Moral and Ethical Issues in Living-Donor Liver Transplant in Egypt

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Abstract

Objectives: **Since brain-death criteria are not accepted in Egypt, only organs acquired from living donors can be used for transplant. Our objective was to highlight the ethical issues raised by living-donor liver transplant.**

Materials and Methods: **The study was conducted by reviewing publications from centers performing living-donor liver transplant in Egypt and by consulting with a group of experts in the fields of liver transplantation, clinical ethics, and religious scholarship.**

Results: **The first successful living-donor liver transplant in Egypt was performed at the National Liver Institute in 1991; however, this program did not continue because of poor early results. In August 2002, transplants began at Dar-Al-Foaud Hospital; since then, almost 500 cases of living-donor liver transplant have been performed at 9 centers. Although the donor risk is estimated to be low, 2 donors died (0.4%). The ethical principle that best applies to living-donor liver transplant is *primum non nocere* (first, not to harm), as the donor derives emotional benefit from donation and the opportunity to save a life. It is important to stress that the alternative to living-donor liver transplant in Egypt is not deceased-donor liver transplant. There are no doubts that this is a beneficial procedure for the recipient with acceptable risks to the donor.**

Conclusions: **It is ethically appropriate to perform liver transplant using living donors.**

Key words: *Donor, Recipient, Autonomy, Informed consent, Voluntarism*

An increasing number of centers worldwide are starting to perform living-donor liver transplants for selected patients. This provides potentially life-saving therapy to many patients who otherwise would die awaiting organs from deceased donors (1). In Egypt, living-donor liver transplant has been performed more frequently during the past few years, driven by the absence of a law that permits use of deceased donor organs and by the need to decrease mortality of patients with end-stage liver disease. Because of the risk that donors are exposed to, various medical and ethical issues are raised (2).

Donors are confronted with a major operation, and they incur a considerable health risk without any potential health benefit. Although many studies have considered the medical or anatomic criteria for donor selection, few studies have examined the moral and ethical issues related to living-donor liver transplant (3). Until now, there has not been systematic in-depth research on the donor's motives before transplant.

The objective of this study was to highlight the moral and ethical issues raised by living-donor liver transplant in Egypt. Knowledge of these issues would advance the understanding of this unique situation, contribute to more-precise donor evaluation, and provide tools for preventing psychosocial complications.

Materials and methods

This study was conducted by reviewing publications from centers performing living-donor liver transplant in Egypt (4-6) and by consulting with a group of 10 experts selected for their experience and

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expertise in the fields of liver transplantation, clinical ethics, and religious scholarship. The experts included 5 transplant surgeons, a hepatologist, a pediatric hepatologist, and 3 religious scholars. Discussions were held to examine the moral issues and ethical concerns of living-donor liver transplant in view of the absence of a law that permits deceased donor organ donation in Egypt.

Donor Selection

When potential donors present with the willingness to donate, the transplant team first explains to the donors the risks they will be incurring and the implications of their decision on the recipient. Donors should make their decisions voluntarily; they are advised that they can withdraw without explanation up to the moment of anesthesia. The basic requirements that the donor must fulfill include age between 18 and 55 years and either a spouse or a family member within the third degree of consanguinity with the recipient. The donor-recipient pair must be blood-group identical or compatible.

Most centers in Egypt divide donor evaluation into 3 phases. In the first phase, the potential donor is evaluated to ascertain compatibility of blood type, medical history, body size, general condition, and psychosocial circumstance. More than one-half of all potential donors are excluded during the first phase. In the second phase, the potential donor undergoes a complete history and physical examination, psychosocial evaluation, electrocardiogram, chest radiograph, laboratory tests, and one or more imaging studies to assess the liver size (hepatic mass) and vascular supply. Ultrasound with Doppler, magnetic resonance imaging, and computed tomography have been used for these purposes. The third phase is devoted to invasive procedures required to investigate potential problems discovered during the first and second phases. These procedures may include liver biopsy to assess for hepatic steatosis, hepatic angiography to assess arterial and venous drainage, endoscopic retrograde cholangiopancreatography to assess biliary tract anatomy, and additional consultations or procedures.

