Restrictive Blood Transfusion Practices in Cardiac Surgery: Is Less Better?

Tait Chamberlain | Deepak Krishnan | Andrew Lin
Omkar Sunkersett | Jeremy Wolverton

University of Michigan
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Abstract

In recent years, blood transfusions during cardiac surgery have undergone much scrutiny. Several studies have shown that the likelihood of adverse outcomes increases with transfusions. Transfusions have been linked to mortality, complications after surgery, and increased the length of stay. This has caused a number of institutions to implement more stringent guidelines when it comes to transfusing patients. The University of Michigan Health System is one of these institutions. In 2009, the triggers for transfusion were reevaluated and tightened. This left a striking disparity in the number of units that were being transfused per patient pre and post 2009. Prior to 2009, up to 70% of patients were given blood transfusions during surgery. And as recent of the restrictive practices, as 2015, that percentage has declined significantly to as low as 10%. This study is meant to interpret those data to determine if patient outcomes changed as a result of these newer guidelines. The study looks at 3600 Valve and CABG operations between 2005 and 2015. Our Analysis has excluded 2009 data because this was largely a transitional period, and the exact date of the newer guidelines is unknown for various surgeons and departments.

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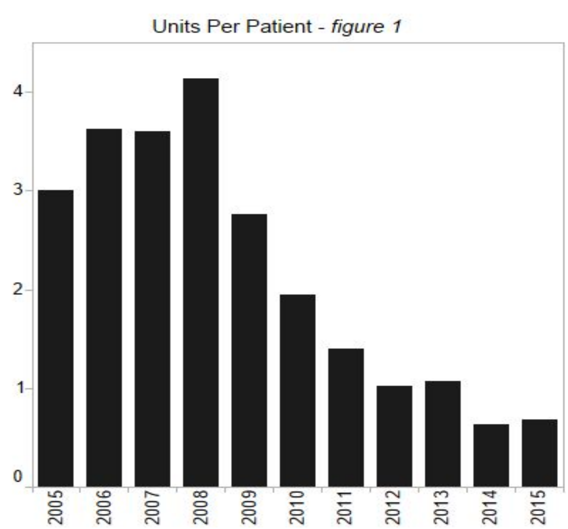
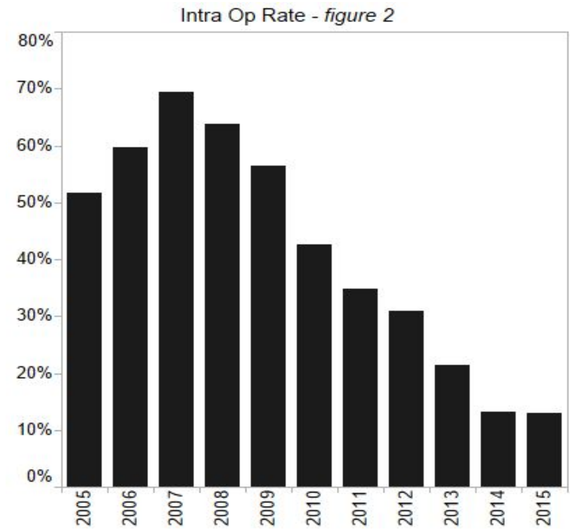
I. INTRODUCTION

Blood transfusions are sometimes a very necessary part of having successful cardiac surgery. However, blood transfusions have also been directly linked to increased hospital length of stay and mortality following a cardiac operation in multiple studies. Therefore it begs the question, *Is less blood better?* It is a very difficult question to answer for many reasons. One reason is that there's no definitive way of knowing that if the patient is not given a blood transfusion if they will survive. However, you can look retrospectively at blood use and attempt to decipher if less may mean better.

