# Effect of the use of fresh frozen plasma in cardiac surgery on the postoperative serum creatinine values

## *Kalp cerrahisinde taze donmuş plazma kullanımının ameliyat sonrası kan kreatinin değerleri üzerine etkisi*

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***Background:*** In this study, we evaluated the effect of fresh frozen plasma use on postoperative serum creatinine values.

***Methods:*** A total number of 160 patients (49 females, 111 males; mean age 61.5±10.7 years; range 41 to 82 years) that underwent coronary artery bypass surgery (88 off-pump and 72 on-pump cases) between October 2006 and March 2009 were evaluated. Fresh frozen plasma or whole blood was administered to these patients as necessary. The preoperative and postoperative serum creatinine values were then compared.

***Results:*** The postoperative serum creatinine values were significantly increased in the off-pump patient group that received only whole blood. The postoperative serum creatinine values did not change significantly in the off-pump group that received both whole blood and fresh frozen plasma. In the on-pump group receiving whole blood and fresh frozen plasma, the postoperative creatinine values dropped significantly.

***Conclusion:*** In cardiac surgery, fresh frozen plasma does not impair renal functions when compared with whole blood.

*Key words:* Cardiac surgery; creatinine; fresh frozen plasma.

***Amaç:*** Bu çalışmada taze donmuş plazma kullanımının ameliyat sonrası kan kreatininin değerleri üzerine etkisi incelendi.

***Çalışma planı:*** Ekim 2006 ile Mart 2009 tarihleri arasında koroner arter bypass ameliyatı (88 pompasız ve 72 pompalı) uygulanan toplam 160 hasta (49 kadın, 111 erkek; ort. yaş 61.5±10.7 yıl; dağılım 41-82 yıl) değerlendirildi. Bu hastalara gereksinime göre tam kan ya da taze donmuş plazma verildi. Bunun ardından, ameliyat öncesi ve sonrası serum kreatinin değerleri karşılaştırıldı.

***Bulgular:*** Sadece tam kan verilen pompasız hasta grubunda ameliyat sonrası serum kreatinin değerleri anlamlı olarak yükseldi. Tam kan ve taze donmuş plazma verilen pompasız grupta serum kreatinin değerleri anlamlı bir değişiklik göstermedi. Tam kan ve taze donmuş plazma verilen pompalı grupta ameliyat sonrası kreatinin değerleri anlamlı şekilde azaldı.

***Sonuç:*** Kalp cerrahisinde kullanılan taze donmuş plazma tam kana göre böbrek fonksiyonlarını bozmaz.

*Anahtar sözcükler:* Kalp cerrahisi; kreatinin; taze donmuş plazma.

A problem faced frequently in cardiac surgery is increased postoperative morbidity which develops after the transfusion of blood and blood products.[1,2] Postoperative complications related to the use of blood and its products are increased infection risk, pulmonary dysfunction, gastrointestinal complications, renal failure, and even increased mortality.[2-5] Moreover, extraoperative use of blood and its products may cause hemolytic and non-hemolytic transfusion reactions.[6] Therefore, it is worth investigating which complications occurred after the use of specific blood and blood products.

In this study, pre- and postoperative blood urea nitrogen and creatinine values were compared among patients who received blood or blood plus fresh frozen plasma (FFP) when undergoing off-pump or on-pump coronary artery bypass graft (CABG) surgery.

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## PATIENTS AND METHODS

Between October 2006 and March 2009, a total number of 160 patients (49 females, 111 males; mean age 61.5±10.7 years; range 41 to 82 years) who underwent CABG surgery (88 off-pump, 72 on-pump) in the Department of Cardiovascular Surgery, Atatürk Training and Research Hospital were evaluated retrospectively.

Patients were categorized into off-pump and on-pump groups. Both groups were further divided into three subgroups: blood-only receivers, blood plus FFP receivers and control. Thus, six subgroups were formed, and investigative parameters were compared within these six subgroups.

When considering the postoperative needs, 33 patients received whole blood, 23 patients received whole blood plus FFP, and 32 patients received no blood product in the off-pump group. In the on-pump group, 25 patients received whole blood, 28 patients received whole blood plus FFP and 19 patients received no blood product. Clinical and demographic characteristics of these patients are shown in table 1.

