

"Does Donation of a Kidney affect the Health of the Donor?"

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The History of Kidney Donation by Living Donors

At the beginning of the twentieth century, following the introduction of anesthesia and the ability to perform major surgery, several researchers began to investigate the possibility of transplanting organs into ailing subjects. As mammals, including humans, have two kidneys, one could consider transplanting one kidney from a healthy individual into a patient with kidney failure. The initial experiments were in dogs, in which the kidney was disconnected from the blood supply and then reconnected. The kidney function was restored in spite of the fact that the nerve supply to the kidney had been cut. However, the transplantation of a kidney from one dog to another dog was followed within a short period of time by cessation of function of the transplanted kidney, most likely due to an immunologic mismatch.

After World War II researchers once again started to investigate the transplantation of kidneys. There were a few attempts to transplant the kidneys of deceased donors into patients with advanced kidney disease. The transplanted kidney was rejected in all cases. There were also attempts to transplant kidneys from living related donors into patients with kidney failure. The transplanted kidneys functioned for only a few weeks. Most of these attempts at transplanting kidneys were performed in Paris, France. Another experimental center was in Boston in the USA. In 1954 a patient with kidney failure and an identical twin brother were referred to the clinic in Boston. The investigators decided to transplant one of the kidneys of the healthy twin into the body of his sick brother. The transplanted kidney functioned immediately and continued to function for 8 years, when the patient died of recurrence of his kidney disease. The donor died a few years ago at the age of 79, 54 years after donating the kidney.

This successful transplantation stimulated investigators to seek methods of preventing rejection. Several methods, such as radiation and new medications, which suppressed rejection, were developed in the 1950's and 1960's. This led to the transplantation of kidneys from deceased and living donors. The introduction of treatment with hemodialysis (removal of waste products from the body by means of

an artificial kidney) extended the survival of patients with kidney failure. Another method of cleansing the blood by introducing fluid into the abdominal cavity (peritoneal dialysis) was developed. Thus by end of the 1960's it was possible to treat patients with kidney disease using these methods. Initially the results were not encouraging and the survival of patients treated using dialysis or transplantation

was relatively short. Over the ensuing years the hemodialysis equipment was improved resulting in improved survival. At the same time new medications for preventing rejection were developed as well as new methods for identifying the tissue typing of the donor and recipient. These developments resulted in improved survival of the transplant patients and their survival exceeded that of dialysis patients. The Figure shows the expected remaining lifetime in years of healthy males, transplanted

patients and patients on dialysis in the USA (the numbers are taken from the American Renal Data System¹). As can be seen the survival of transplanted patients, although less than that of the general population is greater than that of dialysis patients at all ages.

Kidney Transplantation in the Treatment of Patients with Kidney Disease

It is accepted today that kidney transplantation is the preferred form of treatment for patients with kidney failure as far as improved survival and improved quality of life are concerned. Since the transplantation of kidneys from deceased donors became an accepted form of treatment, great efforts have been made to obtain a sufficient number of organs from deceased donors in order to treat all the patients who are transplant candidates. These efforts have not been successful and the number of patients who are transplant candidates increases annually. In the last few years there has been an increase in the number of individuals who have donated one of their kidneys during their lifetime. Even the addition of these donors has not matched the ever-increasing number of patients waiting for a kidney transplant. In the USA, 82,000 patients were listed as waiting for a kidney transplant in 2012¹. During the same year 17,200 transplants were performed, 11,600 from deceased donors and 5,600 from living donors. During the

Expected Remaining Lifetime (yrs) White Males USA, 2013

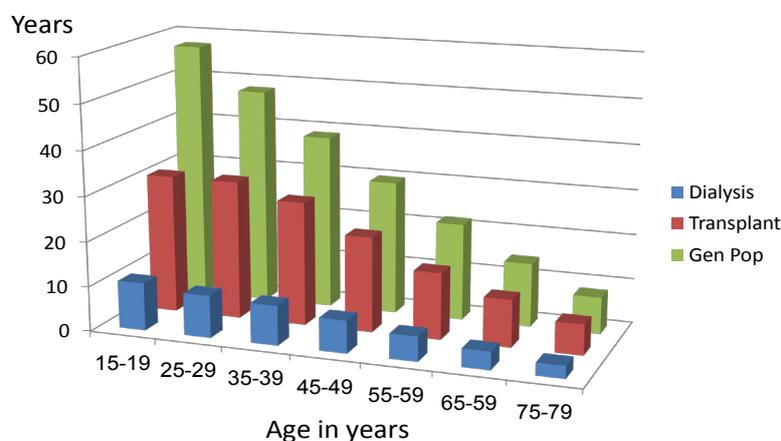


Figure: Expected remaining lifetime in years in the USA of white males in the general population, after kidney transplantation and on dialysis treatment.

same year 29,000 patients were added to the wait list. In Israel 849 patients are listed as candidates for a kidney transplant. (See Table 1 – The numbers are taken from the annual report of Israel's National Transplant Center). Over the last few years approximately 200 kidney transplants have been performed annually in Israel. Over the past four years there has been a dramatic increase in the number of living donors and they now provide 55-65% of the organs available for transplantation. In spite of the growth in the number of transplants, the number of patients waiting continues to increase.

