

# Long Term Success of Kidney Transplantation after Triple Cold and Triple Warm Ischemic Time

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## Abstract

The number of elderly and multi-morbid patients on the list for kidney transplantation has increased rapidly over the past decade. The presented case is about a 64-year old patient, suffering from chronic kidney disease due to benign nephrosclerosis. After eight years on list for kidney transplantation, a 43-year old deceased donor was accepted and the patient was assigned for kidney transplantation. Intraoperatively the kidney transplantation turned out to be unexpectedly challenging due to severe arteriosclerosis of the recipient iliac vessels while the donor graft quality was excellent. The kidney transplantation was stopped after the second attempt due to repeated intima dissection of the iliac artery. The kidney graft was reperfused with UW-solution after each attempt. After the second attempt the flow of the iliac vessels was compromised. In order to maintain the arterial flow of the iliac vessels, a crossover bypass was required, which was performed without any impairment of the lower extremities' blood perfusion. The patient could be discharged 12 days after the surgery. The remaining kidney-graft, with total cold ischemic time of 25 hours and total warm ischemic time of 85 (25+35+25) minutes, was transplanted to a 61-years old female patient. The primary graft function was excellent with decreasing serum creatinine level and sufficient diuresis. The doppler-duplex scanning showed good perfusion of the graft. The patient was discharged eight days after transplantation. On the 10-years follow-up, the patients had still an excellent graft function with creatinine value of 1.5 mg/dl. Although one case is not enough to make conclusions, it shows that the transplantation of such kidney-grafts with multiple cold and warm ischemic times to another patient should be considered as an option in these situations.

**Keywords:** Multimorbid; Kidney-graft; Nephrosclerosis; Hypertension; Creatinine

## Background

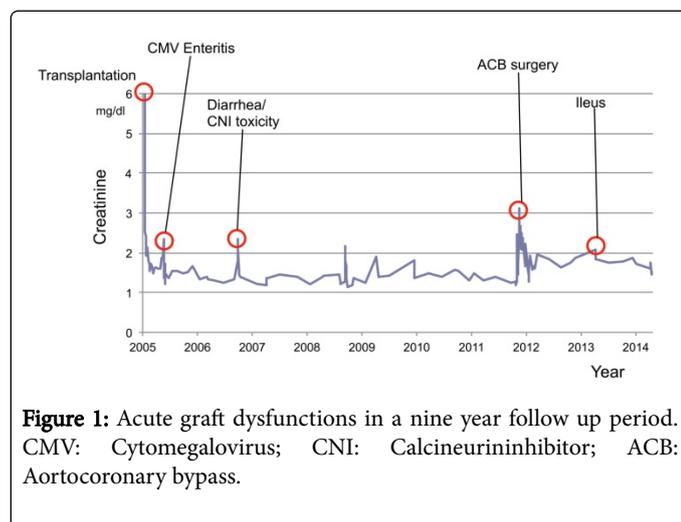
The number of elderly patients on the list for kidney transplantation has increased rapidly over the past decade. Consequently the risk for intraoperative, especially vascular complications, has risen significantly due to multiple co-morbidities such as hypertension, diabetes and arteriosclerosis of the recipients [1,2]. In such cases vascular reconstructions are often necessary, which are frequently associated with prolonged warm ischemic times or even breakup of a transplantation. The key issue in such a situation is what to do with the remaining kidney-graft. One option is the transplantation of the kidney to another patient after multiple cold and warm ischemic times. With regards to the severe organ shortage at present, this possibility should be considered. However there is no data about the outcomes of grafts with multiple cold and warm ischemic times.

## Case Report

A 64-year old female patient, suffering from chronic kidney disease due to benign nephrosclerosis, had been on the list for kidney transplantation since August 1997. On the 1<sup>st</sup> of January 2005 a suitable organ offer from a 43-year old deceased donor was accepted and the patient was assigned for kidney transplantation. The routine preoperative tests included blood test, Electrocardiography (ECG) and X-ray of the thorax, all with negative results. Intraoperatively the kidney transplantation turned out to be unexpectedly challenging due

