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CORONARY ARTERY BYPASS GRAFTING SURGERY FOR PATIENTS WITH SYSTEMIC AUTOIMMUNE DISEASES: INSTITUTIONAL EXPERIENCE

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Abstract

Aim: Systemic autoimmune diseases are risk factors for cardiovascular diseases and have also been identified as a factor that worsens perioperative outcomes in various surgical specialities. This study investigated the effects of systemic autoimmune diseases on coronary surgery outcomes.

Methods: One hundred fifty-one patients were included in this study. hundred-forty-four patients without autoimmune disease were in the first group and seven patients with systemic autoimmune disease who underwent isolated coronary surgery were in the second group. Hospital Electronic recording systems were used for data collection. The follow-up period is 12 months. A statistically significant P value was taken as 0.05.

Results: The two groups were comparable preoperatively, only the prevalence of hypertension and diabetes was significantly higher in the second group. There was no significant difference between the two groups in terms of intraoperative variables. Perioperative complications (excluding stroke), 30-day mortality and post-operative cardiopulmonary resuscitation rate were significantly higher in the second group, however there was no difference between the two groups in terms of 12-month survival.

Conclusions: Despite systemic autoimmune diseases being found a factor that increases complications in terms of coronary surgery, coronary surgery is promising with its success in 12-month survival and repeated revascularization rate in these patients.

Keywords: *Autoimmune disease, myocardial revascularization, coronary artery bypass grafting, ischemic heart disease.*

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Introduction

Autoimmune diseases promote endothelial dysfunction and contribute to plaque forming on endothelial surfaces via chronic inflammation[1]. In addition, current medical therapy of autoimmune diseases might be involving coronary artery disease occurring, because steroid based medications are frequently used for these patients[2]. Autoimmune diseases and coronary artery disease relationship is shown in various studies in the literature[3-5]. Perk et al. concluded that autoimmunity increases the two-fold risk of cardiovascular events (CVEs)[3]. Furthermore, Lindhardsen et al. found that rheumatoid arthritis has the same risk of myocardial infarction as diabetes mellitus[4]. Thence coronary artery disease management is important for patients with autoimmune diseases.

At present, there are no specialized guidelines for managing coronary artery disease in patients with autoimmune diseases. Moreover, unfortunately, there is a huge knowledge gap in the literature in terms of revascularization for these patients, especially surgical revascularization. On the interventional coronary revascularization side, Autoimmune diseases have been identified as a risk factor for major cardiac events, repeated revascularization due to restenosis, and mortality[5-7]. Ma et al.[6] conducted a meta-analysis study involving 11 studies and 824,745 participants, which found that autoimmune diseases are a significant risk factor for major cardiac adverse events, repeat revascularization, myocardial infarction, restenosis, and death in both the short and long term[6]. In Pepe et al.'s comprehensive review, autoimmune diseases were identified as a strong factor associated with in-stent restenosis and long term mortality[7]. However, on the other side of revascularization, coronary artery bypass surgery in patients with autoimmune disease has a paradoxically improved outcomes and satisfactory results. Aguayo et al. conducted a study with the US national database and they found paradoxically improved CABG perioperative outcomes in patients with autoimmune diseases[8]. Sponga et al. found that despite a higher incidence of postoperative complications cardiac surgery in patients with autoimmune diseases can still yield satisfactory short- and long-term outcomes[9]. Nevertheless, current literature needs to studies for filling knowledge gap on coronary surgery efficiency in patients with autoimmune diseases[8,9].

This study is a single-center study aiming to contribute to the literature by retrospectively investigating the effects and outcomes of coronary artery surgery in patients with autoimmune diseases.

Materials and Methods

Study Design

The study enrolled 151 patients with ischemic heart disease who underwent coronary bypass grafting surgery. The primary objective was to investigate the impact of autoimmune diseases on perioperative outcomes, while the secondary goal was to assess the efficacy of surgical revascularization in improving survival outcomes in these patients.

Ethical Approval

We submitted an application to the clinical research ethics committee of the hospital for this retrospective study. After a thorough review of the study, the committee granted ethical approval, which was assigned the number " ESH/GOEK 2023/2 ".

Patients

The study population consisted of 151 patients with multivessel ischemic heart disease who underwent isolated coronary bypass surgery for their condition between 2020 and 2022. In this study, seven patients were in the patients with systemic autoimmunity group and one hundred thirty-seven patients were in the control group.

