 1.778, 95%CI 1.314-2.406, Fig. 8). No significant difference was found in single-arm BM (0.220, 95%CI 0.145-0.296, Fig. 9) and PB (0.364, 95%CI 0.187-0.541) studies.

Twelve studies (Bashey et al., 2017; Castagna et al., 2014; Ciurea et al., 2012; Gaballa et al., 2016a,b; Munchel et al., 2011; O'Donnell et al., 2016; Raiola et al., 2014; Cieri et al., 2015; Gaballa et al., 2016a,b; Raj et al., 2014; Solomon et al., 2015a,b; Sugita et al., 2015) reported data on the grade III-IV acute GVHD involving a total of 1337 patients. The pooled OR of grade III-IV acute GVHD from comparative retrospective studies showed a significantly higher incidence of grade III-IV acute GVHD in the PB group (OR = 1.741, 95%CI 1.032-2.938, Fig. 10). No significant difference was found in single-arm BM (0.045, 95%CI 0.025-0.066, Fig. 11) and PB (0.070, 95%CI 0.028-0.112) studies.

3.8. Engraftment

Twelve studies (Bashey et al., 2017; Bradstock et al., 2015; Castagna

Table 1
Characteristics of studies included.

Study	Country	Study arm	Number of Patients	Median Age	Study design	Diagnosis	Conditioning regimen	GVHD prophylaxis	Recruitment period	NOS score
Cieri 2015	Italy	PB	40	55(21-78)	cohort	AML(22), ALL(5), MDS(1), CML(1), HD (6), NHL(5)	treosulfan + Flu + Mel	Cy + MMF + sirolimus	November 2012 to July 2014	6
Sugita 2015	Japan	PB	31	48 (21-65)	perspective	AML(17), ALL(8), MDS(4), other (2)	TBI(2 Gy) + Cy + Flu + Bu	Cy + MMF + tacrolimus	NA	6
Solomon 2015	USA	PB	30	46 (24-60)	prospective	AML(16), ALL(6), CML(5), MDS(1), NHL (2)	TBI(12 Gy) + Flu	Cy + MMF + tacrolimus	NA	5
Gaballa 2016	USA	PB	50	49 (21-65)	retrospective	AML(27), ALL(14), MDS(3), NHL(5), AA(1)	TBI(12 Gy) + Cy	Cy + MMF + tacrolimus	March 2007 to December 2014	6
Raj 2014	UK2016	PB	55	49 (14-69)	retrospective	AML(16), HL(9), ALL(2), MDS(5), NHL (12), SAA(4), CLL(4), CML(3),	TBI(2 Gy) + Cy + Flu	Cy + MMF + tacrolimus	March 2009 to February 2013	5
Gaballa 2016	USA	BM	60	45(20-63)	prospective	ALL(7), NHL(8), HL(2), other(10)	TBI(2 Gy) + Cy + Flu	Cy + MMF + tacrolimus	January 2010 through August 2014	6
Ciurea 2012	USA	BM	32	11 (6–28)	retrospective	AML(16), ALL(4), CML(5), NHL(3),HD (2), other(2)	THIO + Mel	Cy + MMF + tacrolimus	February 2009 and March 2011	6
McCurdy 2017	USA	BM	372	55 (18-75)	retrospective	AML(91),ALL(26),MDS(33), NHL(123), CLL(51), HL(37), other (11)	NMAC	PT Cy	2002 and 2012.	5
Munchel 2017	USA	BM	210	52 (1-73)	prospective	NA	TBI(2 Gy)+Cy + Flu	Cy + MMF + tacrolimus	NA	5
Raiola 2014	Italy	BM	92	44(15-71)	retrospective	AL(39), Lymphoma(25), MDS(10), other (18)	71 THIO + Bu + Flu/Bu + Cy 21 TBI(2 Gy) + Cy + Flu + THIO (+ Mel)	Cy + MMF + CyA	January 2006 and July 2012	6
Bashey2017	USA	BM	481	58(18-76)	prospective	AML(193), ALL(70), MDS(40), NHL (143), HL(50)	Bu, Cy with or without Flu(65) TBI(≥10 Gy)+ Cy(15) TBI(≥10 Gy)+ Flu(11) TBI(2 Gy)+Cy + Flu(405)	Cy + MMF + Calcineurin inhibitor	2009-2014	7
		PB	190	47(19-73)		AML(107), ALL(29), MDS(18), NHL(27), HL(10)	Bu, Cy with or without Flu(45) TBI(≥10 Gy)+ Cy(5) TBI(≥10 Gy)+ Flu(53) TBI(2 Gy)+Cy + Flu(88)			
Castagna2014	Italy	BM	46	44(19-68)	retrospective	HL(23), NHL(15), CLL(1), AML(2),MM (2) ALL(2),	TBI(2 Gy)+Cy + Flu	Cy + MMF + tacrolimus	April 2009 until April 2013	6
		PB	23	54(25-65)		HL(6), NHL(9), CLL(3), AML(2),MM(2),				
Bradstock2015	Australia	BM	13	53(27-63)	retrospectiv	AML(10), NHL(2),CML(1)	TBI(2 Gy) + Cy + Flu	Cy + MMF + tacrolimus	NA	6
		PB	23	44(23-69)		AML(9), NHL(4),ALL(4), MDS(2), HL(1), SAA(2), other(1)				
O'Donnell2016	USA	BM	43	49(7-70)	retrospectiv	AML(20), ALL(4), HL(7), other(13)	NMAC	NA		6
		PB	43	49(14-68)		AML(13), ALL(3), HL(8), NHL(3), other (16)				