This study will try to do just that. It will look at 3600 cardiac operations at University of Michigan Hospital from 2005 to 2015. It is well documented in this data set that U of M surgeons drastically reduced the number of blood transfusions they were giving patients in 2009. This created two distinct periods that can be analyzed. Prior to 2009 the average number of units a patient



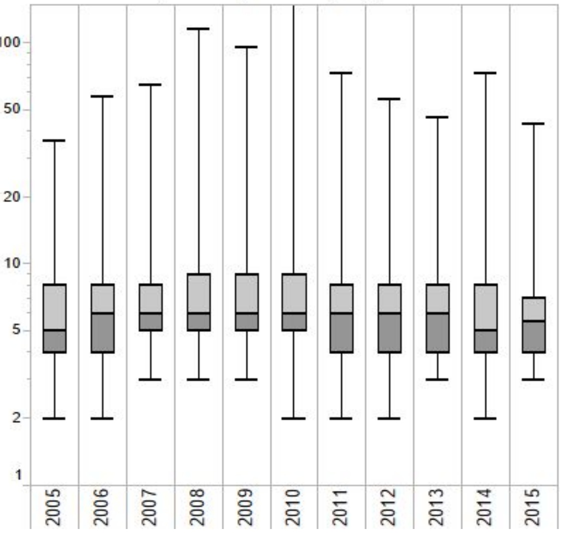
received was 3. After 2009 that number



dropped to as low as .5 units per patient (See figure 1). Also, the rate and the number of patients receiving blood transfusions drastically decreased as well (See figure 2). It's quite clear that a more restrictive blood transfusion practice was put into place at this institution, but how has that changed patient outcomes? If at all.

Our study team is very interested in attempting to answer this question. The literature indicates that more blood transfusions overall will have a negative impact on cardiac surgery outcomes. We were anticipating that these data would reflect this. We expected that patient outcomes would at least be better post-2009 than pre-2009. A yearly breakdown of the length of stay data did not appear to be

Hospital Length of Stay - *figure 3*



affected on account of reduced blood transfusions (See figure 3). We used several tools and methods that were introduced to us in SI 544. Mainly, we used the open source statistical analysis package R to run a linear regression. Then we conducted an ANOVA test to identify key variables. We will cover these methods more in depth in the next few sections.

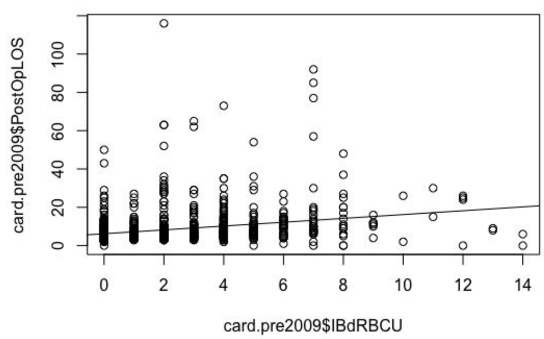
II. METHODOLOGY

We began by studying the dataset and fetching a list of significant variables. We split the data into two frames-one which was prior to the implementation of the restrictive blood transfusion practices (in 2009) and the other post-2009.

We then further split the data into pre-operative factors (those measurements taken before and during the operation, such as Age, Sex, Weight, and Body Surface Area, see Appendix Figure 6), post-operative factors that were not binomial (the two measurements in our data taken after the operation, the total number of hours the patient stayed on a ventilator post-operation, and the total length of stay (see Appendix Figure 7), and finally the post-operative factors that were binomial (such as whether the patient suffered from paralysis, stroke, or renal failure after the surgery, see Appendix Figure 7). Splitting the post-operative factors into binomial and non-binomial groups allowed us to run linear regressions on the variable factors, and a generalized linear model on the binomial factors to ensure the accuracy of our correlations.