Data Collecting

Following approval from the ethics committee, patient data was obtained from the national electronic registry system. The preoperative data included the patient's age, gender, body mass index, hypertension, carotid artery disease, history of atrial fibrillation, left ventricular ejection fraction, diabetes mellitus, chronic obstructive pulmonary disease, renal conditions based on glomerular filtration rate (GFR), and urgency of case. There also patients sample variables such as haemoglobin, GFR, c reactive protein (CRP), albumin, haematocrit was taken as preoperative variables. Postoperative outcomes were also recorded, including intraoperative death, 1-year revascularization requirement, acute kidney injury, cardiopulmonary resuscitation needing, postoperative complications, stroke, 30-day mortality, postoperative haematocrit, intubation time, intensive care unit (ICU) duration, length of stay, and 12-month overall survival. We also reviewed intraoperative notes for each patient to obtain intraoperative variables such as number of distal anastomoses, cardiopulmonary bypass (CPB) time, aortic cross-clamp (ACX) time and low cardiac output (LCO) syndrome.

Statistical Analysis

The chi-square test was used for categorical parameters between the control group and the osteoporosis group, and the Student-t test was used for continuous ones. Log-rank Kaplan-Meier test was used for survival. $P<0.05$ was taken for statistical significance.

Results

Preoperative Characteristics

The average age of the study cohort was 61.4, and the female patient rate was 26.5%(n=40). In this study, 4.6% of patients who received coronary artery bypass surgery had a systemic autoimmune disease. The mean age was 61.3 in the control group (CG) and 63.1 in the patients with the autoimmune disease group (AuG) (P=0.115). The demographic data, including body mass index (29.0 vs. 27.3, P=0.935), and gender distribution (26.4% female rate in the CG vs. 28.6 female rates in the AuG, P=0.868), were not significantly different among the groups. Except for the prevalence of hypertension (47.9% in the CG vs. 100.0% in the AuG, P=0.007) the groups were similar in terms of cardiovascular comorbidities, such as carotid artery disease (15.3% in the CG vs. 28.6% in the AuG, P=0.348), previous atrial fibrillation (13.2% in the CG vs. 0.0% in the AuG, P=0.304), and left ventricular ejection fraction (56.4% in the CG vs. 53.3% in the AuG, P=0.993). Excluding diabetes mellitus (43.8% in the CG vs. 85.7% in the AuG, P=0.030), which was higher in the autoimmune group. The prevalence of non-infectious chronic diseases such as chronic obstructive pulmonary disease (24.3% in the CG vs. 14.3% in the AuG, P=0.543), and decreased renal functions (64.6% in the CG vs. 28.6% in the AuG, P=0.054) was similar among the groups. blood values, including haemoglobin, CRP, albumin, and haematocrit, did not differ significantly among the groups($P>0.05$) (see table 1). Surprisingly, the mean glomerular filtration rate (83.6 ml/min in the CG vs. 87.0 ml/min in the AuG, P=0.008) was found high in the patients with the autoimmune diseases group. (see table 1).

Intraoperative Results

The mean number of distal anastomoses performed is 2.9. The average duration of ACX time and CPB time in the CG and AUG were 51.7 and 86.5 minutes, respectively. There were no significant differences observed between the groups in terms of the number of distal anastomoses (2.9 in the CG vs. 2.9 in the AuG P=0.479), CPB time (85.6 min in the CG vs. 104.9 in the AuG min, P=0.684), ACX time (51.4 min in the CG vs. 58.0 min in the AuG, P=0.867), and incidence of low cardiac output syndrome (LCOS) (3.5% in the CG vs. 14.3 in the AuG, P=0.153), as shown in table 2.

