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# RISK MATTERS



# Organ Transplantation – Improving Life and Reducing Risk

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Transplantation is necessary for patients who suffer from life-threatening organ failure, including, for example, kidney, heart, lung, pancreas, liver failure or severe blood disease. Impaired function of organs can also cause various associated diseases and restrictions in life. This problem could also be solved by replacing damaged organs with healthy and functioning organs that prevent further complications.

# **History of transplantation**

The first experiments in exchanging diseased body parts for healthy ones were probably discussed as early as 600 B.C. By the sixteenth century surgeons had notable success with skin replacement. The first to try kidney transplantation from human to human was surgeon Yu Yu Voronoy in the Ukraine in 1933.<sup>1</sup> Unfortunately, many mistakes during Voronoy's experiment, such as blood group mismatch, and a big gap in time between the surgery and the donor's death, led to failed surgery. Voronoy tried various other procedures, none of which resulted in a successfully functioning transplantation.<sup>2</sup> The first successful kidney transplantation took place on December 23, 1954 and was done by Joseph Murray.<sup>3</sup> The success of this surgery was a great inspiration for several other surgeons, not only for kidney transplants but also for undergoing other organ transplantations.

# **Transplantation today**

With the help of better medical technologies, such procedures as advanced immunosuppressive therapies, strong monitoring of transplant patients after surgery, kidney and bone marrow transplantation, became usual in medical care units. Two of the main problems in transplant surgery are, first, the difficulty of finding a matching donor and then the immunosuppression therapy post transplantation. On the one hand, patients with an organ transplant have a better survival rate than people who take medicine for a failing organ or who are on dialysis.<sup>4</sup> However, even with huge medical improvements and new medical technology over the years, studies and registries show that some types of transplantation surgery – such as lung and heart-lung transplants – have a poor outcome after a few years. According to the International Society for Heart and Lung Transplantation (ISHLT), the median survival rate for a lung transplant after



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five years is approximately 54%.<sup>5</sup> The mortality rate for heart-lung transplantation is even worse than lung transplantation. Nowadays, it is known that increased mortality rate, infection rate and graft failure is significantly higher in the first few years after any organ transplant.<sup>6</sup> Predicting the long-term outcome of an organ transplant in the early days after the procedure is an impossible thing to do in many cases. Making an underwriting decision at that stage will require substantial safety margins. Therefore, it seems more reasonable to postpone such cases until a more reliable prognosis can be made. Transplant patients can live a long time with the donor organ, but at some point (approximately 20 years) rejection, re-transplantation and mortality rate increases significantly. One study found that most survivors after 20 years of transplantation had a high cardiovascular risk, chronic kidney disease with low glomerulus filtration rate and renal insufficiency of different stages.7

#### Transplantation: ups and downs

A great advantage of organ transplantation is that patients can have a relatively normal and healthy quality of life. Studies have found that patients with a kidney transplant have lower mortality rate and better quality of life than patients who undergo dialysis. Moreover, constant dialysis causes severe problems when patients have additional diseases, such as cardiovascular disease, hypertension or diabetes mellitus.8 However, organ recipients need lifelong immunosuppression therapy because the recipient could react at any point against the donor organ, which could cause rejection of the transplant. A re-transplantation might have an even less successful outcome than a one-time transplantation, and again, lifetime intake of medicines to suppress the immune system after organ transplantation will be crucial. As the immune system is generally weak after a transplant, an increased rate for infections, malignancy and health disorders are seen in patients with immunosuppressive medication.9 After the transplant surgery, both the infection rate and the mortality rate in the first few years are very high in comparison to the general population. Additionally, death because of cardiovascular disorders is significantly higher among kidney and heart transplant patients.<sup>10</sup>

Many factors are associated with the survival rate of recipients – such as the age, reasons behind the organ failure, associated diseases including high blood pressure or diabetes; and socioeconomic factors including the access to medical care and infection occurring after the transplantation.<sup>11</sup> In kidney transplantation, for example, whether a kidney comes from a living donor vs. deceased donor plays an important role in the survival rate. It is known that patients with a kidney from living donor survive significantly longer than with one from a deceased donor.<sup>12</sup>

