TRANSPLANT INTERNATIONAL

Transplant International ISSN 0934-0874

ORIGINAL ARTICLE

Nighttime procedures are not associated with adverse outcomes in kidney transplantation

Katrin Kienzl-Wagner, Stefanie Schneiderbauer, Claudia Bösmüller, Stefan Schneeberger, Johann Pratschke and Robert Öllinger

Department of Visceral, Transplant and Thoracic Surgery, Center of Operative Medicine, Innsbruck Medical University, Innsbruck, Austria

Keywords
cold ischemia time, kidney transplantation, nighttime, sleep deprivation, surgery.

Correspondence
Johann Pratschke MD, Department of Visceral, Transplant and Thoracic Surgery, Center of Operative Medicine, Innsbruck Medical University, Anichstrasse 35, 6020 Innsbruck, Austria.
Tel.: +43 512 504 22601;
fax: +43 512 504 22602;
e-mail: johann.pratschke@i-med.ac.at

Conflicts of interest
The authors declare no conflict of interest.

Received: 22 November 2012
Revision requested: 23 December 2012
Accepted: 5 May 2013
Published online: 17 June 2013

doi:10.1111/tri.12125

Summary

Surgeries performed during the night are associated with higher complication rates. The aim of this study was to determine the impact of nighttime surgery on the outcome after kidney transplantation. In all, 873 deceased donor kidney transplants were retrospectively analyzed and grouped according to the time of surgery: daytime (8 AM to 8 PM, $n = 610$) versus nighttime (8 PM to 8 AM, $n = 263$). Statistical analysis compared patient/graft survival, rate of delayed graft function (DGF), acute rejection rate, and surgical complications. One and 5-year patient and graft survival did not differ between daytime and nighttime transplants. DGF occurred in 31.1% of daytime compared to 37.6% of nighttime procedures ($P = 0.06$). Acute allograft rejection was observed in 22.6% of daytime compared to 18.3% in nighttime graft recipients ($P = 0.15$). Nighttime procedures were associated with 22.4% complications compared to 22.1% in daytime procedures ($P = 0.92$). Most importantly, if transplantations were postponed until the next morning, cold ischemia time (CIT) would have increased from 16.6 h to 24.6 h ($P < 0.0001$) which would have resulted in decreased long-term survival ($P < 0.02$). Nighttime kidney transplants are neither associated with a higher surgical complication rate nor worse 5-year outcomes than daytime procedures, thus are justified to keep CIT short.

Introduction

The surgical community is facing patient safety issues in the context of the need for continuity of care with a 24/7 coverage of clinical service. This problem is especially present in highly specialized and complex fields such as solid organ transplantation. The healthcare system, trying to reduce costs by staff cuts, on the one hand, and work-hour restrictions, on the other hand, further contributes to this area of conflict. The Institute of Medicine report suggesting that up to 98 000 Americans die each year as a result of medical errors clearly points out the importance of safety measurements in delivering patient care [1]. Bearing in mind that the causes of medical errors are multifactorial, evidence suggests that sleep deprivation and fatigue in the context of excessive duty hours are major potential risk factors. In surgery, sleep deficiency is known to adversely affect cognitive and psychomotor performance and consecutively is associated with higher surgical complication rates. Therefore, rescheduling any overnight operative procedure that is not an emergency to the following day should be the logical consequence.

However, transplant procedures are performed almost regularly after hours or overnight because the timing of the recipient operation is largely dependent on the time of donor death. Postponing organ recovery in a brain dead donor is limited for medical and organizational reasons. Delaying the donor operation poses the risk of cardiocirculatory instability that may render organs unusable, a strategy that seems contradictory in an era when more and more extended criteria are accepted because of organ shortage.

In kidney transplantation, one of the major predictive factors for outcome is cold ischemia time (CIT). It is well

established that with increasing ischemia time, graft survival rates and graft function worsen. In particular, kidney transplants from deceased donors should be performed within 18 h of cold ischemia, as beyond this window, graft survival significantly decreases [2]. To keep CIT as short as possible and improve outcomes, kidney transplantation is performed as emergency surgery also during nighttime.

To date, only two studies with limited numbers of transplants have addressed the impact of nighttime kidney transplant procedures on graft survival and surgical complications, rendering conflicting results [3,4]. To address this gap of evidence, we conducted a retrospective single-center analysis including all deceased donor kidney transplants from January 2000 through January 2010 to evaluate whether performing kidney transplants at night was associated with adverse outcomes for transplant recipients compared with those who undergo daytime operation.

