

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Weekend versus weekday transplant surgery and outcomes after kidney transplantation: a retrospective national database analysis
AUTHORS	Baid-Agrawal, Seema; Martus, Peter; Feldman, Harold; Mattix-Kramer, Holly

VERSION 1 - REVIEW

REVIEWER	Karl L. Womer, MD University of Florida, USA
REVIEW RETURNED	23-Dec-2015

GENERAL COMMENTS	<p>This is a retrospective study with adequate power and based on the US national registry data. The study design and statistical analyses were conducted properly. The conclusion that performance of kidney transplant surgery on weekends does not negatively affect short- or long-term patient outcomes seems valid. Strengths include that the study is the first to investigate whether there is a weekend effect with regard to kidney transplant outcomes. The weaknesses are a lack of positive findings, except for length of stay, and difficulty drawing any major conclusions about the importance of these findings with regard to clinical practice. Thus, it is unclear whether this study alone would lead to any major changes in other surgical fields or within the field of kidney transplantation. The following are just a couple of minor comments:</p> <ol style="list-style-type: none">1. Page 20. The authors should specify the number of years of survival in Table 2.2. Page 22, 23, 24. Please report the results of log rank tests for these KM curves (Figure 1 a, b, c) since it was mentioned in the method section.3. Induction or immunosuppressant drug use was not assessed and compared between the two surgery groups.4. A recent abstract presented at the ASN Kidney Week 2015 in San Diego, CA ("Discard of deceased donor kidneys in the United States: The weekend effect." Abstract SA-PO1013) that was reviewed in several news releases (e.g. http://www.eurekalert.org/pub_releases/2015-11/ason-dom102415.php) found donor kidneys were 20% more likely to be discarded on weekends. Do the authors feel that this phenomenon may impact the finding in their study?
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REVIEWER	Eliyahu Khankin MD, FASN Transplant Institute Division of Nephrology, Department of Medicine Beth Israel Deaconess Medical Center Boston, MA USA
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REVIEW RETURNED	27-Dec-2015
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GENERAL COMMENTS	The format of the manuscript is clear and concise and the question stated is addressed appropriately and elegantly. It would have been more complete if more data were available, as authors stated in their discussion (assessing the impact of night-time transplantation on the outcome was impossible due to the lack of data on the time of transplantation in the UNOS database). That said, I do not feel that missing night time surgery analysis data is a major deficiency. I do wonder if authors could elaborate more on the "root" of noted slightly lower hospital length of stay with transplants performed over the weekend (Saturday and Sunday) vs. the regular workweek (Monday-Friday), as it may be an important finding suggesting that some of the transplants are done in a more efficient way during the weekend without negative influence on the surgery outcomes and provide directions for future clinical process improvement.
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REVIEWER	Klemens Budde Charité Universitätsmedizin Berlin, Germany
REVIEW RETURNED	28-Dec-2015

GENERAL COMMENTS	interesting research question, answered in a large database.
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REVIEWER	Annemarie Weissenbacher Innsbruck Medical University Austria
REVIEW RETURNED	03-Jan-2016

GENERAL COMMENTS	Thank you very much for submitting this retrospective analysis. The idea is very interesting, to show that there are no major differences between weekday and weekend surgery. Comments: In this analysis it needs to be differentiated between night and day surgery as well. I cannot understand that it is not possible to get these data, as is mentioned on page 10 (...owing to the lack of data on the time of transplantation in the UNOS database...). Knife to skin or the wound closure time is always known! Next issue: is there a difference in the working hours of the surgeons. Were these transplants done by "on call" surgeons or were they working on a 24 hours basis? The statistics are not clearly described. How can it be that a median CIT of 18 and 19 hours with exactly the same IQR is highly significantly different? I have the same question for the hospital stay.
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VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Karl L. Womer, MD
University of Florida, USA

Comments:

This is a retrospective study with adequate power and based on the US national registry data. The

study design and statistical analyses were conducted properly. The conclusion that performance of kidney transplant surgery on weekends does not negatively affect short- or long-term patient outcomes seems valid. Strengths include that the study is the first to investigate whether there is a weekend effect with regard to kidney transplant outcomes.

Response: We would like to thank the reviewer for his very helpful comments.