Patients with blood diseases – such as leukemia, anaplastic anemia or thalassemia – have an opportunity to undergo bone marrow transplantation, a surgical procedure that replaces the diseased stem cells of the bone marrow with healthy ones. There are three different types of bone marrow transplantation, based on donor characteristics:

- Syngeneic transplantation, where the bone marrow comes from the identical twin
- Allogeneic transplantation from a sibling, other relatives or non-relatives (genetically similar)
- Autologous, where the patient himself is the donor

Different mortality rates were seen according to the donor source in bone marrow transplantation. Better survival rates were found when the donor was from the monozygotic identical twin compared to autologous or allogenic transplantation.<sup>13</sup> To come up with the most adequate rating for an individual case, it is thus reasonable to differentiate by the source of the transplanted organ.

#### **Rare transplantation type**

Isolated pancreas transplantation is a rare procedure, but there is a surgical option for a diabetes mellitus type 1 patient: A simultaneous transplantation of pancreas and kidney (SPK) is the most common type of pancreas transplantation and appropriate for patients with diabetes type 1 and end stage renal failure. With the help of SPK, diabetes patients have better outcome and lower risk for diabetic retinopathy, kidney, or heart disease.<sup>14</sup> Annual data reports showed that the rehospitalization rate and complications are high after the first few years of isolated pancreas transplantation and SPK surgery.<sup>15</sup> Therefore both the type of transplantation and the time since transplantation should be taken into account when assessing pancreas transplantation risk.

### Living organ donor: Are there risks?

Kidney transplantation, for example, is a treatment for patients who suffer from total and permanent kidney failure. The number of patients who need kidney transplantation is increasing worldwide; sadly, thousands of people in each country can only sit on the kidney transplant waiting list. As mentioned above, dialysis is another choice of treatment for patients who suffer from end-stage kidney disease, but kidney-transplant patients have a better outcome than those who undergo dialysis. Moreover, a better quality of life is also observed for kidney transplant patients.<sup>16</sup>

While the survival rate of kidney transplant patients is well-studied and the research is ongoing, we should also consider what happens with the lives of donors. The quality of life and mortality rate of living donors are not much studied. A long-term study in Norway observed no negative impact on the survival rate of kidney donors. In this study, the living kidney donors were specially selected and carefully examined for different diseases. According to the study, kidney donors had a better quality of life than the normal Norway population.<sup>17</sup> Having said that, the selection of the living kidney donor is not the same in every country worldwide and the mortality rate might vary. Unfortunately, there are not enough data from developing countries where the survival rate of kidney donors is investigated. A long-term survival analysis of 80,347 living kidney donors showed that the risk of death within the first 90-days (early postsurgical death) following nephrectomy was higher in living kidney donors (3.1 deaths per 10,000 donors) in comparison to the matched cohort (control group) (0.4 per 10,000). Beyond the first three to six months postsurgery, studies showed that the survival rate of kidney donors and their risk for end-stage kidney disease was similar to the control group (nonkidney donors).<sup>18</sup> Therefore, kidney donors can be accepted at standard rates six months' after surgery.

#### **Summary**

Transplantation is an important option for patients with chronic organ failure or severe blood disease. A new life can begin post transplantation, albeit with some significant risks that play behind the newly transplanted, functioning donor organ. Either the risk of rejection or the side effects of immunosuppressive therapy – such as malignancy and higher infection rates – mean that organ transplantation is not an easy decision for patients. Assessing cases associated with transplantations is a complex task for underwriters and will often require the involvement of medical doctors. According to new studies and medical expertise, better ratings are possible in many cases – for both patients and donors. Living kidney donors seem to be able to live a normal life like the general population, but they should be assessed carefully because of the significance of their role in the success of transplants: by donating their organs they are literally saving lives. Despite the risks involved, organ transplantation means a chance to life for desperately ill people and an act of humanity by healthy individuals.

Our updated rating guidelines for all types of transplantations referred to in this article will be provided in the next update of Gen Re's underwriting manual CLUE.

#### About the Author



Development. She is engaged in the development

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