Patients and methods

Study design

A retrospective analysis of all kidney transplants performed at the Department of Visceral, Transplant and Thoracic Surgery, Medical University Innsbruck, between January 1, 2000 and December 31, 2009 was conducted. Patients undergoing combined transplants (simultaneous pancreas-kidney transplantation, liver-kidney or heart-kidney) as well as living-donor kidney transplants were excluded. Transplants were stratified by operative time of day: 'daytime' was defined as skin incision between 8 AM and 8 PM, 'nighttime' was defined as skin incision between 8 PM and 8 AM. All kidney transplants were performed by the same group of transplant surgeons ($n = 18$) as soon as negative crossmatch was available, no matter what time of the day.

Data on kidney transplantation and operative variables as well as follow-up data were retrospectively collected by chart and electronic medical record view. The parameters examined included patient and donor demographics, number of transplant, cause of end-stage renal disease, HLA mismatch, operative start time, total operative time (from skin incision to wound closure), surgeons experience (consultant, resident), cold and warm ischemia time. The primary endpoints examined were patient and graft survival. Secondary endpoints included the frequency and type of acute rejection, the incidence of delayed graft function (DGF) as well as the rate of surgical complications. DGF was defined as the need for dialysis in the first week after transplant excluding single early postoperative dialysis performed for hyperpotassemia and ruling out acute rejection or vascular and urinary tract complications [5]. Surgical complication was defined as the need for interventional or surgical treatment. Acute rejection was defined as the clinical need for pulsed steroid treatment or biopsy-proven rejection.

Approval to conduct the study was obtained from the local ethics committee (UN4580 309/4.5).

Statistical analysis

Baseline characteristics were compared using the chi-square test for categorical variables. Continuous variables were tested with the Student *t*-test or Mann–Whitney *U*-test (if assumption of Gaussian distribution was not fulfilled). Patient survival and overall graft survival were estimated by Kaplan–Meier methodology and compared using log-rank tests. For all statistical measures, a P-value < 0.05 was considered significant. All statistical analyses were performed using GraphPad Prism 5.0 (GraphPad Software, La Jolla, CA, USA).

Results

Transplant characteristics

During the observation period, a total of 873 kidney transplants from deceased donors were performed. Of these, 610 transplants were performed during daytime, whereas 263 renal transplants were performed during nighttime. Demographic characteristics of the study population and operative details are summarized in Table 1.

In all, 80.2% of daytime and 76% of nighttime transplant patients received their first renal allograft, whereas the remaining 19.8% and 24.0% of recipients had a retransplant ($P = 0.17$). The majority of retransplants were second kidney transplants (13.9% and 19.4%); 4.3% and 3.8% of daytime and nighttime operations were third kidney transplants; and 1.3% and 0.8% of patients received their fourth kidney. In the daytime group, transplant procedures also included one-fifth and one-sixth renal transplantation. Mean recipient age and sex distribution was similar in daytime and nighttime kidney transplants. The predominant indications for kidney transplantation also did not differ significantly between the two groups. Cause of end-stage renal disease was glomerulonephritis in 38.4% and 35.4% of daytime and nighttime kidney graft recipients, polycystic kidney disease in 11.6% and 12.2%, pyelonephritis in 9.8% and 6.8%, and diabetes mellitus in 6.9% and 9.1% of daytime and nighttime transplants. No difference was seen in donor age, BMI, gender, and the number of HLA mismatches. Mean CIT was similar in the two groups with 16.1 h in daytime procedures compared to 16.6 h in nighttime transplants ($P = 0.24$). Anastomosis time also was independent of operative time of day with a mean of 31 min in both daytime and nighttime kidney transplant procedures ($P = 0.82$). Total operative time from skin incision to wound closure was significantly shorter in kidney transplants performed during nighttime compared with daytime operations (2.8 ± 0.8 h vs. 3.1 ± 0.8 h, $P < 0.0001$).

Table 1. Baseline characteristics. Demographic characteristics of the study population and operative details. Results are presented as mean and standard deviations or as absolute and relative frequencies.