Data Analysis

Because of the lack of standardized means to examine living donors' motivation, moral issues, and ethical issues, qualitative methodology is the appropriate scientific method for describing, understanding, and explaining or interpreting ethical issues and other complex phenomena of psychosocial or psychological natures. Findings are not expected to be statistically projectable.

Results

The first successful living-donor liver transplant in Egypt was performed at the National Liver Institute in 1991; however, this program did not continue because of poor early results. In August 2002, transplants began at Dar-Al-Foaud Hospital; since then, almost 500 cases of living-donor liver transplant have been performed in 9 centers. Although the donor risk is estimated to be low, 2 donors died (0.4%). In 4 major centers of liver transplant in Egypt, from August 2002 to February 2007, 326 living-donor liver transplant procedures were performed. The transplants procedures were performed in 285 adults and 41 children. In the adults, the most common indication for transplant was hepatitis C-related cirrhosis in 251 patients (88.1%); other indications included hepatocellular carcinoma (11 patients, 3.9%), hepatitis B-related cirrhosis (9 patients, 3.2%), Budd-Chiari syndrome (9 patients, 3.2%), primary sclerosing cholangitis (3 patients, 1.0%), and hemochromatosis (3 patients, 1.0%). In the children, congenital biliary atresia represented the most common indication for transplant (26 patients, 87.8%); other indications included hepatoblastoma (2 patients, 4.9%), Byler disease (2 patients, 4.9%), and congenital hepatic fibrosis (1 patient, 2.4%). Two donors died (2 of 326, 0.6%). Repeat laparotomy was necessary in 6 donors (1.8%). The 1-year survival for recipients was 68.8% (224 patients). Biliary complications occurred in 95 recipients (29.1%), and vascular complications, in 33 recipients (10.1%).

From the responses of the 10 individuals interviewed, 4 themes emerged: volunteerism and informed consent, donor-related arguments, recipient-related arguments, and family expectations.

Volunteerism and Informed Consent

Most living donors for pediatric patients are parents, and their voluntary intention is easily understood and justified. For adult recipients, parents are frequently not suitable for donation because of advanced age or underlying diseases, and nonparental donors are more common. Spouses are

the most common voluntary living donors for adult recipients. The higher risk of a more extensive donor operation and the more complex social interrelationship for nonparental donors make the process of obtaining voluntary and informed consent even more important in adult-to-adult living-donor liver transplant. It is important to exclude financial inducement before or after donation.

The primary selection criterion for a living liver donor should be volunteerism. The primary selection stage evaluates the donor's voluntary intent. The donor's social and psychological background should be evaluated by a clinical psychologist or other mental health professional. Protecting the donor's right to withdraw without external pressure by providing a medical excuse not to proceed at any stage is very important. This primary selection process should be completed before the evaluation for medical or surgical suitability commences. Screening of family members for a suitable donor, or simultaneous evaluation of several potential donors to identify the most suitable one, overemphasizes the medical criteria in donor selection and puts undue pressure on the suitable but involuntary donor.

Donor-Related Arguments

For many donors, donation is an attempt to reduce the anxiety and fear of losing a beloved person (the recipient) to a life-threatening disease. Donors expressing this argument try to gain control over feelings of helplessness and weakness toward death. In many cases, donors have experienced these feelings in the past (eg, by losing a parent). In these cases, the donation is influenced by this past experience and is an attempt to avoid the same type of trauma and gain control over the situation.

Furthermore, the wish to maintain the relationship is a common argument often expressed by partners; this also demonstrates their attempt to avoid loneliness. Surprisingly, some donors show a high level of curiosity or eagerness to take on a risk and show an openness to new experiences. The donation is not purely a means to save the recipient's life. It becomes a personal challenge and an opportunity for an exceptional experience, for personal development, to distinguish oneself, and to initiate life changes.

The idea of coping with the recipient's disease and their often extremely reduced health condition seems unbearable for many donors. In some cases, the donation is an attempt to become like the recipient by undergoing an operation and to restore the disturbed balance of the health status in the relationship. By experiencing surgery and suffering, donors feel that they can better approach and understand the recipients. Donation is a way of coping with guilt over their own health or sharing responsibility for the recipient's disease (eg, although one donor's infection two decades ago was cured, the spouse-recipient developed chronic hepatitis). A new beginning seems possible. These donors have a strong concept of justice that has to be protected or restored, and to accomplish that, they want to share their resources with the weaker recipient.