Newcastle-Ottawa Scale = NOS, CML = chronic myeloid leukemia, AML = acute myeloid leukemia, ALL = acute lymphoid leukemia, AL = acute leukemia, MDS = myelodysplastic syndrome, NHL = non-Hodgkin's lymphoma, SAA = severe aplastic anemia, MF = Myelofibrosis. MAC = myeloablative conditioning, NMAC = non-myeloablative conditioning, RIC = reduced intensity conditioning, Cy = cyclophosphamide, Bu = busulfan, TBI = total body irradiation, Mel = melfalan, Flu = fludarabine, THIO = thiotepa, CsA = cyclosporine, MMF = mycophenolate mofetil, NA = not available.

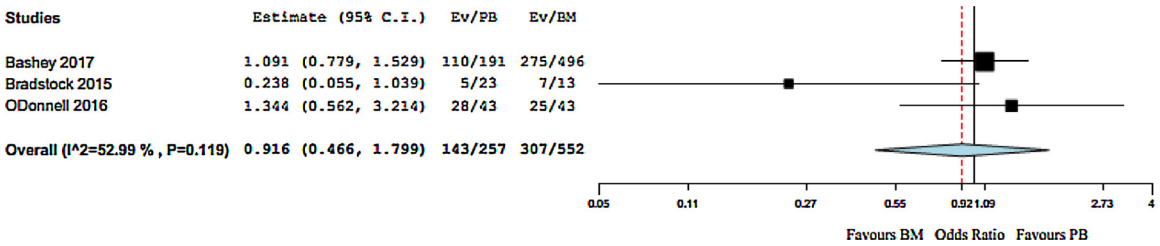

Fig. 2. Overall survival in comparing retrospective studies. A forest plot illustration.

