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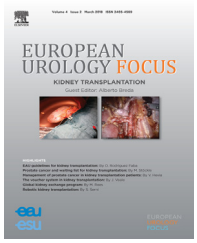

Renal Disease

# Hypothermic Machine Perfusion Results in a Marginal Kidney Transplant Programme

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**Abstract**

*Background:* Hypothermic machine perfusion (HMP) of deceased donor kidneys is associated with a better outcome than static cold storage, predominantly in marginal donors. Nevertheless, there is little evidence supporting whether graft centre of origin and donor category impact HMP results.
*Objective:* To identify factors impacting HMP in transplantation from marginal donors.
*Design, setting, and participants:* Analysis of prospectively collected cohort data of expanded criteria donor (ECD) and donor after circulatory death (DCD) categories II and III was performed. A total of 214 adult recipients of first kidney transplantation with complete data and a minimum of 6-mo follow-up were included.
*Outcome measurements and statistical analysis:* Delayed graft function (DGF) was defined as the lack of decrease in creatinine level in the first 48 h. Graft loss was defined as return to dialysis or creatinine clearance $<$15 ml/min/1.73 m$^2$. Univariate and multivariate logistic regression analyses for DGF were constructed to identify independent risk factors. Recipient and graft survival (GS) analyses were conducted by Kaplan-Meier, and univariate and multivariate Cox regression analyses.
*Results and limitation:* DGF occurred in 32.8% of imported and 20.5% of local grafts ($p = 0.059$). Only donor category (DCD; odds ratio [OR]: 6.6, $p = 0.008$) and haemodialysis (OR: 3.5, $p = 0.002$) were significantly associated with DGF development. The 1-yr GS rate was 92.5% in the local donor group and 84.3% in the imported donor group ($p = 0.050$). Multivariate analysis by Cox proportional hazards model identified only donor category (hazard ratio [HR] 10.99, $p = 0.001$) and donor age (HR 1.07, $p = 0.005$) as predictive variables for GS. The small sample size of the DCD group diminished the statistical power and did not permit a subgroup analysis to determine the impact of specific DCD category on HMP results.
*Conclusions:* DCD donor category, but not donor centre of origin, impacted DGF development and GS in the HMP of deceased donor kidneys.
*Patient summary:* Currently, the number of donors is insufficient to meet the demand for renal grafts. Expanded criteria for donation after brain death and donation after circulatory death (DCD) programmes have been developed as strategies to minimise this problem. Hypothermic machine perfusion has previously demonstrated its usefulness in expanded criteria donation and DCD preservation. DCD type and donor age increase the risk of graft loss.


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## 1. Introduction

Kidney transplantation (KT) is an alternative treatment for patients with end-stage renal disease; it improves both survival and quality of life. However, the number of donors is insufficient to meet the demand for renal grafts [1,2].

Despite their potential to expand the current pool of kidneys, expanded criteria donor (ECD) and donor after circulatory death (DCD) kidneys are associated with more frequent clinical complications, such as delayed graft function (DGF) and primary nonfunction (PNF), resulting in either the patient's return to dialysis or the need for a retransplant. As a result, in recent years, there has been increasing support for the use of hypothermic machine perfusion (HMP) techniques in place of static cold storage (SCS) [3–7]. HMP has been shown to decrease the incidence of PNF and DGF and increase 1-yr graft survival (GS) compared with standard SCS. Additionally, HMP offers the unique possibility of assessing the graft by monitoring perfusion dynamics and/or perfusate biomarkers that may correlate with graft outcome [8–11].

The objective of the present study was to analyse HMP results within the context of a marginal donor programme by presenting the results of HMP use in real-life practice. The damage associated with prolonged cold ischaemia time (CIT) and warm ischaemia in DCD are the main predictors of DGF. As the utility of HMP may be more important for reducing these risk factors, we investigated donor origin (local vs imported) and donor category as risk factors in a predictive model of DGF and GS.

## 2. Patients and methods

### 2.1. Design, setting, and participants

Study data were prospectively collected in a cohort of consecutive ECD and DCD (type II and III categories) KT recipients between February 2012 and September 2017. Ethical approval was obtained from the Ethics Review Board. A total of 214 adult recipients of a first KT with complete data and a minimum follow-up of 6 mo were included in the analysis, as summarised in the flowchart given in Figure 1.

### 2.2. Preservation method

The kidneys were procured locally or imported from another organ procurement hospital. Pulsatile HMP was provided by Life-Port Kidney Transporter (Organ Recovery Systems, Itasca, IL, USA). Local kidneys were placed on Life-Port in the donor's operating room and delivered to the recipient on the pump. Imported kidneys were placed on ice until they reached our transplant centre. Grafts were not discarded on the basis of machine haemodynamic parameters.

### 2.3. Outcome measurements and statistical analysis

#### 2.3.1. Primary endpoint

DGF was defined as the absence of a creatinine level decrease of >10% in the first 48 h. The need for dialysis in the 1st week was also considered.

#### 2.3.2. Secondary endpoints

PNF was defined as the permanent lack of graft function.

#### 2.3.3. Acute rejection

Induction immunosuppression included the systematic use of the monoclonal antibody basiliximab. Maintenance immunosuppression was composed of tacrolimus, mycophenolate-mofetil, and prednisone. Acute rejection (AR) was clinically suspected and confirmed by kidney biopsy.

#### 2.3.4. Creatinine clearance

Creatinine clearance was estimated by means of MDRD-4 IDMS.

#### 2.3.5. Graft survival

Graft loss was defined as the recipient's return to dialysis or creatinine clearance of <15 ml/min/1.73 $m^2$.

Pretransplant biopsy specimens of all allografts were obtained by wedge biopsy. Frozen sections were evaluated for glomerulosclerosis, which was calculated as a percentage (number of obsolete glomeruli divided by the total number of glomeruli with a minimum of 25 glomeruli).

Life-Port calculates the resistive index (RI) by dividing the instantaneous pressure by the instantaneous flow. Flow and RI data were assessed at 15 and 30 min; at 1, 2, and 4 h; and at the end of HMP.

Continuous variables are expressed as the mean and confidence interval or as median and range, as required, and categorical variables as the number and percentage. Univariate and multivariate logistic regression analyses for DGF were constructed to find independent risk factors of DGF. Survival recipient and graft analysis were assessed through Kaplan-Meier, and univariate and multivariate Cox regression

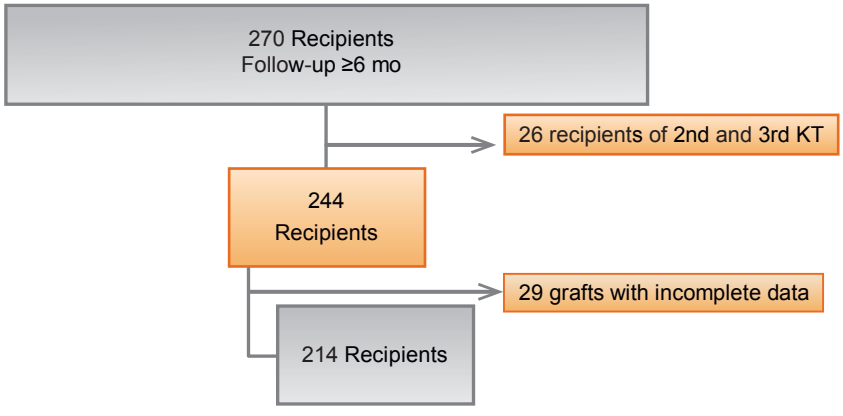


**Fig. 1 – Flowchart of KT recipients included in the study. KT = kidney transplantation.**