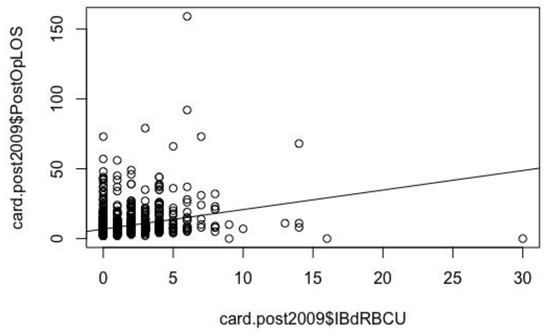
Using this method we were able to establish a strong correlation between the amount of blood transfused during the operation and the patient length of stay. To generalize, we found that pre-2009 for every 350 mL of blood transfused during the cardiac operation, there is an additional day added to the length of stay (Length of stay in days = 6.197 + 1.002*Units of blood transfused).

Length of Stay by transfusion amount pre-2009 - *Figure 3*



Post-2009, we can see that this correlation only strengthens, as the amount of blood transfused lowers overall, increasing the significance of each unit of blood delivered (Length of stay in days = 6.784 + 1.397*Units of blood transfused).

Length of Stay by transfusion amount post-2009- *Figure 4*



Having established a clear correlation between amount of blood transfused and patient outcome as measured by postoperative length of stay, we attempted to verify that the patient outcomes were not affected by the more restrictive blood transfusion practices, as measured by the patients' lengths of stay.

Our null hypothesis was that the mean length of stay pre-2009 was not different than the mean length of stay post-2009. Our test of this hypothesis shows that with 95% confidence we can say the patient length of stay did not change during the two periods.

Hypothesis test for Patient Length of Stay

Y_post = 62.69
Y_pre = 80.01
Mean_post = 7.78
Mean_pre = 8.29
N_post = 1971
N_pre = 1119
SE = 2.77
T-value = 0.1838

After confirming this result, we studied the significant pre-operative variables across the two data frames and observed that there were 4 variables which had high correlation pre-2009 but did not have a statistically significant correlation post-2009.

The variables are:

Significant preoperative variables pre-2009 only - *Figure 5*

Variables	*P-value pre-2009*
Sex	5.16e-08
BSA - Body Surface Area	.1968
Hypertension	.003
CVD - Cerebrovascular Disease	.02158

(For a full list of significant variables, see Appendix Figure 8.)

We observed that prior to 2009, patients' gender, BSA, Hypertension level and whether they suffered from CVD was significantly positively correlated with the amount of blood they received during the operation. After 2009, however, these factors ceased from being significantly correlated.

Nonetheless, we can see that post-2009, indicators of patient outcomes do not change significantly (in other words, while the amount of blood transfused during operations decreases significantly, patient outcomes do not significantly change). Thus it seems clear that these 4 factors which dropped out of significance post-2009 are not highly correlated with patient outcomes.

The one factor that does become significant post-2009 is HCT (the Last Hematocrit prior to the operation). This variable, which is in loose terms the density of red blood cells in the blood, becomes correlated because part of the post-2009 blood transfusion protocols was to lower the threshold of HCT that triggers an additional unit of blood transfusion, going from ~30 to ~22. This increased reliance on a single factor, HCT, to indicate when to transfuse more blood, is particularly interesting, because it shows that HCT is not highly correlated with the 4 variables discussed above. If HCT were merely a leading indicator or otherwise multicollinear with any of those variables, the increased reliance on HCT in determining when to transfuse blood would have increased, rather than decreased, their significance. This further confirms our thesis that the prior 4 variables should not be utilized in decision making on transfusions during operations because the patient outcomes are not adversely affected.

