“Does perioperative patient perfusion obviate the need for kidney machine perfusion?” A retrospective analysis of patients receiving a kidney from ‘donation after circulatory death’ donors

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Declaration of interest: none

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Abstract (245/250)

Background:

Delayed graft function (DGF) remains a clinically relevant problem in the post-transplant period, especially in patients with a renal graft from a 'donation after cardiac death' (DCD) donor. Controversy exists around the optimal perioperative fluid therapy in such patients. These patients may benefit from a perioperative saline loading fluid protocol, which may reduce the risk of DGF.

Methods:

We compared two cohorts of patients who underwent a renal transplantation with a graft from a DCD donor. From January 2003 until December 2012, patients (N=46) were hemodynamically managed at the discretion of the care-giving physician, without a preoperative fluid administration protocol (first study period). From January 2015 until March 2019 (N=26), patients received saline loading pre, during, and after kidney transplantation according to a well-defined saline loading fluid protocol (second study period). The relationship between the use of this perioperative fluid protocol and DGF was analyzed using univariable and multivariable logistic regression models.

Results:

Delayed graft function occurred in 11/46 (24 %) patients in the first study period and in 1/26 (4%) in the second study period ($p < 0.05$). In a multivariable model, correcting for cold ischemia time and KDRI, the use of a saline loading fluid protocol in the perioperative phase, was nearly significantly associated with a decrease in DGF ($P=0.07$).

Conclusion:

In our DCD transplant population, DGF rates were low. Our data further strongly suggest that implementation of a perioperative saline loading fluid protocol was independently associated with a lower risk of DGF.

Keywords

Kidney transplantation, Delayed Graft Function, Donation After Circulatory Death, Graft perfusion, Perioperative hemodynamic management

Declaration of interest: none

Introduction

Today, inadequate post-operative function or 'delayed graft function' of the newly transplanted graft still remains a major concern among patients receiving a kidney graft from a deceased donor.

'Delayed graft function' is most often defined as 'need for dialysis in the first week after transplantation'.[1] The pathophysiology remains unclear, but is thought to be the result of a complex interplay of donor-associated (older age, ischemia, inflammation), technical (storage, ischemia time) and recipient-associated (reperfusion, immunological) factors.[2] In contrast to patients with 'primary non-function', defined as the permanent absence of graft function, patients with DGF will eventually recover to become dialysis-independent. Nevertheless, DGF complicates the post-operative course, and it may be associated with lower long-term patient and graft survival.[3]

In an effort to alleviate donor shortage, the donor pool has been broadened with the use of grafts from 'expanded criteria donors' (ECD) and 'donation after circulatory death' (DCD) donors. DCD donors, also known as non-heart beating donors, are donors in which a circulatory arrest occurred before graft harvesting. As opposed to grafts from 'donation after brain death' (DBD) donors, DCD grafts suffers from a first period of warm ischemia before explantation, which can aggravate ischemia-reperfusion injury.[4] Consequently, the incidence rate of DGF in patients with a graft from a DCD donor is higher than in patients with a graft from a DBD donor, being around 25% with a DBD donor and ranging from 30 to 80 % with a DCD donor.[5-8]

Unfortunately, there is still little we can do to prevent DGF, and clinical practice guidelines on its management are limited.[9] A poorly defined, but important aspect is perioperative fluid management. The primary goal is to avoid hypovolemia and renal tissue hypoxemia after kidney transplantation which would further aggravate ischemia-reperfusion injury. On the other hand, care should be taken to avoid over-hydration, as patients with end-stage renal disease are prone to complications of fluid overload such as capillary leakage, tissue edema, pulmonary edema, infections and myocardial ischemia.[10] Together, this results in a very narrow therapeutic window for intravenous fluid administration. Moreover, we lack non-invasive, practical tools to adequately guide perioperative fluid therapy. Clinical experience and use of traditional parameters such as blood pressure, heart rate, urinary output and central venous pressure (CVP) have shown to be unreliable.[10, 11]

At the Antwerp University Hospital, there has historically been a tendency to be rather restrictive in administering intravenous fluid therapy in the immediate phase before kidney transplantation. Since 2015, however, we have adopted a new saline prehydration protocol, with deliberate pre- and peri-operative intravenous fluid administration in order to improve early graft perfusion. In this retrospective study, we sought to determine if this saline loading regimen has had an impact on the risk of DGF.