Table 1. Preoperative medical background

Variables	Control group	Patients with systemic autoimmune diseases	p
Age (mean)	61.3	63.1	0.115
Gender (female %)	26.4	28.6	0.868
Body Mass Index (mean)	29.0	27.3	0.935
Hypertension(yes,%)	47.9	100.0	0.007
Carotid Artery Disease(yes,%)	15.3	28.6	0.348
Previous Atrial Fibrillation (yes,%)	13.2	0.0	0.304
Left Ventricular Ejection Fraction (mean %)	56.4	53.3	0.993
Diabetes Mellitus(yes,%)	43.8	85.7	0.030
Chronic Obstructive Pulmonary Disease(yes,%)	24.3	14.3	0.543
Decreased Renal Functions GFR<90 (yes,%)	64.6	28.6	0.054
Urgent Case (yes,%)	9.0	28.6	0.091
Preoperative HB	13.7	11.7	0.177
Preoperative GFR	83.6	87.0	0.008
Preoperative CRP	6.0	4.3	0.262
Preoperative albumin	41.9	39.3	0.689
Preoperative hematocrit	40.7	37.7	0.062

CRP: C reactive protein, GFR: Glomerular filtration rate, HB: Hemoglobin

Table 2. Intraoperative results

Variables	Control group	Patients with systemic autoimmune diseases	P
Number of distal anastomoses (n)	2.9	2.9	0.479
Cardiopulmonary Bypass Time (minute)	85.6	104.9	0.684
Aortic Cross-Clamp Time (minute)	51.4	58.0	0.867
Low Cardiac Output Syndrome (Yes, %)	3.5	14.3	0.153

Postoperative Outcome: Primary endpoint

During the study, no deaths occurred during surgery, however within 30 days after the surgery, 3 patients (2%) passed away. The groups showed no significant difference regarding acute kidney injury (6.2% in the CG vs. 0.0% in the AuG,P=0.495), stroke(5.6% in the CG vs. 0.0% in the AuG,P=0.520), length of hospital stay(9.7 days in the CG vs. 10.5 in the AuG days=0.474), and duration of intensive care unit(5.1 days in the CG vs. 3.6 days in the AuG, P=0.581). However, the group of patients with autoimmune disorders exhibited worse results in terms of needing cardiopulmonary resuscitation (2.1% in the CG vs. 14.3% in the AuG, P=0.050, OR=7.8), postoperative complications (4.9 % vs. 28.6%, P=0.010, OR=7.8), intubation time (8.9 hours in the CG vs. 15.9 in the AuG hours, P=0.013), postoperative haematocrit levels (29.3 in the CG vs. 26.5 in the AuG, P=0.043), and in-hospital mortality (1.4% in the CG vs. 14.2% in the AuG, P=0.017, OR=11.8). (see table 3)

Coronary surgery success: secondary endpoint

We used the 12-month rate of repeated revascularization and 12-month survival as indicators of the success of coronary surgery based on the parameters in our existing database. There was no significant difference between the groups in terms of 12-month repeated revascularization rate (0.7% in the CG vs. 0.0% in the AuG, P=0.824) and 12-month survival rate (85.7% in the AuG vs. 95.8% in the CG, P=0.151, OR=1.5). (see table 3 and figure 1)

Table 3. Postoperative outcomes

Variables	Control group	Patients with systemic autoimmune diseases	p	Hazard Ratio
Intraoperative Death	0.0	0.0	-	-
1-year revascularization requirement	0.7	0.0	0.824	-
Acute kidney injury	6.2	0.0	0.495	-
Cardiopulmonary resuscitation(in-hospital)	2.1	14.3	0.050	7.8
Postoperative complications including bleeding	4.9	28.6	0.010	7.8
Stroke	5.6	0.0	0.520	-
Thirty-day mortality	1.4	14.2	0.017	11.8
Postoperative Hct	29.3	26.5	0.043	
Intubation Time(hours)	8.9	15.9	0.013	
ICU duration (Days)	5.1	3.6	0.581	
Length of Stay inc. ICU duration (Days)	9.7	10.5	0.474	
12-month survival	85.7	95.8	0.151	1.5