Research steps:

1) Plotted the dataset to see general trends
2) Divided the data set into pre-2009 and post-2009 periods
3) Divided the variables into pre-operative factors, post-operative factors, and postoperative-binomial factors
4) Performed a regression on blood transfusion amounts (*IBdRBCU*) against the 27 factors (variables) that we have in our dataset pre- and post-2009
5) Used anova tests to verify the elimination of nonsignificant variables pre- and post-2009
6) Performed separate regressions on pre- and post-2009 for pre-operative variables, postoperative outcomes, and postoperative binomial outcomes
7) Compared the significant variables between the periods for pre-operative variables
8) Performed regressions based on patient length of stay pre- and post-2009 to verify that patient outcomes have not been significantly affected by the policy change
9) Performed regressions on preoperative variables to confirm if correlations maintained their significance pre- and post-2009

III. RESULTS

We posit that doctors are unnecessarily taking into account these factors when deciding how much blood to transfuse during an operation, either directly or indirectly. With the more restrictive practices in place, we can see that these factors no longer correlate to the amount of blood transfused.

Since we can see from the data that patient outcomes are largely unchanged by the introduction of more restrictive transfusion practices (that is, patient outcome variables remain steady despite lower blood transfusion rates), it seems clear that even if there is an unknown corollary between these 4 factors and blood transfusion rates, doctors can safely not take into account these factors when making blood transfusion decision during operation. In a stressful surgery environment, it may be helpful to know which factors do not significantly affect patient outcomes with regard to blood transfusion rates.

IV. CONCLUSION

Based on our analysis of this sample, we find a basic correlation between the amount of blood transfused during cardiac operations and patient outcomes as measured by “Length of Stay”. Still, overall we observe that the correlation between blood transfusions and postoperative outcomes is low. This translates into the more restrictive blood transfusion practices instituted in 2009 not significantly either improving or negatively impacting patient outcomes.

Research, however, has shown that increased blood transfusions have produced more unfavorable outcomes. Our analysis and the data of University of Michigan patients have not been able to reproduce these findings. Outcomes remain unchanged regardless of the volume of blood transfusions given to patients.

Still, from our research we can draw some positive and significant conclusions. One conclusion is that the transfusion triggers before 2009 are too loose. This means that patients are more likely to receive blood transfusions unnecessarily based on their pre-existing conditions. Another conclusion is that with the decrease in the amount of blood units used, there would be a significant cost savings in health care with no impact on outcomes. While less imperative for patient care, reducing costs without harming patient outcomes is a high priority for hospital administrations, and can free up significant capital to further the hospital’s mission and impact on the larger community.

We suspect that a major reason we cannot see a high correlation between blood transfusion amounts during surgery and post-surgery outcome variables is because our dataset variables are highly endogenous. Because of the difficulty of running clinical trials on this data, it may be advisable to attempt to find an instrument variable that is highly correlated with our explanatory variable (blood transfusion amounts), but not correlated with our patient outcome variables (e.g., morbidity).

V. FURTHER STUDY

It may be that the preoperative variables (we discovered), which do not change between pre- and post-2009 periods, are such instruments. This is because patient outcomes have not become significantly worse post-2009, indicating that these variables are highly correlated with blood transfusion amounts but not with patient outcomes. Using one of these variables as an instrument, it may be possible to counteract the endogeneity in our data set and show a negative correlation between blood transfusion amounts and patient outcomes.

Further avenues of future study would include determining the extent that preoperative risk factors affect the amount of blood transfused during operations. If these risk factors are significant and can be corrected for in the regressions, the correlation between blood transfusions and patient outcomes may become much more pronounced. In other words, the impact of blood transfusions in our current model may be drowned out by the fact that patients going into surgery with significant risk factors require more blood to be transfused than low-risk patients but may not have significantly worse outcomes post-surgery than low-risk patients, skewing the blood-transfusion correlation.

Finally, it would be helpful to better understand the extent to which our data set variables are endogenous, and how much they suffer from multicollinearity. While we suspect that this has greatly complicated our analysis, we aver that further researching the extent of each is beyond the scope of this study.