Materials and methods

Patients and study period

From January 1st, 2003 until December 31st, 2012 and from January 1st, 2015 until March 31st, 2019, 548 patients underwent renal transplantation in the University Hospital of Antwerp, Antwerp, Belgium. Two distinct cohorts are described based on the period of renal transplantation. In the first study period (January 1st, 2003 until December 31st, 2012), all patients were hemodynamically managed at the discretion of the care-giving physician, typically without preoperative saline loading, further referred to as the "historical cohort". From 2015 on, a 'saline loading' perioperative fluid protocol was introduced in our center. All patients who underwent renal transplantation after implementation of this new protocol are referred to as the "saline loading cohort". After excluding pediatric patients, patients who underwent a combined transplantation (kidney and pancreas and/or heart); patients who received a graft from a living donor or from a DBD donor, and patients who underwent a pre-emptive transplantation (transplantation date before the start of renal replacement therapy), 73 patients were kept in the final analysis of the current study (see figure 1).

The implemented perioperative fluid protocol

In clinically euvolemic patients, the 'saline loading' perioperative fluid protocol starts 4 hours prior to transplantation with the infusion of saline (0,9% NaCl) at a maximum rate of 1000 mL/hour to target an increase in body weight of 1,5 to 3%. After this pretransplant saline loading has been completed, saline infusion is continued perioperatively at a maximum 600 mL/h until a CVP target of 5-10 cm H20 is reached. The infusion rate is then reduced to 30 mL/h to maintain the CVP target during transplantation. In the first 8 hours after completion of surgery, fluid therapy is

guided by the patient's CVP and diuresis. If the CVP is below 5 cmH2O, an infusion of 500ml of saline is given over 1h. If the CVP is above 5 cmH20 and diuresis is higher than 20 mL/h, an infusion with a mixture of 0,45% NaCl and 5% Glucose is given at a maximal rate of 200 mL/h; if diuresis is lower than 20 mL/h, the rate of this infusion is set at 30 mL/h and an single infusion of Furosemide (250mg) is given. After 8 hours the rate of this infusion is set at 40 mL/h or 80 mL/l if the patient's diuresis is less or more than 20 mL/l, respectively.

Immunosuppressive therapy

In case of DCD transplantation, standard induction therapy consisted of rabbit antithymocyte globulin (rATG) and intravenous methylprednisolone. Occasionally, monoclonal interleukin 2 receptor antibodies (IL2Ra) were used instead of rATG according to the physicians' discretion. Standard maintenance therapy consisted of mycophenolic acid (MPA), steroids and delayed introduction of tacrolimus (Tac) or cyclosporine A (CsA) in case of ATG administration. Until 2013, rATG was administered as rATG-Fresenius S® (dose 2 mg/kg/day) from day 0 to day 8. From 2013 on, Thymoglobulin® was used at 1.0-1.25 mg/kg/day from day 0 to day 6. The first rATG dose was administered in the operating room, after induction of narcosis, and given over a 6 to 8 hours period. Basiliximab was administered as 20 mg on day 0 and day 4. Daclizumab was administered at a dose of 1 mg/kg on days 0, 14, 28, 42, and 56. Corticosteroid therapy consisted of intravenous methylprednisolone 250 mg on day 0, methylprednisolon 125 mg on day 1, oral prednisolone 20 mg/day from day 2-14 and later tapering. Under rATG, the introduction of Tac or CsA was delayed until the graft regained function, defined as decrease of serum creatinine levels by 50 % from baseline, or at the end of the first week at latest regardless of graft function. In case of IL2Ra induction, CsA or Tac was started within the first 24 hours. CsA was started as 3 mg/kg BID with target C2 levels of 1000 ng/ml. Tac was started as 0.15 mg/kg/day with target trough levels of 10 ng/mL. MPA was dosed at 2500 mg/day when combined with CsA and 2000 mg/day when combined with Tac.

Data collection and processing

After inclusion, patients' baseline demographics and characteristics and study outcomes were collected in a local database.

The outcome 'delayed graft function' or DGF was defined as the need for renal replacement therapy in the first 7 days after transplantation, regardless of indication and duration. Duration of DGF was defined as the time (days) from transplantation until the last day of dialysis. Patients with 'primary non-function' were defined as patient with a permanent lack of graft function after transplantation.

For each donor, we calculated the Kidney Donor Risk Index (KDRI). It has the advantage to combine several donor-related characteristics (age, height, weight, race, history of hypertension, history of diabetes, cause of death, terminal serum creatinine, HCV status and donation type (donation after brain or circulatory death)) in order to estimate the relative risk for graft failure as compared with the median donor of the preceding year in DonorNet (reference donor).[12] In addition, recent data indicate that the KDRI is also a good predictor of the occurrence of DGF.[13] To compare KDRI scores across different years, we used the median donor of 2017 as reference donor.

