Turkish Journal of Thoracic and Cardiovascular Surgery 2020;28(4):586-592
http://dx.doi.org/doi: 10.5606/tgkdc.dergisi.2020.19814

Original Article / *Özgün Makale*

Did blood transfusion increase mortality in patients with diabetes undergoing isolated coronary artery bypass graft surgery? A propensity score-matched analysis of 816 patients

İzole koroner arter baypas greft cerrahisi yapılan diyabet hastalarında kan transfüzyonu mortaliteyi artırdı mı? 816 hastanın eğilim skoru eşleştirme analizi

Muharrem Koçyiğit[1], Halim Ulugöl[1], Seher İrem Kıran[1], Cem Alhan[2], Fevzi Toraman[1]

[1]Department of Anesthesiology and Reanimation, Acıbadem Mehmet Ali Aydınlar University, Istanbul, Turkey
[2]Department of Cardiovascular Surgery, Acıbadem Mehmet Ali Aydınlar University, Istanbul, Turkey

ABSTRACT

Background: The aim of this study was to compare clinical outcomes of blood transfusion in patients with diabetes mellitus undergoing isolated on-pump coronary artery bypass grafting.

Methods: The medical records of a total of 1,912 patients (1,300 males, 612 females; mean age 60.7±10.0) with diabetes who underwent isolated on-pump coronary artery bypass grafting between January 1999 and June 2019 were retrospectively analyzed. The patients were divided into two groups as patients with and without blood transfusions. The mortality rates were compared between the two groups.

Results: The mortality rate was 14 times higher in the patients receiving blood transfusion (odds ratio: 14.80; 95% confidence interval 5.05 to 43.34; p<0.001). However, in the multivariate logistic regression analysis, there were no statistically significant difference in mortality between the patient groups, when diabetes mellitus was a covariate factor (Odds ratio: 8.34; 95% confidence interval 3.94 to 17.66 vs. odds ratio 8.36; 95% confidence interval 3.95 to 17.70).

Conclusion: The propensity score-matched analysis of patients with diabetes showed that clinical outcomes were more severely affected by blood transfusion.

Keywords: Blood transfusion, coronary artery bypass grafting, diabetes mellitus, mortality.

ÖZ

Amaç: Bu çalışmada izole on-pump koroner arter baypas greftleme yapılan diyabet hastalarında kan transfüzyonunun klinik sonuçları karşılaştırıldı.

Çalışma planı: Ocak 1999 - Haziran 2019 tarihleri arasında izole on-pump koroner arter baypas greftleme yapılan toplam 1912 diyabet hastasının (1300 erkek, 612 kadın; ort. yaş 60.7±10.0 yıl) tıbbi kayıtları retrospektif olarak incelendi. Hastalar kan transfüzyonu yapılan ve yapılmayan hastalar olmak üzere iki gruba ayrıldı. Gruplar arasında mortalite oranları karşılaştırıldı.

Bulgular: Kan transfüzyonu yapılan hastalarda ölüm oranı 14 kat daha yüksek idi (olasılık oranı: 14.80; %95 güven aralığı 5.05 ila 43.34; p<0.001). Bununla birlikte, çok değişkenli lojistik regresyon analizinde, diabetes mellitus bir eş değişken faktör olduğunda, hasta grupları arasında mortalite açısından istatistiksel olarak anlamlı bir fark yoktu (olasılık oranı: 8.34; %95 güven aralığı 3.94-17.66'ya kıyasla olasılık oranı: 8.36; %95 güven aralığı 3.95-17.70).

Sonuç: Eğilim skoru eşleştirme analizi, diyabet hastalarında kan transfüzyonunun klinik sonuçları daha kötü bir şekilde etkilediğini gösterdi.

Anahtar sözcükler: Kan transfüzyonu, koroner arter baypas greftleme, diabetes mellitus, mortalite.

