

Early morning kidney transplantation: Perioperative complications

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Summary

Introduction: To reduce cold ischemia time (CIT), many kidney transplants are performed in the early morning. Conducting complex surgeries in the early morning may influence the surgeon's technical capacity and rate of surgical complications (SC). **Aim:** Evaluate the influence of surgery start hour (SSH) regarding duration of surgery (DS), immediate diuresis (ID), SC and acute rejection (AR); evaluate the influence of CIT regarding SC, ID, and AR. **Methods:** 2855 cadaveric transplants performed between June 1980 and March 2018 were retrospectively evaluated. Regarding SSH, two groups were created: Group M (00: 00h-05.59h, n = 253) and Group D (06: 00h - 23: 59h, n = 2602). Analyzing the impact of SSH on DS, ID, SC and AR. Evaluate the relationship between CIT (< 18h, 18-30h and > 30h) on ID, SC and AR utilizing univariate and multivariate statistical analysis with SPSS. **Results and Conclusion:** Groups M and D were comparable in all evaluated demographic variables ($p > 0.05$), except cold ischemia time (Group M with higher CIT, $p < 0.001$). Regarding univariate analysis, Surgery start hour did not influence DS ($p = 0.344$), and SC ($p = 0.264$), but related with higher ID ($p = 0.028$) and AR ($p = 0.018$). CIT related with immediate diuresis ($p = 0.020$) and acute rejection ($p < 0.001$) but did not relate with complications ($p = 0.734$). Regarding multivariate analysis, SSH only influenced immediate diuresis ($p = 0.026$) and did not influenced acute rejection ($p = 0.055$). CIT influenced immediate diuresis ($p = 0.019$) and acute rejection ($p < 0.001$). Surgery start hour influences Immediate diuresis. With this study, we conclude that the priority must be a short cold ischemia time.

KEY WORDS: Early morning transplantation; Kidney transplantation; Kidney transplant complications; Immediate diuresis; Surgery starting hour.

Submitted 9 January 2021; Accepted 23 February 2021

INTRODUCTION

Medical error and its influence on the health of patients is an important and current subject in modern medicine. In 1999, the Institute of Medicine of the United States of America reported that medical errors were responsible for one hundred thousand annual deaths and had a global cost of 29 billion dollars (1). Sleep deprivation increases the risk of medical error, so far as being called the Achilles heel of the medical profession (2). Sleep deprivation

can have serious consequences on the surgeon, affecting his ability to maintain his mental and motor abilities. Studies show that sleep deprivation can have the same effect as alcohol intoxication on the surgeon's abilities (3-6). It has been reported that there is an increase in the number of surgical complications and mortality when surgeries are performed after the professionals normal working hours (4-6).

Kidney transplant (KT), although not being an urgent procedure, is most of the times executed at late hours, even at dawn. The reasons for such are several and include: the complex organization needed to distribute renal grafts, elective surgery that occupies surgical theatre and the need to prepare the receptor for surgery (7). The main reason for such high number of late procedures is the need to reduce cold ischemia time (CIT) as much as possible in KT, as larger CIT relates to worst graft function, smaller survival time of graft and higher patient mortality (8). Although, studies show that with an 18 hours window of CIT there isn't a significant difference in outcomes (9, 10). On the other hand, it has been described that surgical factors and the existence of complications influence the outcome of KT (11, 12). As such, it is pertinent to address what can be more favourable, having the lowest CIT possible or having a "fresh" surgical team with hypothetically smaller number of complications. For reason external to the surgical team, CIT was longer in specific cases up to the point where it was relevant to decide between performing surgery at night or in the morning. If waiting until morning could cause CIT to be considered unsafe, procedures were conducted at later hours, being the group with the largest CIT the one that could not wait any more time. To our knowledge, there are only five large scale studies that studied this problem concerning Kidney Transplantation, with conflicting results and comparing different hours from the ones in this work (7, 13-16).

MATERIALS AND METHODS

Study design

Retrospective analyses of all KT occurring in the Urology and Kidney Transplant Service of the "Centro Hospitalar e Universitário de Coimbra", Portugal, between June 1980

No conflict of interest declared.

and July 2018. Patients with combined transplant (pancreas, lung, heart and liver) and from living donor were excluded, being selected 2855 consecutive transplants. The resulting population was divided into two groups based on the surgery start hour (SSH): Group M (00:00h-05:59h) and Group D (06:00h-23:59h). Four outcomes were defined and measured based of SSH: duration of surgery (DS), the number of surgical complication (SC), immediate diuresis (ID) measured on the operating table and acute rejection (AR) of the graft.

The population was equally studied on the CIT and its influence in the ID, AR and DS.

Surgical team composition was not gathered in this study, but in the institution where the analysis was performed the presence of residents is not dependant of the hour of transplant. Being most teams composed of a senior surgeon and a resident.

Data collected was inserted in multiple labour laws, surgeons on the transplantation department are exclusively allocated to the task after normal working hours, having the right to rest after night procedures.