Statistical analysis

All variables are outlined as frequencies and percentages, means and standard deviations or medians and interquartile ranges, as appropriate. Data were compared with Pearson Chi Square, Fisher Exact test, Student t test or non-parametric testing (Wilcoxon rank-sum test). Statistical analysis was performed with the use of SPSS (version 23 for Mac) and JMP (version 14). A two-sided p value <0,05 was considered statistically significant. We restricted the multivariable analysis to 3 variables to avoid overfitting of the model.

Results

Study population

A total of 72 patients who received a kidney from a DCD donor were kept for final analysis of which 46 patients were transplanted between 2003 and 2012 and hemodynamically managed according to the historical fluid protocol. Twenty-six patients received a renal transplantation after 2015 and before march 2019 and were perioperatively treated according to the saline loading fluid protocol. Baseline demographics and characteristics of both cohorts were comparable and are listed in table 1.

Incidence of delayed graft function

None of the patients experienced primary non-function. Delayed graft function (DGF) occurred in 12 patients (16,7%) of which 11 took place in the historical cohort (11/46; 23,9%) and 1 in the saline loading cohort (1/26; 3,8%) (Figure 2, p <0,05). The main indications for starting post-operative dialysis were hyperkaliemia (3/12; 25%) and hypervolemia (3/12; 25,0%) or a combination of both (3/12; 25%). One patient had symptomatic uremia (8,3%), one patient suffered from medically uncontrollable hyperphosphatemia (8,3%) and one patient had ongoing high levels of serum creatinine. The median duration of DGF, defined as the time from transplantation until the last day of dialysis, was 6,5 days with an interquartile range of 2,2 to 13,5 days. Kidney transplant biopsy was performed in 6 patients during the period of DGF. In only two patients, histological analysis was conclusive on the underlying cause. Both patients had clear histological signs of acute tubular necrosis.

Risk factors of delayed graft function

In univariable analysis, the presence of donor arterial hypertension (OR 7,42; 95% CI 1,71 – 32,29) and a higher body weight of the donor (OR 1,03; 95% CI 1,00 – 1,07) were significant predictors of delayed graft function (p <0,05 for both predictors). The odds for developing delayed graft function were 7,7 times lower for patients in the saline loading fluid protocol as compared with patients in historical fluid cohort (p=0,05).

In order to estimate the independent effect of the new saline loading protocol on DGF prevention, a multivariable analysis was performed. Because of the relatively low number of DGF events, we limited the number of covariables to only two, to avoid overfitting of the model. We decided to use cold ischemia time (CIT), which is the most important risk factor for DGF known from the literature[14], and the KDRI, because it incorporates the two factors that were statistically significant in the univariable analyses, such as donor history of hypertension and donor weight. In this model, there was a clear trend towards an independent effect of the saline loading protocol on the risk of DGF (p=0.07).

Discussion

In this study we showed that the incidence of DGF following a DCD transplantation decreased from 23,9% to 3,8% after implementation of a saline loading perioperative fluid protocol. A multivariable analysis, correcting for CIT and donor quality (based on KDRI), suggested that the new fluid protocol may indeed have had an independent role in DGF prevention. Of note, KDRI has recently been show, in an analysis of more than 50.000 kidney transplant recipients, to be a good predictor of DGF across a wide range of CIT.[13]

The rationale for prehydratation in the immediate phase before and during engraftment is to avoid hypovolemia and renal tissue hypoxemia, which would further aggravate the ischemia-reperfusion injury. Hemodynamic changes during anesthesia and surgery can negatively influence graft perfusion.[15] Mediators that accumulate during the ischemia period can lead to vasodilation and increased vascular permeability after reperfusion, which may contribute to the decline in central venous pressure (CVP) that is often seen in the immediate postoperative period.[16] Furthermore, the transplanted kidney is denervated and lacks neurogenic regulation of the renal blood flow, which makes it more vulnerable to hypoperfusion.[17]

Nevertheless, it is unlikely that our low DGF rate is solely due to the saline loading protocol, because the DGF rate was already relatively low before its implementation. Indeed, observed rates of DGF with DCD transplantation in the current literature mostly range between 30% and 80% [5, 6]. Therefore, delayed introduction of calcineurin-inhibitors under the umbrella of ATG induction therapy, standard procedure in our clinic in patients with a high risk of DGF, may also have contributed to the low DGF rates.[18] Although the number of patients in our series who did not receive ATG was too low to show the efficacy of this strategy in the present study, a meta-analysis of calcineurin-sparing strategies has convincingly shown that CNI-sparing strategies are associated with less delayed graft function (OR 0.89; 95% CI 0.80–0.98; *P* 0.02)[19]. In addition, cold-ischemia times were kept relatively short. Indeed, over half of the grafts in our study had a cold ischemia time of less than 12 hours.

