Transplant International

ORIGINAL ARTICLE

The weekend effect in kidney transplantation outcomes: a French cohort-based study

Simon Ville[1,2], Julien Branchereau[1,2], Adeline Cornuaud[3], Jacques Dantal[1,2], Christophe Legendre[4], Fanny Buron[5], Emmanuel Morelon[5], Valérie Garrigue[6], Moglie Lequentrec[6], Laetitia Albano[7], Elisabeth Cassuto[7], Sophie Girerd[8], Marc Ladrière[8], Denis Glotz[9], Carmen Lefaucher[9], Clarisse Kerleau[1,2], Yohann Foucher[2,3] & Magali Giral[1,4,10] for the DIVAT consortium

1 CRTI UMR 1064, Université de Nantes, ITUN, RTRS Centaure, Inserm, Nantes, France
2 INSERM UMR 1246 - SPHERE, Nantes University, Tours University, Nantes, France
3 Centre Hospitalier Universitaire de Nantes, Nantes, France
4 Kidney Transplant Center, Necker University Hospital, APHP, RTRS Centaure, Paris Descartes and Sorbonne Paris Cité Universities, Paris, France
5 Nephrology, Transplantation and Clinical Immunology Department, RTRS Centaure, Edouard Herriot University Hospital, Hospices Civils, Lyon, France
6 Nephrology, Dialysis and Transplantation Department, Lapeyronie University Hospital, Montpellier, France
7 Department of Nephrology and Renal Transplantation, Hospital Pasteur, Nice, France
8 Renal Transplantation Department, Brabois University Hospital, Nancy, France
9 Department of Nephrology and Renal Transplantation, CHU Paris-GH St-Louis Lariboisière, Paris, France
10 Centre d'Investigation Clinique en Biothérapie, Nantes, France

Correspondence
Magali Giral, ITUN - 30, bd Jean Monnet, 44093 Nantes Cedex 01, France.
Tel.: +33 2 40 08 47 69;
e-mail: mgiral@chu-nantes.fr

SUMMARY

Numerous studies have reported a weekend effect on outcomes for diseases treated at hospitals. No study has been conducted in France for kidney transplantation. We therefore performed a cohort-based study to evaluate whether outcomes of kidney transplant recipients display a weekend effect. Data were extracted from the French DIVAT cohort. Patients aged 18 years and older, transplanted with a single kidney from deceased donors between 2005 and 2017 were studied. Linear regression, logistic regression, and cause-specific Cox model were used. Among the 6652 studied patients, 4653 patients were transplanted during weekdays (69.9%) versus 1999 during weekends (30.1%). The only statistically significant difference was the percentage of patients with vascular surgical complication(s) at 30 days: 13.3% in the weekend group versus 16.2% in the weekday group 0.79 (95% CI: 0.68; 0.92). We did not observe other significant differences for the other outcomes: patient or graft survival, the risk of acute rejection episodes, the 30-day percentage of urological complications, and the 1-year estimated glomerular filtration rate. Our study highlights a small protective weekend effect with less post-surgery vascular complications compared to weekdays. This paradox might be explained by a different handling of weekend transplantations.

Transplant International 2020; 33: 1030–1039

Key words
cohort-based analysis, kidney transplantation, weekend effect

Received: 11 December 2019; Revision requested: 13 January 2020; Accepted: 11 May 2020;
Published online: 13 July 2020

Simon Ville and Julien Branchereau have contributed equally.
Données Informatisées et VAlidées en Transplantation (DIVAT), Collaborators listed in Acknowledgments section.

doi:10.1111/tri.13653

Introduction

Over the last several decades, the issue of the "weekend effect" has been proposed by several studies, primarily British ones, which have reported an increased global mortality in patients admitted to hospitals during the weekend compared to weekdays [1]. Other articles studying specific medical conditions, such as myocardial infarction and stroke, have confirmed this effect [2,3]. Worse outcomes during the weekend have also been reported for both elective and urgent surgical interventions [4,5]. This effect could be explained on the one hand by a difference in the caregivers' skill level (nursing and medical staff), that is, less experienced on the weekend, and on the other hand, by the restricted availability of diagnostic and therapeutic procedures.

Organ transplantation from deceased donors is currently performed irrespective of the day of the week and at any time during the day, in order to minimize the cold ischemic time thus improving allograft function and transplantation survival [6]. Therefore, surgical procedures (procurement and graft) are frequently performed on the weekend, and this may lead to concerns that these graft outcomes may be worse. In 2016, Mohan et al. [7] reported that in the United States, deceased donor kidney discard rates were significantly higher on weekends and may have been due to compensation for a potential weekend effect. Likewise, as published in the British media [8], proposed weekend transplants were in some cases denied by candidates due to fear of complications or death.

In kidney transplantation setting, studies aimed at assessing the weekend effect on post-transplant outcomes concluded that recipients transplanted during weekends in hospitals did not suffer any adverse outcomes in comparison to those transplanted during weekdays [9–11]. However, most previously published studies suffer from the same methodological pitfall, whereby the conclusions were based on multivariate models for adjusting on confounders that were in some cases not "true confounders" (e.g. cold ischemia time - CIT). Indeed, CIT is on the pathway of the weekend effect on graft and patient outcomes. The inclusion of such a variable in multivariate regression, in order to estimate the causal weekend effect, results in an over-adjustment, which can lead to an under-estimation of the true effect [12]. Moreover, none of these studies was specifically conducted on the French health organization.