The weaknesses are a lack of positive findings, except for length of stay, and difficulty drawing any major conclusions about the importance of these findings with regard to clinical practice. Thus, it is unclear whether this study alone would lead to any major changes in other surgical fields or within the field of kidney transplantation.

Response:

The weekend effect has raised significant concerns in recent years, not only for emergency procedures, but also for elective surgeries. Since kidney transplantation involves complex peri-operative care and technically advanced procedures, it may be more sensitive to the weekend effect. Furthermore, deceased donor kidney transplantation provides a unique setting for studying the differences in quality of care during weekends, as it differs from acute critical illness in that the patients coming for transplantation are typically clinically stable. Therefore, in this situation, confounding due to differences in severity of illness at the time of admission is much less likely compared to other clinical situations. We interpret the lack of weekend effect found on the kidney transplant outcomes in our study as a very positive finding and an indication of consistency in quality of care irrespective of the day of the week if standardized protocols and interdisciplinary team effort are in place. The operationalization of deceased donor kidney transplantation may provide a model for other emergency or elective procedures that are performed over weekends, and help improve outcomes. Therefore, we do believe that our study is an important contribution to the literature and holds strong clinical implications for other surgical fields as well as policy makers.

The following are just a couple of minor comments:

1. Page 20. The authors should specify the number of years of survival in Table 2.

Response: Thanks for this suggestion. We have now revised the Table 2 to include the number of years of survival (Revised version, page 20).

2. Page 22, 23, 24. Please report the results of log rank tests for these KM curves (Figure 1 a, b, c) since it was mentioned in the method section.

Response: Thanks for pointing it out. We have now included the results of log rank test for the KM curves in the figure 1 (Revised version, pages 22-24).

3. Induction or immunosuppressant drug use was not assessed and compared between the two surgery groups.

Response: We agree with the reviewer that induction and immunosuppressant drug use are important variables to assess. Therefore, we did the analyses for induction and maintenance immunosuppressants in the two groups. The differences in immunosuppressants between the two groups were quite small and some reached statistical significance just because we had over 136,000 people in the analysis. Furthermore, in the multivariate analysis, we found the null findings to be robust even for adjustment for immunosuppressants. Therefore, the association between outcomes and weekday status that we found is very robust for adjustment for covariates. No matter how we define it or what variables we add to the model, there is still no association between the day of the week and outcomes. Since we wanted a more parsimonious model, we left immunosuppressants out of the model.

4. A recent abstract presented at the ASN Kidney Week 2015 in San Diego, CA ("Discard of deceased donor kidneys in the United States: The weekend effect." Abstract SA-PO1013) that was reviewed in several news releases (e.g. http://www.eurekalert.org/pub_releases/2015-11/ason-dom102415.php) found donor kidneys were 20% more likely to be discarded on weekends. Do the authors feel that this phenomenon may impact the finding in their study?

Response: We thank the reviewer for mentioning this interesting abstract. The increased discard of the donor kidneys found in this study would lead to fewer kidney transplants on the weekends. Interestingly, the kidneys that were discarded during weekends were found to be of a higher quality than those discarded during the rest of the week. Therefore, this phenomenon may theoretically have adverse effects on the outcomes of the transplants performed over weekends. However, the lack of an observed weekend effect in our study is all the more remarkable given the possible influence of fewer high quality kidneys for weekend transplant recipients. Nonetheless, it should be noted that these findings are still available only as an abstract, and an accurate interpretation of the findings may be possible only after the availability of detailed analysis.

Reviewer: 2

Eliyahu Khankin MD, FASN
Transplant Institute, Division of Nephrology, Department of Medicine

Comments:

The format of the manuscript is clear and concise and the question stated is addressed appropriately and elegantly. It would have been more complete if more data were available, as authors stated in their discussion (assessing the impact of night-time transplantation on the outcome was impossible due to the lack of data on the time of transplantation in the UNOS database). That said, I do not feel that missing night time surgery analysis data is a major deficiency.

Response: We are thankful to the reviewer for his supporting comments.

I do wonder if authors could elaborate more on the "root" of noted slightly lower hospital length of stay with transplants performed over the weekend (Saturday and Sunday) vs. the regular workweek (Monday-Friday), as it may be important finding suggesting that some of the thighs are done in more efficient way during the weekend without negative influence on the surgery outcomes and provide directions for future clinical process improvement.