	Day (n = 610)	Night (n = 263)	P-Value
Demographic characteristics of study population			
Recipient age (years)	50.9 ± 14.1	50.3 ± 14.3	0.55
Recipient sex: male	406/67%	172/65%	0.74
Cause of ESRD			
Glomerulonephritis	234/38.4%	93/35.4%	0.40
Polycystic kidney disease	71/11.6%	32/12.2%	0.82
Pyelonephritis/reflux nephropathy	60/9.8%	18/6.8%	0.16
Diabetes mellitus	42/6.9%	24/9.1%	0.25
Hypertension/renovascular	36/5.9%	17/6.5%	0.74
Interstitial nephritis	22/3.6%	9/3.4%	0.89
Other	60/9.8%	26/9.9%	0.98
Unknown	85/13.9%	44/16.7%	0.29
No. of transplant			
First transplant	489/80.2%	200/76.0%	0.17
Retransplant	121/19.8%	63/24.0%	
Second transplant	85/13.9%	51/19.4%	
Third transplant	26/4.3%	10/3.8%	
Fourth transplant	8/1.3%	2/0.8%	
Fifth transplant	1/0.2%	0/0%	
Sixth transplant	1/0.2%	0/0%	
HLA-MM	2.7 ± 1.5	2.9 ± 1.5	0.03
Operation characteristics			
Total time (skin incision–wound closure) (h)	3.1 ± 0.8	2.8 ± 0.8	<0.0001
Warm ischemia time (min)	31 ± 10	31 ± 10	0.82
Cold ischemia time (h)	16.1 ± 4.6	16.6 ± 6.0	0.24

Patient and graft survival for nighttime compared with daytime kidney transplantation

Patient survival in nighttime kidney graft recipients was not inferior to that in daytime graft recipients with a 1-year patient survival of 94.6% and 95.9% and a 5-year survival of 86.3% and 88.0%, respectively (P = 0.73, Fig. 1a). Graft survival also did not differ significantly between nighttime and daytime transplants with 90.4% and 90.3% graft survival at 1 year, and 78.1% and 78.3% at 5 years, respectively (P = 0.78, Fig. 1b).

Acute rejection and incidence of DGF

Acute rejection was observed in 18.3% of nighttime kidney graft recipients compared to 22.6% of daytime allografts (P = 0.15) (Table 2). Of the 174 acute rejection episodes observed in the daytime group, 116 were biopsy-proven, whereas the remaining 58 rejection episodes were clinically diagnosed. The majority of rejection episodes were classified as T cell-mediated (74%, n = 128), 22% were classified as antibody-mediated, and 8 rejection episodes could not be classified retrospectively. Kidney transplants performed during nighttime displayed a total of 65 acute rejection episodes with 48 episodes being biopsy-proven and 17 diag-

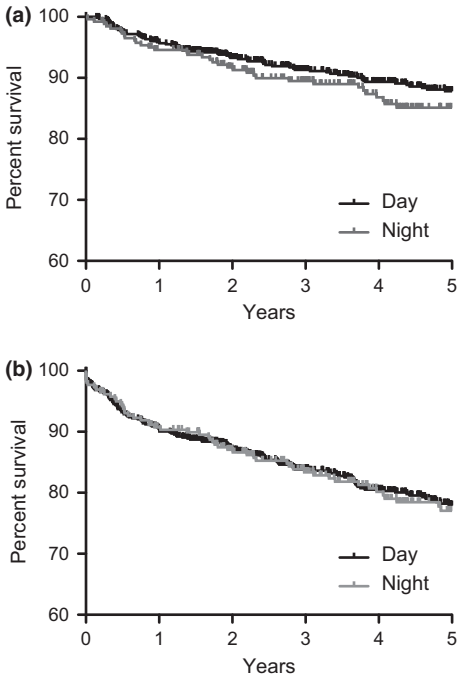

Figure 1 (a) Patient and (b) kidney graft survival. Kaplan–Meier survival estimates stratified by time of operation.

Table 2. Transplant outcome.