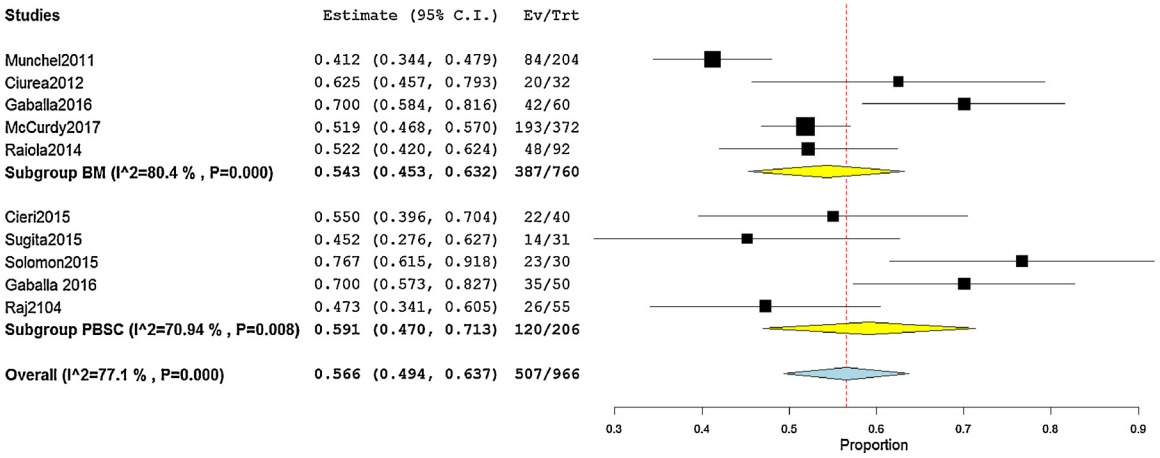

Fig. 3. 2-year overall survival in single-arm studies. A forest plot illustration.

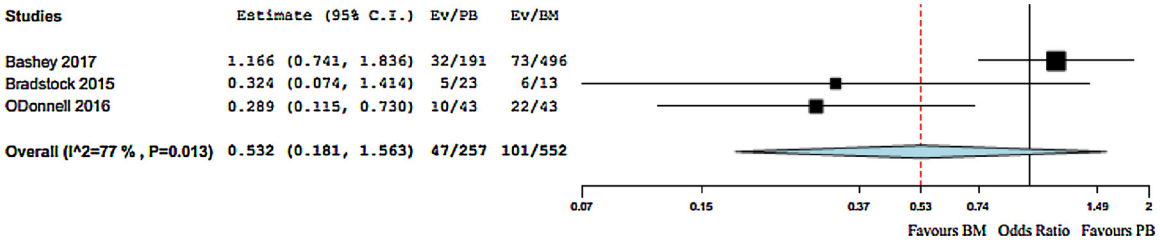

Fig. 4. Relapse incidence in comparing retrospective studies. A forest plot illustration.

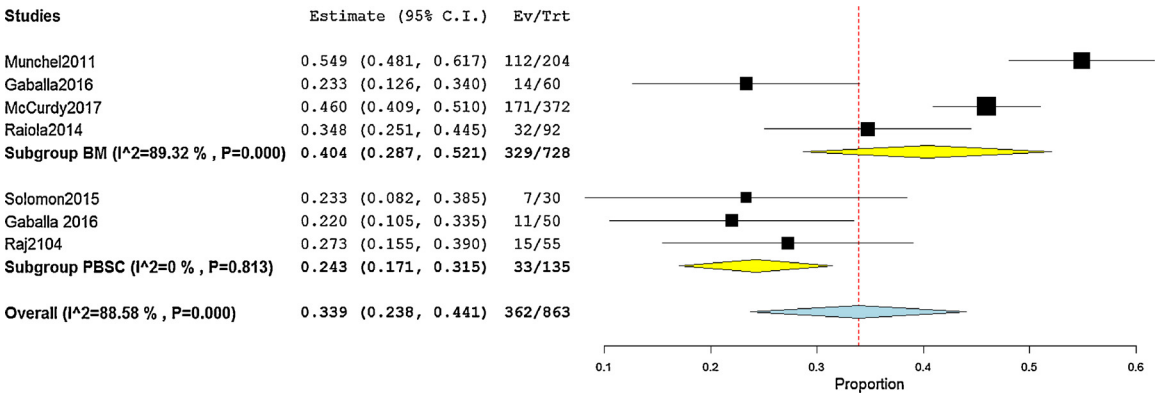

Fig. 5. Relapse incidence in single-arm studies. A forest plot illustration.

et al., 2014; Ciurea et al., 2012; Gaballa et al., 2016a,b; Munchel et al., 2011; O'Donnell et al., 2016; Cieri et al., 2015; Gaballa et al., 2016a,b; Raj et al., 2014; Solomon et al., 2015a,b; Sugita et al., 2015) reported data on the engraftment rate involving a total of 1364 patients. The pooled outcomes in comparing retrospective studies showed a significantly higher rate of engraftment in the PBSCT group (OR = 1.856, 95%CI 1.075-3.204, Fig. 12). No significant difference was found in the single-arm BM (0.914, 95%CI 0.857-0.972, Fig. 13) and PB (0.974, 95%CI 0.952-0.996) studies.