Therefore, we evaluated the impact of the weekend on the outcome of kidney transplantation graft surgery by respecting methodological standards in causal inference [13] and using a multicentric French cohort.

Patients and methods

Studied population

Data were extracted from the French DIVAT cohort (www.divat.fr, approved by CNIL, no 914184) consisting of kidney transplant recipients followed-up in Nantes, Paris (Necker and Saint-Louis), Nancy, Lyon, Montpellier, and Nice. The quality of the DIVAT data bank was validated by an annual audit. All participants gave informed consent. The included patients were adults at the time of their kidney transplantation performed between 2005 and 2017. Only kidney transplantations from deceased donors were considered. Multiple organ transplants were not included. The time of the surgery was determined from the operative report. Weekend surgery was defined as the date of surgery being a Saturday or Sunday and weekday surgery as the date of surgery being Monday to Friday. We determined the time of the surgery from the operative report. The weekend transplantations were the surgeries started at 0:00 am on Saturday and ended at 11:59 pm on Sunday.

French kidney allocation process

Briefly, the first kidney, considered as the local kidney, is proposed to the patients of the center that harvested (classified according to a score, see below). The second kidney is proposed first for national priorities (emergency, national priority immunization) and then for regional priorities (regional priority immunization, pediatric recipient for donors aged 18 to 30 years). If a retrieved organ does not trigger at any national or regional priorities, a national list is established via a points-scoring system that takes into account the age of registration, the number of HLA incompatibilities, the age differential, an indicator of difficulty of access to transplantation, combined with a geographical score.

Available data

Donor characteristics were age, gender, last Serum Creatinine (SCr) level, and cause of death. Recipient characteristics were age, gender, body mass index (BMI), comorbidities (diabetes, hypertension, dyslipidemia, neoplasia, cardiovascular history), duration of dialysis before transplantation, type of dialysis before

transplantation (No dialysis or peritoneal or hemodialysis), pre-transplantation anti-class I or class II Human Leucocyte Antigen (HLA) immunization (anti-class I or class II - HLA) and initial renal disease. Transplantation parameters were CIT and number of HLA-A-B-DR incompatibilities.

Outcomes

The main outcome was the patient and graft survival, defined by the time between the transplantation and the first event between return to dialysis, pre-emptive re-transplantation and patient death. We also studied (i) the risk of acute rejection defined by the time between the transplantation and the first occurrence of acute rejection (return to dialysis, pre-emptive re-transplantation and all-cause death with a functioning graft were right-censored), (ii) the proportion of patients with urological complication within the 30 days post-transplantation (collection, lymphocele, vesical-ureteral reflux on the transplant, ureteral stenosis, urinoma), (iii) the proportion of patients with vascular complications within the 30 days post-transplantation (arteriovenous fistula, bleeding from surgical site, arterial dysfunction, partial or complete arterial or venous thrombosis or aneurysm), and (iv) the estimated glomerular filtration rate (eGFR) at 1-year post-transplantation by using the CKD-EPI formula [14].

Statistical analyses

The characteristics at the time of transplantation between the two groups of interest (weekend versus weekday transplantation) were compared using Chi-square tests for categorical variables and, Student *t*-tests for continuous variables. Linear regression (for the 1-year eGFR), logistic regressions (for the 30-day complications), and cause-specific Cox models (for the times-to-event) were used.

Our principal aim was to describe the causal effect of transplantations performed during weekends versus weekdays. The previous list of variables, such as the cold ischemia time or the donor characteristics, are the consequences of the transplantation day. It does not constitute confounders: They are on the pathway between the exposure and the outcomes. Therefore, the raw associations between the transplantation day and the outcomes were unbiased. They consisted in the principal analyses of our study. All the results in the next section were unadjusted. Note that in case of significant results, we further performed an over-adjusted model, by fitting a multivariable regression including all the variables at transplantation associated with the outcome (univariate analyses, $P < 0.10$). The aim of this secondary analysis was to explore the potential mechanism for the weekend effect. Only adjusted indicators were defined as adjusted, the other were by default unadjusted.

Non-agreement with the log-linearity assumption was defined when the Bayesian Information Criterion (BIC) criteria decreased using natural spline transformation compared to the inclusion of the covariate in its natural scale. In case of violation, variables were categorized. Hazard proportionality was graphically checked by plotting log-minus-log survival curves according to the two groups of interest and studying the Schoenfeld residuals. The analyses were performed using Plug-Stat® software (www.labcom-risca.com) and R software.