Hct: Hematocrit, ICU: intensive care unit

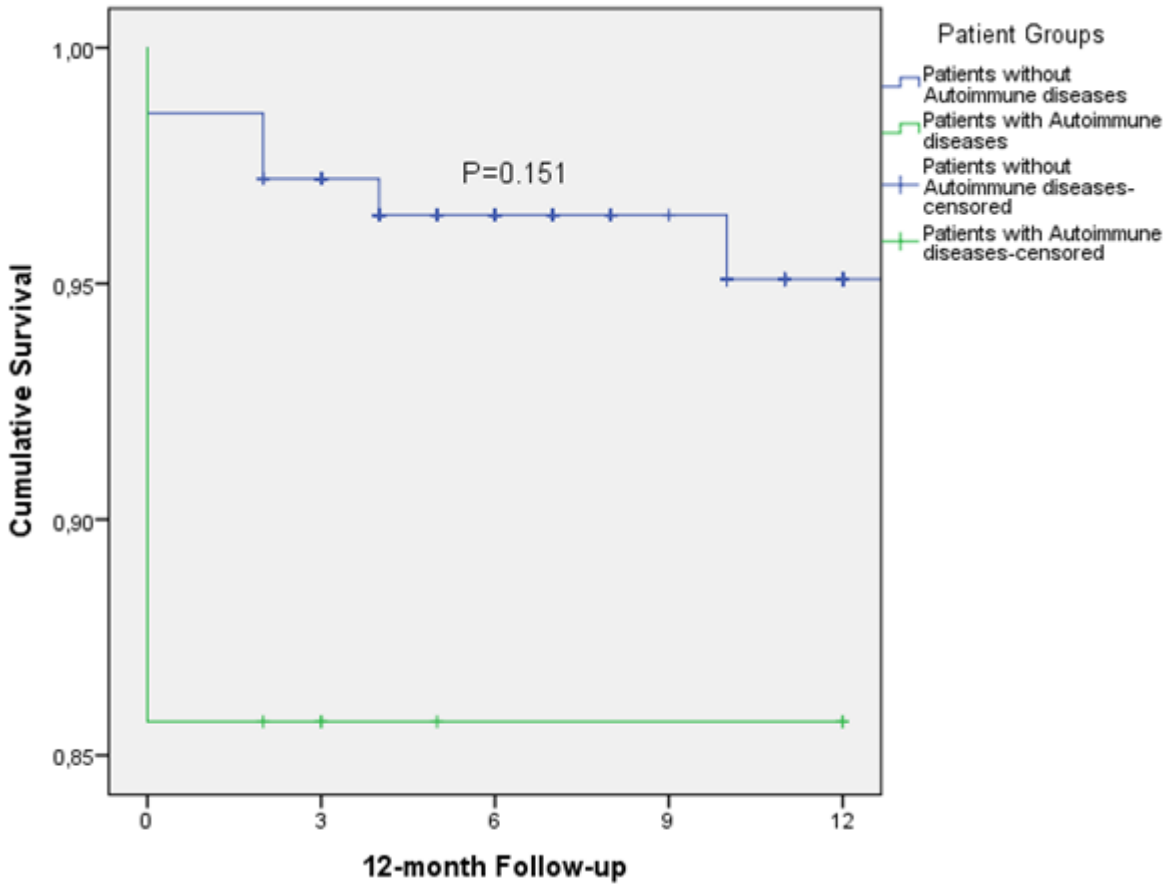

Figure 1. 12-month follow-up survival analysis

Discussion

Autoimmune diseases are known to be associated with cardiovascular risk. Traditional risk factors such as diabetes and hypertension are shown to be of higher prevalence in patients with autoimmune conditions[10], which is also evidenced by our study (Table 1). Chronic inflammation and immune dysregulation lead to accelerated atherosclerosis[11], and long-term use of steroid-based immunosuppressants has cardiovascular effects12.

Among the 151 patients with coronary artery disease that underwent isolated CABG in our cohort, 7 were identified to have an autoimmune disease, representing a prevalence of 4.6%. Given the association with cardiovascular morbidity, it is expected for these patients to be overrepresented in revascularization procedures, although it is interesting that in the two nationwide studies investigating CABG outcomes[8,13] the prevalence of autoimmune conditions was relatively low (0.57% and 1.8%, respectively) despite the large sample size. Furthermore, Wassif et al.[14] demonstrate that in acute coronary syndrome (ACS), patients with rheumatic conditions were less likely to undergo coronary angiography and revascularization (both PCI and CABG). These findings suggest a predominantly less invasive management of ACS in these patients, which is worthy of further investigation given the non-inferior and, in some cases, even surprisingly better CABG outcomes in the autoimmune group shown by multiple studies.

Indeed, Varghese et al.[15] demonstrate that in patients undergoing CABG, those with RA had 49% less in-hospital mortality, a shorter

length of stay by 1.36 days, and reduced total hospital charges, compared to the control group. This is supported by the nationwide study of the Society of Thoracic Surgeons[8] that included 2,101,591 patients, which not only showed that the connective tissue diseases group was not associated with increased mortality, however, had also paradoxically improved cardiovascular, neurologic, and infectious complications, except the antiphospholipid syndrome group. The earlier study of Birdas and associates[16] also shows no differences between the autoimmune and the control group in terms of 30-day mortality and overall postoperative complications.

