

Professor Luuk Hilbrands, chair of the DESCARTES working group of the ERA-EDTA, discusses the hurdles that remain in kidney transplantation and how they might be overcome



Strategies to improve patient outcomes in kidney transplantation

The DESCARTES working group of the ERA-EDTA ("European Renal Association – European Dialysis and Transplant Association") plays an active role in the advancement of kidney science and care. The ultimate aim is to sustainably improve the outcome of patients who have received a kidney transplantation. Major hurdles we have to overcome in transplantation in order to reach this aim are rejection and cardiovascular disease.

Rejections still pose a challenge

The main challenge patients face after receiving a kidney transplant is that the new organ starts and continues to work, preferably for many years, if not decades. There is also the question of patient survival – in short, what is the use of a working kidney graft, if the patient dies of cardiovascular complications or of cancer a few years after receiving the organ? The magic word is 'outcome', so we need to strive for better patient and graft survival after transplantation.

There are many different causal factors for the loss of transplanted organs. Acute rejection plays a role in the first year after transplantation, especially. About 20% of the patients have an acute rejection episode within the first three to six months. Often they feel absolutely powerless and helpless, because they have not sensed any signs of rejection, which is usually detected by regular monitoring of kidney function and biomarkers in the blood. Whenever there is a deterioration of renal function, rejection is one possible reason. If rejection is detected early, it can usually be treated effectively, and the donated kidney can be saved. This is something we have to communicate to the patients to enhance adherence to regular monitoring. Chronic rejections are a major



problem in practice. As soon as these become clinically apparent, there is hardly any therapy that can be considered promising, and the ultimate outcome in most cases is loss of the organ. The great challenge for the future will be to detect chronic rejection in the subclinical phase and to develop better treatment strategies for high-risk patients. Many research groups are focusing on these issues, among them members of the DESCARTES working group.

Communication is vital for strengthening patients' adherence

Compliance also plays a key role in the frequency of post-kidney transplant complications, especially when it comes to rejection. For that reason, many strategies have been developed with the aim of strengthening patients' adherence. Monitoring the side effects of medication is of utmost importance in this regard. If patients experience side effects,

they are less inclined to take the drug in question regularly. It is also advisable to simplify the drug regimen. In some cases, for example, one can switch to a drug that can be taken once a day rather than two or three times per day. This may help to improve compliance, but the most important measure for improving adherence is to talk to the patient.

In my clinic, we try to explain the drug regimen from the first day after the transplantation. The patient needs to understand what kind of drugs he/she has to take, what their mechanisms of action are (as well as possible side effects) and for what reason the patient has to take them. The earlier one starts to explain this to patients, the earlier one knows if she/he will be able to adhere or not.

While the patient is still in hospital, we can evaluate which patients can manage the drug intake themselves and which not. With some

patients, it becomes quite apparent during their hospitalisation that they need some support when at home. If this is the case, we in the Netherlands have the option of sending a nurse who visits the patient regularly at home and helps him/her to ensure appropriate intake of their medication. Of course, if the patient is not compliant, in the sense of actively refusing to take the pills and refusing the support being offered, then that patient is difficult to help. But for patients who cannot manage proper intake of their medication, due to cognitive dysfunction, for example, it can be very helpful to have this home care.

A standardised immunosuppressive regime is not a 'cure-all' - sometimes variation is the key to success

Standard practices in kidney transplantation vary between European countries – and DESCARTES is often asked what can be done to overcome this. In my opinion, however, we first have to ask whether it is really necessary to have the same immunosuppressive regimen for all patients. Even in the Netherlands we have some variation after the first three months. While the regimen is pretty much the same everywhere in Europe for the first 12 post-transplant weeks, it varies considerably after this initial phase. There are some centres that follow one schedule and others which follow another. The reason for this variation is that there is no regimen that has proved to be far better than others. In the scientific literature, many immunosuppressive therapies have been described and analysed – many with similar results. Even the guidelines leave room for variation, therefore, and do not recommend one and the same therapy for all.