Results

Cohort description

This study was performed on a cohort of 6652 patients who met the inclusion criteria, and the patient characteristics at the time of transplantation are listed in Table 1. Among these, 4653 patients were transplanted during weekdays (69.9%) versus 1999 during weekends (30.1%). The two groups can be considered comparable (the small *P*-values were due to the important sample size). The median follow-up time was 4.0 years (ranging from 0.0 to 13.0). During follow-up, 632 patients died with a functioning graft, (including 185 in the weekend group), 868 returned to dialysis (including 256 in the weekend group) and 14 patients were pre-emptively re-transplanted (including 5 in the weekend group).

Patient and graft survival

There was no significant difference in patient and graft survival up to 10 years post-transplantation between patients transplanted on weekends versus weekdays. As illustrated in Fig. 1. The probability of patient and graft survival at 10 years post-transplantation in the weekday group was 0.55 (95% CI: 0.52; 0.57) versus 0.54 (95% CI: 0.50; 0.58) in the weekend group. As illustrated in Fig. 2, the Hazard Ratio (HR) was 1.01 for patients transplanted during weekends versus those during weekdays (95% CI: 0.90; 1.13).

Given the large time frame of transplants included, we did a subgroup analysis considering graft performed before or after 2012. The HR related to the patient end

Table 1. Patients characteristics.

	Whole sample (n = 6652)			Weekend (n = 1999)			Weekday (n = 4653)			
	NA	n	%	NA	n	%	NA	n	%	P-value
Male recipient	0	4142	62.3	0	1232	61.6	0	2910	62.5	0.4829
Recurrent causal nephropathy	7	1796	27.0	1	535	26.8	6	1261	27.1	0.7625
Pre-emptive transplantation	15	610	9.2	4	179	9.0	11	431	9.3	0.6863
History of diabetes	0	1196	18.0	0	342	17.1	0	854	18.4	0.2253
History of hypertension	0	5537	83.2	0	1651	82.6	0	3886	83.5	0.3546
History of vascular disease	0	1219	18.3	0	382	19.1	0	837	18.0	0.2785
History of cardiac disease	0	2003	30.1	0	605	30.3	0	1398	30.0	0.8577
History of cardiovascular disease	0	2633	39.6	0	805	40.3	0	1828	39.3	0.4520
History of malignancy	0	802	12.1	0	239	12.0	0	563	12.1	0.8689
History of dyslipidemia	0	2576	38.7	0	811	40.6	0	1765	37.9	0.0429
History of hepatitis (B or C)	0	454	6.8	0	128	6.4	0	326	7.0	0.3712
Positive recipient CMV serology	78	4361	66.3	19	1304	65.9	59	3057	66.5	0.5899
Positive recipient EBV serology	99	6375	97.3	28	1925	97.7	71	4450	97.1	0.2116
Positive anti-class I immunization	634	2427	40.3	187	722	39.8	447	1705	40.5	0.6157
Positive anti-class II immunization	728	2312	39.0	221	654	36.8	507	1658	40.0	0.0204
Male donor	13	3932	59.2	1	1160	58.1	12	2772	59.7	0.2039
ECD donor	72	2978	45.3	28	895	45.4	44	2083	45.2	0.8729
Donation after Circulatory Death	70	256	3.9	20	76	3.8	50	180	3.9	0.8926
Vascular cause of donor death	24	3589	54.1	8	1112	55.9	16	2477	53.4	0.0684
Donor hypertension	286	2075	32.6	92	615	32.2	194	1460	32.7	0.7006
Positive donor CMV serology	33	3597	54.3	10	1098	55.2	23	2499	54.0	0.3572
Positive donor EBV serology	67	6323	96.0	23	1898	96.1	44	4425	96.0	0.9320
HLA-A-B-DR incompatibilities ≥ 4	69	919	14.0	20	275	13.9	49	644	14.0	0.9214
Re-transplantation	0	1346	20.2	0	368	18.4	0	978	21.0	0.0151
Depleting induction	0	4041	60.7	0	1238	61.9	0	2803	60.2	0.1955
Calcineurin inhibitor at surgery	10			5			5			0.3606
Ciclosporine		1333	20.1		917	19.7		416	20.8	
Tracrolimus		5165	77.8		3631	78.1		1534	76.7	
No		144	2.1		100	2.2		44	2.3	
Transplant center										0.0121
A		1099	16.5		373	18.7		726	15.6	
B		1283	13.9		356	17.8		927	19.9	
C		727	10.9		220	11.0		507	10.9	
D		1473	22.1		445	22.3		1028	22.1	
E		1380	20.7		384	19.2		996	21.4	
F		283	4.3		86	4.3		197	4.2	
G		407	6.1		135	6.8		272	5.8	
	NA	**Mean**	**SD**	**NA**	**mean**	**kdSD**	**NA**	**Mean**	**SD**	
Recipient age (years)	0	52.3	13.6	0	52.3	13.8	0	52.4	13.6	0.7791
Recipient BMI (kg.m-2)	47	24.8	5.8	8	24.9	4.5	39	24.8	6.2	0.5746
Duration on waiting list (months)	150	27.7	25.5	41	27.8	26.3	109	27.6	25.1	0.8083
Donor age (years)	25	53.3	20.6	10	53.3	16.6	15	53.3	22.1	0.9950
Donor creatinemia (µmol/l)	51	91.6	58.9	12	89.3	54.0	39	92.6	60.9	0.0267
Cold ischemia time (hours)	28	18.6	7.4	8	18.2	7.2	20	18.7	7.5	0.0122