To refuse donation may be extremely threatening to the potential donor's self-image and self-esteem. Two donors who withdrew their availability to donate reported that they could not live "peacefully" knowing they probably could have saved the recipient's life by donating. Both received psychological support. Refusal to donate could raise feelings of guilt or the sense of not acting according to self-expectations or social expectations. Donors protect their personal integrity by maintaining their ideals and expectations of themselves.

Recipient-Related Arguments

Recipient-related arguments often occur in cases where the recipient is a child or young adult. The donor argues that the recipient is too young to die. An early death, depriving the recipient from experiencing and enjoying life, does not seem fair to the donor. In a similar way, other donors argue that it is not fair for older recipients to die, because they have not had the opportunity to enjoy life to the fullest, because of obligations to family or work or because of the disease itself. Donation represents a chance for the recipients to experience the pleasant side of life that they deserve and to fulfill personal wishes. These donors represent the recipients as being worthy of the donation, as they will regain time and chances.

Especially in cases of adult child-to-parent donations, the donation is a way to express love or gratitude and to honor the efforts invested in raising the donor. A further argument used by many donors is the wish to relieve the recipient's suffering. The donors often have their own experience of the rapidly deteriorating health of the recipient and develop a strong wish to comfort them.

We identified donors who take on a stabilizing role in the family. They want to protect younger family members from pain caused by the potential death of a recipient whose existence is of vital importance to them. Interestingly, this is an argument used by donors who themselves experienced the loss of a loved one in their childhood or youth.

Finally, we identified donors who justified their wish to donate with higher religious and moral principles and beliefs, or they ascribed a spiritual character to the donation. For them, donation held meaningful ethical aspects.

Family Expectations

Potential donors are usually aware of family expectations, even if the expectations are not articulated by the family members. In most cases, families restrained themselves from expressing expectations openly to potential donors, because of fears that they could pressure them to decide for donation but also because of their own ambivalence and concerns about the risk of surgery for donors.

We have formulated some guidelines to be applied for a donor's preselection within the family, as suggested by the interviewed experts.

1. In the case of more than one potential donor within the family, usually the one emotionally closest to the recipient is preferred.
2. The youngest or weakest family members are protected from donating unless there is no alternative.
3. Family members who carry more responsibility within the family or who have protective roles are preferred as donors.
4. Families usually do not consider as potential donors family members whose social and occupational life or relationships to third persons would probably severely suffer if postoperative complications occurred.

Discussion

Living-donor liver transplant for pediatric recipients was pioneered in the late 1980s and early 1990s as a way to reduce the high mortality rate of children on waiting lists for deceased donor transplant (1). After the first successful living-donor transplant of a left lateral liver segmentectomy was performed in Australia in 1989 (7), a formal prospective clinical study of adult-to-child living-donor liver transplant was performed at the University of Chicago (8). The first successful adult-to-adult living-donor transplant using a right hepatic lobe was performed in the United States in 1997 (8).

Living-donor liver transplant has aroused criticism about the risk that it imposes on healthy persons, because the goal of zero morbidity and mortality for a living liver donor would never be attainable (9). *Primum non nocere* (first, not to harm) is a tenet in medicine held most sacred by physicians. Although it is a widely held misconception that this Latin phrase is part of the Hippocratic Oath, it nonetheless is an important philosophy believed in contemporary medicine. On the surface, adult-to-adult living-donor liver transplant challenges this tenet, because a healthy individual undergoes a major operation for no physical benefit to himself or herself (10).

To date, 3 donor deaths after living-donor liver transplant have been reported in the United States, 2 of which occurred within the first postoperative month and were clearly related to the procedure, for an overall mortality of 0.15% (3 deaths in 2000 donors) (11). One donor died from complications of aspiration pneumonia, and one donor died of complications due in part to sepsis. One donor died of recreational drug use or suicide 23 months after donation (8). Worldwide, other donor deaths have been reported in Europe and Asia, but the exact number is not known. In Egypt, two donor deaths have been reported for a prevalence of 0.4% (12).