Received: April 07, 2020 *Accepted*: August 30, 2020 *Published online*: October 21, 2020

Correspondence: Muharrem Koçyiğit, MD. Acıbadem Mehmet Ali Aydınlar Üniversitesi, Anesteziyoloji ve Reanimasyon Anabilim Dalı, 34684 Ataşehir, İstanbul, Türkiye. Tel: +90 532 - 782 42 48 e-mail: muharremkocyigit@hotmail.com

Cite this article as:
Koçyiğit M, Ulugöl H, Kıran Sİ, Alhan C, Toraman F. Did blood transfusion increase mortality in patients with diabetes undergoing isolated coronary artery bypass graft surgery? A propensity score-matched analysis of 816 patients. Turk Gogus Kalp Dama 2020;28(4):586-592

Diabetes mellitus increased the risk of cardiovascular disease with insulin resistance, inflammation and endothelial dysfunction.[1] The risk of cardiovascular diseases is 1.6 to 2.6 times higher in patients with diabetes, particularly among younger age and in women.[2] After cardiac surgery, the incidences of morbidity and mortality in these patients are higher than those without diabetes.[3,4]

Blood transfusion are associated with postoperative wound infections, pneumonia, renal dysfunction, multiple organ failure, and increased hospital stay.[5] Additionally, perioperative blood transfusions are known to be associated with an increased morbidity and mortality after cardiac surgery.[6,7]

In the present study, we aimed to compare clinical outcomes of blood transfusion in patients with diabetes mellitus who underwent isolated on-pump coronary artery bypass grafting (CABG).

PATIENTS AND METHODS

Between January 1999 and June 2019, a total of 6,148 patients underwent isolated on-pump CABG in Department of Cardiovascular Surgery of Acıbadem Mehmet Ali Aydınlar University. Of these, 1,912 patients (1,300 males, 612 females; mean age 60.7±10.0 year) with diabetes were included in this retrospective study. Patients who underwent off-pump CABG or concomitant surgery were excluded. Patients who had revision for bleeding were also excluded to eliminate the negative outcomes caused by bleeding with hemodynamic instability or blood transfusions. Study flow chart is shown in Figure 1. The medical records were retrieved from the electronic registry and hospital database. A written informed consent was obtained from each patient. The study protocol was approved by the Institutional Review Board of Acıbadem Mehmet Ali Aydınlar University, ATADEK. The study was conducted in accordance with the principles of the Declaration of Helsinki.

The patients were divided into two groups as those with (n=515, 26.94%) and without (n=1,397, 73.06%) blood transfusions. Demographic data, EuroSCORE scores, ejection fraction (EF), hematocrit, creatinine levels, use of medication, and the presence of comorbidities were analyzed. The durations of cross-clamp (CC) and cardiopulmonary bypass (CPB) during surgery, durations of endotracheal intubation and intensive care unit (ICU) stay, and morbidity, mortality rates were evaluated.

All operations were performed by a single surgical team. All patients received a balanced anesthesia using clinical protocols. Standard CPB was established and antegrade cold blood cardioplegia was used for myocardial protection. Blood transfusion was not driven by a numerical trigger value alone, but by a restrictive red blood cell (RBC) transfusion policy based on hematocrit levels and hemodynamic parameters. If the hematocrit value was below 17% during the hypothermic period of CPB and below 20% after CPB, RBCs were transfused. The patients receiving at least one unit of RBC were included in the blood transfusion group. All patients were transferred to the ICU after surgery.

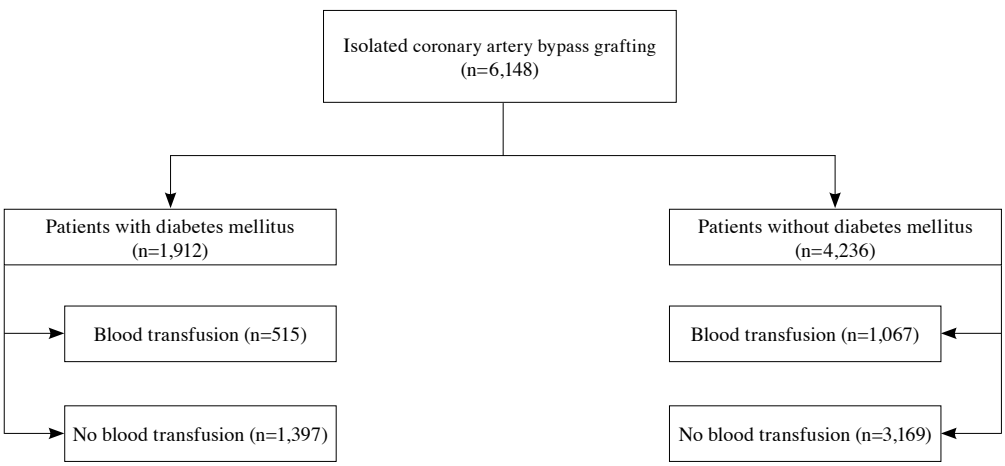

Figure 1. Study flowchart.