BMI, Body Mass Index; CMV, Cytomegalovirus; EBV, Epstein-Barr Virus; ECD, Expanded Criteria Donor; HLA, Human Leucocyte Antigens; NA, Not Available; SD, Standard Deviation.

graft survival for weekends versus weekdays was 1.06 (95% CI: 0.93; 1.20) before 2012 versus 0.86 (95% CI: 0.69; 1.07) after 2012 (Table S1). Because one can discuss the center as a possible confounder, the percentage of transplantations performed during the weekend ranging from 27.7 to 33.9% in each center, we also

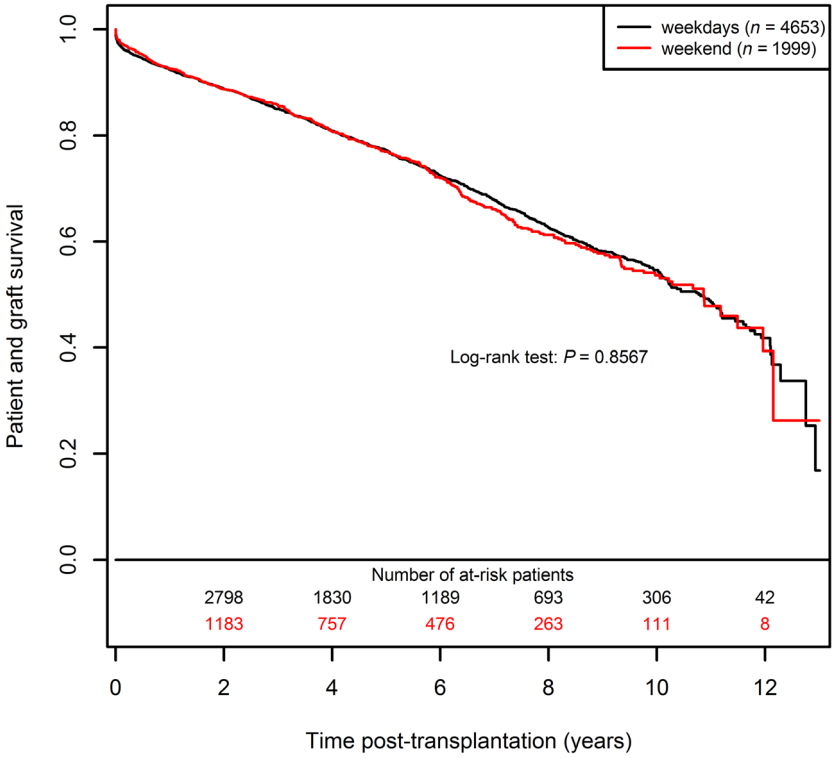

Figure 1 Patient and graft survival curves for weekday and weekend groups.

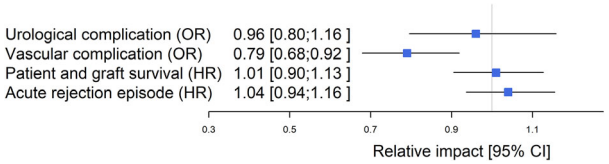

Figure 2 Unadjusted Hazards Ratios (HR) and Odds Ratios between weekday and weekend groups.

consider the center effect. The results were unchanged (Table S2).

Urological and vascular complications within the first 30 days post-transplantation

The overall percentage of patients with urological surgical complications was 8.6%. It was 8.4% (95% CI: 7.3%; 9.7%) in the weekend group versus 8.7 % (95% CI: 7.9%; 9.5%) in the weekday group. The corresponding Odds Ratio (OR) was 0.96 (95% CI: 0.79; 1.15). The description of the urological complications is listed in Table 2.

In contrast, the overall percentage of patients with vascular surgical complications was 15.4% and ranged from 13.3% in the weekend group (95% CI: 11.9%; 14.9%) to 16.2 % in the weekday group (95% CI: 15.2%; 17.3%). The corresponding OR was 0.79 (95% CI: 0.68; 0.92). The description of the vascular complications is listed in Table 3. The primary vascular complication accounting for almost two-thirds of the total was the occurrence of bleeding requiring transfusion or re-intervention, followed by arterial dysfunction (11.8%) referring in trouble in performing the arterial anastomosis that required surgical repair or more rarely angioplasty. On the post-op doppler during the first week post-transplantation, either systematic or for cause and whatever the daytime of the week, partial arterial thrombosis accounted for 11.4% and venous thrombosis for 6.6% of all vascular complication. Finally, complete arterial thrombosis leading to a technical graft failure accounted for only 2.8 %.

As detailed in the methods section, we re-analyzed the significant results by considering the CIT, i.e. the only significant risk factor of vascular complications. By comparing two recipients with the same CIT, where one was transplanted during the weekend and the other during the week, the corresponding adjusted OR between these two patients was estimated at 0.79 (95% CI: 0.67; 0.92). The non-adjusted and adjusted OR were similar, meaning that the weekend effect was not due to CIT.