I, personally, think that the road to success is actually to adjust the therapy to the needs of the individual patient – in accordance with the individualised medicine approach. For example, we give steroids to all patients and usually continue this therapy after the first phase. But if a patient develops severe side effects (diabetes, osteoporosis), we discontinue this treatment and change the regimen. Unless one regimen proves to be superior to all others we believe that an individualised approach should be the standard – and to achieve that it is good to have an array of options for treating patients.

It is not all about preventing rejections - decreasing patients' cardiovascular risk is just as important

Besides chronic rejection, the second main cause for premature loss of organ transplants is death

with a functioning transplant.¹ The mortality of patients with kidney transplants is high and is mainly attributable to cardiovascular factors. These patients basically have a triple risk profile. As in the general population, their cardiovascular health is determined by the classical CV risk factors (age, familial disposition, gender, diabetes, hypertension, nicotine abuse, hyperlipidaemia, etc.). In addition to those factors, however, there are also risk factors associated with CKD (anaemia, proteinuria, malnutrition, microinflammation, endothelial damage) and transplantation-specific risks, such as post-transplantation diabetes. Patients, for example, who develop post-transplant diabetes within the first year are known to have a significantly worse outcome.² Comprehensive aftercare, including measures to lower patients' cardiovascular risk, is therefore crucial if we are to improve kidney transplantation outcomes.

Better outcomes by intensifying living donation?

Living donor kidney transplantation achieves better overall results than the transplantation of deceased donor organs. Many efforts have therefore been made to expand the pool of living kidney donors in European countries. In the Netherlands, especially, we have a very high rate of living donors, dating back to the time when we had a long waiting list for deceased donors. We developed very good information programmes and ensured that donors are supported in many ways; for example, we compensate them for any loss of income while in hospital, and we provide special insurance schemes. One of the latest initiatives is that we have home-based educational teams. They visit end-stage renal disease patients at home and inform the patients, their families and friends about all the renal replacement therapy options – including living donor kidney transplantation.

However, if a patient has found a donor among his or her family (or friends), a problem regularly encountered is that the blood groups are not compatible. In order to overcome the limits imposed by ABO-incompatibility and thus to increase the number of living donations, two main strategies have been developed. First, there are cross-over donation programmes. In the Netherlands, for example, about 10% of living donor kidney transplantations are performed as cross-over donations, which demonstrates their success. These programmes have been established in many countries, but most often the exchange is limited to two donor-recipient couples. Apart from cross-over programmes, there is also the 'medical solution', which is to overcome ABO-incompatibility by removing antibodies against the

blood group antigens. This is meanwhile being done in every European country.

But when it comes to living donation, there is also the other side of the coin – in this case the donor. To do no harm is a fundamental part of the Hippocratic oath, which is why some European countries are rather reticent about promoting living donation, especially given some recent concerns regarding the long-term safety of living donors. This is why DESCARTES published a position paper on this topic last year.³ The DESCARTES board members emphasised the importance of optimal risk-benefit assessment and proper information for the prospective donor, which should also include recommendations on health-promoting behaviour post-donation.

We believe education is the key to better outcomes in kidney transplantation

Improving outcomes has many different facets and aspects. It is not about changing one parameter only but involves complex follow-up care that takes many issues into consideration. Doctors who manage patients before, during and after transplantation need up-to-date knowledge, specific clinical skills and ethical commitment. This explains the DESCARTES working group's focus on education. We organise CME courses throughout the year in different countries. In October, there is one in Edinburgh, Scotland, on 'Making the right decision in kidney transplantation: current controversies on clinical and ethical issues'.⁴ Apart from organising educational events, we publish opinion papers and literature reviews and are involved in the guideline work carried out by 'European Renal Best Practice' (ERBP). For further information on our working group, please visit <http://www.era-edtaworkinggroups.org/en-US/group/descartes#sthash.yK94PU10.dpbs>.

References

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