



# Deceased Donor Transplantation: Patient Selection, Ethics, and New Approaches

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RENAL transplantation was a hot topic at the 60<sup>th</sup> European Renal Association (ERA) Congress 2023, which took place both virtually and in-person in Milan, Italy, between 15<sup>th</sup>–18<sup>th</sup> June. One such session saw experts in transplant medicine, surgery, and transplant ethics deliver presentations on deceased donor kidney transplantation. Co-chaired by Marta Crespo, Hospital del Mar, Barcelona, Spain, and Christophe Mariat, University Hospital Saint-Étienne, Saint-Priest-en-Jarez, France, this symposium delivered invaluable insights into donor selection, transplant ethics, and approaches to improve graft viability and implementation.

## INTRODUCTION

One of the main challenges faced by those working in solid organ transplantation and those on the waiting list to receive a transplant is the discrepancy between the number of donor organs needed and the number of organs available. Increasing the number of available donor organs is of key, and ongoing work is required to reduce donor organ discard rates, improve public confidence in organ donation, and enhance donor graft viability. This challenge will require multidisciplinary collaboration and ongoing clinical research.

eloquently discussed the challenges associated with donor-recipient matching. Whilst it is well-known that the best treatment for end-stage renal disease is renal transplantation, this is not always achievable. Messa commented: “The real problem, as we know, is that the number of patients on the waiting list is by far higher than the number of organs available each year.” To highlight this point, Messa provided data from the USA, showing that approximately 80,000 patients with end-stage renal disease were registered on the renal transplant waiting list between 2010–2020, and <24,000 organs were available in that period. This 3:1 ratio of demand versus supply is similar in Europe.

## DONOR AND RECIPIENT SELECTION

The transplantation process is complex, lengthy, and involves several stakeholders. Crespo poignantly stated: “The success of transplantation starts much before transplantation,” highlighting that there are multiple factors that need to be considered and optimised even before the point of surgery is reached.

Alongside this, poor utilisation of available organs is also a concern. Messa explained that data from the USA have stably shown that approximately 20% of the total number of kidneys recovered are not transplanted. Messa added that this is likely to be similar in Europe. Addressing this will be a key factor in closing the gap between the number organs needed and the number of organs available.

A key factor in this process is selecting the right donor for the right recipient. Piergiorgio Messa, Università degli Studi di Milano, Italy,

There is a need to balance equity and efficiency in renal transplant to ensure all patients have the same chance of receiving an organ, but also avoid organ misassignment or underutilisation.



This balance can be difficult to achieve in donor-recipient matching and organ allocation. For example, there are challenges around the projected recipient life expectancy and estimated donor organ longevity.

Another consideration for donor-recipient matching is donor quality. Historically, the expanded criteria donors and standard criteria donors have been used. However, Messa noted that this dichotomous system could risk an excess of discarded organs based on assumption of non-suitability. More recently, a continuous evaluation of both donor and recipient using the Kidney Donor Profile Index (KDPI) and estimated post-transplant survival score (EPTS) has been proposed. KDPI provides an estimate of how long a kidney is expected to function once transplanted, while EPTS estimates the length of time that a candidate is likely to benefit from a donor kidney. Both measures are scored on a scale of 0–100%, with lower scores indicating longer estimated transplant function and

longevity of benefit, respectively. This provides a method to ensure that the donor organ goes to the ideal recipient.

However, this model is not without its limitations, as some components of the scores have greater weight than others, limiting the real predictive value of KDPI. Moreover, Messa discussed that the biggest limitation is that in real practice, users of the KDPI will have a threshold at which they judge a graft to be bad. Often, this threshold is a score of 85%, which can result in increased organ discard rates.

Messa stated that, presently, the main way to improve donor-recipient matching is to increase the number of organ donations. They discussed several ways in which this could be tackled, including increasing donation after cardiac death (DCD), living organ donation, reducing organ discard rates, and overcoming the opposition to organ donation.

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## IMPROVING GRAFT VIABILITY

In agreement with Messa, Gabriel Oniscu, CLINTEC, Karolinska Institutet, Stockholm, Sweden, also highlighted the increased demand, as well as demonstrable inequity, persistent wait list mortality, and poor utilisation of currently donated organs as key concerns for the transplant community.