4. Discussion

We performed a systematic review and meta-analysis of studies to examine the efficacy of PB and BM in haploidentical HSCT patients using PTCy. To the best of our knowledge, this is the first meta-analysis exploring stem cell source, PB or BM, specifically, which is the better

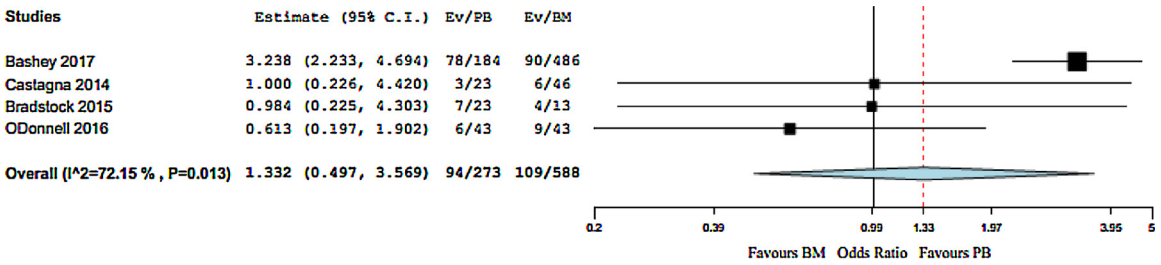

Fig. 6. Chronic GVHD in comparing retrospective studies. A forest plot illustration.

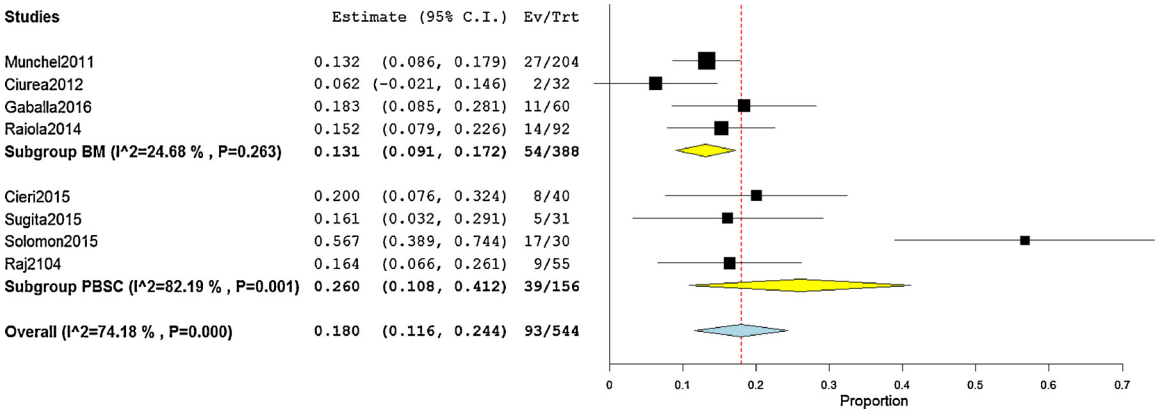

Fig. 7. Chronic GVHD in single-arm studies. A forest plot illustration.

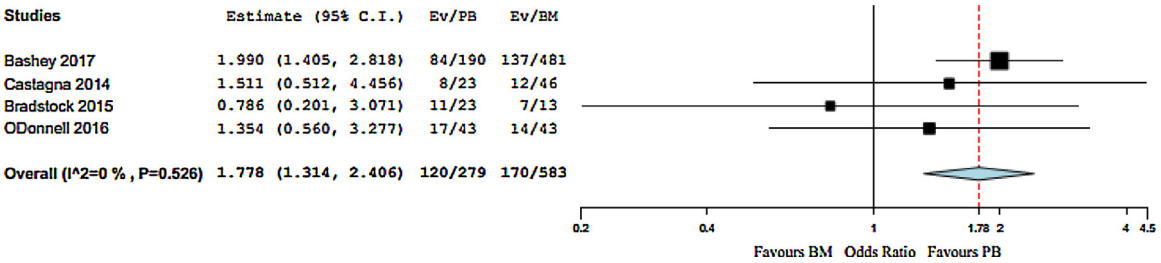

Fig. 8. GradeII-IVacute GVHD in comparing retrospective studies. A forest plot illustration.