Another possible explanation for the low DGF rate could be that we might have applied very strict acceptance criteria for DCD donors, therefore using only young or otherwise high-quality donors in case of DCD. However, median donor age in our most recent cohort was 50 years, which is comparable to the median age of deceased donors used for a transplant in Eurotransplant nowadays and median KDRI was 0.99 (95 % CI 0.82-1.19), indicating

that the quality of these donor kidneys is comparable to the quality of the median deceased donor used for transplant in the U.S. in 2017. Therefore, it seems unlikely that our low DGF rate is to a large extent explained by a strict selection of DCD donors.

Our study has a number of limitations. First, it is a retrospective observational study extending over a relatively long time period. Therefore, there may have been other evolutions in medical management over time that have influenced the risk of DGF beyond the new fluid management. These parameters are not well known and thus are not easy to grasp in this analysis. Second, the sample size is relatively small with only a low number of DGF events, therefore limiting the reliability of the multivariable model. Strengths of this study include the relatively uniform immunosuppressive treatment, good adherence to the saline loading protocol and detailed data on the quality of the donor grafts.

There is increasing evidence that new preservation strategies, particularly hypothermic machine perfusion (HMP) of the allograft, reduces the risk of delayed graft function, both in grafts from DCD and DBD donors, with the greatest reduction in DCD donors. A recent Cochrane systematic review and meta-analysis documented that HMP reduces the risk of DGF in kidneys from DCD donors (7 studies, 772 participants: RR 0.75; 95% CI 0.64 to 0.87; P = 0.0002; high certainty evidence), as well as kidneys from DBD donors (4 studies, 971 participants: RR 0.78, 95% CI 0.65 to 0.93; P = 0.006; high certainty evidence). [20] Indeed, the incidence of DGF decreased from 50,1% to 36,4% with DCD donors and from 34,2% to 26,8% with DBD donors.[20] Nevertheless, today machine perfusion is not yet widely performed because of logistic difficulties and substantial costs. Interestingly, our experience shows that it is possible to achieve DGF rates that are at least as low as those described with machine perfusion, with just static cold storage. Our study raises the possibility that “patient perfusion” might obviate the need for kidney “machine perfusion”, particularly when combined with rATG and delayed introduction of calcineurin inhibitors and if cold ischemia time can limited to 12 hours or less.. The potential economical benefit of implementing HMP as standard-of-care practice is still a matter of debate.[21, 22] If further studies confirm that low DGF rates can be achieved with classic static cold storage, such as in our experience, HMP may not be cost-effective.

In summary, we believe that implementation of a perioperative hemodynamic management strategy to optimize early graft perfusion as described here, together with reducing cold ischemia time and delayed introduction of calcineurin inhibitors will contribute to keep the incidence of DGF low in recipients of DCD kidneys.

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Figures:

Figure 1: patient selection criteria

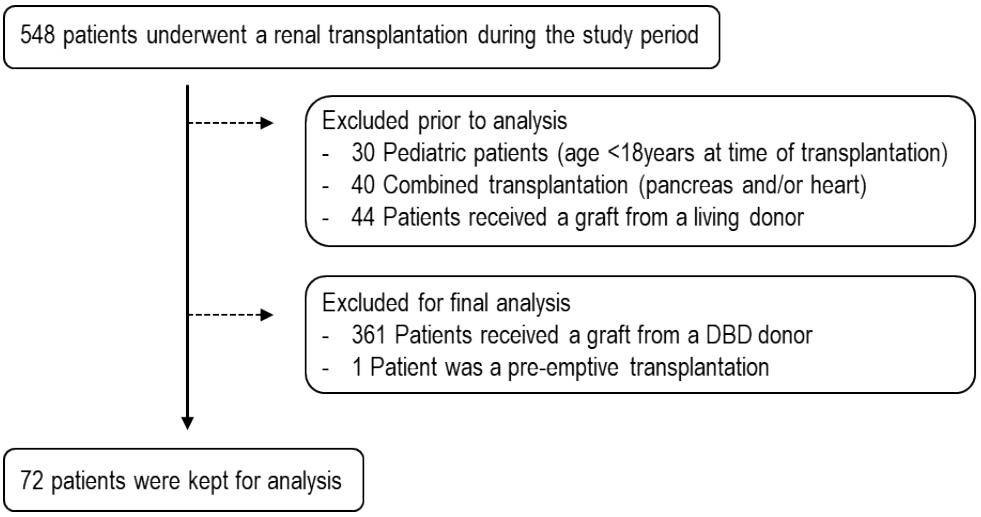
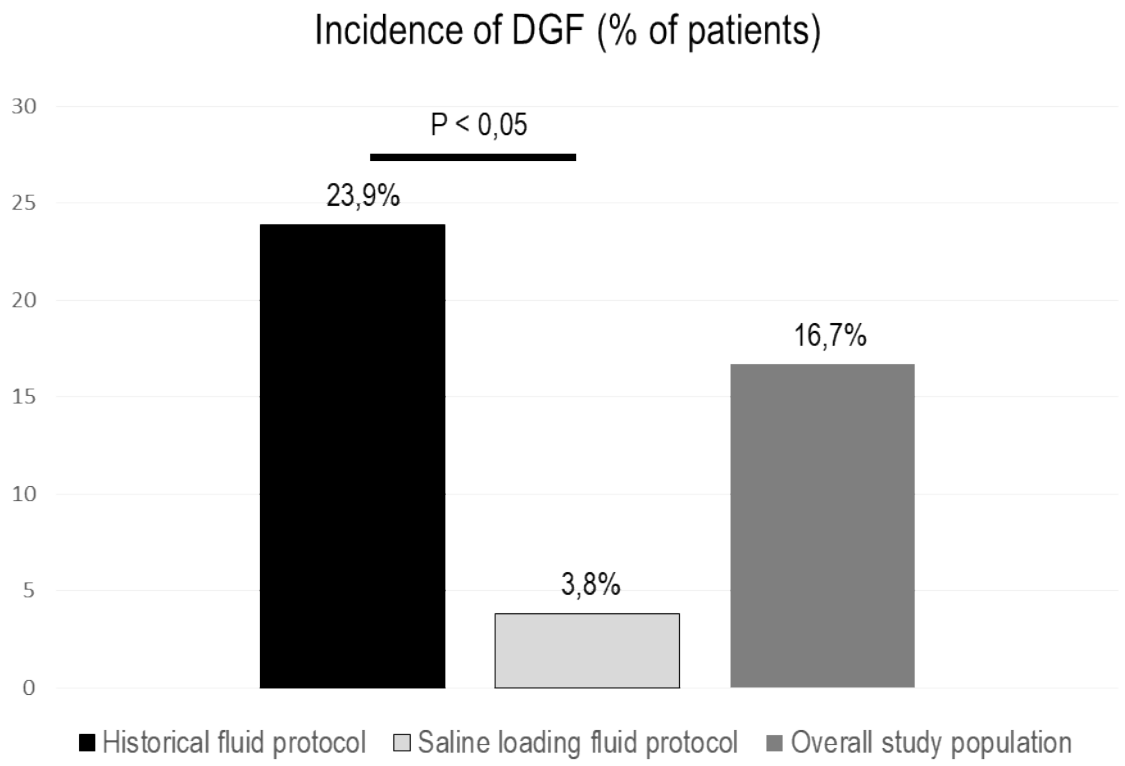


Figure 2: incidence of delayed graft function (DGF)



Tables:

Table 1: Baseline demographics and characteristics [a]

	Historical fluid protocol (n=47)	Saline loading fluid protocol (n=26)	p-value
Male recipient	27 (58,7%)	16 (61,5%)	0,81
Recipient age, years	50 (40-60)	55 (47-61)	0,12
Recipient BMI, kg/m^2	25,8 (22,3-28)	25,2 (23,5-28,4)	0,45
Black orgin	0 (0%)	1 (3,8%)	0,18
Recipient history			
Diabetes	8 (17,4%)	3 (11,5%)	0,50
Hypertension	42 (91,3%)	23 (88,5%)	0,70
Duration RRT, days	743 (406-1167)	720 (449-1373)	0,74
Male donor	33 (71,7%)	17 (65,4%)	0,57
Donor age, years	44 (31-52)	50 (41-55)	0,29
Donor weight, kg	80 (69,5-92,7)	70 (59,7-85,6)	0,06
Donor history of hypertension	9 (19,6%)	1 (4,3%)	0,09
Donor cause of death			
CVA/stroke	11 (23,9%)	3 (11,5%)	0,20
Other	35 (76,0%)	23 (88,5%)	
Donor creatinine, mg/dl	0,68 (0,58-0,82)	0,63 (0,47-0,70)	0,09
Induction			
rATG	32 (69,6%)	23 (88,5%)	0,07
IL2	14 (30,4%)	3 (11,5%)	
Maintenance			
Calcineurine I	46 (100%)	25 (96,2%)	0,18
mTOR I	0 (0%)	1 (3,8%)	
Current PRA			
>5%	1 (2,2%)	2 (7,7%)	0,26
>30%	1 (2,2%)	0 (0%)	0,45
Warm ischaemia time, minutes	31 (28-37)	30 (23-39)	0,63
Cold ischaemia time, hours	12,08 (7,69-15,17)	11,05 (7,71-16,01)	0,84
HLA mismatches	3 (2-3,25)	3 (2-3)	0,68
Graft rank			
First graft	42 (91,3%)	23 (88,5%)	0,69
Regraft	4 (8,7%)	3 (11,5%)	
KDRI	1 (0,79-1,19)	0,99 (0,82-1,22)	0,98

Footnotes

[a] All continuous variables are displayed as median with interquartile ranges between brackets. All categorical values are illustrated as proportion of total in percentages.