Table 1. Baseline demographic and clinical characteristics of patients with and without blood transfusion

	Before propensity matching							After propensity matching						
	No transfusion (n=1,397)			Blood transfusion (n=515)				No transfusion (n=408)			Blood transfusion (n=408)			
	n	%	Mean±SD	n	%	Mean±SD	*p*	n	%	Mean±SD	n	%	Mean±SD	*p*
Age (year)			61.8±8.9			64.3±8.3	<0.001			64.6±8.8			64.1±8.3	0.430
Body mass index (kg/m^2)			29.7±9.8			29.7±24.1	0.980			30.5±15.0			30.0±27.0	0.770
Sex							<0.001							0.720
Female	378			234				177			182			
Male	1019			281				231			226			
EuroSCORE logistics (%)			3.6±5.5			5.4±8.6	<0.001			4.7±6.4			4.4±5.3	0.390
NYHA Class 3 and 4 (%)	192	13.7		111	19.6		0.004	75	18.4		70	17.2		0.710
Previous cardiac surgery (%)	19	1.3		22	4.2		<0.001	12	2.9		10	2.5		0.670
EF <30 (%)	35	2.5		25	4.9		<0.001	17	4.2		15	3.7		0.850
Hypertension (%)	1022	73.2		379	73.6		0.840	317	77.7		299	73.3		0.140
Hypercholesterolemia (%)	871	62.3		334	64.9		0.330	254	62.3		274	67.2		0.160
COPD (%)	95	6.8		60	11.7		0.001	45	11.0		44	10.8		1.000
Smoking (%)														
Smokers	305	21.8		77	15		< 0.001	86	21.1		60	14.7		0.050
Former smokers	583	41.7		189	36.7			140	34.3		154	37.7		
Never smoked	509	36.4		259	48.3			182	44.6		194	47.5		
Medications														
Beta blockers (%)	751	53.8		288	55.9		0.390	225	55.1		235	57.6		0.520
Calcium canal blockers (%)	283	20.3		101	19.6		0.650	95	23.3		91	22.3		0.800
ACE inhibitors (%)	470	33.6		173	33.6		0.980	140	34.3		139	34.1		1.000
Aspirin (%)	848	60.7		292	56.7		0.115	222	54.4		233	57.1		0.480
Clopidogrel (%)	31	2.2		6	1.2		0.130	7	1.7		4	1.0		0.540
Elective surgery (%)	1270	90.9		457	88.7		0.070	372	91.2		371	90.9		1.000
Preoperative hematocrit level (%)			40.3±4.5			38.0±4.7	< 0.001			38.3±4.8			38.3±4.4	0.940
Preoperative creatinine level (mg/dL)			0.9±0.4			1.0±0.5	< 0.001			0.9±0.4			1.0±0.5	0.300
CC time (min)			39.8±16.2			40.2±16.9	0.680			38.9±16.2			40.3±17.7	0.260
CPB time (min)			68.9±24.8			71.4±29.0	0.060			67.0±23.7			70.1±27.2	0.080
Number of distal anastomoses			3.3±1.0			3.4±0.9	0.040			3.3±1.0			3.5±0.9	0.003

SD: Standard deviation; NYHA: New York Heart Association; EF: Ejection fraction; COPD: Chronic obstructive pulmonary disease; ACE: Angiotensin-converting enzyme; CC: Cross-clamp; CPB: Cardiopulmonary bypass.