The age, gender, comorbidity, pre- and postoperative creatinine values, blood urea nitrogen (BUN) values, type of operation, postoperative amount of drainage, duration of hospital stay, duration of intensive care unit (ICU) stay, existence of postoperative revision, postoperative intra-aortic balloon pump (IABP) use, amount of transfused blood, and FFP within the postoperative first 24 hours were recorded for each patient. Groups were compared regarding age, pre- and postoperative creatinine values, pre- and postoperative BUN values, pre- and postoperative ejection fraction (EF), along with the amount of transfused blood and FFP. Postoperative values at the 24$^{th}$ hour were taken into account for the postoperative period. Patients with preoperative creatinine values of more than 2 mg/dl were excluded. Other exclusion criteria included mortality during the preoperative period, congestive heart failure in the preoperative period, preoperative ejection fraction (EF) of less than 35%, the use of preoperative IABP counterpulsation, and emergency operations.

Patients whose condition worsened according to postoperative renal function test results were referred to the Nephrology Department.

Patients were transfused with blood whenever their hematocrit values dropped below 24%. Fresh frozen plasma was used for patients thought to be experiencing coagulopathy and excessive drainage (≥250 ml within first hour) in order to correct the problem and replace fluid loss.

### Surgical technique

All patients were operated on under general anesthesia. Median sternotomy was applied, and on-pump or off-pump CABG surgery was performed. The left internal mammary artery and great saphenous vein were used as arterial and venous grafts, respectively. Patients that were revascularized on a beating heart were heparinized (100-200 IU/kg), keeping the activated clotting time (ACT) beyond 250 seconds, while patients that underwent conventional surgery were heparinized (300-400 IU/kg), keeping the ACT value beyond 450 seconds. Some patients needed reoperation for bleeding, and some patients received postoperative IABP therapy on an as needed basis.

### Statistical analysis

The Statistical Package for Social Sciences (SPSS) for Windows version 15.0 (SPSS inc., Chicago, Illinois, USA)

**Table 1. Clinical and demographic data of the patients**

| | Off-pump | | | | | | On-pump | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Blood | | Blood + FFP | | Control | | Blood | | Blood + FFP | | Control | |
| | n | Mean±SD | n | Mean±SD | n | Mean±SD | n | Mean±SD | n | Mean±SD | n | Mean±SD |
| Mean age (year) | | 62.64±10.35 | | 62.65±13.31 | | 61.06±11.21 | | 58.32±9.42 | | 63.04±9.57 | | 60.95±10.15 |
| Gender | | | | | | | | | | | | |
| Male | 17 | | 21 | | 13 | | 21 | | 22 | | 17 | |
| Female | 16 | | 2 | | 19 | | 4 | | 6 | | 2 | |
| Hypertension | 17 | | 10 | | 18 | | 13 | | 10 | | 9 | |
| Hyperlipidemia | 9 | | 6 | | 6 | | 7 | | 5 | | 4 | |
| Smoker | 15 | | 10 | | 12 | | 15 | | 16 | | 12 | |
| COPD | 3 | | 1 | | 1 | | – | | 3 | | 2 | |
| History of MI | 14 | | 9 | | 16 | | 4 | | 4 | | 6 | |
| Cardiac surgery | 2 | | 1 | | – | | 2 | | 3 | | – | |
| CVO | 1 | | 1 | | 2 | | – | | 2 | | 2 | |
| DM | 7 | | 1 | | 3 | | 8 | | 3 | | 4 | |

FFP: Fresh frozen plasma; SD: Standard deviation; COPD: Chronic Obstructive Pulmonary Disease; MI: myocardial infarction; CVO: Cardiovascular occlusion; DM: Diabetes mellitus.