In our study, in-patient outcomes were inferior in the autoimmune disease group, with a significantly higher prevalence of 30-day mortality, postoperative complications including bleeding and need for cardiopulmonary resuscitation, as well as lower post-operative HCT, and longer intubation times (table 3). Nevertheless, there were no significant differences in terms of the need for repeat revascularization and most importantly, 12-month survival. The apparent discrepancy between the short and mid-term mortality results can be explained by the fact that, out of 7 patients in our cohort with autoimmune diseases, only 1 died in the hospital. Interestingly, this patient was not receiving any immunosuppressant/modulatory drugs pre- or postoperatively (Table 4).

The risk of a systemic inflammatory response syndrome (SIRS) after cardiopulmonary bypass is well-established, and the possible clinical benefits of prophylactic administration of corticosteroids for patients undergoing on-pump cardiac surgery are discussed in the literature[17]. Therefore, it is possible to speculate that the lack of post-operative steroid therapy in patients already with an autoimmune/inflammatory condition might have had an impact on the 30-day mortality. Moreover, the possible positive effect on mortality of receiving corticosteroids in patients with rheumatoid arthritis (RA) has already been suggested by Varghese et al., and Birdas et al. find that immunomodulating medications had a significant protective effect against re-interventions. Although evidence is needed to support this hypothesis. The increased in-hospital complications we found point to the importance of a multidisciplinary approach in the post-operative management of these patients, with a particular vigilance in terms of systemic inflammation related to CPB and its sequelae [17,18]. It is important to note that wide literature evaluating percutaneous coronary interventions (PCI) outcomes in autoimmune patients is also available; the meta-analysis6 of numerous controlled studies shows a higher likelihood of restenosis, repeat ischemia, and other adverse events in the autoimmune group.

Table 4. Autoimmune patients

Patient No:	Diagnosis	NSAİİ	Steroids	Thirty-day mortality
1	Rheumatoid Arthritis	+	+	No
2	Rheumatoid Arthritis	+	-	No
3	Rheumatoid Arthritis	-	-	*Yes*
4	Vasculitis	-	+	No
5	Psoriasis	-	-	No
6	Psoriasis	-	-	No
7	Autoimmune inflammatory disease	-	-	No

(Patient-1 has been on nsaii and steroids after postoperative day-1. However patient 2 and patient 3 did not take any medications for autoimmunity)

Therefore, given the relatively younger age and underlying endothelial dysfunction of this population possibly predisposing to restenosis of stents, it is suggested that these patients should receive CABG if indicated, as good outcomes are demonstrated not only by our study in terms of 12-month mortality and repeat revascularization, however also widely by the literature.

Conclusion

In conclusion, we found that although the autoimmune disease is associated with elevated perioperative complications in coronary artery bypass surgery, coronary surgery is promising and satisfactory in terms of therapeutic outcomes of coronary disease, such as 12-month survival and 12-month repeat revascularization. We suggest that administering anti-inflammatory drugs before and after surgery for autoimmune patients may provide benefits and emphasize the importance of coordinated planning and management of these patients with specialists from cardiology, heart surgery, internal medicine, intensive care, and anesthesiology departments.

Limitations

Although the small number of patients in our autoimmune patient group is a significant limitation of our study, we think that it has made an important contribution to the literature with results. We also state that the results of our study need to be confirmed by prospective and multicentre studies with larger number of patients.

Conflict of interest
The author declare that they have no conflict of interest.

Ethical approval
Ethical approval was obtained from Eskisehir City Hospital Ethics Committee with the protocol number ESH/GOEK 2023/2.