Transplant International 2020; 33: 1030–1039

Table 2. Descriptive urological surgical complications according to study groups.

	Whole sample (*n* = 6652)		Weekdays (*n* = 4653)		Weekend (*n* = 1999)	
	n	%	*n*	%	*n*	%
Drainage of fluid collection	70	1.05	45	0.97	25	1.25
Lymph collection (drainage or surgery)	199	2.99	143	3.07	56	2.80
Vesicoureteral reflux (endoscopic treatment or surgery)	5	0.08	4	0.09	1	0.05
Ureteral stenosis	98	1.47	73	1.57	25	1.25
Urine collection (fistula/ureteral necrosis)	197	2.96	136	2.92	61	3.05
Missing values	2	0.03	2	0.04	0	0.00
Overall	569	8.58	401	8.66	168	8.40

Acute rejection occurrence

The cumulative probabilities of acute rejection are plotted in Fig. 3. The value at 1-year post-transplantation in the weekday group was 0.20 (95% CI: 0.19; 0.21), and the same in the weekend group (95% CI: 0.19; 0.22). The HR was 1.04 between patients transplanted during weekends versus those during weekdays (95% CI: 0.94; 1.16).

eGFR at 1-year post-transplantation

Among the 6652 included patients, 729 patients were excluded because of a follow-up lower than 1-year post-transplantation, 162 excluded due to death before 1-year post-transplantation, 76 patients were excluded because of missing data on the outcome, even if the follow-up was enough. During the first-year post-transplantation, 299 patients returned to dialysis, and the 1-year eGFR was established at 5 ml/min/1.73m^2 for these patients.

The overall mean 1-year eGFR was 51.4 ml/min/1.73m^2 (95% CI: 50.8; 51.9). We observed no significant difference between the two groups: 52.1 ml/min/1.73m^2 (95% CI: 51.2; 53.1) in the weekend group versus 51.0 ml/min/1.73m^2 (95% CI: 50.4; 51.7) in the weekday group. The mean difference was estimated at −1.16 ml/min/1.73m^2 (95% CI: −2.32; 0.01).

Discussion

Our French cohort-based study demonstrated that graft and patient survival was similar regardless of whether the transplantation occurred on weekends or on weekdays. It confirmed the results of previous studies that raised this question in other countries. In the United States, Baid-Agrawal et al. [9] analyzed a cohort of 136,715 adult recipients of deceased donor single organ kidney transplants between 1994 and 2010. They studied patient and/or graft survival, hospitalization length, delayed graft function (DGF), and acute rejection within

Table 3. Descriptive vascular surgical complications according to study groups.

	Whole sample (*n* = 6652)		Weekdays (*n* = 4653)		Weekend (*n* = 1999)	
	n	%	*n*	%	*n*	%
Arterial aneurysm	4	0.06	3	0.06	1	0.05
Arteriovenous fistula (surgery or radiologic intervention)	9	0.14	7	0.15	2	0.10
Bleeding requiring blood transfusion or re surgery	666	10.01	491	10.55	175	8.75
Arterial dysfunction (surgery or radiologic intervention)	121	1.82	91	1.96	30	1.50
Arterial thrombosis	146	2.19	115	2.47	31	1.55
Partial arterial thrombosis	117	1.76	91	1.96	26	1.30
Complete arterial thrombosis	29	0.44	24	0.52	5	0.25
Venous thrombosis (partial or complete)	67	1.01	44	0.95	23	1.15
Missing values	9	0.14	5	0.11	4	0.20
Overall	1013	15.36	751	16.25	262	13.31

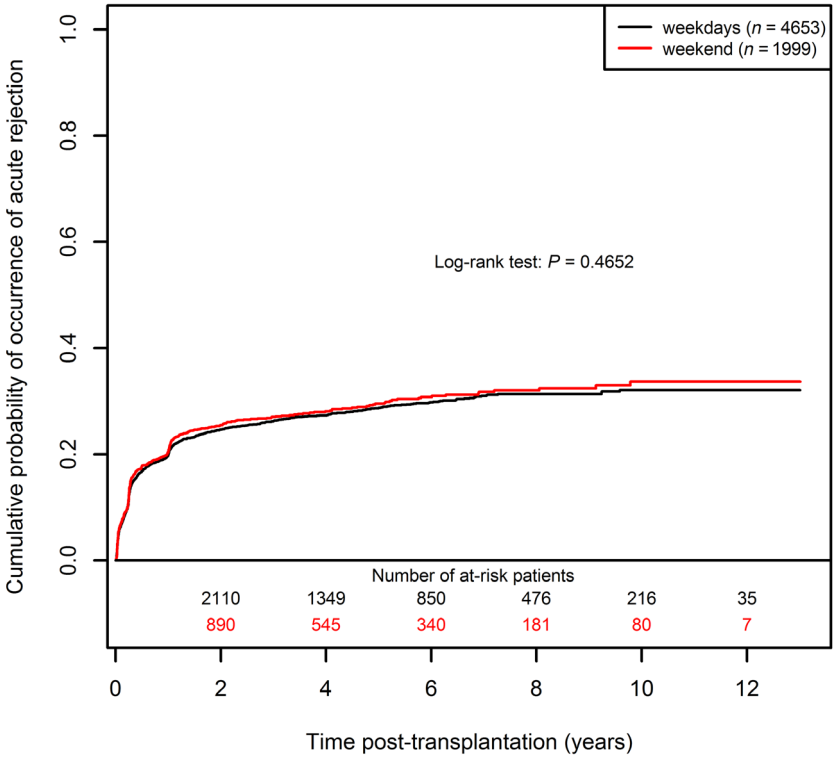

Figure 3 Cumulative probability of acute rejection for weekday and weekend groups.