	Day (n = 610)	Night (n = 263)	*P*-Value
Overall patient survival			0.73
At 1 year	95.9%	94.6%	
At 5 years	88.0%	86.3%	
Overall graft survival			0.78
At 1 year	90.3%	90.4%	
At 5 years	78.3%	78.1%	
DGF	31.1% (190/610)	37.6% (99/263)	0.06
Acute rejection	22.6% (138/610)	18.3% (48/263)	0.15
Acute rejection episodes	174	65	
BPAR	116	48	
Clinically suspected AR	58	17	
T-cell-mediated AR	128	48	
Antibody-mediated AR	38	17	
Unclassified AR	8	0	

nosed clinically. Also, 74% of rejection episodes were classified T cell-mediated and 26% antibody-mediated. However, operative time of day seems to be related to the incidence of DGF. Nighttime kidney transplants displayed DGF in 37.6% of cases, whereas only 31.1% of daytime allografts developed DGF. Nevertheless, this trend did not reach statistical significance (P = 0.06) (Table 2).

Risk of surgical complications associated with nighttime kidney transplantation

No statistically significant difference in risk of surgical complications was observed when nighttime operations were compared with daytime operations (Table 3). Surgical complications requiring reoperation or interventional treatment occurred in 22.4% of nighttime procedures compared to 22.1% of daytime operations (P = 0.92). The most common surgical complications in both groups included ureteral stenosis and reflux, hematomas, lymphoceles and seromas, as well as wound dehiscence or infection.

Table 3. Surgical complications (P = 0.92). Surgical complications are related to the number of transplants in the respective group; details of surgical complications are related to the total number of complications in the respective group.

Surgical complications	Day 135/610 (22.1%)	Night 59/263 (22.4%)
Venous thrombosis	0	1
Stenosis of transplant artery	3	2
Arterial thrombosis	0	0
Rupture of vascular anastomoses	4	2
Ureteral stenosis	53	17
Ureteral necrosis	4	3
Vesicular leakage	7	3
Vesicular tamponade	1	0
Reflux	18	3
Hematoma	19	8
Wound dehiscence/wound infection	15	11
Lymphocele/seroma	22	15
Incisional hernia	10	5
Other	7	4

Shift of cold ischemia time

If kidney transplants were not performed as emergency procedures during nighttime, but were delayed to the following morning with skin incision at 8 AM according to our definition of daytime surgery, mean CIT would have risen from 16.6 ± 6 h to 24.6 ± 7 h in the nighttime group with a considerable number of kidneys transplanted after a CIT > 18 h (from 37% up to 79% if delayed; Fig. 2a).

Among the 873 transplants, CIT < 18 h revealed significantly better 5-year graft survival (81.1%) than when CIT was >18 h (72.9%, P = 0.02) (Fig. 2b).

Surgeon's experience

In all, 66% of daytime kidney transplants were performed by a consultant compared to 70% of nighttime procedures (P = 0.23); 27% of daytime transplants were assisted by a consultant compared to 20% of nighttime procedures

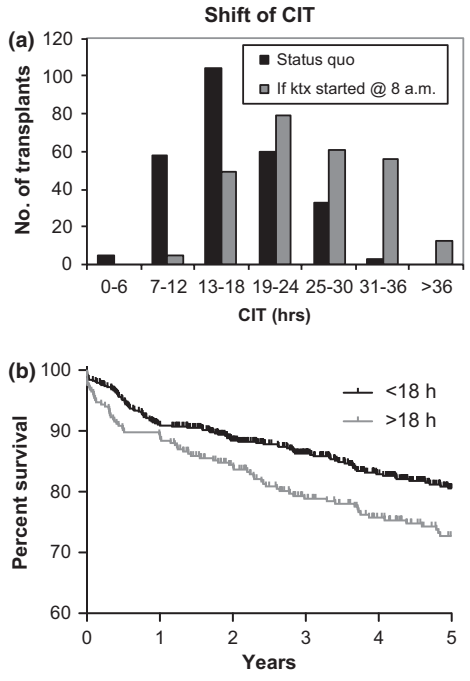

Figure 2 (a) Shift of cold ischemia time (CIT) if nighttime kidney transplants were performed the following morning. (b) Kidney graft survival. Kaplan–Meier survival estimates stratified by CIT < 18 h or >18 h.

Table 4. Kidney transplants stratified by seniority of operating surgeon.