Definitions

Marginal donor was defined as having at least one of the following characteristics: over 60 years old, over 50 years and arterial hypertension, death by cerebral vascular accident or serum creatine level of over 1.5 mg/dl (17, 18).

Acute rejection was defined as worsening of graft function on the first year, having been admitted a clinical diagnosis (increase in creatine blood level, imagological alteration, need for corticoid treatment) or histologic (kidney biopsy). Immediate diuresis was defined by the observation of urinary output in patients with no need for dialysis on the first week after kidney transplant. Surgical complications were divided in: urologic (urinary fistula, ureteric stenosis, ureteric necrosis), vascular (arterial or venous thrombosis, arterial stenosis, vascular anastomosis dehiscence), lymphocele, haemorrhage (need of surgical revision or transfusion), wound dehiscence, incisional hernia and others.

Statistical analysis

Baseline and demographic characteristics of group M and D were compared using the chi-squared test for categorical variables and the student's T test for continuous variables. Univariate analysis of the effects of SSH and CIT in outcomes were described using the chi-squared test. Multivariate analysis was conducted by applying the logistic regression method.

RESULTS

Demographic characteristics

Between 00:00 hours and 05:59 hours there were 253 cadaveric transplants in contrast to 2602 in the other time period. Demographic characteristic of Group M and Group D are summarized in Table 1. In comparison, more patients from the group M presented CIT superior to 30 hours ($p < 0.001$). All other characteristics were similar. Mean surgical time for group (group D is further divided) is summarized in Table 2.

Table 1.
Demographic characteristic of the population.

Populational demographic characteristic	Group M	Group D	p value
Number of patients	253	2602	
Marginal donor (%/n)	50.6% (128)	50.2% (1307)	0.932
Age of receptor (y)	46.6 ± 13.9	45.6 ± 13.7	0.291
Sex of receptor			0.458
Male	69.2% (175)	66.9% (1740)	
Right side implant	79.8% (202)	2131 (81.9%)	0.828
Number of transplants (%/n)			0.608
1	94.5% (239)	5.5% (14)	
> 1	94.4% (2457)	14.6% (155)	
Number of arteries of the graft			0.953
1	78.3% (198)	22.7% (55)	
> 1	78.7% (2047)	21.3% (553)	
Cold ischemia time (%/n)			< 0.001
< 18h	38.3% (97)	38.7% (1004)	
10-30h	53.9% (134)	58.6% (1521)	
> 30h	8.7% (22)	2.8% (72)	

Table 2.
Mean surgery duration time in relation to surgical starting time.

Surgery start hour	% (n)	Mean duration of surgery (min)
Grupo M		
00:00-05:59	8.8% (253)	157.2(45-330)
Grupo D		
06:00-11:59	12.9% (366)	165.9 (55-555)
12:00-17:59	40.3% (1151)	149.1 (45-615)
18.00-23:59	38.0% (1085)	152.1 (45-390)
Total	2855	153.5 (45-615)

Univariate analysis

The effects of surgical star hour in the outcomes defined (DS > 3 hours, ID, SC e AR) are summarized in Table 3. The effects of CIT on the same outcomes (except duration of surgery) are summarized in Table 4.

Multivariate analysis

The effects of SSH and CIT when analysed together (multivariate analysis) are summarized in Table 5.

Table 3.
Effect of surgery starting hour in outcomes of renal transplant.

	Group M	Group D	p value
Surgery duration > 3 hours	20.6% (52)	18.1% (472)	0.344
Immediate diuresis	71.1% (180)	79.0% (2055)	0.028
Surgery complications	20.9% (53)	18.1% (471)	0.264
Vascular	5.9% (15)	4.1% (107)	
Urologic	5.5% (14)	6.5% (168)	
Lymphocele	2.0% (5)	1.4% (37)	
Bleeding	6.3% (16)	3.3% (85)	
Wound dehiscence	1.2% (3)	1.6% (42)	
Abscess	-	0.4% (11)	
Hernia	-	0.4% (11)	
Other	-	0.4% (10)	
Acute rejection	25.3%	18.9%	0.018

Table 4.
Effects of cold ischemia time in the outcomes of kidney transplant.

Cold ischemia time	< 18h	18-30h	> 30h	p
Immediate diuresis	81.4% (900)	77.2% (1277)	66.0% (62)	0.020
Surgery complications	18.4% (203)	18.1% (299)	21.3% (20)	0.734
Acute rejection	14.4% (159)	22.0% (364)	41.5% (39)	< 0.001

Table 5.
Multivariate analysis of the effect of surgery starting hour and cold ischemia time in the outcomes of kidney transplant.

