Valorisation addendum
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This chapter will touch upon the return of investment prospects for society from the knowledge gathered during this PhD-trajectory. The findings in this thesis are not only relevant from a scientific point of view, but also have social and economic value. The subject of the thesis, critical issues in organ donation after circulatory death, is of great importance for the health care community and also for the society as a whole. Insight in and improvement of the different aspects of the process of donation after circulatory death (DCD) can expand the use of organs from DCD donors and improve the donation procedure, which eventually will benefit patients on the transplant waiting list. This chapter will describe the relevance of the performed research in a broader perspective.

At the end of 2014, there were 1043 patients on the transplant waiting list in the Netherlands. Within the Eurotransplant region (the Netherlands, Belgium, Croatia, Germany, Luxembourg, Austria, Slovenia, Hungary) 14 928 patients were waiting for an organ transplant.\(^1\)\(^2\) The majority of these patients needed a kidney.

Kidney transplantation is the optimal therapy for patients with end-stage renal disease. It results in superior life expectancy and quality of life, compared to dialysis treatment.\(^3\)\(^4\) Next to improvement of the overall survival rates and quality of life, renal transplantation is a cost saving alternative compared with dialysis, even if only DCD kidney transplantation is compared to dialysis.\(^5\)\(^6\) A patient on dialyses costs about 55 000 euro per year, and the costs of nephrologic care after the patient is transplanted is about 8000 euro every year, after the first year. This means that every additional year of graft survival stands for a saving of 47 000 euro. (costs adapted from the Dutch Transplant Society).

In 2014 there were 271 post mortal organ donors in the Netherlands and 2041 organ donors within the Eurotransplant region.\(^1\)\(^2\) These numbers are by far not sufficient to treat all patients on the waiting list. As a result, patients die while waiting for an organ; in the Netherlands, there were 130 patients and within Eurotransplant 1318 patients who died in 2014 on the waiting list.

In the Netherlands, DCD increased over the last decades, and over the last years the number of DCD donors is equal to or exceeds the number of donors after brain death (DBD). Within the Eurotransplant region, the percentage DCD donor is only 10%. Procurement of kidneys from DCD donors holds the potential to expand the donor pool 2.5 to 4 times.\(^7\) However, an increased incidence of delayed graft function (DGF) and primary non function (PNF) is seen compared to kidney transplantation from conventional brain dead donors, due to the warm ischemic injury in DCD organs.\(^8\)\(^9\) Although the survival of functioning grafts is similar between DCD and DBD, the expansion of DCD kidney donation has not reached to its full potential. A study from Snoeijis et al. showed that patients who receive a standard criteria DCD kidney live
longer, the overall mortality rate was reduced by 56%, compared to patients who continue dialysis treatment with the option of waiting for a conventional DBD kidney transplantation.\textsuperscript{10} Widespread implementation of DCD may increase the life expectancy of patients on the waiting list for a kidney transplant by reducing the waiting times for transplantation.

The studies in Chapter 8 and 9 focus on the European perspective on DCD. From its results it was concluded that DCD is not fully utilized yet within Europe. With the implementation of DCD in more countries, reduction of the waiting list can be realized. Implementation of solid protocols, supported by the responsible authorities, transplant and intensive care professionals may result in a further increase with DCD transplantation in Europe. Countries with less expertise with DCD can learn from the countries with a long experience with DCD. Therefore, with a group of experts on DCD from different countries, recommendations on several key aspects of the DCD process were formulated, a clinical pathway for DCD developed, and requirements to implement a DCD programme formulated.

We have shown that increasing the donor potential by the implementation of a DCD programme for patients who die after unsuccessful resuscitation, should not be restricted by the consent rate of the family. The consent rate of the family is not lower if a patient dies unexpectedly. The number of patients who die after failed resuscitation is higher than the number of intensive care patients, who die after withdrawal of treatment and meet donor criteria, and therefore a great potential to expand the donor pool.\textsuperscript{11}

An important aspect of DCD donation is the uncertainty whether a potential donor will die within a restricted time period after withdrawal of treatment. If a donation procedure will be abandoned, this obviously also has financial and logistic consequences, like the reservation of an operating room and operating team. With the multicentre study we performed, variables were identified that increased the odds of dying within 60 or 120 minutes after withdrawal of treatment of a potential DCD donor. However, in clinical practice, we cannot predict the time of death of a potential donor with absolute certainty, and therefore initiation of a donation procedure in every potential donor is important given the shortage of organs. Around 20 % of the initiated DCD procedures do not lead to transplantation because the potential donor does not die within 120 minutes after withdrawal of treatment\textsuperscript{1}. Further research is needed to develop an accurate and generalizable instrument to improve the predictions of death after withdrawal of treatment and the donation after circulatory death eligibility.\textsuperscript{12} Because kidneys from DCD donors are inevitably associated with warm ischemic damage, due to the period of circulatory arrest prior to preservation, it is important to use the best available method for preservation. In a retrospective study we showed that
direct aortic cannulation is the preferred preservation method for controlled DCD, compared to preservation with the double-balloon-triple-lumen catheter. The preservation method of choice depends on logistic, ethical, financial and legal jurisdictional circumstances. In a review about the currently used techniques to preserve kidneys, we concluded that the normothermic regional perfusion seems a promising technique and may improve the viability of marginal donor kidneys. Further improvement should be made to optimize the quality and further expansion of the potential donor pool and thereby realize an increase in the organ donor rate.
References