

## CASE WITH COMMENTARY

### When Is It Appropriate to Put a Live Donor at Risk to Help Another Patient?

Commentary by Anjay Khandelwal, MD

#### Abstract

This article considers the nature and scope of ethical decision making in monozygotic sibling (MZS) skin grafting. Although rare, identical twin-to-twin skin grafting has been reported with excellent survival rates in burn patients. Of 16 cases published to date, only a few address the ethical decision making process that is involved with monozygotic sibling skin grafting; this article discusses clinical indications and ethical challenges.

#### Case

Shara, age 16, has been in the burn unit as a patient of Dr. Fran for 3 days, with mostly third-degree burns covering 85% of her total body surface area (TBSA); her neck, groin, axilla, and some spots of her scalp are not burned. She has had one surgery to excise the burn but is scheduled for several more. She's responding well to fluid administration and is currently intubated and sedated.

During teaching rounds, Dr. Fran explains to the students that once tissue debridement is complete, Shara will need about 15 more graft surgeries during a 4- to 6-month stay in the unit. If there are complications, such as infections, she will likely need to stay longer. "Now an interesting thing about Shara," Dr. Fran continues, "is that she has an identical twin sister who could be a potential skin donor. Her name is Alia. A decision we need to make about this patient's care is whether and how to talk with Shara, Alia, and their parents about the possibility of recruiting Alia to donate skin."

One student asks what would be involved. Dr. Fran clarifies, "We would need to harvest Alia's skin from both her legs and back. Removing from Alia the amount of skin we'd need for Shara means that Alia would suffer a lot of pain and become, for all intents and purposes, a second critical wound care patient. That is, the required amount of skin removal from Alia's legs and back would result in the equivalent of substantial TBSA second-degree burns, infection risk, and pigment changes. If Alia would agree to taking on this pain, risk, and hospital stay with her sister, the benefit to Shara, if all goes well, would be a reduction in risk for possible complications: isografting (grafting using genetically identical tissue), like autografting (grafting using the patient's own tissue), would avoid immunologic responses seen with allogeneic (nongenetically identical) tissue and lead to greater long-term graft acceptance. In addition, Shara's hospital stay

would likely be reduced to less than 2 months with only 5 to 6 surgeries, since she will not require the additional procedures to harvest skin. Reduced hospital time and not utilizing cadaveric tissue would probably reduce exposure to infection. Overall, it could be a good option to reduce risk of graft failure, pain, and infection, among other complications.”

One student, Min, who has met Shara’s family, adds, “I’ve learned that Shara’s family members are recent immigrants. I don’t know about their insurance status, but my guess is that the decrease in costs that would probably accompany a shorter hospital stay, at least for Shara, if all goes well, could be an important factor for this family. I don’t know whether it would be appropriate to bring that up during a discussion with them, however.”

“Thanks for adding those important points, Min,” Dr. Fran responds. “So, team, if you were me, how would you help this family understand the risks and benefits of the different options? How would you talk to Shara about this? What would you say to Alia?”

### **Commentary**

The term “identical twin-to-twin skin grafting” has been used in the past to describe instances in which an identical twin has donated skin to assist with skin grafting to cover large total body surface area (TBSA) burns sustained by his or her identical twin. However, in light of several case reports involving triplets,<sup>1,2</sup> the author proposes to use the term monozygotic sibling (MZS) skin grafting.

A review of the literature identified numerous reports of MZS skin grafting, although only 5 of 18 published articles discussed ethics, and the 16 articles with multiple patients mostly focused on pediatric cases and revolved around the issue of informed consent.<sup>1-16</sup> Only one article addressed multiple complex ethical issues in a pediatric case.<sup>15</sup> Here, we discuss clinical indications and ethical challenges relevant to MZS skin grafting in the case scenario involving a pediatric patient.

### **Skin Grafting for Burn Care**

Before exploring the ethical challenges, it is imperative to first understand the role of skin grafting in modern burn care. The process of early excision of burns with skin grafting has had a great impact on outcomes, given that early wound closure reduces morbidity and mortality.<sup>17</sup> Wound coverage can be achieved by various methods and can be temporary or permanent. Nonbiological temporary coverage involves the use of dressings, while the more common biologic temporary coverage can be accomplished through the use of *xenografting*, *allografting*, or the use of skin substitutes. Xenografting refers to transplantation of tissue grafts from one species—most commonly porcine in the United States—to another. Allografting involves transplantation of tissue grafts from a genetically nonidentical donor of the same species. For burn patients, the most