Table 2. Postoperative data of patients with and without blood transfusion

	Before propensity matching							After propensity matching						
	No transfusion (n=1,397)			Blood transfusion (n=515)				No transfusion (n=408)			Blood transfusion (n=408)			
	n	%	Mean±SD	n	%	Mean±SD	*p*	n	%	Mean±SD	n	%	Mean±SD	*p*
Intubation time (h)			7.0±13.8			11.7±43.0	<0.001			8.2±22.2			9.3±33.5	0.610
Chest tube output (mL)			495.8±213.9			742.5±545.4	<0.001			462.4±201.7			659.8±372.3	<0.001
Blood transfusion unit			0.0±0.0			2.2±2.2	<0.001			0.0±0.0			1.9±1.6	<0.001
ICU duration (h)			21.6±13.1			38.4±58.3	<0.001			22.5±15.1			31.2±54.7	0.002
New onset stroke (%)														
Transient	7	0.5		5	1.0		0.030	2	0.5		3	0.7		0.540
Permanent	0	0.0		2	0.4			0	0.0		1	0.2		
Postoperative AF (%)	199	14.2		115	22.3		<0.001	67	16.4		84	20.6		0.140
New onset dialysis (%)														
Transient	2	0.1		6	1.2		0.001	2	0.5		2	0.5		0.600
Permanent	1	0.1		3	0.6			0	0.0		1	0.2		
Pulmonary complications (%)	5	0.3		5	0.9		0.130	3	0.7		3	0.7		0.220
Sternal dehiscence (%)	16	1.1		5	1.0		1.000	6	1.5		4	1.0		0.750
Overall infections (%)	30	2.1		34	6.6		<0.001	11	2.7		25	6.1		0.020
Vasoactive agent infusion >4 h (%)	143	10.2		103	20.0		<0.001	51	12.5		68	16.7		0.280
Discharge hematocrit level (%)			28.3±4.0			27.0±3.5	<0.001			27.8±3.9			27.0±3.4	<0.001
Discharge creatinine level (mg/dL)			0.9±0.4			1.1±0.8	<0.001			0.9±0.5			1.0±0.6	0.210
Hospital duration (days)			6.4±4.6			7.4±6.8	<0.001			6.7±4.7			7.0±4.8	0.320
ICU readmission (%)	32	2.3		31	6.0		<0.001	11	2.7		23	5.6		0.030
Reintubation (%)	11	0.8		20	3.9		<0.001	3	0.7		12	2.9		0.019
Hospital readmission (%)	45	3.2		26	5.0		0.070	13	3.2		20	4.9		0.210
Mortality (%)	4	0.3		21	4.1		<0.001	2	0.5		8	2.0		0.050

SD: Standard deviation; ICU: Intensive care unit; AF: Atrial fibrillation.

Statistical analysis

Statistical analysis was performed using the SPSS version 10 software (SPSS Inc., Chicago, IL, USA). Data were presented in mean ± standard deviation (SD), median (min-max) or number and percentage. Univariate comparisons were made using the chi-square (χ^2) test or Fisher's exact test for categorical variables, and the t-test was used for continuous variables. Transfused patients were matched with non-transfused patients using the propensity score matching analysis to control for the imbalance between the groups. The propensity score was estimated using a regression model. Variables with a *p* value of <0.1 were entered into the logistic regression analysis. A multinomial logistic regression analysis was used to examine the relationships between diabetes mellitus, blood transfusion, and mortality. A two-sided *p* value of <0.05 was considered statistically significant.

RESULTS

Baseline demographic and clinical characteristics of the patients are presented in Table 1. There was no statistically significant difference between the groups in terms of age, sex, body mass index, and pre- and intraoperative values after the propensity score matching.

Before propensity score matching, the length of ICU stay, infection rates (odds ratio [OR]: 3.22; 95% confidence interval [CI]: 1.95 to 5.32; p<0.001), hospital stay, and mortality (OR: 14.80; 95% CI: 5.05 to 43.34; p<0.001) were significantly higher in the blood transfusion group (Table 2). After propensity score matching, the length of ICU stay was significantly higher in the blood transfusion group than the non-transfusion group; however, there was no significant difference in the duration of hospitalization between the two groups. Additionally, the infection rates were higher in patients who received blood transfusions than those who did not receive blood transfusions (OR: 2.35; 95% CI: 1.14 to 4.85; p=0.017).

Furthermore, the mortality rates were four times higher in the patients who received blood transfusions than those who did not receive blood transfusions (OR: 4.06; 95% CI: 0.85 to 19.23; p=0.05). However, the multivariate logistic regression analysis revealed no statistically difference in mortality between the groups, when diabetes mellitus was a covariate factor (OR: 8.34; 95% CI: 3.94 to 17.66 vs. OR: 8.36; 95% CI: 3.95 to 17.70).

DISCUSSION

The higher incidence of mortality in patients with diabetes after cardiac surgery was reported in previous studies.[8-11] In a meta-analysis, Zhang et al.[11] found that the incidence of morbidity and mortality was higher in patients with diabetes than those without after CABG.