to severe arteriosclerosis of the recipient iliac vessels while the donor graft quality was excellent. After completed anastomosis and reperfusion there was no blood-flow on the renal artery and no graft perfusion. Suspicion of intima dissection of the iliac artery led to the decision of graft explantation. The graft was re-perfused by the University of Wisconsin Solution (UW) [3]. The intima dissection was confirmed macroscopically. The reconstruction of the recipient iliac artery was done by end-to-end anastomosis. The intraoperative doppler-duplex sonography showed good blood flow after reconstruction. Hence the decision was made to attempt a second transplantation. The arterial anastomosis was performed now more distal on the iliac artery. However, even after the second attempt no sufficient perfusion could be attained. The kidney graft was again explanted and re-perfused by UW-Solution. The arterial flow of the iliac vessels was then significantly compromised and required a crossover bypass reconstruction, which was successfully performed. Thereafter excellent flow on the iliac vessels was detected. Considering the extremely complex vascular situation, the risk for the patient as well as the risk of graft loss was assessed to be too high and the transplantation was stopped at that point. The case was reported to Eurotransplant, which decided to apply a rescue allocation to the organ immediately in order to prevent organ loss due to significantly increased ischemic time. Therefore a 61 years old female patient was prepared, who had been waiting on the list for five years and additional five years inactive due to breast cancer. She should receive the rescue allocated kidney, which had to this point undergone three periods of cold and two periods of warm ischemic times. In the further course of the second surgery no further complications arose. Transplantation

was performed in standard technique of our centre into the left fossa iliaca, anastomosed to the external iliac vein and artery [4]. Total cold ischemic time of the kidney graft amounted 25 hours and total warm ischemic time 85 (25+35+25) minutes. The HLA matching presented four mismatches. Both patients could be transferred from the Intensive Care Unit (ICU) to the normal ward on the first postoperative day. The radiological findings of the patient's crossover bypass showed an excellent flow without any impairment of the lower extremities' blood perfusion. The first patient was discharged 12 days after surgery. The second patient showed an excellent primary graft function with decreasing serum creatinine level and sufficient diuresis. The immunosuppressive therapy was based on an induction by the anti-interleukin-2-receptor-antibody basiliximab and a standard immunosuppression based on tacrolimus, prednisone and mycophenolate mofetil. The postoperative routinely performed doppler-duplex scanning showed good perfusion of the graft. There was no acute rejection of the graft or any other postoperative complication. The patient was discharged eight days after transplantation from the surgical ward. In the course of the following ten years a number of acute graft dysfunctions arose. The first graft dysfunction in the first year with increase of the creatinine was caused by enteritis based on Cytomegalovirus (CMV) infection, which was treated successfully. The second dysfunction was caused by diarrhea and calcineurin inhibitor (CNI) toxicity in the second postoperative years. The kidney biopsy has shown no signs for donor specific antibodies (DSA) and recovered from this graft dysfunction soon. The patient underwent combined aortocoronary bypass (ACB) surgery and mitral valve reconstruction, six years after kidney transplantation, which led to an oliguric acute graft failure temporarily requiring hemodialysis. In the further course graft function recovered and has remained on an excellent level, with last Creatinine value of 1.5 mg/dl measured in 2014 (Figure 1).



## Discussion

Arteriosclerosis of the iliac artery has become more prevalent in patients with chronic kidney disease on dialysis with increasing age [5]. Traditionally, severe arteriosclerosis has been considered as relative

contraindication for kidney transplantation [6]. Several recently published data reported combined kidney transplantation and vascular reconstruction in patients with arteriosclerosis resulting in promising outcome [7,8]. However, in some cases it is more beneficial to stop the kidney transplantations due to high risk for patient and graft. Such decision is difficult and requires careful considerations. It is known that prolonged cold and warm ischemic time leads to delayed graft function [9]. However there are no data in the literature describing the effect of multiple cold and warm-ischemic times. One may speculate whether repeated cold and warm ischemic periods may have protective effect on the graft similar to preconditioning. An important factor for the excellent patient- and graft survival in our case (10 years) is the excellent quality of the kidney prior transplantation, but one case is not enough to make conclusion about the right strategy. However this case demonstrates the importance of a diligent preoperative work-up including the vascular status, in particular before transplant surgery. In patients with history of severe arteriosclerosis a surgeon with vascular surgery experience should perform the transplantation. If multiple attempts are required, the graft should be of good quality in order to compensate prolonged cold and warm ischemic times due to vascular reconstruction. With regards to the promising results also new developments such as machine perfusion or perfusion solution itself should be discussed for the case of multiple cold and war ischemic times [10].

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