Table 1: Candidates for Kidney Transplants, and number of Transplants performed in Israel, 2007-2014

Year	Waiting for Transplant	Transplants from Deceased Donors	Transplants from Living Donors	Total no. of Transplants
2007	534	59	68	127
2008	598	100	56	158
2009	690	93	69	162
2010	733	53	78	131
2011	729	128	119	247
2012	755	57	108	165

The main conclusion is that in spite of all of the efforts, the number of transplant candidates continues to grow. In addition, organs from deceased donors cannot be relied on to provide the necessary number of kidneys. Thus there must be a major effort to increase the number of deceased and living kidney donors.

Should the removal of a kidney from a healthy donor and the transplantation of that kidney in a sick individual be considered a morally acceptable act?

There is much debate on this subject in the medical literature. In spite of the fact that some people consider requesting a healthy person to donate one of his kidney to be ethically unsound, most investigators support the donation of a kidney under the following conditions²:

1. The individual must be willing to donate his kidney, without coercion.
2. The individual must be given all the relevant information about the risks and benefits of donating a kidney and the benefits to the recipient, taking into account that there are other therapeutic options.
3. He must be a suitable candidate medically and psychologically.
4. The benefits to the donor and recipient must outweigh the risks of the donation and transplantation.

Following this consensus, a meeting was held in Amsterdam and the conditions for caring for living donors were published³. The next meeting was held in Istanbul in 2008. The participants condemned the commercialization

of kidney transplantation and payment for the donation⁴. As payment to kidney donors was declared illegal in the Israeli Transplant Law of 2008, efforts have been made to remove the disincentives, by reimbursing the donor for loss of working days, for the payment of additional insurance, and other expenses. Following the approval of this law, the Ministry of Health in Israel, published a directive in which these legal compensations were detailed.

What are the consequences of the removal of one kidney from the living donor?

If we want to continue to promote the donation of kidneys by living donors we have to investigate the effects on the survival and quality of life of the donor.

What are the effects on short and long-term survival and on development of kidney disease?

For many years it has been known that if an infant is born with one kidney, that kidney will be larger and functionally superior to that of each kidney in a healthy individual. Moreover, if one kidney of an adult is removed the remaining kidney will hypertrophy (increase in size), on condition that it is not diseased. During a period of advanced study in the USA over 40 years ago, my colleagues and I investigated the hypertrophy of the remaining kidney in living donors. Initially we examined the effect of the removal of one kidney on the size of the remaining kidney⁵. Over the ensuing years after the removal of the kidney there was an increase in size of the remaining kidney. This hypertrophy was not affected by the age of the donor. We then examined the effects on the function of the remaining kidney⁶. We found that the function of the kidney increased within the first few days to three weeks after the removal of the contralateral kidney and got to about 66% of the original function of both kidneys. The age of the donor did not affect this functional hypertrophy. When these donors were followed for an additional 4 years it became clear that there is an additional slow increase in function and that this is dependent on the donor's age. The number of subjects in our investigation was relatively small but it was clear that in healthy donors, there was a compensatory increase in the function of the remaining kidney after the removal of one kidney.

Over the last few years many investigators have summarized the effects of donation of a kidney on the mortality and morbidity of the donor. I have examined many articles summarizing the results in large groups of kidney donors and have included the main conclusions of some of these articles published before 2013 (Sommerer et al⁷, Gai et al⁸, Segev et al⁹, and Delanaye et al¹⁰) in Table 2.

However, since these articles were published there have been additional studies, which have investigated the effects of removing a kidney. In 2014 Muzaale et al published the results of a study in which they compared almost 100,000 living donors in the USA to approximately 20,000 healthy individuals¹¹. They found that the donors had an increased risk of developing kidney failure. However, this risk was considered small. This same group had previously reported that the long-term survival of the living donors was greater than that of matched controls⁹.

Table 2. The effects of removal of a kidney on the donor

	Summary of Recent Articles.			
	Sommerer et al, 2004 ⁷	Gai et al, 2007 ⁸	Segev et al, 2010 ⁹	Delanaye et al, 2012 ¹⁰
Morbidity and Mortality after removal of a kidney	Morbidity: Serious complications are rare. Most complications are minor (hemorrhage and infections) Mortality: Very rare, less than 0.02%	Small number of complications after surgery. Laparoscopic surgery may be superior. Mortality rate: 0.03%	Mortality rate: 0.03%	Small incidence of complications. Mortality 0.03%.
Long-term Mortality	Mortality less than in the general population	No change in long-term mortality	Long-term mortality less than control group	All summaries showed no difference in mortality as compared to general population
The risk of Renal failure	Over the years a small number, similar to that in the general population, developed renal failure.	The risk for developing chronic kidney disease is 0.5%		Small risk
Function of the Remaining Kidney	After a small initial decrease in the total kidney function it remains stable for many years.	Initial small decrease, then stabilization and even a small increase over the years. There is a question of increased risk for donors with initial decreased kidney function		Summarised previous works and found similar conclusions, small initial decrease in function followed by an increase and stabilization.
Excretion of Protein in the Urine	There is an increase in excretion of protein in some of the donors	Increased protein excretion. Not clear whether this is a risk		Increased excretion of protein in a minority of donors.
Blood Pressure	There is a slight increase in blood pressure in some of the donors	Increased but the prevalence of hypertension similar to the general population		Slight increase in blood pressure.
Quality of Life		Good		Slight increase in number of suicides.
Conclusions	The risks are minimal for both a short and long period.	The donation is considered to be safe with small risk.	Even in the presence of changes such as urine protein excretion no change in mortality	Risk for complication low and removal of a kidney for donation is considered a safe procedure.