**Table 2. Comparison of pre- and postoperative creatinine values and blood products administered**

| | Preoperative values | | | Postoperative values | | | Blood product given (units) | | |
|---|---|---|---|---|---|---|---|---|---|
| | n | Mean±SD | *p* | n | Mean±SD | *p* | Pre- and postoperative *p* value | Blood | FFP |
| Blood + FFP on-pump | 28 | 1.02±0.22 | 0.637 | 28 | 0.95±0.25 | 0.190 | 0.044 | 4.36 | 3.71 |
| Blood (on-pump) | 25 | 1.06±0.24 | 0.637 | 25 | 1.06±0.24 | 0.190 | 0.938 | 3.48 | – |
| Control (on-pump) | 19 | 1.08±0.19 | 0.637 | 19 | 1.05±0.18 | 0.190 | 0.356 | – | – |
| Blood + FFP (off-pump) | 23 | 1.11±0.20 | 0.009 | 23 | 1.13±0.28 | 0.142 | 0.607 | 2.78 | 2.26 |
| Blood (off-pump) | 33 | 0.96±0.20 | 0.009 | 33 | 1.26±0.34 | 0.142 | 0.000 | 2.27 | – |
| Control (off-pump) | 32 | 0.97±0.17 | 0.009 | 32 | 1.10±0.37 | 0.142 | 0.013 | – | – |

FFP: Fresh frozen plasma; SD: Standard deviation.

was used for analysis. All data was summarized with tables and graphs. Normally distributed quantitative data was compared between groups using one-way ANOVA (post-hoc Bonferroni) statistical analysis. A paired sample t-test was used for pre- and postoperative creatinine values. With a confidence interval of 95%, a p value of less than 0.05 was considered statistically significant.

## RESULTS

Regarding gender distribution, no significant differences among the three subgroups in the on-pump group were noted (p>0.05), but in the off-pump group, blood plus FFP receivers showed a significant difference compared to other subgroups (p<0.05). The mean age of patients was similar in all the subgroups (p>0.05).

In the off-pump group, the preoperative creatinine values showed significant differences among the subgroups (p=0.009). Among the subgroups, blood plus FFP receivers had a higher mean creatinine value than both the blood-only and control groups, which was statistically significant (p<0.05; Table 2).

Although the preoperative creatinine values were high in the blood and FFP receiving subgroups of the off-pump group, the postoperative values showed no statistical significance (p>0.05).

The pre- and postoperative BUN values showed no statistical significance among the three subgroups in the off-pump group.

In the off-pump group, when comparing the pre- and postoperative creatinine values of the blood plus FFP receivers with the control group, no significant difference was noticed. However, the postoperative creatinine values were found to be significantly higher than the preoperative values among the blood receivers and controls (p<0.05; Table 2).

The preoperative and postoperative creatinine values among the three subgroups in the on-pump group showed no significant difference (p>0.05).

In the on-pump group, the postoperative mean creatinine values were significantly lower than the preoperative values among the blood plus FFP receivers (p=0.044; Table 2), but the pre- and postoperative mean creatinine values did not differ between the blood receivers and controls (p>0.05).

In the on-pump group, the pre- and postoperative BUN values of the three subgroups showed no significant differences.

The amounts of blood or blood plus FFP transfused in all groups are shown in table 3. Correlation analyses concerning the postoperative creatinine values and amount of blood or blood plus FFP transfused in all patients showed no significant correlation (p>0.05).

Comparing the preoperative ejection fractions (EF) of the patients, no statistical significance was detected among the groups (p>0.05; Table 3). Moreover, a correlation analysis of the preoperative EF values and postoperative creatinine levels showed no significant correlation (p>0.05). The remaining postoperative data is summarized in table 4.

## DISCUSSION

In recent years, although both pharmacological and technical measures have been undertaken to promote a reduction in the use of blood and blood products, blood transfusions with their associated complications are still a serious problem.[7,8]

Many studies stated that using blood products increases the risk for reoperation due to bleeding, gastrointestinal complications, non-cardiac reoperations, prolonged ventilatory support, acute renal failure, pneumonia, and sepsis.[5,9-12] Consistent with the literature, both the off-pump and on-pump groups along with the in blood and blood plus FFP subgroups had mean extubation times which were significantly longer compared with the control subgroups.

**Table 3. Comparison of preoperative ejection fraction values of patients**

| Group | n | Mean±SD | *p* | *p* |
|---|---|---|---|---|
| Blood + FFP (on-pump) | 28 | 48.93±9.06 | | |
| Blood (on-pump) | 25 | 50.80±8.74 | 0.422 | |
| Control (on-pump) | 19 | 47.37±7.70 | | 0.538 |
| Blood + FFP (off-pump) | 23 | 48.48±9.94 | | |
| Blood (off-pump) | 33 | 46.36±10.33 | 0.732 | |
| Control (off-pump) | 32 | 46.56±11.18 | | |

FFP: Fresh frozen plasma; SD: Standard deviation.