the first-year post-transplant. They concluded that surgeries performed on weekends did not negatively affect outcomes. Similar results were published by Anderson et al. [11] on a comparable population of 12,902 kidney transplant recipients performed in England between 2003 and 2014. They reported no difference in the 30-day mortality, 1-year mortality, 1-year allograft failure or rejection, DGF, hospitalization length, or the risk for re-hospitalization. Likewise, an absence of a weekend effect on the 3-year patient and graft survival, DGF, acute rejection, and the 1-year estimated glomerular filtration rate (eGFR) was also reported by Schütte-Nütgen et al. [10], based on a mono-centric German cohort of 580 patients transplanted between January 2007 and December 2014.

After it was first identified in the 70s, the weekend effect has been the subject of an increasingly intense debate, particularly since 2010. Indeed, English studies reporting an increase in mortality of patients admitted to hospital during the weekend have resulted in a profound reform of the National Health Service [15]. More recently, this concept was challenged by rigorous studies using more extensive databases. These suggested that the weekend effect could be mainly attributable to differently distributed patient illness severity and comorbidity conditions between the weekend and weekday [16]. Despite this, a weekend effect has been shown to be associated with specific pathologies such as myocardial infarction, whereby it was associated with increased short-term mortality and was directly correlated with the speed of the coronary revascularization procedure [17]. Consequently, the study of the weekend effect on surgical complications is an important consideration for kidney transplant recipients. In contrast with Schütte-Nütgen et al. [10], who reported a higher rate of complications after weekend surgical procedures, we observed no significant difference in urological complications, but significantly less vascular complications for weekend transplantations.

While we showed that this protective effect was not due to a lower weekend group CIT, how to explain this unexpected finding.

This result can be due to differences in the organization of the operating room on the one hand and the experience of the surgeons on the other. Some clues could be provided by studies comparing graft outcomes and surgical complications depending on the time of the surgery [18–21]. Indeed, similarly to the weekend days, human, and material resources are limited during the night. Except one [18], these studies reported similar outcome whatever the time of the day. Interestingly, the most recent and well-conducted study [20] revealed

Transplant International 2020; 33: 1030–1039

significantly less pure technical graft failures on nighttime (defined as graft loss within ten days after the transplantation without signs of acute rejection, excluding cases of primary non-function and non-viable kidney). These results from the Netherlands are coherent with our findings since vascular complications explained most graft failures. Authors suggested that this difference could be due to a more quiescent operation room during nightly hours, which is possibly associated with positive impacts on surgical performances [22,23]. Differences in the surgeons' experience could also explain this paradox. In France, during the week-days, kidney transplants are mainly performed by the surgical students under the supervision of senior surgeons, while for better efficiency, weekends surgical organization often differs, and transplantations are mostly performed by the latter. Transplant surgery has become more complex, especially at the vascular level due to the aging of donors and recipients [24]. Kulu et al. [25] reported the young age of a surgeon as a risk factor of vascular and hemorrhagic complications after kidney transplantation.

In relation to this, Lim et al. [26] explored the two-way interaction between vascular disease and weekend transplants using a large study of over 6,000 deceased donor kidney transplant recipients from the ANZDATA registry (Australia and New Zealand). While early and late graft failures were not different between weekday and weekend transplants in the entire cohort, early graft failure attributed to vascular complications were more common for transplantations performed on the weekend in patients with a history of vascular disease (15% of the entire cohort). Compared to our observations, these apparently conflicting results could be due to different hospital procedures. A deeper analysis will be required to explore this idea, nevertheless, the corresponding data (precise recipient vascular history, duration of time to anastomosis which was reported associated with the graft survival [27], recipient surgery complexity, surgical expertise, etc.) are not collected in our database.

Importantly, even though we demonstrated a statistically significant difference in the percentage of vascular surgical complications between the weekend and the weekday groups, this absolute difference was only 2.9% (95% CI: 1.1%; 4.8%; $P = 0.0023$). While our sample size was high, the small effect may be clinically irrelevant. Our analysis may have additional limitations. Firstly, we did not explore all possible outcomes, for instance, the hospitalization length was not analyzed. Secondly, we did not study DGF, which is defined in our database as the need for at least one dialysis session in the first seven days post-transplantation, because this criterion is not available for pre-emptive transplantations and patients under peritoneal dialysis before transplantation.