V. APPENDIX

Figure 6. Pre-operative variables:

Surgeon Code	Code number for the surgeon who performed the operation
IBdRBCU	Number of Red Blood Cell Units transfused intra operative (1 unit = 350mL)
BdRBCU	Number of Red Blood Cell Units transfused post the operation
Status	The acuity of the surgery. 1-elective, 2-urgent, 3-emergent
Age	Age of the patient undergoing surgery
Sex	Gender of the patient undergoing surgery
Weight (in Kg)	weight in kilograms of the patient undergoing surgery
BSA	Body surface area of the patient undergoing surgery
RFHemoglobin	The last hemoglobin value from blood test prior to enter the operating room
Hct	Last Hematocrit prior to OR
WBC	Last White Blood Cell Count
CreatLst	Last Creatinine
Dialysis	If the patient is on dialysis before the operation
Hypertn	If the patient has hypertension
PVD	Peripheral Vascular Disease
CVD	Cerebrovascular Disease
Incidence	1 = First time cardiac operation, 2 - 2nd, etc.

Figure 7. Post-operative variables:

VentHrsTot	Total number of hours patient was on a ventilator after the operation

PostOpLOS	How long the patient was in the hospital after surgery
COpReBld	Patient had to be taken back to the operating room after surgery for bleeding
CNStrokP	Patient suffered a stroke after operation
CNParal	Patient suffered paralysis after operation
CRenFail	Patient suffered renal failure after operation
CPPneum	Patient suffered pneumonia after operation
COtArrst	Patient went into Cardiac Arrest after operation
COtMSF	Patient had multi system failure (many organ failures)
COtAFib	Patient suffered from Atrial Fibrillation after operation
MtOpD	Patient died after operation, and related to the operation

Figure 8. Significant variables

pre-2009	**post-2009**
Surgeon Code	*Surgeon Code*
Status	*Status*
Age	*Age*
RFHemoglobin	*RFHemoglobin*
ProcedureType	*ProcedureType*
Sex	
BSA	
Incidence	
WBC	
Hypertension	