Thakar et al.[13] created a scoring system to predict the risk of acute renal failure in cardiac surgery. According to this system, female gender, a preoperative EF value of less than 35%, congestive heart failure, a history of previous cardiac surgery, preoperative IABP use, diabetes mellitus (DM), emergency surgery, and a preoperative creatinine value of more than 2.1 mg/dl are risk factors for postoperative renal failure. The mean EF of all included patients was greater than 45%, and the mean preoperative creatinine value was less than 1.5 mg/dl. Moreover, patients with preoperative congestive heart failure, preoperative IABP use, and those scheduled to undergo emergent operations were excluded from this study. Twenty-six patients had diabetes as a risk factor for renal failure due to diabetic nephropathy, but the number of diabetic patients was similar in all the groups.

A study by Kuduvalli et al.,[14] investigated the effects of blood use in CABG surgery on postoperative mortality and morbidity rates. The incidence of postoperative renal failure was found to be 2.6% among patients receiving blood whereas it was 0.2% among patients who did not. This difference was statistically significant.

In another study by Whitson et al.,[5] it was found that using blood products increased the incidence of acute renal failure. Accordingly, the ratio of acute renal failure in the group that did not receive any blood products was 1.8% whereas it was calculated at 8% in the group of blood product recipients, which was statistically significant.

Many other studies have shown that the probability of postoperative renal dysfunction increases with the use of blood in cardiac surgery.[1,15-19] In our study, although there wasn't any significant difference between preoperative and postoperative serum creatinine values in the on-pump group blood-only subgroup (consistent with the literature), postoperative mean serum creatinine values were significantly higher than the preoperative values in the off-pump group blood-only subgroup.

In another study conducted by Godet et al.,[19] risk factors for acute renal failure were investigated among patients undergoing thoracic and thoracoabdominal aortic surgery. According to the results of this study, an average of seven units of packed red blood cells was used in the group which was free of acute renal failure whereas 11 units were used in the group which developed it. This difference was statistically significant. A mean of 2.1 L of FFP was used in the group which was free of acute renal failure whereas, in those where it developed, 2.9 L of FFP was used. This difference was statistically significant as well. However, in our study, the postoperative mean serum creatinine values were not higher than the preoperative values of blood plus FFP subgroups of both the on-pump and off-pump groups.

**Table 4. Remaining postoperative values of patients**

| | Off-pump | | | | | | On-pump | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Blood | | Blood + FFP | | Control | | Blood | | Blood + FFP | | Control | |
| | n | Mean±SD | n | Mean±SD | n | Mean±SD | n | Mean±SD | n | Mean±SD | n | Mean±SD |
| MAD (ml) | | 689±177 | | 936±242 | | 393±75 | | 926±179 | | 1360±497 | | 397±106 |
| Reoperation | 1 | | 2 | | – | | 2 | | 3 | | – | |
| IABP use | 1 | | 2 | | – | | 2 | | 3 | | 1 | |
| Postoperative inotropic support | 8 | | 9 | | 8 | | 6 | | 7 | | 5 | |
| MET (h) | | 7.88±2.47 | | 7.96±2.40 | | 5.97±1.82 | | 11.20±2.33 | | 9.93±2.88 | | 5.58±1.54 |
| Mean ICU stay (d) | | 2.70±1.21 | | 2.91±1.04 | | 2.28±0.85 | | 3.08±1.22 | | 3.68±1.87 | | 2.37±0.68 |

FFP: Fresh frozen plasma; SD: Standard deviation; IABP: Intraaortic balloon pump; MAD: Mean amount of drainage; MET: Mean extubation time; ICU: Intensive care unit.

In conclusion, blood and its products are widely used in cardiac surgery. One of the many complications of blood and blood product usage is the development of postoperative renal failure. Based on our study, we think that the use of FFP is safer than blood in terms of renal function impairment.

