

Impact of Donor and Recipient Sex and Parity on Outcomes of HLA-Identical Sibling Allogeneic Hematopoietic Stem Cell Transplantation

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ABSTRACT

Allogeneic hematopoietic stem cell transplantation (SCT) may cure patients with hematologic malignancies, but it carries significant risks. Careful donor selection is an important component of the clinical transplantation decision-making process and includes evaluation of HLA typing and other criteria, the most controversial of which is parity. We examined the effect of donor sex and parity on outcomes of HLA-identical sibling SCT. Because the effect of recipient sex/parity has never been explicitly evaluated, we also analyzed the effect of recipient sex/parity on outcomes of transplantation. We found that (1) parous female donors result in an increased risk of chronic graft-versus-host disease (GVHD) in all recipients, (2) the magnitude of this increased risk is similar in male and female recipients, and (3) nulliparous female donors increase the risk of chronic GVHD in male recipients to a degree comparable to that from parous donors. A decrease in the risk of relapse was not observed, and there was no effect on overall survival, acute GVHD, or transplant-related mortality. Recipient parity had no independent effect on any endpoint. Until the effects of pregnancy on the maternal immune system are better understood, it is appropriate whenever possible to avoid parous female donors and to choose male donors for male recipients in HLA-identical related donor SCT.

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KEY WORDS

Allogeneic stem cell transplantation • Graft-versus-host disease • Pregnancy

INTRODUCTION

Allogeneic hematopoietic stem cell transplantation (SCT) is a curative therapy for patients with hematologic malignancies but results in significant morbidity and mortality. Donor selection is an important way that the risks may be decreased and is therefore a key component of the clinical practice of transplantation. In general, HLA-identical siblings are the preferred donors, but some patients have more than

one HLA-matched sibling. Thus, it is important to understand the contribution of donor factors other than HLA matching to outcomes after SCT. Criteria proved or hypothesized to affect outcomes after SCT include age, cytomegalovirus (CMV) serostatus, ABO compatibility, and sex and parity. Of these, sex/parity is the most controversial, and it is not clear which of these factors should outweigh the others. Some investigators have found an increased risk of acute or

Table 1. Summary of Previous Studies of Sex and/or Parity in Allogeneic SCT

Study	Year	n	Sex/Parity Combinations Considered in Study	GVHD Endpoint	Results†
Gale et al [1]	1987	2036	Sex mismatching Alloimmunized* female donor → male vs female recipients	Acute	Increased risk of aGVHD in female → male transplants vs all other combinations Increased risk of aGVHD in alloimmunized female → male vs female recipients Increased risk of aGVHD in non-alloimmunized female → male vs female recipients No increased risk of aGVHD in alloimmunized vs non-alloimmunized female → female recipients
Flowers et al [2]	1990	136	Donor sex/parity → any recipient Parous female donor → male vs female recipients	Acute	Increased risk of aGVHD in recipients of parous vs nulliparous female donor grafts No increased risk of aGVHD in recipients of parous female vs male donor grafts No increased risk of aGVHD in recipients of parous female donor → male vs female recipients
Atkinson et al [3]	1986	2534	Sex mismatching Alloimmunized donor	Chronic	Increased risk of cGVHD in alloimmunized female donors → male vs female recipients
Weisdorf et al [4]	1991	469	Sex mismatching Alloimmunized donor	Acute	Increased risk of aGVHD in all combinations other than female donor/female recipient Increased risk of aGVHD in alloimmunized vs non-alloimmunized donor into all recipients
Nash et al [5]	1992	446	Sex mismatching Donor parity/recipient sex	Acute	Increased risk of aGVHD in female recipients of male grafts and in male recipients of parous female grafts
Carlens et al [6]	1998	451	Female donor → male recipient vs all others Alloimmunized female donor vs all other combinations	Chronic	Increased risk of cGVHD in alloimmunized vs non-alloimmunized donor into all recipients
Remberger et al [7]	2002	679	Alloimmunized female donor → male recipient vs all other combinations	Chronic	Increased risk of cGVHD in male recipients of alloimmunized female donor transplants
Przepiorka et al [8]	1999	160	Donor sex Female donor → male recipient vs all other combinations Alloimmunized donor Alloimmunized donor → male recipient vs all other combinations	Acute	No effect of donor sex or parity on aGVHD
Bross et al [9]	1984	136	Sex mismatching	Acute	Sex mismatching (either direction) increases risk of aGVHD
Randolph et al [10]	2004	3238	Sex mismatching	Acute and chronic	Increased risk of aGVHD and cGVHD in male recipients of female grafts

*Alloimmunized refers to previous pregnancy or transfusion.

†aGVHD indicates acute graft-versus-host disease; cGVHD, chronic GVHD.

chronic graft-versus-host disease (GVHD) associated with donor parity [1-7], although it is uncertain whether this risk applies just to male recipients or to all patients. Conversely, in other studies, parity was

not a risk factor for GVHD [8]. Further, some studies have focused on sex mismatching only, without incorporating parity [9,10]. These results, summarized in Table 1, are generally from single centers, contain small

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