Table 2: Predictors of delayed graft function

			Unadjusted model (univariable)			Adjusted model (multivariable)		
	No DGF (n=60)	**DGF (n=12)**	**OR**	**CI**	**p-value**	**OR**	**CI**	**p-value**
Male recipient	38 (63,3%)	5 (41,7%)	0,41	0,12 – 1,46	0,17			
Recipient age, years	53 (44,2 – 60,7)	50,5 (39,5 – 59)	0,99	0,93 – 1,04	0,60			
Recipient BMI, kg/m^2	25,4 (22,7 – 27,7)	27,6 (22,7 – 30,5)	1,13	0,95 – 1,34	0,18			
Recipient history								
Diabetes	8 (13,3%)	3 (25,0%)	2,17	0,48 – 9,74	0,31			
Hypertension	54 (90,0%)	11 (91,7%)	1,22	0,13 – 11,18	0,86			
Duration RRT, days	728 (414 – 1255)	634,5 (436,5 – 1157,25)	1,00	1,00 – 1,00	0,62			
Male donor	41 (68,3%)	9 (75,0%)	1,39	0,34 – 5,72	0,65			
Donor age, years	46 (37 – 54,7)	48 (40,7 – 55,5%)	1,01	0,96 – 1,06	0,64			
Donor weight, kg	75 (66 – 85)	91,5 (69,7 – 113)	1,03	1,00 – 1,07	0,04			
Donor history of hypertension	5 (8,8%)	5 (41,7%)	7,42	1,71 – 32,29	0,01			
Donor cause of death								
CVA/stroke	11 (18,3%)	3 (25,0%)	1,48	0,34 – 6,40	0,60			
Donor creatinine, mg/dl	0,66 (0,55 – 0,80)	0,63 (0,51 – 0,79)	0,89	0,17 – 4,53	0,88			
Induction therapy								
rATG	14 (23,3%)	3 (25,0%)	1,10	0,26 – 4,61	0,90			
Maintenance therapy								
Calcineurine I	59 (98,3%)	12 (100%)	/[b]					
Current PRA								
>5%	3 (5,0%)	0 (0%)	/[c]					
>30%	1 (1,7%)	0 (0%)	/[c]					
Warm ischaemia time, minutes	30 (27 – 37)	32 (30 – 41)	1,04	0,95 – 1,14	0,37			
Cold ischaemia time, hours	12,0 (7,8 – 15,3)	10,5 (6,9 – 18,3)	1,01	0,90 – 1,14	0,82	1,02	0,90 – 1,15	0,80
HLA mismatches	3 (2 – 3)	3 (2 – 3,75)	1,06	0,60 – 1,88	0,85			
Regraft	5 (8,3%)	2 (16,7%)	2,20	0,38 – 12,95	0,38			
KDRI	0,98 (0,81 – 1,19)	1,1 (0,95 – 1,21)	1,73	0,18 – 16,94	0,63	1,38	0,11 – 16,89	0,80
Saline loading fluid protocol	25 (41,7%)	1 (8,3%)	0,13	0,02 – 1,05	0,05	0,14	0,02 – 1,18	0,07

Footnotes

[a] All continuous variables are displayed as median with interquartile ranges between brackets. All categorical values are illustrated as proportion of total in percentages.