	Day (n = 610)	Night (n = 263)	P-Value
Transplant performed by consultant	404 (66%)	185 (70%)	0.23
Transplant assisted by consultant	166 (27%)	52 (20%)	0.02
Consultant present	570 (93%)	237 (90%)	0.08
No consultant	36 (6%)	24 (9%)	0.01
Missing data	4 (0.7%)	2 (0.8%)	

(P = 0.02). Taken together, 93% of daytime kidney transplants were performed in the presence of a senior surgeon (either operating surgeon or assisting surgeon) compared to 90% of nighttime kidney transplants (P = 0.08). Only 9% of nighttime transplants were performed without a consultant compared to 6% of daytime transplants (P = 0.01, Table 4).

Discussion

To our knowledge, this study constitutes the largest analysis in kidney transplantation relating transplant outcomes to operative time of day. We found no difference in patient and graft survival when comparing daytime and nighttime kidney transplant procedures. This contrasts the results of Fechner *et al.* who observed a significantly higher risk of long-term graft failure in recipients transplanted during nighttime compared with recipients who underwent daytime operation [3]. In our cohort, nighttime kidney transplantation was not associated with a greater risk of surgical complications than daytime procedures, which is in line with data from Seow *et al.* [4], but is contradictory to findings from Fechner *et al.* reporting a higher incidence of – predominantly vascular – complications in nighttime kidney transplant procedures [3]. With respect to allograft rejection, nighttime surgery again did not adversely impact outcomes with 22.6% of daytime graft recipients having an acute rejection compared to 18.3% of nighttime graft recipients. The incidence of DGF was slightly higher in the group of nighttime kidney transplants, but did not reach statistical significance. The reasons for this observation are not yet clear, although one possible explanation might be that this slightly higher incidence of DGF results from a higher proportion of marginal kidneys consequently being transplanted at nighttime, as in this subgroup, all efforts are made to keep CIT short. The definition of DGF used in this study is based on the need for postoperative dialysis. Although this definition is widely accepted by the transplant community [5], it is limited by its subjectivity compared to more quantitative definitions such as no fall in serum creatinine concentration of 10% or more per day within two consecutive 24-h periods. However, no significant difference in donor age or BMI was observed between kidneys transplanted during the night or day.

Evidence of the impact of nighttime surgery on outcomes is very limited in the transplant literature. Apart from the two studies in kidney transplantation mentioned above, Lonze *et al.* have presented a detailed analysis of the risks of nighttime operation in liver transplantation [6]. Comparing two 12-h time strata, complications were not significantly different, but nighttime operations were associated with a twofold greater risk of early postoperative death (odds ratio 2.9), whereas long-term patient survival was unaffected by operative time of day. For thoracic organ transplantation, a large UNOS database cohort study including more than 27 000 heart and lung transplant recipients did not reveal any significant association between nighttime heart or lung transplantation and 1-year mortality [7].

It is common sense that excessive duty hours and extended work shifts (24 h or more) inevitably lead to sleep deprivation and fatigue that in turn result in reduced performance. This is supported by various scientific publications: Survival rates from in-hospital cardiac arrest are significantly lower during nights and weekends compared with daytime and evening [8]. Interns make 35.9% more serious medical errors when working extended work shifts of 24 h or more [9]. Conversely, eliminating interns' extended work shifts significantly decreases attentional failures [10]. However, the surgical literature on the impact of sleep deprivation on surgical outcomes and performance gives conflicting results [11–16].

Simulation-based methods are a means to objectively assess psychomotor and cognitive skill performance. It was the landmark paper by Dawson *et al.* that presented a vivid picture and therefore an easily grasped index of the relative impairment associated with fatigue. After 24 h of sustained wakefulness, cognitive psychomotor performance decreases to a level equivalent to the performance deficit observed at a blood alcohol concentration of roughly 0.10% [17].

As an association of fatigue and surgical performance has been published [18–21], the reasons for our results demonstrating no difference in surgical outcomes in nighttime kidney transplantation (compared to daytime procedures) need to be explored. One possible explanation is that standard surgical procedures are comprised of a distinct course of movements and surgical steps that – once they are automatized – do not require higher cognitive capacity, especially as at our center 120–140 kidney transplants are being carried out per year by a small number of surgeons. During nighttime, under sleep-deprived conditions, these automatized movements and steps together with surgical training and expertise ensure optimal utilization of cognitive resources [22]. Furthermore, probably any surgeon has

developed strategies to adapt to and cope with fatigue during his training [23]. Optimizing performance after excessive hours of wakefulness can be and is equally trained as surgical skills [24]. So, for sure, training and experience compensate fatigue.