Blood transfusions have been shown to be associated with a high incidence of infection, transfusion-related lung injury, pneumonia, sternal infections, leg wound infections, circulatory overload, low cardiac output syndrome, renal dysfunction, atrial fibrillation, stroke, and short and long-term mortality rates.[12-14] The independent risk factors for blood transfusions are age, female sex, low body surface area, low EF (<35%), emergency operation, anemia, redo cardiac surgery, use of extracorporeal circulation, prolonged bypass time, and re-exploration for any reason.[15,16] Blood transfusions are also associated with worse survival and increased risk factors, leading to prolonged hospital stay after cardiac surgery.[17-19]

Hemorheological alterations of the storage of RBCs may disturb the microcirculation.[20] Additionally, endothelial dysfunction causes microvascular complications and disturbs the microcirculation in patients with diabetes.[21] A randomized-controlled trial showed that correcting CPB-induced dilutional anemia with blood transfusions in patients with diabetes undergoing CABG increased the risk of renal injury due to the microcirculatory derangements caused by the transfusions.[22] Additionally, this patient population is at an increased risk of renal injury compared to those without diabetes due to possible end-organ damages.[9] Although blood transfusions and diabetes mellitus are associated with a high incidence of renal injury, in our study, there were no statistically significant differences in discharge creatinine levels or the number of new-onset dialysis between the patients with diabetes who received blood transfusion and who did not.

In their study, Vranken et al.[23] reported that the rate of infections increased in female patients, smokers, and patients with advanced age, diabetes mellitus, obesity, chronic obstructive pulmonary disease, low EF, prolonged CPB time, and perioperative administration of inotropes after cardiac surgery. They also reported that the number of blood transfusions was associated with infections in patients after cardiac surgery. Blood transfusions are a predominant factor for all types of postoperative infections. Likosky et al.[24] observed that the incidence of pneumonia increased for every unit of

transfused RBCs after cardiac surgery. Additionally, the impaired chemotaxis and phagocytosis of neutrophils increase the risk of infections in patients with diabetes.[11] In our study, there were no significant differences in pulmonary complications, such as pneumonia, between the groups; however, infections were higher in the patients receiving blood transfusion.

A multi-center study in Europe reported that at least one unit of RBCs and a transfusion rate of 40.2% was recorded in patients who underwent CABG surgery.[8] In our study, a blood transfusion rate of 25.7% was recorded in all isolated CABG patients. Additionally, the length of ICU stay, chest-tube drainage, postoperative atrial fibrillation, new-onset dialysis and stroke, hospital readmission, ICU readmission, and mortality rates in the patients who received blood transfusions were higher than those who did not in our study.

In addition, in the current study, the patients were matched for propensity scores using perioperative risk assessments. Based on propensity score-matched analyses, the ICU stay, ICU readmission, reintubation, and mortality rates were statistically higher in the patients with diabetes who received blood transfusions compared to the others.

One of the strengths of the study was that the patient sample was from a single center, and all operations were done by the same surgeons and anesthesiologists using similar practices for blood transfusion. However, the main limitation includes its retrospective design.

In conclusion, propensity score-matched analysis of the patients with diabetes shows worse clinical outcomes due to blood transfusion, although mortality remains comparable between those who receive blood transfusion and those who do not. Nonetheless, further, large-scale, prospective studies are needed to confirm these findings.

Declaration of conflicting interests

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding

The authors received no financial support for the research and/or authorship of this article.