[b] No events in patients with mTOR inhibitor as maintance therapy

[c] No events in patients with PRA >5% or PRA >30%

Figure 1: patient selection criteria

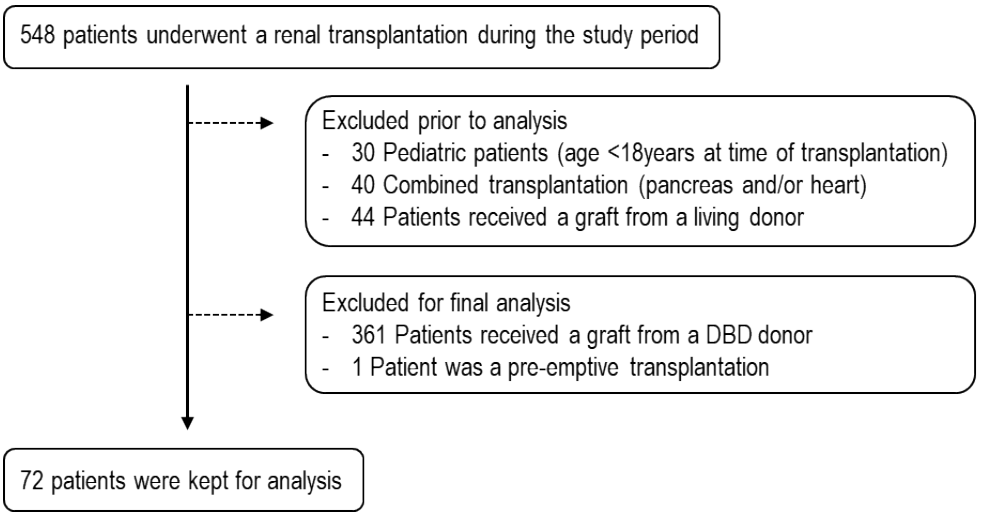


Figure 2: incidence of delayed graft function (DGF)

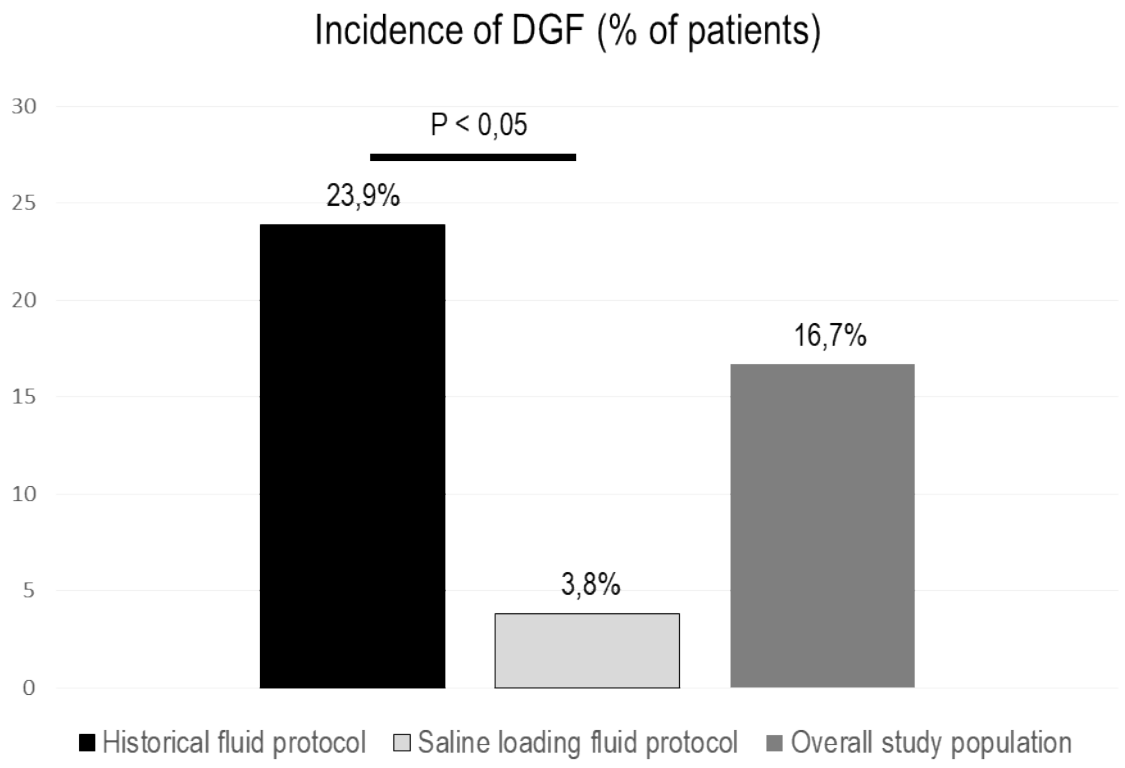


Table 1: Baseline demographics and characteristics [a]

