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## INTRODUCTION

Delayed graft function (DGF) continues to pose a significant challenge to the practice of kidney transplantation and it has important implications for early and late graft and patient outcomes.

Epidemiological studies have indicated that DGF is associated with a 41% increased risk of graft loss, and a 38% increase in the risk of acute rejection.

Differences in early graft function between kidney transplant recipients previously managed with either haemodialysis (HD) or peritoneal dialysis are well described.

However, whether a similar disparity exists between patients treated with extended hour ( $\geq 24$  hours/week) and conventional HD remains unknown, since only two small, single-centre studies have compared outcomes between these groups, reporting conflicting results.

Therefore, this study was conducted to examine the effect of pre-transplant HD modality on graft and patient outcomes using data from the Australia and New Zealand Dialysis and Transplant Registry.

## METHODS

This was a multicentre study including all HD patients who were transplanted in Australia or New Zealand between 2000 - 2014.

The primary outcome was DGF, defined as an ordinal outcome, as either a spontaneous fall in serum creatinine of less than 10% within 24 hours, or the need for dialysis within 72 hours following transplantation.

Secondary outcomes included post-transplant dialysis within 72 hours, acute rejection, renal function at 12 months, death-censored graft failure, all-cause and cardiovascular mortality, and a composite of graft failure and mortality.

Ordinal logistic regression was used to examine the primary outcome. Dialysis requirement within 72 hours following transplantation was evaluated with binary logistic regression.

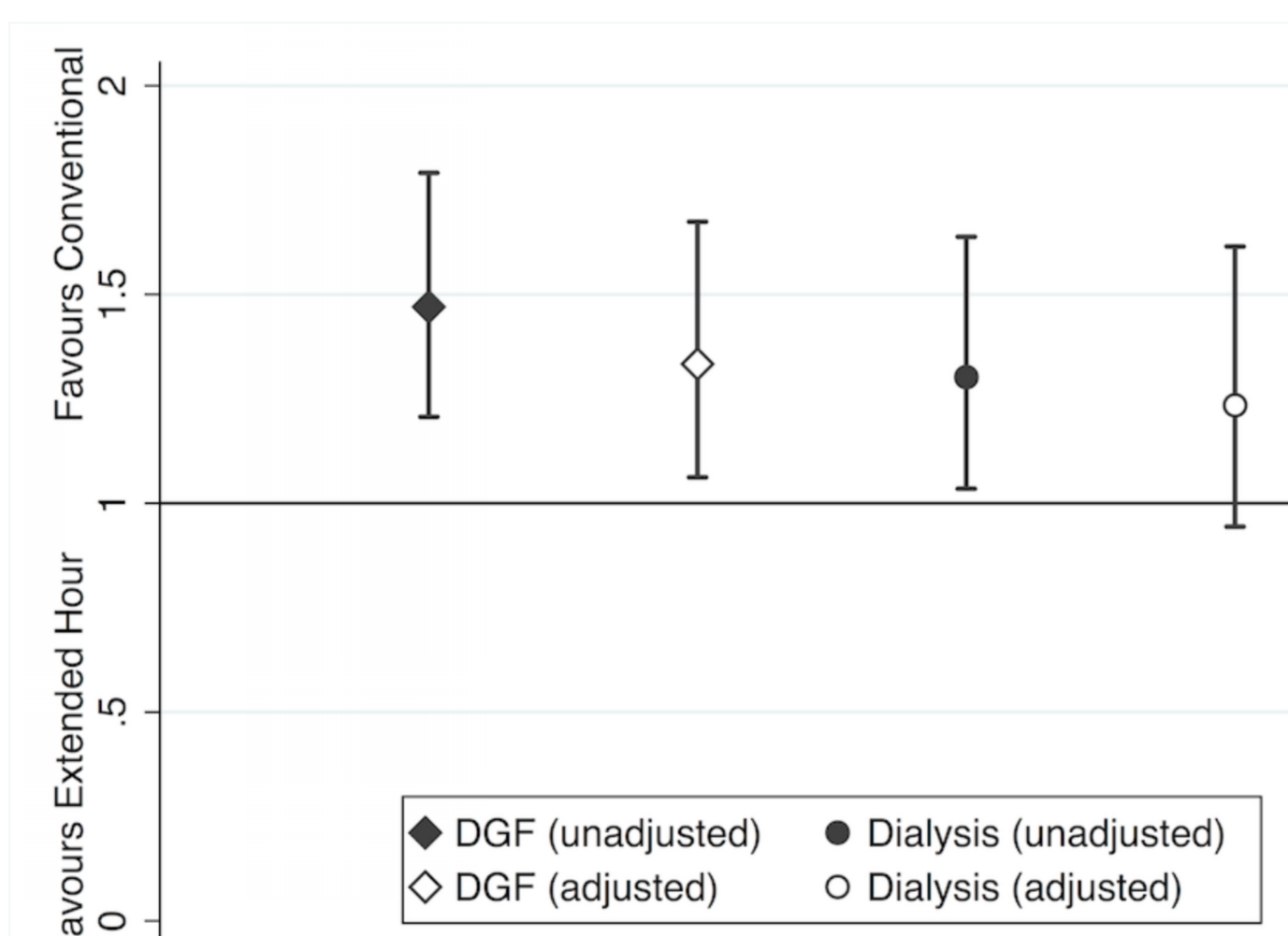
Negative binomial regression was used to compare acute rejection rates. Graft function at 12 months was examined using a linear regression model. Graft and patient survival were evaluated by Cox regression models.