References

1. Sherer Y, Shoenfeld Y. Mechanisms of disease: atherosclerosis in autoimmune diseases. Nature clinical practice Rheumatology. 2006;2(2):99-106. https://doi.org/10.1038/ncprheum0092
2. Bulkeley BH, Roberts WC. The heart in systemic lupus erythematosus and the changes induced in it by corticosteroid therapy. The Am J Med. 1975; 58: 243-64. https://doi.org/10.1016/0002-9343(75)90575-6
3. Perk J, De Backer G, Gohlke H et al. European guidelines on cardiovascular disease prevention in clinical practice. Eur Heart J. 2012;33:1635-701. https://doi.org/10.1093/eurheartj/ehs092
4. Lindhardsen J, Ahlehoff O, Gislason G, et al. The risk of myocardial infarction in rheumatoid arthritis and diabetes mellitus: a Danish nationwide cohort study. Annals of the rheumatic diseases. 2011;70(6):929-34. https://doi.org/10.1136/ard.2010.143396
5. Frostegard J. Atherosclerosis in patients with autoimmune disorders. Arteriosclerosis, thrombosis, and vascular biology. 2005;25(9):1776-85. https://doi.org/10.1161/01.ATV.0000174800.78362.ec
6. Ma G, Zhao H, Fei Y, et al. Autoimmune diseases may increase adverse cardiovascular events after percutaneous coronary intervention: a systematic review and meta-analysis. Heart, Lung and Circulation. 2019;28(10):1510-24. https://doi.org/10.1016/j.hlc.2018.07.012
7. Pepe M, Napoli G, Carulli E, et al. Diseases in patients undergoing percutaneous coronary intervention: A risk factor for in-stent restenosis? Atherosclerosis. 2021;333:24-31. https://doi.org/10.1016/j.atherosclerosis.2021.08.007
8. Aguayo E, Dobaria V, Sareh S, et al. National Analysis of Coronary Artery Bypass Grafting in Autoimmune Connective Tissue Disease. Ann Thorac Surg. 2020;110(6):2006-12. https://doi.org/10.1016/j.athoracsur.2020.03.120
9. Sponga S, Ferrara V, Dagenais F, et al. Autoimmune Connective Tissue Diseases and Cardiac Surgery. Circulation. 2021; 144(Suppl_1):A13880-A13880. https://doi.org/10.1161/circ.144.suppl_1.13880
10. Baena-Díez JM, Garcia-Gil M, Comas-Cufi M, et al. Association between chronic immune-mediated inflammatory diseases and cardiovascular risk. Heart. 2018;104.2:119-26. https://doi.org/10.1136/heartjnl-2017-311279
11. Shoenfeld Y, Gerli R, Doria A, et al. Accelerated atherosclerosis in autoimmune rheumatic diseases. Circulation. 2005;112(21),3337-47. https://doi.org/10.1161/Circulationaha.104.507996

12. Elezaby A, Dexheimer R, Sallam K. Cardiovascular effects of immunosuppression agents. Frontiers in Cardiovascular Medicine. 2022;9: 981838 https://doi.org/10.3389/fcvm.2022.981838
13. Lai CH, Lai WW, Chiou MJ, et al. Outcomes of coronary artery bypass grafting in patients with inflammatory rheumatic diseases: an 11-year nationwide cohort study. The Journal of Thoracic and Cardiovascular Surgery. 2015;149(3):859-66. https://doi.org/10.1016/j.jtcvs.2014.11.038
14. Wassif H, Saad M, Desai R, et al. Outcomes Following Acute Coronary Syndrome in Patients with and without Rheumatic Immune-Mediated Inflammatory Diseases. Journal of the American Heart Association. 2022;11(18):e026411. https://doi.org/10.1161/JAHA.122.026411
15. Varghese JJ, Koneru S, Scaife SL, et al. Mortality after coronary artery revascularization of patients with rheumatoid arthritis. The Journal of thoracic and cardiovascular surgery. 2010;140(1):91-6. https://doi.org/10.1016/j.jtcvs.2009.09.036
16. Birdas TJ, Landis JT, Haybron D, et al. Outcomes of coronary artery bypass grafting in patients with connective tissue diseases. The Annals of thoracic surgery. 2005;79(5):1610-4. https://doi.org/10.1016/j.athoracsur.2004.10.052
17. Chai T, Zhuang X, Tian M, et al. Meta-Analysis: Shouldn't Prophylactic Corticosteroids be Administered During Cardiac Surgery with Cardiopulmonary Bypass? Frontiers in Surgery. 2022;9:832205. https://doi.org/10.3389/fsurg.2022.832205
18. Kaya İ. New Heart Centre: Eskisehir City Hospital-First Results. Koşuyolu Heart Journal. 2019; 22(3): 193-7. https://doi.org/10.5578/khj.68859