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## REFERENCES

1. Whitson BA, Huddleston SJ, Savik K, Shumway SJ. Bloodless cardiac surgery is associated with decreased morbidity and mortality. J Card Surg 2007;22:373-8.
2. Murphy GJ, Reeves BC, Rogers CA, Rizvi SI, Culliford L, Angelini GD. Increased mortality, postoperative morbidity, and cost after red blood cell transfusion in patients having cardiac surgery. Circulation 2007;116:2544-52.
3. Rogers MA, Blumberg N, Heal JM, Hicks GL Jr. Increased risk of infection and mortality in women after cardiac surgery related to allogeneic blood transfusion. J Womens Health (Larchmt) 2007;16:1412-20.
4. Scott BH, Seifert FC, Grimson R. Blood transfusion is associated with increased resource utilisation, morbidity and mortality in cardiac surgery. Ann Card Anaesth 2008;11:15-9.
5. Whitson BA, Huddleston SJ, Savik K, Shumway SJ. Risk of adverse outcomes associated with blood transfusion after cardiac surgery depends on the amount of transfusion. J Surg Res 2010;158:20-7.
6. Norda R, Tynell E, Akerblom O. Cumulative risks of early fresh frozen plasma, cryoprecipitate and platelet transfusion in Europe. J Trauma 2006;60:S41-5.
7. Winton TL, Charrette EJ, Salerno TA. The cell saver during cardiac surgery: does it save? Ann Thorac Surg 1982;33:379-81.
8. Aach RD, Kahn RA. Post-transfusion hepatitis: current perspectives. Ann Intern Med 1980;92:539-46.
9. Ferraris VA, Ferraris SP, Saha SP, Hessel EA 2nd, Haan CK, Royston BD, et al. Perioperative blood transfusion and blood conservation in cardiac surgery: the Society of Thoracic Surgeons and The Society of Cardiovascular Anesthesiologists clinical practice guideline. Ann Thorac Surg 2007;83:S27-86.
10. Leal-Noval SR, Rincón-Ferrari MD, García-Curiel A, Herruzo-Avilés A, Camacho-Laraña P, Garnacho-Montero J, et al. Transfusion of blood components and postoperative infection in patients undergoing cardiac surgery. Chest 2001;119:1461-8.
11. Zacharias A, Habib RH. Factors predisposing to median sternotomy complications. Deep vs superficial infection. Chest 1996;110:1173-8.
12. Michalopoulos A, Stavridis G, Geroulanos S. Severe sepsis in cardiac surgical patients. Eur J Surg 1998;164:217-22.
13. Thakar CV, Arrigain S, Worley S, Yared JP, Paganini EP. A clinical score to predict acute renal failure after cardiac surgery. J Am Soc Nephrol 2005;16:162-8.
14. Kuduvalli M, Oo AY, Newall N, Grayson AD, Jackson M, Desmond MJ, et al. Effect of peri-operative red blood cell transfusion on 30-day and 1-year mortality following coronary artery bypass surgery. Eur J Cardiothorac Surg 2005;27:592-8.
15. Cosgrove DM, Loop FD, Lytle BW, Gill CC, Golding LR, Taylor PC, et al. Determinants of blood utilization during myocardial revascularization. Ann Thorac Surg 1985;40:380-4.
16. Magovern JA, Sakert T, Benckart DH, Burkholder JA, Liebler GA, Magovern GJ Sr, et al. A model for predicting transfusion after coronary artery bypass grafting. Ann Thorac Surg 1996;61:27-32.
17. Moskowitz DM, Klein JJ, Shander A, Cousineau KM, Goldweit RS, Bodian C, et al. Predictors of transfusion requirements for cardiac surgical procedures at a blood conservation center. Ann Thorac Surg 2004;77:626-34.
18. Landoni G, Bove T, Crivellari M, Poli D, Fochi O, Marchetti C, et al. Acute renal failure after isolated CABG surgery: six years of experience. Minerva Anestesiol 2007;73:559-65.
19. Godet G, Fléron MH, Vicaut E, Zubicki A, Bertrand M, Riou B, et al. Risk factors for acute postoperative renal failure in thoracic or thoracoabdominal aortic surgery: a prospective study. Anesth Analg 1997;85:1227-32.