A wide range of complications in donors after living-donor liver transplant has been reported in the literature. The prevalence of complications ranged from 0% to 67%, with an overall crude complication prevalence of 31% (10). Biliary complications including bile leaks and strictures have been reported in 0% to 7% of donors. Complications related to major abdominal surgery, including wound infections, small bowel obstruction, pneumonia, and incisional hernia, occurred in 9% to 19% of donors. There have been anecdotal reports of aborted donor hepatectomy at the time of surgery as a result of unexpected findings, including the presence of significant hepatic steatosis, but comprehensive figures of such occurrences have not been collected (13).

In a study assessing donor quality of life after living-donor liver transplant, virtually all donors stated that they would donate again, irrespective of

recipient outcomes (10). Almost all donors (96%) were able to return to work by a mean of 10 weeks after surgery. A majority of donors (71%) reported abdominal symptoms several months after surgery that were attributed to surgery (10).

Three factors determine a donor's motivation under the unique circumstances concerning living-donor liver transplant: the social environment, the relationship to the recipient, and the donor's personal attitude and benefit. These factors possess their own dynamics in underlying a donor's motivation and influencing the attitudes of the recipient's family and the medical staff. Similar findings were reported concerning living kidney donors (11). Under these circumstances, the complete absence of coercion, a purely autonomous decision, or a simply altruistic attitude seems unrealistic. A situational, relational, and emotional-affective concept of autonomy seems more appropriate—and appropriately more complex—for donor evaluation (11).

Because of the possibility of living-donor liver transplant, the medical system delegates to potential donors the decision regarding life or death of a related or beloved person. The choice between donation and refusal often becomes a hypothetical one. All donors, even the ambivalent ones, tried to embed their choice or eagerness to donate in a context that is emotionally and ethically meaningful for them and that can help them follow through with their decision. Highly motivated, unambivalent donors seem to create a coherent context for their decision under the given circumstances, albeit to a varying extent among individuals. In contrast, ambivalent donors' justifications seem inconsistent, contradictory, and not rewarding. A mature donor-recipient relationship seems to provide a meaningful and mutually beneficial context in which to embed donation and to view living-donor liver transplant as a worthwhile opportunity. Nevertheless, donors expressed further motives, reported in part by previous authors (13). We identified 2 important issues, namely,

1) What constellations of motivation offer a sufficiently strong basis for donors to justify their decision for donation and to cope with the transplant process and any outcomes? and

2) Which motives are the medical system and society ready to accept? The study's results support the belief that assessment of the donor's motivation and autonomy should focus on 3 key aspects: the donor-recipient relationship; benefit to the donor (emotional, moral, or other); and the family dynamics (13).

Clinicians must be aware that the medical staff itself takes part in the dynamics of decision making around living-donor liver transplant and has a decisive influence on who is selected as a donor and how a potential donor makes the decision for or against donation. It is necessary to create an adequate environment for donors to express fears, doubts, or anxiety. In each case, clinicians should maintain an adequate emotional distance and bear in mind the medical and psychosocial risks of living-donor liver transplant and the imbalance of power between physician and patient (10). We agree that the professional who provides informed consent for donation or who evaluates donors and their families psychosocially should be a neutral third person (11).

Furthermore, clinicians should also be able to express their doubts if a donation appears too risky. Not only potential donors but also medical staff at transplant centers can be subjected to the pressure of living-donor liver transplant dynamics (eg, staff can experience pressure from families who see living-donor liver transplant as the only alternative to the recipient's imminent death) (14).

The benefit received by the donor is basically psychological, because he or she feels rewarded by the satisfaction of having helped save the life of a loved one. In a broader context, this satisfaction is experienced not only by the donor but by the entire family, including extended family members and friends. Society likewise benefits when a disabled person with end-stage liver disease is able to return to productive life after successful liver transplant. In Asia, where the family systems are particularly closely knit, living-donor liver transplant has become a novel way of strengthening the social dynamics that keep families together (14).