Mjoen et al published in the same year their study of 1901 kidney donors in Norway, compared to over 30,000 individuals, who were considered to have been suitable for donating a kidney¹². They showed that there was an increased, but relatively small risk for long-term death and development of kidney failure.

Many important investigators have commented on these latest findings and have outlined their approach to living kidney donors. The major problem with most of the publications is that the living donors are compared to different control groups and in most of the studies a high proportion of the donors are related to the recipient

and thus may have some genetic predisposition for the development of kidney disease. I have decided to rely on the commentary of Gaston et al, which was published this year¹³. They summarized past studies as showing that there is a very low immediate surgical risk and that long-term survival and quality of life were excellent. The latest studies of Muzaale et al and Mjoen et al both have limitations. However, the results should not be ignored and new well-planned studies are required to investigate the risks of donation of a kidney. It is important to inform all potential donors of these significant but small risks and to ensure that the investigation and preparation of the donors is of the highest standard in order to minimize risks.

What is the influence of the removal of a kidney on the function of the remaining kidney?

As I showed many years ago and has since been confirmed by many investigators, there is an initial increase in the function of the remaining kidney and over the years it may reach 70 to 80% of the function of both kidneys prior to removal. There is thus only a relatively small reduction in total kidney function as compared to that of healthy adults. It is important to stress the fact that this function remains stable over the course of many years. It is unlikely that this small reduction in kidney function is a risk factor for kidney disease.

Are there other effects?

An increase of urinary excretion of protein has been described in some of the donors. A long follow-up of at least 10 years is required in order to be sure that this mild increase in the excretion of protein is not a marker for increased risk of kidney disease. The investigators who have examined this finding concluded that this is not a risk factor. There is also a mild increase in blood pressure in some of the donors. However, the prevalence of hypertension (consistent blood pressure levels greater than accepted levels), is similar to that of the general population.

Is the removal of a kidney a risk factor for the development of cardio-vascular disease?

A group of physicians from Canada investigated the development of heart disease in over 2000 donors by matching them with over 20,000 healthy individuals (10 non-donors was matched to each donor)¹⁴. The risk for death or severe heart disease was lower in the donors than in the non-donors.

Does the presence of hypertension before donation influence post-donation blood pressure and kidney function?

A group of investigators from The Netherlands compared a small group of donors with hypertension prior to the donation to a group of donors, who were not hypertensive¹⁵.

The blood pressure and kidney function levels were similar in both groups one and five years after the donation.

Conclusions

The decision to donate a kidney to a sick individual is a difficult decision. The donation of a kidney to an individual with end-stage renal failure, who is being treated with dialysis, or who is about to begin treatment, is truly an altruistic gift, which very significantly improves the survival and quality of life of the recipient. Recent developments in the matching of the donor to the recipient, and in the treatment of rejection of the foreign organ have contributed to the success of the transplantation of kidneys both from deceased and living donors. Insufficient organs from deceased donors and the success of transplantation from living donors has led to an on-going increase in the number of donations from altruistic donors.

One of the first lessons, which is taught to medical students is that one must not cause unnecessary damage or suffering. Thus we are obliged to ask the question whether it is permissible to remove a kidney from an otherwise healthy individual. The decision is simpler when the donor is related to the recipient. Most investigators have shown that the absence of one kidney does not affect the survival of the individual. Moreover, there is sufficient data showing that the donation of one kidney does not affect or may have a minimal effect on survival. The recent publications which showed a slight decrease in long-term survival in kidney donors as compared to healthy individuals show a very little effect on the eventual survival of the donor. The risk for surgical complications is very small and these are mostly not serious. Although it is known that the donors have a higher risk for the development of urinary excretion of protein and increased blood pressure, there does not seem to be an increased risk for kidney disease. The conclusion is that there is a small risk to the donor but that benefits to the recipient and the feeling of a contribution to society by the donor far outweigh all the potential risks.

Every potential donor undergoes a series of tests in order to show that he has normal kidney function, that he does not have signs of latent or overt kidney disease or other diseases, which may endanger him in the short or long-term. There are guidelines which instruct the physicians in carrying out these tests and most transplantation centers have prepared strict protocols for the preparation of kidney donors. Adherence to the protocols for preparing the donor undoubtedly minimizes the risks.

Saving the life of an individual is a virtuous deed and leaves the donor with a feeling of satisfaction.

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