Improving graft viability is a strategy to overcome the discrepancy in organ availability and patients on the waitlist. Oniscu explored several potential solutions for improving graft viability and implementation. One key strategy is the use of machine perfusion. Machine perfusion strategies can be employed at retrieval, preservation, or time of transplant, and can take place at normothermic, sub-normothermic, and hypothermic temperatures.

Messa discussed increasing DCD donors as a potential solution to increasing organ donations. Oniscu stated that there has already been an increase in DCD across Europe, and discussed that whilst outcomes have been good, warm and cold organ ischaemia remains a challenge. Oniscu further explained that to overcome this, circulation can be restored to the organ for some time before organ retrieval with an extracorporeal circuit, using normothermic regional perfusion to induce a scenario closer to that of donation after brainstem death. This scenario could enable a greater number of organs to be recovered from donors, contributing towards decreasing the gap between organs required and organs donated. To build on this further, Oniscu presented data from the UK which showed that graft failure halved, delayed graft function was lower, and there was a significant 1-year estimated glomerular filtration rate benefit in DCD with normothermic regional perfusion compared with DCD without normothermic regional perfusion. In this study, estimated glomerular filtration rate improved by 6.3 mL/min/1.73 m<sup>2</sup> at the end of the first year, translating to an additional 4 years of graft life free from dialysis. Other strategies discussed were donor hypothermia, which has been shown to be inferior to machine perfusion strategies, hypothermic oxygenated perfusion, and normothermic machine perfusion.

Oniscu further discussed the potential of sustainable organ perfusion services for donor

organs, highlighting that implementation would be complex and require funding, education, and training. Additionally, they explored whether there could be role for developing purpose-built organ repair/reconditioning centres to help optimise utilisation of currently donated organs.

Oniscu also provided insight into potential future focuses, including functional and injury markers, functional MRI, near infrared spectroscopy, laser speckle imaging, anti-microRNA therapy, and nanoparticles for immunomodulation.

Although organ perfusion is now established in clinical practice, it remains unclear which strategy is best in different scenarios. Oniscu suggested that further work needs to be done to help unpick this, as there are benefits to each approach. Despite this, they concluded that rapid progress is being made towards understanding graft injury and identifying mitigating therapies.

## ETHICAL CONSIDERATIONS

Not only does organ transplantation require meticulous consideration regarding donor-recipient matching and patient and organ optimisation, but considerable ethical input is also required. Mehmet Sukru Sever, İstanbul School of Medicine, Türkiye, explored donor, family, and allocation ethics, highlighting how these may conflict, and detailing the complexities of transplantation ethics.

Some of the key factors discussed were donation decision-making, the definition of death, and allocation criteria. Sever shared the definitions of circulatory death as when circulatory and respiratory functions have permanently ceased, and brain death as cessation of all functions of the entire brain. The latter is pivotal in legitimising organ removal from bodies in which circulatory and respiratory function is ongoing. There are three further sub-categories defining brain death: brainstem death, whole brain death, and higher brain death. Sever explained how these different definitions can cause public confusion, and discussed the need for uniformity in determining brain death globally.

The dead donor rule has been used deontologically to underline that the donor must be dead before organs are retrieved or that

retrieval should not cause death of the donor. Sever highlighted that whilst this helps maintain public trust, it can contradict autonomy, neglect utility, and misuse non-maleficence. They discussed how such academic controversies can have harmful impacts, such as a reduction in organ donation, and discussed how provision of simple, concise, and transparent information to the community would be more effective in preventing public misunderstandings.

As well as discussing the ethics and potential harms associated with directed and conditional donation, Sever also explored opt-in and opt-out strategies for organ donation. Sever spotlighted that Spain is the most successful country in terms of organ donation, and that whilst they adopt an opt-out strategy, they have reported that donation rates are not different to rates seen with an opt-in strategy.

Sever concluded by discussing the ethical considerations for organ allocation. They stated: "Developing ethically and legally approved organ allocation systems is a must," and explained

that policies for reducing disparities should be balanced with utility, cost, and efficiency. Sever commented that "the optimal strategy for increasing organ donation should combine utilitarian considerations with deontological and ethical rules."

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## CONCLUSION

Renal transplantation is complex and multifaceted. Improving donor-recipient matching, and reducing the discrepancy between donor organ supply and demand, remains a key challenge for those in the field. With ongoing research and new strategies and approaches, there is hope that this gap can be reduced in the future. ●

