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Original Article: Clinical Investigation

Our experience with third renal transplantation: Results, surgical techniques and complications

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Background: Despite the popularity of kidney transplantation in the current era, second and third kidney transplantation are not yet widely accepted and practiced. Each center has its own regulations and experiences and there is no accepted protocol for third kidney transplantation. We report here our 15 years of experience with third kidney transplantation.

Methods: This is a report of all the third kidney transplantations performed in Baqiyatallah Hospital, Tehran, Iran, between 1991 and 2006. Demographic data, surgical techniques, complications and outcomes are reported.

Results: Of the nine third kidney transplant patients, six were male. The median age was 43 years (32–52). All of the patients received kidney from living donors. All operations were performed by a midline incision and the grafts were placed at the midline, in the intraperitoneal space. For arterial anastomosis, we used internal iliac, right common iliac and both the right external iliac and inferior mesenteric artery in 4, 4 and 1 case(s), respectively. For venous anastomosis, we used vena cava, common iliac and external iliac veins in 3, 5 and 1 case(s), respectively. During the follow up period (38 months), 6 grafts (66.6%) were functioning. None of the graft rejections were due to surgical complications. Wound dehiscence occurred in two patients. No other surgical complications including infection, lymphocele or hemorrhage were observed.

Conclusion: Third kidney transplantation is a field that has not been fully explored. The rate of complications seems to be not much higher than the first transplantation. Defining a standard protocol seems necessary.

Key words: kidney transplantation, multiple transplantations, renal transplantation, surgery, third transplantation.

Introduction

The number of kidney transplant failures each year continues to grow due to the increasing number of surviving renal transplant recipients.[1] It is reported that about 14% of the patients undergoing renal transplantation require a second[2] or higher number of retransplantations.[3] Of this number, few of them go back on the waiting list or are retransplanted.[4] One reason is that despite the general agreement on first transplantation, performing multiple renal transplantations is not accepted worldwide and reports of third renal transplantations are rare.[5–7]

We report here our experience with the third living renal transplantation and related patient and graft outcomes in our center.

Patients and methods

We retrospectively studied all cases of third renal transplantation, performed in Baqiyatallah Hospital, Tehran, Iran, from February 1991 to March 2006. From 2157 kidney transplantations, nine were third renal transplantations.

As a routine, all of the candidates for retransplantation (including third transplantation) must meet the following criteria:

a. the cause of kidney transplant rejection for the past ones must be chronic allograft rejection
b. the recipient must have negative panel reactive antibody.

We also try to minimize the number of Heuman Leukocyte Antigen (HLA) mismatches between donor and recipient when performing retransplantations.

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We extracted demographic and disease specific data along with surgical techniques, including the graft placement and the anastomosis of arteries, veins and ureters, surgical complications and outcomes for the purpose of this study.

We also calculated the graft survival rate of the third kidney transplanted patients using the Kaplan-Meyer method. We compared these results with the graft survival rate of the first and second kidney transplantation in our center, performed in the same interval, using the log–rank test.

Results

Patients

Among the nine patients, six were male and three were female (M/*F* = 2/1), with an average age of 43.3 years (32–52 years). The first and second grafts functioned for a mean duration of 4 (0–10) and 3.5 (0–17) years, respectively. The mean interval between the first to second and the second to third graft transplantation were 11 and 26.5 months, respectively. All patients received the kidney from a living donor. The immunosuppression regimen was mycophenolate mofetil (MMF), prednisolone and cyclosporine. One patient received azathioprine instead of MMF.

Surgical techniques

All surgeries were performed with a midline incision and the grafts were placed in the intraperitoneal space at midline. For arterial anastomosis, we used internal iliac artery in four (three right and one left) and right common iliac artery in four cases. In one case, the right external iliac artery and the inferior mesenteric artery were both used. Five end-to-end anastomosis and four end-to-side anastomosis were performed.

Table 1 Graft survival rate of the patients for the first, second and third kidney transplantation

Interval after kidney transplantation	First	Second	Third
6 months	91%	81%	88%
12 months	89%	76%	88%
24 months	83%	66%	66%
36 months	79%	60%	58%

For venous anastomosis, we used vena cava in three cases, common iliac vein in five cases (four left and one right) and left external iliac in one case, all with end-to-end anastomosis.

All ureters were anastomosed to the middle posterior part of the bladder with stent placement and the Lich Gregoir extravesical anastomosis technique. None of the previous grafts had been removed.

Complications and outcomes

Wound dehiscence, probably due to multiple previous abdominal surgeries, occurred in two patients which was repaired immediately and had no effect on graft functioning. No other surgical complications such as infection, lymphocele or hemorrhage were observed. The mean follow up period was 38 (2–140) months. At the last follow up, six grafts (66.6%) were functioning with the mean creatinine level of 1.3 mg/dL (0.9–1.9 mg/dL). Three patients had graft rejection; 6 months, 2 and 10 years after the second transplantation (mean = 4.1 years), all of which were due to immunological problems (acute rejection).