## RESULTS

4935 patients (378 extended hour, 4557 conventional) were transplanted during the study period and followed for a median of 5.1 (IQR 2.4-8.4) years.

Compared to conventional HD, patients who received extended hour HD were more likely to be male, obese, and to have had a longer waiting time. They were less like to be Aboriginal or Torres Strait Islander (ATSI) race.

	Extended hour (n=378)	Conventional (n=4557)
Male (n,%)	282 (75)	2975 (65)
Age (years $\pm$ SD)	47.9 $\pm$ 11.9	49.6 $\pm$ 12.9
BMI (n,%)		
<18.5	5 (1)	134 (3)
18.5-30	248 (67)	3265 (73)
>30	119 (32)	1064 (24)
Race (n,%)		
-Caucasian	317 (84)	3572 (78)
-ATSI	2 (0.5)	212 (5)
-Other	59 (15)	773 (17)
Diabetes (n,%)	49 (13)	831 (18)
IHD (n,%)	51 (14)	787 (17)
Waiting time (months, IQR)	47.1 (30.0-75.1)	36.3 (19.5-65.7)
Donor type (n,%)		
-Live	89 (24)	1266 (28)
-DBD	230 (61)	2813 (62)
-DCD	59 (16)	478 (11)
Donor age (years, $\pm$ SD)	46.6 $\pm$ 15.7	46.8 $\pm$ 15.7
Ischaemia time (hr $\pm$ SD)	9.7 $\pm$ 5.2	10.1 $\pm$ 6.1
HLA mismatches (n,%)		
0-2	139 (37)	1570 (35)
3-4	108 (28)	1651 (36)
5-6	131 (35)	1336 (29)



**Table 1:** Baseline characteristics of 4935 HD patients who underwent renal transplantation between 2000 and 2014

**Figure 1:** Logistic regression analysis of DGF and requirement for dialysis within 72 hours. Estimates shown include odds ratios with 95% confidence intervals