An increase in kidney discard rate during the weekends has been previously reported in the United States, suggesting that organ selection could hide an otherwise detrimental weekend effect on outcomes[7,28]. While transplantation discard rate cannot be established in our cohort, such selectivity could partially explain the observed inter-center variability in the proportion of transplantation performed on the weekend, ranging from 27.7 to 33.9%. However, as recently demonstrated, the organ acceptance rate in France is higher than in the United States [29] and we did not observe either difference in the donor quality according the time of the week nor center effect. Otherwise, studies on organ acceptance patterns in the United States demonstrated that transplants are harder to place during the weekends [30,31]. While French allocation rules are different, we do not know whether similar concern prevails. However, we reported a shorter cold ischemic time for transplantations performed during weekends than those during weekdays, suggesting the absence of differences in the organ acceptance between weekends and weekdays.

In summary, our study demonstrated no significant difference in patient or graft survival between weekend or weekday surgeries, but we did observe a small significantly lower risk of vascular surgical complications in transplantations performed during weekends. This observation may be specific to this French cohort, and this needs further exploration to identify possible reasons for this protective weekend effect, and whether this could be translated into improved weekday surgeries and clinical/hospital management.

Funding

This work was partially supported by a public grant overseen by the French National Research Agency (ANR) to create the Common Laboratory RISCA (Research in Informatic and Statistic for Cohort Analyses, http://www.labcom-risca.com, reference: ANR-16-LCV1-0003-01) involving the development of PlugStat® software.

Conflict of interest

The authors declare that they have no conflict of interest.

Acknowledgments

We wish to thank members of the clinical research assistant team (S. Le Floch, A. Petit, J. Posson, C. Scellier, V. Eschbach, K. Zurbonsen, C. Dagot, F. M'Raiagh, V. Godel, X. Longy, P. Przednowed). We are also grateful to Roche Pharma, Novartis and Sanofi laboratories for supporting the DIVAT consortium as the CENTAURE foundation (www.fondation-centaure.org). We thank also E Savoye from agence de la biomedicine.

DIVAT Consortium: Lyon E. Hériot: Lionel Badet, Maria Brunet, Fanny Buron, Rémi Cahen, Sameh Daoud, Coralie Fournie, Arnaud Grégoire, Alice Koenig, Charlène Lévi, Emmanuel Morelon, Claire Pouteil-Noble, Thomas Rimmelé, Olivier Thaunat ; Montpellier: Sylvie Delmas, Valérie Garrigue, Moglie Le Quintrec, Vincent Pernin, Jean-Emmanuel Serre; Nancy: Pascal Eschwege, Luc Frimat, Sophie Girerd, Jacques Hubert, Marc Ladriere, Emmanuelle Laurain, Louis Leblanc, Pierre Lecoanet, Jean-Louis Lemelle ; Nantes: Gilles Blancho, Julien Branchereau, Diego Cantarovich, Agnès Chapelet, Jacques Dantal, Clément Deltombe, Lucile Figueres, Claire Garandeau, Magali Giral, Caroline Gourraud-Vercel, Maryvonne Hourmant, Georges Karam, Clarisse Kerleau, Aurélie Meurette, Simon Ville, Christine Kandell, Anne Moreau, Karine Renaudin, Anne Cesbron, Florent Delbos, Alexandre Walencik, Anne Devis; Nice: Laeticia Albano, Elisabeth Cassuto; Paris Saint-Louis: Denis Glotz, Carmen Lefaucheur; Paris-Necker: Lucile Amrouche, Dany Anglicheau, Olivier Aubert, Lynda Bererhi, Christophe Legendre, Alexandre Loupy, Frank Martinez, Rébecca Sberro-Soussan, Anne Scemla, Claire Tinel, Julien Zuber.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Table S1. Hazards Ratios (HR) between weekday and weekend groups according to the calendar period of the transplantation.

Table S2. Hazard Ratios (HR) related to the patient and graft survival between weekday and weekend groups according to the center.