Unlike the situation in the United States, where organ donation from living donors who are absolute strangers to recipients has been accepted (12), donation of liver grafts only from relatives or spouses is the accepted practice in Egypt. In Japan, a country where donation from living donors has been the sole option for liver transplant and where relationships are not defined by law, organ donation from living donors has long been widely accepted by the public. The only requirement stipulated by Japanese law is

that the transplant program undergo evaluation and approval by the respective ethics committee of each institution. So far, liver donation from a living yet unrelated donor (unrelated by blood or marriage) has not been reported from Japan. Similarly, in Korea, the law does not restrict the relationship between the donor and recipient; however, commercial transactions (ie, trade or purchase) are strictly prohibited (12).

Although the demand for living-donor liver transplant is perhaps higher in Egypt than in Europe and the United States, the ethical principles governing the act of living donation (15) should be the same everywhere. The autonomy of the donor's decision based on informed consent should be respected. For this reason, the physician is obliged to provide objective and unbiased information to the donor regarding the risks and benefits of living-donor liver transplant. It is on the basis of this information that donors should make their decisions. A thorough psychological assessment is an essential part of the process of donor evaluation, to guard against any form of coercion on the potential donor to donate. Certainly, the virtues of charity, altruism, generosity, sincerity, and magnanimity that come into play in the donation process are not measurable. However, potential donors who demonstrate intelligent and sound judgment should probably be given the opportunity to give something of themselves, provided that they understand the risks of donation (1). If the donor operation can be performed while minimizing risk, the indications for transplant are clear, and the living donor gives voluntary informed consent, living-donor liver transplant is justified. Moreover, the practice is self-perpetuating, because as outcomes improve, more people become aware of the feasibility of this transplant option, and donor volunteerism is encouraged. Just as health care providers are bound to do no harm, they are also expected to do the best that their talent and expertise allow, and they are continuously honing their skills and improving their knowledge to better serve their patients. On the part of surgeons, the temptation to perform living-donor liver transplant for motives that are more egocentric than altruistic may exist (10). Ultimately, it is the surgeons' responsibility to act conscientiously in the practice of their profession. This is a universal ethical principle of professional practice that perhaps is more crucial in the context of living-donor liver transplant, because the demand is increasing and the mandate of the public already exists (12).

Two important issues involve deciding what constitutes an acceptable risk of mortality to the donor and who determines what level of risk is acceptable. In medicine, we draw comparisons to similar procedures that are considered acceptable. The perspectives of the potential recipient and donor are important to consider in living-donor liver transplant. The donor must be informed of the risks associated with the procedure. Coercion of the donor should be excluded during an independent, confidential evaluation. But what mortality rate is acceptable when the donor understands the risks and coercion has been excluded? Donors may be willing to accept high rates of mortality if the life of a loved one is in jeopardy. Risk incurred by the donor must be balanced against what is acceptable to society and the medical community and the burden that the recipient is willing to bear (11).

The possibility of being unable to transplant the graft into the intended recipient because of intraoperative death or other causes should be covered in the preoperative consent discussion with a potential donor. In addition, the possibility of this situation arising should be included in a prospective protocol at all institutions performing adult-to-adult living-donor liver transplant (14). Clearly, if the recipient has a high probability of intraoperative death, the operation should not be undertaken. In any case, to address the possibility of unforeseen complications arising during the operation, the sequence of steps in the operation should be structured to avoid removal of the donor graft until the recipient hepatectomy has been performed and the recipient's survival is likely (14). Despite these safeguards, if the recipient dies intraoperatively and this possibility has not been covered in the preoperative consent discussion, the surgical team must obtain oral and written consent from the donor or the donor's family to reallocate the organ (14).

Conclusions

In Egypt, where deceased donor grafts are not available, the demand for living-donor liver transplant will continue. However, there are significant risks to the living donor, including the risk of death and substantial morbidity, that must be taken into account before patients, physicians, and

transplant programs embark on living-donor liver transplant. It is important, therefore, to uphold the highest medical and ethical standards in the programs' transplant practices to obtain maximum benefit for both donor and recipient. On the basis of our results, we suggest that preoperative and postoperative psychosocial evaluations of all donors should be mandatory in all transplant programs, and such evaluations should have a role in ensuring high-quality care and in maintaining ethical standards in living-donor liver transplant.

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