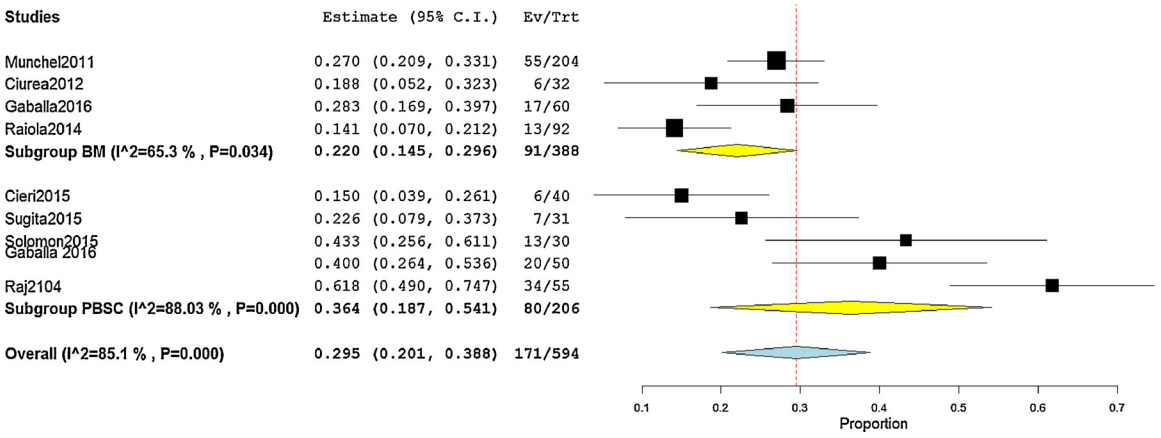

Fig. 9. GradeII-IVacute GVHD in single-arm studies. A forest plot illustration.

choice, in haploidentical HSCT patients using PTCy. The results of our study are partially consistent with previous a meta-analysis examining the effects of PBSCT and BMT in MUD and MRD patients of hematological malignancies.

Our study demonstrated that PBSCT is associated with a higher engraftment rate compared to BMT. It is well known that PB consists of a higher content of mononuclear cells, CD34+ stem cells and T cells compared with BM, which may lead to faster engraftment and immune reconstitution. Wu and colleagues (Wu et al., 2015) also revealed the superiority of PBSCT compared to BMT, which is consistent with our results. Several studies also revealed that PBSC presented a shorter time of neutrophil and platelet recovery.

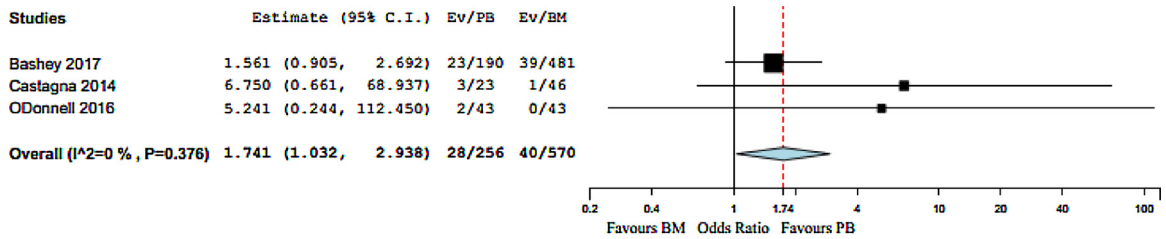

Fig. 10. Grade III-IVacute GVHD in comparing retrospective studies. A forest plot illustration.