Table 1 shows the graft survival rate of the first, second and third kidney transplantation. The graft survival rate for the third kidney transplantation was not significantly different from the first transplantation ($P = 0.867$), but it was significantly better than the second kidney transplantation ($P = 0.047$). Kidney rejected patients returned to hemodialysis.

Discussion

Third renal transplantation comprises around 0.4% of all transplants performed in our center, which is similar to other reports.[8] Ethical concerns,[9] uncertain outcome measures,[10] cost effectiveness concerns,[11] lack of a standard surgical technique and complexity of the procedure for this kind of transplantation[12] are among the causes of this low rate.

In performing re-transplantation, each center has its own experiences. For such a procedure, as well as not having enough experience with the third transplantation, surgeons deal with problems like adhesion bands and lack of space in either iliac fosses for the third transplanted kidney. In some cases, surgeons try to perform nephrectomy and replace the previous graft with the new one, using the same anastomosis.[13,14] By placing the new allograft at midline, we got over the spatial problem and avoided previous graft nephrectomy.

Despite the difficulty to expose, we used internal iliac artery for arterial anastomosis, with an end-to-end manner, so the other accessible arteries remained intact. Internal iliac artery, common iliac artery,[13,14] splenic artery, native renal artery and inferior mesenteric artery were the preferred options in other studies.[12,15] Direct anastomosis to aorta, because of increased risk of stricture at their junction, is not recommended.[16]

We do not usually approach the left common iliac vein in first and second transplantations, so we found it more accessible and easier to expose than the right one for venous anastomosis. In this way, we avoided any infra-umbilical incisions; so, the main abdominal vessels remained intact. The other choices could be inferior vena cava, right common iliac and external iliac veins.[17]

In some multiple transplantations, there is no way to use the pelvic or abdominal vessels for anastomosis. In these situations, orthotopic techniques are recommended.[15] In such multiple transplantations, it is better to evaluate the anatomy of important vessels by CT-scan or angiography before surgery.[17]

In our experience, the rate of surgical complications was lower than other studies.[3,18,19] This may be partly due to the surgery technique and the experience of the transplant surgeons.

In our study, the graft survival rate of the third kidney transplantation was similar to the first transplantation. We also found that the graft survival rate for the third renal transplantation to be better than the second transplantations. This could be the effect of the low sample size in the group of second and the third transplantation. Another reason could be that one of our patients had a graft survival of more than 10 years. This could have a major effect on the results. Previous studies have questioned the survival rates of the third renal transplantation. While the older studies reported a lower survival,[20] newer studies did not find a noticeable difference in patient and graft survival of the multiple transplanted kidneys, compared to the first transplantation.[21] This could be due to a better immunosuppression regimen in the new studies. Finding that the major cause of graft loss in multiple transplantations is immunological problems could be proof of this.[7,17] Our study showed similar results. We found that immunological problems, not surgical complications, are the common causes of graft loss. For example, one patient after 10 years of successful third kidney transplantation and functioning graft stopped immunosuppression therapy by his own and lost his third transplanted kidney.

When interpreting the results of our study, researchers should note that the graft survival rate of the third kidney transplantation was good and comparable to first and second transplantation. The technical problems were not prominent, however the small sample size of the third transplantation patients has limited the generalizability of our results to the real-world practice. In performing third kidney transplantation some issues must be kept in mind. One important issue is the cause of the first and second graft loss. When the cause is de-novo nephritis, or when there is an immunological risk factor for rejection of the graft, performing the third transplant could not lead to a better outcome than the past ones. The other important issue is the state of organ availability.[9,22,23] We did not encounter any ethical issue in terms of the allograft shortage or allocation for third kidney transplantation. This is due to the current regulations in Iran which have removed the waiting list for kidney transplantation.[24] Approaching the issue in other countries with different regulations is still a matter for debate.

Conclusions

Although third renal transplantations are rare and technically difficult to perform, the results are acceptable, so it could be recommended when the underlying disease process and the ethical issues allow.

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Editorial Comment

This is a report of the nine cases who received third renal transplantation at Baqiyatallah Hospital in Tehran over the last 15 years. The surgical technique for third renal transplantation and the results are described concisely. The authors' efforts should be honored, and the article is worth being accepted for publication in the *International Journal of Urology*; however, I thought that this manuscript would be better if each clinical course of those nine patients were described 'in detail' instead of 'mean values' of graft survivals and intervals. I would also like to know whether the living donors were related or un-related and how old they were.

Whenever we read these kinds of articles, we have to consider the differences between nations, including legal, cultural and religious backgrounds. In Japan, we have little opportunity for performing second and third renal transplantation. This is probably (and mainly) due to a shortage of organ donors. The number of organ donors in Iran might be more than that in Japan.

The graft survivals of the second and third grafts shown in this article suggest that we do not have to worry so much about the second and third set phenomena. For all who hope for a chance to receive organ transplantation, the effort to increase the number of organ donors is essential.

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