	Historical fluid protocol (n=47)	Saline loading fluid protocol (n=26)	p-value
Male recipient	27 (58,7%)	16 (61,5%)	0,81
Recipient age, years	50 (40-60)	55 (47-61)	0,12
Recipient BMI, kg/m^2	25,8 (22,3-28)	25,2 (23,5-28,4)	0,45
Black orgin	0 (0%)	1 (3,8%)	0,18
Recipient history			
Diabetes	8 (17,4%)	3 (11,5%)	0,50
Hypertension	42 (91,3%)	23 (88,5%)	0,70
Duration RRT, days	743 (406-1167)	720 (449-1373)	0,74
Male donor	33 (71,7%)	17 (65,4%)	0,57
Donor age, years	44 (31-52)	50 (41-55)	0,29
Donor weight, kg	80 (69,5-92,7)	70 (59,7-85,6)	0,06
Donor history of hypertension	9 (19,6%)	1 (4,3%)	0,09
Donor cause of death			
CVA/stroke	11 (23,9%)	3 (11,5%)	0,20
Other	35 (76,0%)	23 (88,5%)	
Donor creatinine, mg/dl	0,68 (0,58-0,82)	0,63 (0,47-0,70)	0,09
Induction			
rATG	32 (69,6%)	23 (88,5%)	0,07
IL2	14 (30,4%)	3 (11,5%)	
Maintenance			
Calcineurine I	46 (100%)	25 (96,2%)	0,18
mTOR I	0 (0%)	1 (3,8%)	
Current PRA			
>5%	1 (2,2%)	2 (7,7%)	0,26
>30%	1 (2,2%)	0 (0%)	0,45
Warm ischaemia time, minutes	31 (28-37)	30 (23-39)	0,63
Cold ischaemia time, hours	12,08 (7,69-15,17)	11,05 (7,71-16,01)	0,84
HLA mismatches	3 (2-3,25)	3 (2-3)	0,68
Graft rank			
First graft	42 (91,3%)	23 (88,5%)	0,69
Regraft	4 (8,7%)	3 (11,5%)	
KDRI	1 (0,79-1,19)	0,99 (0,82-1,22)	0,98

Footnotes

[a] All continuous variables are displayed as median with interquartile ranges between brackets. All categorical values are illustrated as proportion of total in percentages

Table 2: Predictors of delayed graft function

			Unadjusted model (univariable)			Adjusted model (multivariable)		
	No DGF (n=60)	**DGF (n=12)**	**OR**	**CI**	**p-value**	**OR**	**CI**	**p-value**
Male recipient	38 (63,3%)	5 (41,7%)	0,41	0,12 – 1,46	0,17			
Recipient age, years	53 (44,2 – 60,7)	50,5 (39,5 – 59)	0,99	0,93 – 1,04	0,60			
Recipient BMI, kg/m^2	25,4 (22,7 – 27,7)	27,6 (22,7 – 30,5)	1,13	0,95 – 1,34	0,18			
Recipient history								
Diabetes	8 (13,3%)	3 (25,0%)	2,17	0,48 – 9,74	0,31			
Hypertension	54 (90,0%)	11 (91,7%)	1,22	0,13 – 11,18	0,86			
Duration RRT, days	728 (414 – 1255)	634,5 (436,5 – 1157,25)	1,00	1,00 – 1,00	0,62			
Male donor	41 (68,3%)	9 (75,0%)	1,39	0,34 – 5,72	0,65			
Donor age, years	46 (37 – 54,7)	48 (40,7 – 55,5%)	1,01	0,96 – 1,06	0,64			
Donor weight, kg	75 (66 – 85)	91,5 (69,7 – 113)	1,03	1,00 – 1,07	0,04			
Donor history of hypertension	5 (8,8%)	5 (41,7%)	7,42	1,71 – 32,29	0,01			
Donor cause of death								
CVA/stroke	11 (18,3%)	3 (25,0%)	1,48	0,34 – 6,40	0,60			
Donor creatinine, mg/dl	0,66 (0,55 – 0,80)	0,63 (0,51 – 0,79)	0,89	0,17 – 4,53	0,88			
Induction therapy								
rATG	14 (23,3%)	3 (25,0%)	1,10	0,26 – 4,61	0,90			
Maintenance therapy								
Calcineurine I	59 (98,3%)	12 (100%)	/[b]					
Current PRA								
>5%	3 (5,0%)	0 (0%)	/[c]					
>30%	1 (1,7%)	0 (0%)	/[c]					
Warm ischaemia time, minutes	30 (27 – 37)	32 (30 – 41)	1,04	0,95 – 1,14	0,37			
Cold ischaemia time, hours	12,0 (7,8 – 15,3)	10,5 (6,9 – 18,3)	1,01	0,90 – 1,14	0,82	1,02	0,90 – 1,15	0,80
HLA mismatches	3 (2 – 3)	3 (2 – 3,75)	1,06	0,60 – 1,88	0,85			
Regraft	5 (8,3%)	2 (16,7%)	2,20	0,38 – 12,95	0,38			
KDRI	0,98 (0,81 – 1,19)	1,1 (0,95 – 1,21)	1,73	0,18 – 16,94	0,63	1,38	0,11 – 16,89	0,80
Saline loading fluid protocol	25 (41,7%)	1 (8,3%)	0,13	0,02 – 1,05	0,05	0,14	0,02 – 1,18	0,07

Footnotes

[a] All continuous variables are displayed as median with interquartile ranges between brackets. All categorical values are illustrated as proportion of total in percentages.

[b] No events in patients with mTOR inhibitor as maintance therapy

[c] No events in patients with PRA >5% or PRA >30%