REFERENCES

1. Bell CM, Redelmeier DA. Mortality among patients admitted to hospitals on weekends as compared with weekdays. *N Engl J Med* 2001; **345**: 663.
2. Saposnik G, Baibergenova A, Bayer N, Hachinski V. Weekends: a dangerous time for having a stroke? *Stroke* 2007; **38**: 1211.
3. Kumar G, Deshmukh A, Sakhuja A, *et al*. Acute myocardial infarction: a national analysis of the weekend effect over time. *J Am Coll Cardiol* 2015; **65**: 217.
4. Groves EM, Khoshchehreh M, Le C, Malik S. Effects of weekend admission on the outcomes and management of ruptured aortic aneurysms. *J Vasc Surg* 2014; **60**: 318.
5. Aylin P, Alexandrescu R, Jen MH, Mayer EK, Bottle A. Day of week of procedure and 30 day mortality for elective surgery: retrospective analysis of hospital episode statistics. *BMJ* 2013; **28**: f2424.
6. Debout A, Foucher Y, Trébern-Launay K, *et al*. Each additional hour of cold ischemia time significantly increases the risk of graft failure and mortality following renal transplantation. *Kidney Int* 2015; **87**: 343.
7. Mohan S, Foley K, Chiles MC, *et al*. The weekend effect alters the procurement and discard rates of deceased donor kidneys in the United States. *Kidney Int* 2016; **90**: 157.
8. Queen Elizabeth HospitalTransplant patients 'refusing weekend operations' fearing they are more likely to die - Birmingham Live [Internet]. [cited 2019 Jul 16]. Available from: https://www.birminghammail.co.uk/news/midlands-news/queen-elizabeth-hospital-transplant-patients-10590430.
9. Baid-Agrawal S, Martus P, Feldman H, Kramer H. Weekend versus weekday transplant surgery and outcomes after kidney transplantation in the USA: a retrospective national database analysis. *BMJ Open.* 2016; **6**: e010482.
10. Schütte-Nütgen K, Thölking G, Dahmen M, *et al*. Is there a "weekend effect" in kidney transplantation? *PLoS One* 2017; **12**: e0190227.
11. Anderson BM, Mytton JL, Evison F, Ferro CJ, Sharif A. Outcomes after weekend admission for deceased donor kidney transplantation: a population cohort study. *Transplantation* 2017; **101**: 2244.
12. Schisterman EF, Cole SR, Platt RW. Overadjustment Bias and Unnecessary Adjustment in Epidemiologic Studies. *Epidemiol Camb Mass* 2009; **20**: 488.
13. Pearl J. Introduction to Causal Inference. *Int J Biostat* 2010; **6**: 2.
14. Levey AS, Stevens LA, Schmid CH, *et al*. A new equation to estimate glomerular filtration rate. *Ann Intern Med.* 2009; **150**: 604.
15. Black N. Higher mortality in weekend admissions to the hospital: true, false, or uncertain? *JAMA* 2016; **316**: 2593.
16. Mohammed M, Faisal M, Richardson D, *et al*. Impact of the level of sickness on higher mortality in emergency medical admissions to hospital at weekends. *J Health Serv Res Policy* 2017; **22**: 236.
17. Sorita A, Ahmed A, Starr SR, *et al*. Off-hour presentation and outcomes in patients with acute myocardial infarction: systematic review and meta-analysis. *BMJ* 2014; **21**: f7393.
18. Fechner G, Pezold C, Hauser S, Gerhardt T, Müller SC. Kidney's nightshift, kidney's nightmare? Comparison of daylight and nighttime kidney transplantation: impact on complications and graft survival. *Transplant Proc.* 2008; **40**: 1341.
19. Kienzl-Wagner K, Schneiderbauer S, Bösmüller C, Schneeberger S,

Pratschke J, Ollinger R. Nighttime procedures are not associated with adverse outcomes in kidney transplantation. *Transpl Int* 2013; **26**: 879.
20. Brunschot DMDÖ, Hoitsma AJ, van der Jagt MFP, *et al*. Nighttime kidney transplantation is associated with less pure technical graft failure. *World J Urol*. 2016; **34**: 955.
21. de Boer J, Van der Bogt K, Putter H, *et al*. Surgical quality in organ procurement during day and night: an analysis of quality forms. *BMJ Open* 2018; **25**: e022182.
22. Zheng B, Panton ONM, Al-Tayeb TA. Operative length independently affected by surgical team size: data from 2 Canadian hospitals. *Can J Surg* 2012; **55**: 371.
23. Cassera MA, Zheng B, Martinec DV, Dunst CM, Swanström LL. Surgical time independently affected by surgical team size. *Am J Surg* 2009; **198**: 216.
24. Lejay A, Thaveau F, Caillard S, *et al*. How can a vascular surgeon help in kidney transplantation. *J Cardiovasc Surg (Torino)* 2017; **58**: 351.
25. Kulu Y, Fathi P, Golriz M, *et al*. Impact of surgeon's experience on vascular and haemorrhagic complications after kidney transplantation. *Eur J Vasc Endovasc Surg* 2019; **57**: 139.
26. Lim WH, Coates PT, Russ GR, *et al*. Weekend effect on early allograft outcome after kidney transplantation-a multi-centre cohort study. *Transpl Int* 2019; **32**: 387.
27. Heylen L, Pirenne J, Samuel U, *et al*. The impact of anastomosis time during kidney transplantation on graft loss: a eurotransplant cohort study. *Am J Transplant* 2017; **17**: 724.
28. Brennan C, Husain SA, King KL, *et al*. A Donor utilization index to assess the utilization and discard of deceased donor kidneys perceived as high risk. *Clin J Am Soc Nephrol CJASN* 2019; **14**: 1634.
29. Aubert O, Reese PP, Audry B, *et al*. Disparities in acceptance of deceased donor kidneys between the united states and france and estimated effects of increased US acceptance. *JAMA Intern Med* 2019; **179**: 1365.
30. Cohen JB, Shults J, Goldberg DS, Abt PL, Sawinski DL, Reese PP. Kidney allograft offers: Predictors of turndown and the impact of late organ acceptance on allograft survival. *Am J Transplant* 2018; **18**: 391.
31. King KL, Husain SA, Cohen DJ, Mohan S. Deceased Donor Kidneys Are Harder to Place on the Weekend. *Clin J Am Soc Nephrol CJASN*. 2019; **14**: 904.