The striking argument in kidney transplantation for performing transplants at any time of the day is CIT [2,25–29]. Based on the findings from the Collaborative Transplant Study, the risk of graft failure rises to relative risk 1.09 for kidneys preserved for 19–24 h, to 1.16 for CIT of 25–36 h, and even further to 1.3 for >36 h of cold ischemia [2]. The relatively great window of 18 h of 'safe' CIT might allow for postponing the kidney transplant until the following morning. But, in fact, the current allocation system often leads to long hours of transportation, thereby closing the initially great window and mandating immediate transplantation after arrival of the kidney. In busy transplant centers that cover all abdominal organs, even kidneys derived from in-house donors represent a certain challenge because if transplanted only during daytime hours, they would run into ischemia times beyond 18 h, as the liver and pancreas always go first for obvious reasons. Furthermore, the number of marginal organs is dramatically increasing and the window may come down to 12 h of CIT or even less. In our cohort, CIT > 18 h was a significant risk factor for decreased long-term survival. There are data that machine perfusion ameliorates the detrimental effects of cold ischemia. For reasons of the small number of kidneys placed on the pump in our study cohort ($n = 4$), we cannot assess its effect on outcome measures. We would only consider machine perfusion as a means to deliver treatment, not to prolong CIT.

Certainly, the findings from our study are limited by its retrospective design and potential misclassification bias. The definition of daytime and nighttime procedure is a purely arbitrary one. We have chosen a skin incision at 8 AM as cut-off time point for daytime surgery because at our institution, this best resembles at what time an elective procedure would start. Independently of the model used, any definition lacks the degree of sleep deprivation of the responsible surgeon and merely represents a poor surrogate for rested or fatigued. For most cases, a nighttime surgical procedure that starts at 3 AM will incorporate a sleep-deprived surgeon. But, an operation classified as daytime because of skin incision at 9 AM that is performed post nighttime certainly does not resemble a well-rested state. However, we assume, as the European work law prohibits us to do surgery after 24 h shifts, that none of the daytime procedures were carried out under sleep deprivation. Significantly more transplants were assisted during daytime, whereas significantly more transplants were carried out in the absence of a consultant during the night with no impact on complication rate or survival. These data may allow conclusions on the consultants' behavior (which was not the focus of our study), but should not be included in the decision whether a kidney transplant should be carried out during the night or not.

In summary, herein we report that nighttime kidney transplantation is not associated with a greater risk of surgical complications than daytime kidney transplantation. Furthermore, patient and graft survival do not relate to the operative time of the day. Based on our results, kidney transplant procedures must inevitably be performed as emergency operation regardless of the time of day, as this is the only possibility to keep CIT at a minimum and to warrant optimal transplant outcomes.

Authorship

KK-W, RÖ, JP: conceived and designed the study. KK-W, RÖ: wrote the manuscript. SS, CB: collected the data. RÖ, SS, JP: critically revised and finally approved the article.

Funding

No funding was received for conducting this study.

References

1. Kohn LT, Corrigan JM, Donaldson MS. *To Err is Human: Building a Safer Health System*. Washington, DC: National Academy Press, 2000.
2. Opelz G, Dohler B. Multicenter analysis of kidney preservation. *Transplantation* 2007; **83**: 247.
3. Fechner G, Pezold C, Hauser S, Gerhardt T, Muller 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.
4. Seow YY, Alkari B, Dyer P, Riad H. Cold ischemia time, surgeon, time of day, and surgical complications. *Transplantation* 2004; **77**: 1386.
5. Perico N, Cattaneo D, Sayegh MH, Remuzzi G. Delayed graft function in kidney transplantation. *Lancet* 2004; **364**: 1814.
6. Lonze BE, Parsikia A, Feyssa EL, *et al.* Operative start times and complications after liver transplantation. *Am J Transplant* 2010; **10**: 1842.
7. George TJ, Arnaoutakis GJ, Merlo CA, *et al.* Association of operative time of day with outcomes after thoracic organ transplant. *JAMA* 2011; **305**: 2193.
8. Peberdy MA, Ornato JP, Larkin GL, *et al.* Survival from in-hospital cardiac arrest during nights and weekends. *JAMA* 2008; **299**: 785.
9. Landrigan CP, Rothschild JM, Cronin JW, *et al.* Effect of reducing interns' work hours on serious medical errors in intensive care units. *N Engl J Med* 2004; **351**: 1838.