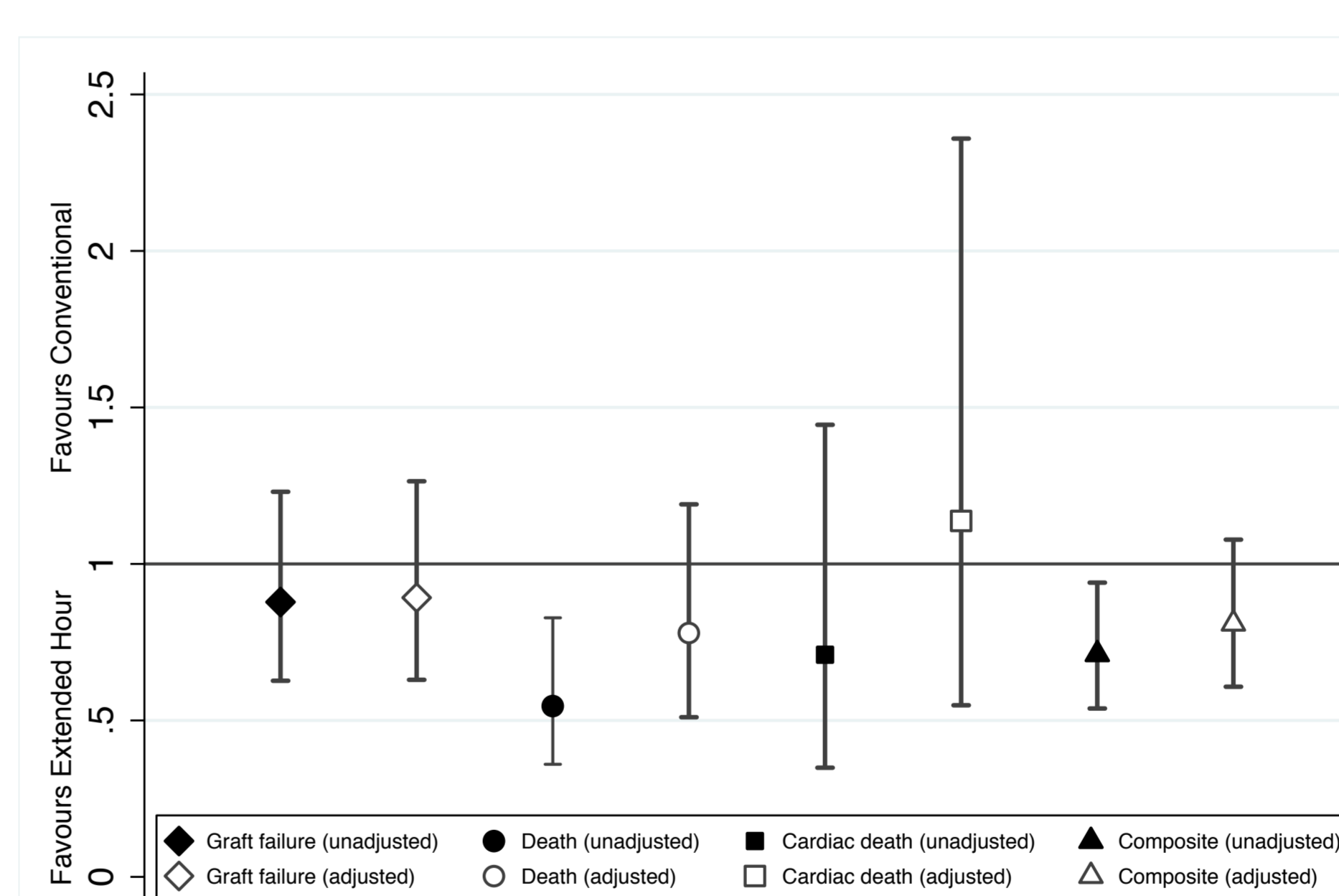
In total, 1979 patients developed DGF (191 extended hour, 1788 conventional). Extended hour HD was associated with a higher likelihood of DGF (OR 1.33, 95% CI 1.06-1.67) and dialysis at 72hr (OR 1.23, 95% CI 0.94-1.61).

	Extended hour (n=378)	Conventional (n=4557)
Acute rejection episodes		
- 0	275 (73)	3287 (72)
- 1	71 (19)	902 (20)
- 2	22 (6)	251 (5)
- $\geq 3$	10 (2)	117 (3)
Graft failure	36 (9)	582 (13)
All-cause mortality	23 (6)	629 (14)
Cardiovascular mortality	8 (2)	170 (4)
Composite outcome	52 (14)	1047 (23)

**Table 2:** Frequency of HD patients reaching the secondary outcomes

There was no difference in the acute rejection rate between conventional and extended hour HD patients (adjusted IRR 0.95, 95% CI 0.77-1.17).

Mean estimated glomerular filtration rate at 12 months was not significantly different between transplant recipients managed with extended hour or conventional HD prior to transplantation ( $52.3 \pm 18.9$  vs  $54.1 \pm 18.9$  ml/min/1.73m<sup>2</sup> p=0.10).



**Figure 2:** Association between extended hour HD and death-censored graft failure, all-cause death, cardiac death and a composite of graft failure or death. Estimates shown include hazard ratio with 95% confidence intervals

There was no difference in the time to death between extended hour and conventional HD patients (HR 0.82, 95% CI 0.53-1.25). Similarly, time to cardiovascular death was comparable between groups (HR 1.15, 95% CI 0.56-2.40)

## CONCLUSIONS

In this large cohort of HD patients from Australia and New Zealand undergoing kidney transplant, extended hour HD was associated with an increased risk of DGF compared to conventional HD.

Post-transplant dialysis requirement, acute rejection, renal function at 12 months, death-censored graft failure, all-cause and cardiovascular mortality, and a composite of graft failure and mortality were not different.

Since extended hour HD is associated with improved BP control, reduced vascular resistance and extravascular volume, and increased weekly sodium removal, patients may be at increased risk of intraoperative hypotension.

Calcineurin inhibitors may further amplify allograft hypoperfusion through dysregulation of intra-glomerular pressure and arteriolar vasoconstriction.

These concepts have important clinical implications because hypovolemia and intraoperative hypotension are preventable and easily modifiable.

Adequate intravascular volume should be ensured both pre-operatively and intra-operatively. Ultrafiltration should be avoided prior to surgery.

Intraoperative hypotension should be managed promptly with fluid and vasopressor support to maintain graft perfusion.

The physiological benefits of extended hour HD are well described, however when patients receiving extended hour HD undergo renal transplantation, consideration should be given to the potentially increased risk of DGF.