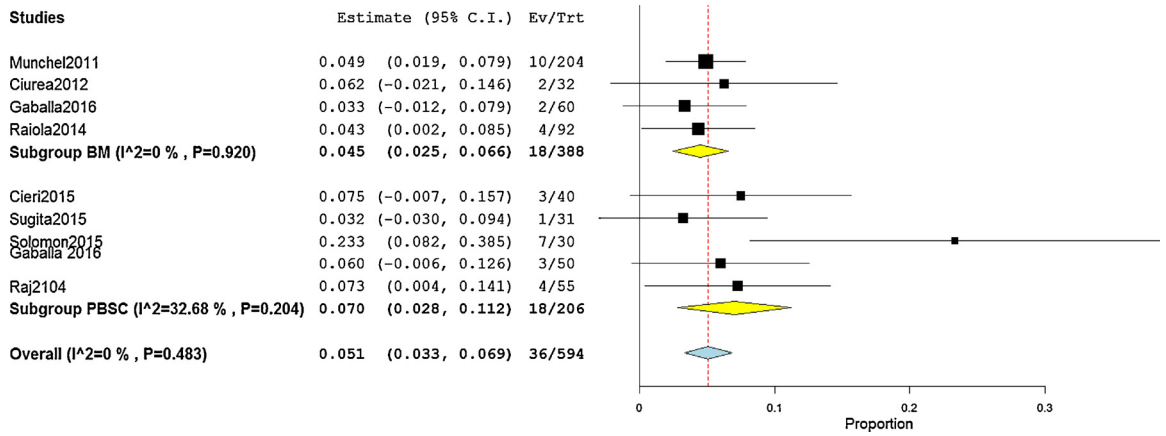

Fig. 11. Grade III-IVacute GVHD in single-arm studies. A forest plot illustration.

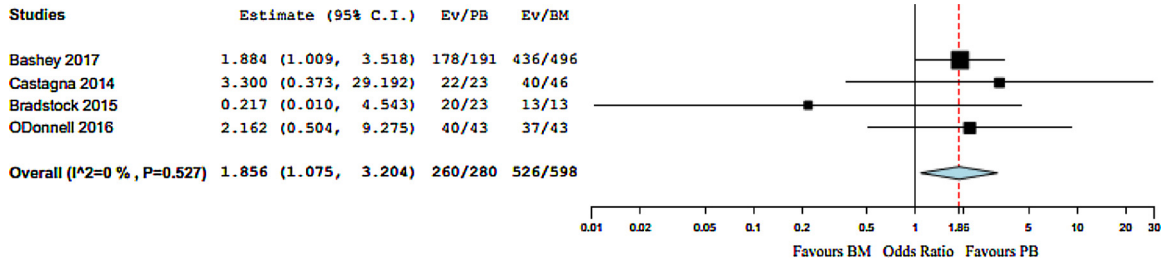

Fig. 12. Engraftment rate in comparing retrospective studies. A forest plot illustration.

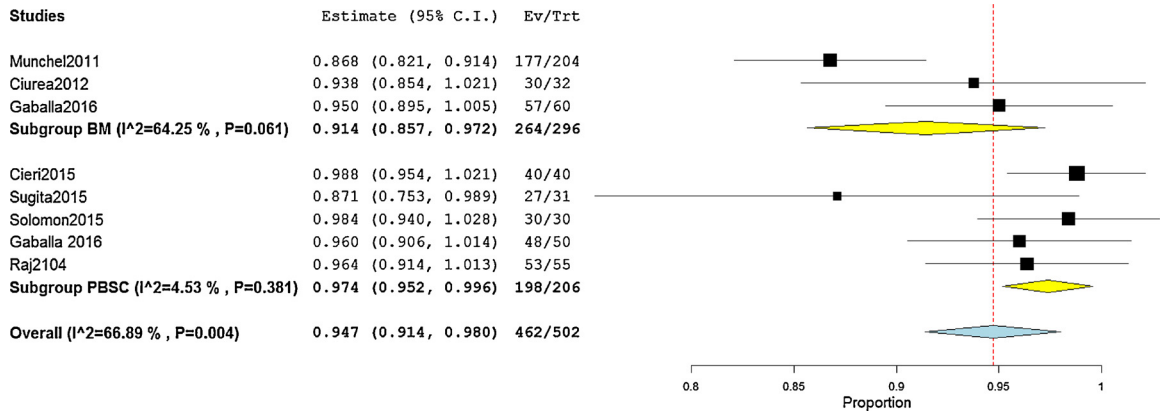

Fig. 13. Engraftment rate in single-arm studies. A forest plot illustration.