CVD	
	HCT

Figure 9. Select R code

```
# Read in the data file
card = read.csv("/users/taitcha/Desktop/cardsurg.csv")

# Run initial regression analysis to find significant variables
pre_lm = lm(MtOpD ~ SurgeonCode + IBdRBCU + BdRBCU + Status + Age + Sex + WeightKg + BSA + RFHemoglobin+ Hct +WBC +CreatLst +Dialysis +Hypertn +PVD +CVD+Incidence+ProcedureType_new,data = project_dataset)

summary(pre_lm)

pre_lm_2 = lm(MtOpD ~ SurgeonCode +IBdRBCU + BdRBCU + Age + Hct + PVD +ProcedureType_new ,data=na.omit(project_dataset[ , all.vars(formula(pre_lm))]))

summary(pre_lm_2)

#run anova tests to verify insignificant variables
anova(pre_lm, pre_lm_2)

post_lm = lm(MtOpD ~ VentHrsTot  + PostOpLOS +COpReBld +CNStrokP +CNParal +CRenFail +CPPneum +COtArrst +COtMSF +COtAFib ,data = project_dataset)

post_lm_2 = lm(MtOpD ~ VentHrsTot  + PostOpLOS +COpReBld +CNStrokP +CRenFail +CPPneum +COtArrst +COtMSF,data = project_dataset)

#run anova tests to verify insignificant variables
anova(post_lm, post_lm_2)

summary(post_lm_2)

#Check fit
fit_pre_2 = predict(pre_lm_2)
res_pre_2 = project_dataset$MtOpD - fit_pre_2
plot(fit_pre_2,res_pre_2)


fit_post_2 = predict(post_lm_2)
res_post_2 = project_dataset$MtOpD - fit_post_2
plot(fit_post_2,res_post_2)
```

```
# Split the data into pre- and post-2009 periods for analysis
card.pre2009 <- card[card$SurgYr<2009,]
card.post2009 <- card[card$SurgYr>2009,]

# Run a linear regression on the pre-operative factors for pre-2009
card.pre2009.lm = lm(card.pre2009$BdRBCU~card.pre2009$Age
                     +card.pre2009$Sex
                     +card.pre2009$Hct
                     +card.pre2009$WeightKg
                     +card.pre2009$WBC
                     +card.pre2009$Incidence
                     +card.pre2009$Status
                     +card.pre2009$CreatLst
                     +card.pre2009$RFHemoglobin
                     +card.pre2009$BSA)

summary(card.pre2009.lm)

# Run a linear regression on the pre-operative factors for post-2009
card.post2009.lm = lm(card.post2009$BdRBCU~card.post2009$Age
                     +card.post2009$Sex
                     +card.post2009$Hct
                     +card.post2009$WeightKg
                     +card.post2009$WBC
                     +card.post2009$Incidence
                     +card.post2009$Status
                     +card.post2009$CreatLst
                     +card.post2009$RFHemoglobin
                     +card.post2009$BSA)

summary(card.post2009.lm)

# Run a linear regression on the non-binomial post-operative factors for pre-2009
card.pre2009.postop.lm = lm(card.pre2009$IBdRBCU~card.pre2009$VentHrsTot
                     +card.pre2009$PostOpLOS)

#plotting for just length of stay pre-2009
card.pre2009.postop.lm = lm(card.pre2009$PostOpLOS~card.pre2009$IBdRBCU)
plot(card.pre2009$PostOpLOS~card.pre2009$IBdRBCU)
abline(card.pre2009.postop.lm )
summary(card.pre2009.postop.lm)

# Run a linear regression on the non-binomial post-operative factors for post-2009
card.post2009.postop.lm = lm(card.post2009$IBdRBCU~card.post2009$VentHrsTot
                     +card.post2009$PostOpLOS)
```

```
summary(card.post2009.postop.lm)

#Plotting for just length of stay post-2009
card.post2009.postop.lm = lm(card.post2009$PostOpLOS~card.post2009$IBdRBCU)
plot(card.post2009$PostOpLOS~card.post2009$IBdRBCU)
abline(card.post2009.postop.lm )
summary(card.post2009.postop.lm)

# Run a generalized linear model on the binomial post-operative factors for pre-2009
card.pre2009.postop.glm <- glm(card.pre2009$IBdRBCU~card.pre2009$MtOpD
                               +card.pre2009$COtAFib
                               +card.pre2009$COtMSF
                               +card.pre2009$COtArrst
                               +card.pre2009$CPPneum
                               +card.pre2009$CRenFail
                               +card.pre2009$CNParal
                               +card.pre2009$CNStrokP
                               +card.pre2009$COpReBld,
                               family=binomial())
summary(card.pre2009.postop.glm)

# Run a generalized linear model on the binomial post-operative factors for post-2009
card.post2009.postop.glm <- glm(card.post2009$IBdRBCU~card.post2009$MtOpD
                               +card.post2009$COtAFib
                               +card.post2009$COtMSF
                               +card.post2009$COtArrst
                               +card.post2009$CPPneum
                               +card.post2009$CRenFail
                               +card.post2009$CNParal
                               +card.post2009$CNStrokP
                               +card.post2009$COpReBld,
                               family=binomial())
summary(card.post2009.postop.glm)

surgery = read.csv("C:/Users/Deepak/Documents/U Mich Docs/544/Final Project/2016-12-03 - Cardiac Surgery.csv")
y_post = var(surgery$PostOpLOS[surgery$SurgYr>2009])
y_pre = var(surgery$PostOpLOS[surgery$SurgYr<2009])
n_pre = length(surgery$PostOpLOS[surgery$SurgYr<2009])
n_post = length(surgery$PostOpLOS[surgery$SurgYr>2009])
mean_pre = mean(surgery$PostOpLOS[surgery$SurgYr<2009])
mean_post = mean(surgery$PostOpLOS[surgery$SurgYr>2009])

SD = sqrt(((y_post)^2/n_post) + ((y_pre)^2/n_pre))
T_val = (mean_pre-mean_post)/SD
```