Outcome	Variable	p
Immediate diuresis	SSH	0.026
	CIT	0.019
Surgery complications	SSH	0.282
	CIT	0.796
Acute rejection	SSH	0.055
	CIT	< 0.001

DISCUSSION

This work presents the highest number of patients analysed in relation to surgery start hour and its possible effects in kidney transplantation. Defined SSH was different when compared with other articles. In two different studies *Kienzl-Wagner et al.* and *Fechner et al.* divided patients in groups of 08:00h-19:59h and 20:00h-07:59h (7,14). *Seow et al.* divided SSH in 07:30h-17:59h; 18:00h-23:59h; 00:00h-07:29h (13), while *Shaw et al.* and *Emmanouilidis* divided the groups into periods of 3h (15, 16). We chose to divide SSH in two blocks of 00:00h-05:59h and 06:00-23:59h such as to reinforce the effects of physical tiredness and sleep deprivation at dawn. Although, group M clearly presented a smaller number of patients, the high number of patients allows for reliable comparisons. Other distinct aspects are the outcomes studied, as most studies analyse the perioperative complications and renal graft survival. In this article we found favourable to try and relate fatigue of the surgeon and short-term outcomes, such as surgery duration, immediate diuresis and surgical complications. As short to median term outcome we evaluated the rate of AR.

The M and D groups are comparable in relation to all variables studied, except in CIT of the graft (Table 1), it being superior in group M. These results are logical, as they represent grafts that were implanted “at any hour” as a way to prevent achieving critical CIT time that could possibly stop the realization of the transplant.

Utilizing univariate analysis, SSH influenced significantly the ID and AR, not having influenced the DS or the number of SC (Table 3). In a similar significant analysis, CIT influenced the same outcomes (Table 4). As group M and D where distinct in relation to CIT, multivariate analysis was conducted (Table 5) showing that SSH influenced the ID but did not alter the rate of AR.

Kienzl-Wagner and *Seow* also did not find a relationship between SSH and the number of surgical complications while *Fechner et al.* demonstrated a larger number of vascular complications in KT conducted during the night

period (7, 13, 14). *Shaw et al.* in their analysis evidenced a larger number of urologic complications during 03:00-05:59h and a higher number of any complications between 00:00-02:59h (15). *Emmanouilidis et al.* also demonstrated higher likelihood for the need of reoperation during the 03:00-05:59h interval (16).

Duration of surgery was not influenced by the SSH, although there isn't sufficient data from literature regarding this specific outcome. One Danish study, analysing the effects of sleep deprivation on the cognitive and technical abilities of surgeons, evidenced that surgeons can compensate for changes to their circadian rhythm, what may explain the results obtained in our study (19).

On this study, SSH significantly influenced ID. In the work by *Kenzl-Wagner* there was also a lower rate of ID in the nocturnal group (63.4% vs. 69.9%), although, without statistical significance. In that review, the author justified that tendency by the existence of a larger number of surgeries with marginal donor in the nocturnal group, what was not observed with our study. One simple justification could be that group M has a higher CIT, but changes to this outcome, ID, are maintain even after multivariate analysis. Notwithstanding the absence of a clear answer for this relation, it is known that a delay of graft function is associated with poorer outcomes and higher risk of graft loss, as show in a previous study done by our transplant centre (20).

The rate of AR in the M and D groups where 25.9% and 18.9%, respectively. On multivariate analysis a distinct association between SSH and AR was not found, consistent with the results from *Kienzl-Meyer et al.* (14).

The key factor that influenced graft function was CIT. As it is showed by our work, CIT has a significant influence in ID and AR (8, 10, 21, 22). Although, studies suggest similar outcomes in the CIT time frame of less than 18h, one study conducted by *Debout et al.* demonstrated that with every hour of CIT the probability of graft failure increases (hazard ratio: 1.013) and that the time frame of 18 hours can be suboptimal (9, 10). The same work stated the existence of a relation between CIT and graft failure (8).

Nevertheless, the recent study by *Emmanouilidis et al.*, demonstrated that in the time frame of less than 23.5 hours of CIT, it is unfavourable to perform KT with the SSH in the 03:00-05:59h period (16).

The effects of sleep deprivation and of SSH has been studied in other specialities and surgeries. Regarding hepatic transplantation, *Lonze et al.* stated that surgery conducted in the nocturnal period was not associated with a higher number of complications but related with longer SD and risk of short term mortality (23). Analysing thoracic organ transplant, *George et al.* did not identify differences between outcomes in patients whose surgery was conducted at night (24). Other works in pancreatic surgery, heart, trauma surgery did not find worst outcome with late SSH (25-28).

There were some limitations to this study, starting with the retrospective analysis of collected data, the definition of early morning surgery (00:00-05:59) is arbitrary and may not relate precisely with the fatigue state of the surgical team. Regarding AR its characterization was expanded to include clinic and histologic diagnoses. It was decided not to assess the relation between SSH and graft survival

as we considered there were no negative outcomes in the short term, and any data extrapolation would be too complex to explain.

CONCLUSIONS

Conducting KT at dawn showed no association with SD, SC or AR. However, it is connected with lower ID. The CIT strongly influences ID and AR. In summary, data collected in this study support that SSH should prioritize CIT, making sure CIT is the lowest possible. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

ACKNOWLEDGMENT

The authors of this article would like to give special reference to *Doctors António Roseiro, Vítor Dias and Francisco Rolo* whom without their continuous and valuable work in the area of Kidney transplant this work would not be possible.

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