With regard to the pooled engraftment rates of single-arm studies in our report, no significant differences were found. Importantly, Sugita's study differs from other studies among PB arm, as shown in the forest plot (Fig. 13). On the one hand, Sugita's study presents the widest CI, which may be attributed to the small sample size. On the other hand, Sugita's study presents the lowest engraftment rate among all included studies in PBSC arm. Given these reasons, we pooled the data again by removing Sugita's study to investigate the stability of our results. The uniform results were still obtained (engraftment rate in PBSC arm, 0.978, 95%CI 0.956-0.999; engraftment rate in BM arm, 0.914, 95%CI 0.857, 0.972, no significant difference was found between single-arm PB and BM group, Supplementary material Fig. A5), which indicates that our results are stable and replicable.

The pooled data reveals that acute GVHD is significantly more likely

to occur in patients receiving PB compared with patients receiving BM. In addition, it is notable that the incidences of chronic GVHD are not significantly different between the two arms; this finding is not completely consistent with previous meta-analysis. Zhang and colleagues (Zhang et al., 2012) demonstrated that PBSCT is associated with a significant increase in the risk of acute GVHD and chronic GVHD. Holtick (Holtick et al., 2015) also found that PB was associated with significantly higher chronic GVHD than BM. Importantly, the number of T cells is ten times higher in PB than in BM. It is clear that the high concentration of CD34+ and T cells in PB not only leads to more rapid neutrophil and platelet engraftment but also may induce stronger GVHD (Cao et al.,2005; Hassan et al., 1996), which interprets the previous outcomes. However, PTCy is extensively used in haploidentical HSCT and is not usually used in MUD or MRD transplantations. It has been proven that Cy presents favorable immunosuppressive properties in the suppression of GVHD, especially after the transplantation, by killing rapidly proliferating cells, especially those in G1 and S phases (Mayumi et al., 1986). Wachsmuth and his colleagues(Wachsmuth et al.,2017) indicated that this reduced functionality of persisting alloreactive T cells may be due in part to the significantly increased frequencies of CD4+CD25+Foxp3+ T cells found in PTCy-treated mice by day +21. In addition, PTCy-treated mice were resistant to reinfusion of 40 or 120 $\times 10^6$ splenocytes at +120-150 days, which supported active suppression being a mechanism underlying the efficacy of PTCy. Based on above reasons, PTCy may kill partial T cells and lead to active suppression in PB so that the high content of T cells did not result in significantly higher chronic GVHD compared to BM, which partially explains the reason why no significant difference was found in chronic GVHD between the two groups.

There are some limitations in our meta-analysis. First, 12 out of the 14 adult studies included were retrospective cohorts that may have had potential confounders and exhibited relatively higher heterogeneity. Second, the sample size of some trials was relatively small, resulting in wide CIs in our meta-analysis. Third, the baseline varied among the studies involved, which indicated that the composition of disease, age, and therapeutic regimens may not be the same. Lastly, the outcomes reported varied among studies, which set barriers for pooling data. Thus, further studies with high methodological quality, such as larger sample sizes, randomized and controlled trials and direct comparison of different graft sources, are needed to investigate the optimal graft source in the haploidentical HSCT.

Based on our study, PB presents superiority in the engraftment rate compared to BM and no significant differences were found on other outcomes, such as OS, DFS, chronic GVHD, relapse and NRM, between the two arms. Furthermore, PB provides a convenience to both doctors and donors, and ensures the safety of the donor, which appears to be more cost–effective.

5. Conclusion

We concluded that the efficacy of PB is not inferior to BM for patients undergoing haploidentical HSCT using PTCy with regard to the primary outcomes, including OS, DFS and relapse. However, with regards to convenience and pain relief, PB graft is suitable for haploidentical HSCT, but with a higher risk of acute GVHD.

Conflict of interest

The authors declared no conflict of interest. The authors are responsible for the content and writing of this article.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.critrevonc.2018.05.017.

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