common form of allograft is a cadaveric allograft. Permanent wound coverage can only be achieved either by allowing the wound to close itself through scarring, which is not ideal, or by *autografting*, the transplantation of tissue from one part of a body to another part of the same body, or *isografting*, the transplantation of tissue to another genetically identical body. Unfortunately, because skin is the most immunological organ in the body, autografting—or MZS skin grafting, in which the genetic make-up of both bodies is identical—represents the only viable option for permanent wound closure, which decreases a patient’s morbidity and mortality risks from a burn injury. Xenografts or allografts are used for burn patients with large TBSA injuries. For example, patients with 75% TBSA burns have, at the most, 25% of their skin that can be used for autografting, but that’s only in cases in which patients’ remaining skin is suitable for harvesting, which is often not the case. Patients with large TBSA burns simply don’t have enough skin to cover their wounds. Surgeons must then wait for harvested sites to heal, which can take as long as three weeks, so that they can “re-harvest” those sites, repeating this process until the wounds are healed. In the interim, xenografts and allografts are used for temporary coverage of the wounds. During this time, due to a severe systemic metabolic insult and risk of infection, patients must be kept in an intensive care unit setting.

In the case scenario, it could be assumed that Shara, with an 85% TBSA burn, only has about 6% to 7% TBSA of skin that is useful as donor sites (assuming that Alia does not serve as a skin donor). Even expanding her harvested skin would only cover perhaps 15% of her body, and therefore the team would still potentially have to wait 2 to 3 weeks to re-harvest her donor sites—to cover another 15% of her body—and this process would need to be repeated until her body is completely covered. The need to repeatedly harvest patients’ skin while allowing the donor sites to heal in the interim leads to extended hospital stays. In addition, the longer the wounds are not completely covered, the longer the patient’s body is tormented by a massive catabolic and inflammatory response. For these reasons, MZS skin grafting, if indicated, should be considered as an adjunct or alternative to autografting.

### **Indications for MZS Skin Grafting**

Unlike traditional organ transplant recipients, whose life depends on whether they receive a transplant, burn patients can survive without MZS skin grafting, albeit at a significant physical cost. Survival and nonsurvival are not two absolutes in this case but represent two ends of a spectrum, with varying degrees of functional impairment and cosmetic alteration in between. When entertaining the notion of MZS skin grafting, the survival, functional, and [cosmetic benefits](#) must be considered in that order.

Although mortality statistics based on age and TBSA burn are available to determine the potential benefit to the recipient, the likelihood of mortality is in constant daily flux for the severely burned patient, and therefore it is difficult to pinpoint a single number upon which to base decisions. From my review of the records of previously reported cases, I

estimated that the projected mortality rate of MZS skin grafting, based on TBSA burn—calculated after the cases were individually reported—ranged from 4.6% to 67.5%, although the end result was that there was 100% survival in all the patients (A.K., unpublished data). Although it is an important question for burn surgeons, it is beyond the scope of this review to discuss at what predicted mortality rate MZS skin grafting should be considered and, even then, the risk of mortality should not be the only or even the primary factor in considering MZS skin grafting.

The main benefit of MZS skin grafting would likely be a significantly shortened time to wound closure, which decreases the likelihood of developing complications commonly associated with a burn injury (eg, sepsis and multi-organ dysfunction) and hence reduces the risk of mortality seen in the later phases of a burn patient's hospitalization.<sup>17</sup> In addition, the recipient would likely undergo far fewer surgeries and his or her hospital stay and hospital costs would be reduced.<sup>17</sup> All of these factors combined would likely lead to improved quality of life for the patient—a benefit that cannot be measured numerically. In Shara's case, MZS skin grafting would likely result in far fewer surgeries and a shorter hospital stay. With an anticipated shorter time to wound closure, she would also face a far less catabolic and inflammatory response, potentially decreasing her risk of morbidity and mortality.

From an ethical viewpoint, the clinician's focus is mainly on the risks to the donor. There are no medical benefits to the donor and, although difficult to quantify, there are inherent medical risks and consequences in harvesting skin, including but not limited to anesthetic risks, [severe pain](#) (which may be prolonged), infection, and permanent scarring or altered pigmentation. These risks must be balanced against the psychological and emotional benefits to the donor such as being responsible for saving a sibling's life, as in Alia's case. At the same time, in the event the skin graft fails or the recipient succumbs to his or her injury, the donor might experience guilt as a result of self-blame or being blamed by family members and friends. This potential negative psychological impact must be weighed against both the benefits of donating and the potential negative psychological impact of not donating if the patient has complications or even succumbs to his or her injury. In addition to experiencing guilt, the donor might also feel neglected or unappreciated, as attention focuses on the more critically ill recipient.<sup>18</sup> In Alia's situation, the risk to her would likely be limited to potential anesthetic or surgical complications and a small risk of infection postoperatively. The most significant factor for her would be pain from the donor sites, which, although not to be trivialized, might not outweigh the psychological benefits of saving her sister's life.

Timing is of utmost importance in cases of large TBSA burns. Unlike most situations involving organ transplantation, in which the donor's medical condition is relatively unchanged on a daily basis, the medical condition of a burn patient is in constant flux. Although historically most cases of MZS skin grafting were performed later in the

hospital course, achieving early wound closure in a burn patient is of paramount importance and can translate into significantly decreased morbidity and mortality.<sup>17</sup> In the above case, if Alia were to donate her skin, the medical team should consider this option sooner rather than later, as time is of the essence for a patient with a large burn injury.