Response: The reviewer is correct that the observed slightly lower hospital length of stay may suggest more efficient transplantation during the weekend. However, we are not clear on the proposed mechanism through which a weekend transplant would lead to efficiencies. However, we did not elaborate more on this finding, as we were cautious in over interpreting very small differences in the study that may have been detected because of the large sample size of the study and may not be clinically meaningful. We have now clarified this point in our Discussion (Revised version, page 10, lines 23-34)

Reviewer: 3

Klemens Budde
Charité Universitätsmedizin Berlin, Germany

Interesting research question, answered in a large database.

The reviewer has no concerns.

Reviewer: 4

Annemarie Weissenbacher
Innsbruck Medical University

Thank you very much for submitting this retrospective analysis. The idea is very interesting, to show that there are no major differences between weekday and weekend surgery.

Comments:

In this analysis it needs to be differed between night and day surgery as well. I cannot understand that it is not possible to get these data, as is mentioned on page 10 (...owing to the lack of data on the time of transplantation in the UNOS database...). Knife to skin or the wound closure time is always know!

Response: We thank the reviewer for her very useful comments. We agree that the impact of day and night on the outcomes is an important aspect and would be desirable to assess. Unfortunately, the time of knife to skin or the wound closure time is not captured in the UNOS database, which we checked again in the data files and confirmed by calling the UNOS office. The only probable way to determine the approximate operative start time would be by adding the cold ischemia time to the cross clamp time at procurement of the organ. However, owing to potential differences in the time zones between the site of procurement and site of transplantation, it would not have been possible to reliably assess the time of surgery and outside the scope of this study. It would certainly be an important topic for another research paper.

Next issue: is there a difference in the working hours of the surgeons. Were these transplants done by "on call" surgeons or were they working on a 24 hours basis?

Response: We agree that the working hours of the surgeons is an important factor to consider. Unfortunately, this data is not captured in the UNOS database. We checked it in the UNOS data files and also confirmed by calling the UNOS office. We have now acknowledged this limitation in our Discussion (Revised version, page 13, lines 3-5).

The statistics are not clear described. How can it be that a median CIT of 18 and 19 hours with exactly the same IQR is highly significantly different? I have the same question for the hospital stay.

Response: The results for both CIT and the hospital stay have been carefully checked and confirmed. For the CIT, even with such a small difference of medians and identical quartiles, the Mann-Whitney test is significant. This is due to the tremendously large sample size. Even if the t-test would not be adequate here, it might be useful to demonstrate this effect: We find a mean difference of 0.32 hours (larger time for weekdays) and a pooled standard deviation of about 9. Thus the observed effect (standardized difference = difference/standard deviation) is $0.32/9 = 0.036$ which is "nothing". However, due to the large sample size, the t-value, which is practically a z-value, becomes 5.6, which leads to a highly significant result.

The situation is a bit more puzzling for the length of stay. Here we do have a significant result in the Mann-Whitney test, but not in the t-test. The effect size of the Mann-Whitney test is mathematically equivalent to the area under the ROC curve (even if no classification is intended usually). For the length of stay, the area under this curve was 0.513 (CI: 0.509-0.518) which is very close to purely random differences between weekdays and weekend, however, it is still significant vs. H_0 : AUROC =

50%.

This is how we can explain the significant differences in CIT and the hospital stay, and have now pointed out in the Discussion that with such large sample sizes, irrelevant effects may become significant (Revised version, page 10, lines 23-34). This however supports our main analysis as with such a large sample size, we found a negative result.

VERSION 2 – REVIEW

REVIEWER	Womer, Karl L University of Florida, USA
REVIEW RETURNED	23-Feb-2016

GENERAL COMMENTS	No further concerns.
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REVIEWER	Eliyahu Khankin MD, FASN Transplant Institute, Beth Israel Deaconess Medical Center/Harvard Medical School, Boston, MA, USA.
REVIEW RETURNED	25-Feb-2016

GENERAL COMMENTS	I would like to thank authors for addressing the suggestions made by his reviewer in the revised manuscript. I have no further suggestions, but would like to make a friendly recommendation to revise the draft for grammatical and typographical errors as well as as minor style improvements to achieve more fluent readability.
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REVIEWER	Annemarie Weissenbacher Innsbruck Medical University
REVIEW RETURNED	22-Feb-2016

GENERAL COMMENTS	Thanks for answering the questions and revising the manuscript.
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