REFERENCES

1. Paneni F, Beckman JA, Creager MA, Cosentino F. Diabetes and vascular disease: pathophysiology, clinical consequences, and medical therapy: part I. Eur Heart J. 2013;34:2436-43.
2. Rao Kondapally Seshasai S, Kaptoge S, Thompson A, Di Angelantonio E, Gao P, Sarwar N, et al. Diabetes mellitus, fasting glucose, and risk of cause-specific death. N Engl J Med 2011;364:829-41.
3. Nagendran J, Bozso SJ, Norris CM, McAlister FA, Appoo JJ, Moon MC, et al. Coronary Artery Bypass Surgery Improves Outcomes in Patients With Diabetes and Left Ventricular Dysfunction. J Am Coll Cardiol 2018;71:819-27.
4. Moazzami K, Dolmatova E, Maher J, Gerula C, Sambol J, Klapholz M, et al. In-Hospital Outcomes and Complications of Coronary Artery Bypass Grafting in the United States Between 2008 and 2012. J Cardiothorac Vasc Anesth 2017;31:19-25
5. Koch CG, Li L, Duncan AI, Mihaljevic T, Cosgrove DM, Loop FD, et al. Morbidity and mortality risk associated with red blood cell and blood-component transfusion in isolated coronary artery bypass grafting. Crit Care Med 2006;34:1608-16.
6. D'Agostino RS, Jacobs JP, Badhwar V, Paone G, Rankin JS, Han JM, et al. The society of thoracic surgeons adult cardiac surgery database: 2017 update on outcomes and quality. Ann Thorac Surg 2017;103:18-24.
7. Dixon B, Santamaria JD, Reid D, Collins M, Rechnitzer T, Newcomb AE, et al. The association of blood transfusion with mortality after cardiac surgery: cause or confounding? (CME). Transfusion 2013;53:19-27.
8. Kinnunen EM, Zanobini M, Onorati F, Brascia D, Mariscalco G, Franzese I, et al. The impact of minor blood transfusion on the outcome after coronary artery bypass grafting. J Crit Care 2017;40:207-12.
9. Gallagher S, Kapur A, Lovell MJ, Jones DA, Kirkwood A, Hassan S, et al. Impact of diabetes mellitus and renal insufficiency on 5-year mortality following coronary artery bypass graft surgery: a cohort study of 4869 UK patients. Eur J Cardiothorac Surg 2014;45:1075-81.
10. Ram E, Kogan A, Levin S, Fisman EZ, Tenenbaum A, Raanani E, et al. Type 2 diabetes mellitus increases long-term mortality risk after isolated surgical aortic valve replacement. Cardiovasc Diabetol 2019;18:31.
11. Zhang X, Wu Z, Peng X, Wu A, Yue Y, Martin J, et al. Prognosis of diabetic patients undergoing coronary artery bypass surgery compared with nondiabetics: a systematic review and meta-analysis. J Cardiothorac Vasc Anesth 2011;25:288-98.
12. Kogan A, Ram E, Levin S, Fisman EZ, Tenenbaum A, Raanani E, et al. Impact of type 2 diabetes mellitus on short- and long-term mortality after coronary artery bypass surgery. Cardiovasc Diabetol 2018;17:151.
13. Bhaskar B, Dulhunty J, Mullany DV, Fraser JF. Impact of blood product transfusion on short and long-term survival after cardiac surgery: more evidence. Ann Thorac Surg 2012;94:460-7.
14. Veenith T, Sharples L, Gerrard C, Valchanov K, Vuylsteke A. Survival and length of stay following blood transfusion in octogenarians following cardiac surgery. Anaesthesia 2010;65:331-6.
15. Vivacqua A, Koch CG, Yousuf AM, Nowicki ER, Houghtaling PL, Blackstone EH, et al. Morbidity of bleeding after cardiac surgery: is it blood transfusion, reoperation for bleeding, or both? Ann Thorac Surg 2011;91:1780-90.

16. van Straten AH, Kats S, Bekker MW, Verstappen F, ter Woorst JF, van Zundert AJ, et al. Risk factors for red blood cell transfusion after coronary artery bypass graft surgery. J Cardiothorac Vasc Anesth 2010;24:413-7.
17. Gallo M, Trivedi JR, Monreal G, Ganzel BL, Slaughter MS. Risk factors and outcomes in redo coronary artery bypass grafting. Heart Lung Circ 2020;29:384-9.
18. Crawford TC, Magruder JT, Fraser C, Suarez-Pierre A, Alejo D, Bobbitt J, et al. Less is more: Results of a statewide analysis of the impact of blood transfusion on coronary artery bypass grafting outcomes. Ann Thorac Surg 2018;105:129-36.
19. Galas FR, Almeida JP, Fukushima JT, Osawa EA, Nakamura RE, Silva CM, de Almeida EP, Auler JO, Vincent JL, Hajjar LA. Blood transfusion in cardiac surgery is a risk factor for increased hospital length of stay in adult patients. J Cardiothorac Surg 2013;8:54.
20. Almac E, Ince C. The impact of storage on red cell function in blood transfusion. Best Pract Res Clin Anaesthesiol 2007;21:195-208.
21. Henning RJ. Type-2 diabetes mellitus and cardiovascular disease. Future Cardiol 2018;14:491-509.
22. Aykut G, Kilercik M, Arıtürk C, Ulugöl H, Aksu U, Kudsioğlu T, et al. Correction of dilutional anemia induces renal dysfunction in diabetic patients undergoing coronary artery bypass grafting: a consequence of microcirculatory alterations? J Nephrol 2018;31:417-22.
23. Vranken NP, Weerwind PW, Barenbrug PJ, Teerenstra S, Ganushchak YM, Maessen JG. The role of patient's profile and allogeneic blood transfusion in development of post-cardiac surgery infections: a retrospective study. Interact Cardiovasc Thorac Surg 2014;19:232-8.
24. Likosky DS, Paone G, Zhang M, Rogers MA, Harrington SD, Theurer PF, et al. Red blood cell transfusions impact pneumonia rates after coronary artery bypass grafting. Ann Thorac Surg 2015;100:794-800.