### **Comparison of Skin Grafting and Organ Transplantation**

Skin grafting is not considered an organ transplant. In accordance with the Organ Procurement and Transplantation Network (OPTN), transplant organs are vascularized tissue such as the heart, lungs, kidneys, and pancreas. In recent times, transplant organs have expanded to vascularized composite allografts (VCAs), including limbs and the face.<sup>19</sup> Cadaveric skin allografts are grouped under human cells, tissue, and cellular and tissue products.<sup>20</sup>

Skin grafting and organ transplantation also differ in terms of regulation. While cadaveric skin allografts are regulated by the Food and Drug Administration (FDA), conventional organ transplantation is regulated by the Health Resources and Services Administration. Importantly, surgeons are not required to take any additional training to perform skin grafts beyond their basic surgical training in either general or plastic surgery. Moreover, skin grafting does not have to be performed in a hospital that meets Centers for Medicare and Medicaid Services (CMS) conditions of participation for organ transplant programs.<sup>21</sup> In fact, many hospitals that are not considered burn centers by the American Burn Association (ABA) nonetheless treat burn patients.<sup>22</sup>

### **Respect for Autonomy in Skin Grafting**

Although a skin graft is not considered an organ transplant, many of the ethical principles relevant to organ transplantation, including respect for autonomy, pertain to skin grafting.

*Living donor advocate.* In 2007, federal regulations mandated that transplant centers have either an independent living donor advocate (ILDA) or a donor advocate team,<sup>21</sup> and, in 2015, the American Society of Transplantation's Living Donor Community of Practice (AST-LDCOP) provided recommendations for the ILDA role.<sup>23</sup> Among other things, these guidelines recommended that: (1) the ILDA must have a certain skill set rather than a specific profession, (2) the ILDA must be educated and demonstrate competence in core knowledge components, (3) the ILDA's primary role should be to assess components of informed consent, and (4) transplant centers must develop a transparent system to define ILDA independence.

Although skin grafting does not fall under the purview of the OPTN, it is certainly justifiable that all MZS donors, adult and pediatric, have an ILDA and that the AST-LDCOP's recommendations be upheld, as skin donors are donating an organ and are

subject to risks and benefits that are similar to those of traditional organ donors. In both MZS skin grafting and organ donation, the medical team might tend to prioritize the recipient or there might be some degree of coercion of the donor. In Alia's case, an ILDA should be appointed and be present for all discussions related to the process of MZS skin grafting, including the conversation during which her assent and her parents' consent to the procedure is given.

*Informed consent.* For pediatric patients, legally, parental permission is all that is required for consent to clinical treatment, although from an ethical standpoint the [minor's assent](#) should also be obtained. The Worldwide Network for Blood and Marrow Transplantation (WBMT) supports that minors can physically and ethically participate as hematopoietic stem cell donors.<sup>24</sup> This recommendation is reiterated by the American Academy of Pediatrics (AAP) and the World Marrow Donor Association (WMDA), although they call for (1) an unbiased health screening and consent process with the parents performed by physicians or equivalent health care practitioners who are not involved in the care of the sibling and (2) assessment of the relative risks and benefits of collection from a given donor by an ILDA, who might not be the health professional screening the patient.<sup>25,26</sup>

The risks of hematopoietic stem cell transplantation, however, are significantly less than the risks of solid organ donation. The American Academy of Pediatrics has put forth five criteria for determining when children may ethically serve as solid organ donors.<sup>27</sup>

1. The donor and recipient are both highly likely to benefit.
2. Surgical risk for the donor is extremely low.
3. All other deceased and living donor options have been exhausted.
4. The minor freely assents to donate without coercion (established by an ILDA).
5. Emotional and psychological risks to the donor are minimized.

Most of these criteria are applicable to MZS skin grafting, although it might not be feasible to exhaust all other deceased donor options, as doing so would consume time and, as mentioned previously, potentially lead to greater morbidity and mortality. Assent of the minor in these situations would require both an explanation of the proposed treatment that would be congruent with the minor's understanding and solicitation of the minor's willingness to accept the proposed care. It is also plausible that the ILDA's opinion could conflict with that of the parents or medical team, in which case referral to the hospital's ethics committee should be considered.

## Conclusion

Overall, the ethical dilemmas in MZS skin grafting are numerous. They revolve mainly around risk-benefit and quality of life analysis as well as respect for autonomy as manifested in appointment of an ILDA and informed consent for the donor and recipient. Although skin grafts are not considered organ transplants, many of same ethical principles governing organ transplantation apply to MZS skin grafting and must be taken into consideration. Early and appropriate involvement of ethical and legal teams, as well as providing an ILDA, is of paramount importance.

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