10. Lockley SW, Cronin JW, Evans EE, *et al.* Effect of reducing interns' weekly work hours on sleep and attentional failures. *N Engl J Med* 2004; **351**: 1829.
11. Sturm L, Dawson D, Vaughan R, *et al.* Effects of fatigue on surgeon performance and surgical outcomes: a systematic review. *ANZ J Surg* 2011; **81**: 502.
12. Komen N, Dijk JW, Lalmahomed Z, *et al.* After-hours colorectal surgery: a risk factor for anastomotic leakage. *Int J Colorectal Dis* 2009; **24**: 789.
13. Ricci WM, Gallagher B, Brandt A, Schwappach J, Tucker M, Leighton R. Is after-hours orthopaedic surgery associated with adverse outcomes? A prospective comparative study. *J Bone Joint Surg Am* 2009; **91**: 2067.
14. Chacko AT, Ramirez MA, Ramappa AJ, Richardson LC, Appleton PT, Rodriguez EK. Does late night hip surgery affect outcome? *J Trauma* 2011; **71**: 447; discussion 53.
15. Chu MW, Stitt LW, Fox SA, *et al.* Prospective evaluation of consultant surgeon sleep deprivation and outcomes in more than 4000 consecutive cardiac surgical procedures. *Arch Surg* 2011; **146**: 1080.
16. Ellman PI, Law MG, Tache-Leon C, *et al.* Sleep deprivation does not affect operative results in cardiac surgery. *Ann Thorac Surg* 2004; **78**: 906; discussion -11.
17. Dawson D, Reid K. Fatigue, alcohol and performance impairment. *Nature* 1997; **388**: 235.
18. Privette AR, Shackford SR, Osler T, Ratliff J, Sartorelli K, Hebert JC. Implementation of resident work hour restrictions is associated with a reduction in mortality and provider-related complications on the surgical service: a concurrent analysis of 14,610 patients. *Ann Surg* 2009; **250**: 316.
19. Grantcharov TP, Bardram L, Funch-Jensen P, Rosenberg J. Laparoscopic performance after one night on call in a surgical department: prospective study. *BMJ* 2001; **323**: 1222.
20. Taffinder NJ, McManus IC, Gul Y, Russell RC, Darzi A. Effect of sleep deprivation on surgeons' dexterity on laparoscopy simulator. *Lancet* 1998; **352**: 1191.
21. Eastridge BJ, Hamilton EC, O'Keefe GE, *et al.* Effect of sleep deprivation on the performance of simulated laparoscopic surgical skill. *Am J Surg* 2003; **186**: 169.
22. Leff DR, Orihuela-Espina F, Athanasiou T, *et al.* "Circadian cortical compensation": a longitudinal study of brain function during technical and cognitive skills in acutely sleep-deprived surgical residents. *Ann Surg* 2010; **252**: 1082.
23. Yuh DD. Effect of sleep deprivation on patient safety: new awakening or tired argument? *Arch Surg* 2011; **146**: 1085.
24. Leff DR, Aggarwal R, Rana M, *et al.* Laparoscopic skills suffer on the first shift of sequential night shifts: program directors beware and residents prepare. *Ann Surg* 2008; **247**: 530.
25. Giblin L, O'Kelly P, Little D, *et al.* A comparison of long-term graft survival rates between the first and second donor kidney transplanted–the effect of a longer cold ischaemic time for the second kidney. *Am J Transplant* 2005; **5**: 1071.
26. Salahudeen AK, Haider N, May W. Cold ischemia and the reduced long-term survival of cadaveric renal allografts. *Kidney Int* 2004; **65**: 713.
27. Ojo AO, Wolfe RA, Held PJ, Port FK, Schmouder RL. Delayed graft function: risk factors and implications for renal allograft survival. *Transplantation* 1997; **63**: 968.
28. Hernandez D, Estupinan S, Perez G, *et al.* Impact of cold ischemia time on renal allograft outcome using kidneys from young donors. *Transpl Int* 2008; **21**: 955.
29. Asderakis A, Dyer P, Augustine T, Worthington J, Campbell B, Johnson RW. Effect of cold ischemic time and HLA matching in kidneys coming from "young" and "old" donors: do not leave for tomorrow what you can do tonight. *Transplantation* 2001; **72**: 674.

