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Comparison of Minimal Extracorporeal Circulation and Conventional Circulatory Systems in Patients with Cardiac Surgery

Kalp Cerrahisi Olan Hastalarda Minimal Ekstrakorporeal Dolaşım ve Konvansiyonel Dolaşım Sistemlerinin Karşılaştırılması

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Öz

Giriş ve Amaç: Kalp cerrahisinde kardiyopulmoner bypass sırasında oluşan sistemik inflamatuar yanıt sendromu ve hemodilüsyon; morbitide ve mortalite üzerinde önemli birer etkendir. Bu sorunu azaltmaya yönelik ekstrakorporeal dolaşım sistemleri modifiye edilmiş ve minimal ekstrakorporeal dolaşım sistemi (MECC) olarak adlandırılmıştır. Çalışmamızda izole koroner arter bypass greft (KABG) cerrahisi geçiren hastalarda; MECC ile konvansiyonel ekstrakorporeal dolaşım sistemi kullanımını karşılaştırarak sonuçlarını paylaşmayı amaçladık.

Gereç ve Yöntemler: Çalışma kliniğimizde 1 Eylül 2013 ile 31 Aralık 2018 tarihleri arasında izole KABG cerrahisi yapılan hastalar üzerinde retrospektif olarak yapıldı. Hastalar; MECC ekstrakorporeal dolaşım sistemi kullanılanlar (Grup 1) ve konvansiyonel ekstrakorporeal dolaşım sistemi kullanılanlar (Grup 2) olarak iki gruba ayrıldı.

Bulgular: Çalışma MECC kullanılan 71 hasta (Grup 1), konvansiyonel ekstrakorporeal dolaşım sistemi kullanılan 69 hasta (Grup 2) olmak üzere toplam 140 hasta üzerinde yapıldı. MECC kullanılan grubun daha ileri yaşlı, kronik obstruktif akciğer hastalığının, ASA ve New York Kalp Derneği fonksiyonel sınıflama değerinin daha yüksek olduğu saptandı, $p<0.05$. Konvansiyonel ekstrakorporeal dolaşım sistemi kullanılan hastalarda aktive pıhtılaşma zamanı, priming solüsyonu, eritrosit transfüzyonu ve taze donmuş plazma transfüzyonu değerlerinin daha yüksektir, $p < 0.05$. Postoperatif veriler için yapılan karşılaştırmada grup 1'in hemotokrit değerinin yüksek, drenajın daha az ve kreatinin değerinin düşük ve entübasyon ile yoğun bakımda yatış süresinin daha kısa olduğu ve bu sonuçların istatiksel olarak anlamlı olduğu saptandı $p<0.05$.

Sonuç: MECC sisteminin konvansiyonel sistem gibi güvenli ve kullanışlı bir ekstrakorporeal dolaşım sistemi olduğunu belirtebiliriz. Bu konuda daha fazla hasta sayısı ve prospektif çalışmalara da ihtiyaç vardır.

Anahtar kelimeler: Kalp cerrahisi, kardiyopulmoner bypass, Minimal Ekstrakorporeal Dolaşım Sistemi.

Abstract

Objective: Systemic inflammatory response syndrome and hemodilution during cardiopulmonary bypass are important factors in morbidity and mortality. Extracorporeal circulatory systems were modified to reduce this problem and the minimal extracorporeal circulatory system (MECC) was developed. Our study aimed to compare the MECC and conventional extracorporeal circulatory systems in patients who underwent isolated coronary artery bypass graft (CABG) surgery.

Materials and Methods: The study was conducted retrospectively on patients who underwent isolated CABG surgery in our clinic between September 1, 2013-December 31, 2018. The patients were divided into those in whom the MECC system (Group 1) and the conventional extracorporeal circulatory system (Group 2) were used.

Results: The study was performed on a total of 140 CABG patients, 71 of which were performed with MECC (Group 1) and 69, with the conventional extracorporeal circulatory system (Group 2). Group 1 had higher mean age, ASA, and New York Heart Association values, and an increased rate of chronic obstructive pulmonary disease ($p<0.05$ for

all). The activated clotting time, priming solution use, as well as the amounts of erythrocyte and fresh frozen plasma transfusion were higher in patients in whom the conventional extracorporeal circulatory system was used ($p<0.05$ for all). Postoperatively, the hematocrit value of Group 1 was higher, they had less drainage, and the creatinine value, and the length of intubated stay in the intensive care unit were shorter compared to Group 2 ($p<0.05$ for all).
Conclusion: Cardiac surgery, Cardiopulmonary bypass, minimal extracorporeal circulatory system

Keywords: Cardiac surgery, Cardiopulmonary bypass, minimal extracorporeal circulatory system.

1. Introduction

Cardiopulmonary bypass (CPB) is defined as the extracorporeal maintenance of the heart's pumping function and the respiratory functions of the lungs for a certain time during cardiac surgery. In this process, the blood of the patient is collected in the reservoir of the heart-lung machine. After being oxygenated and filtered, this blood is returned to the patient. In addition, a bloodless surgical field is provided, which allows for surgical procedures [1]. Inflammatory mediators emerging in the body as a result of the contact of blood with non-epithelialized surfaces in CPB cause systemic inflammatory response syndrome (SIRS) [2, 3]. SIRS is one of the mechanisms that reveal the undesirable effects of CBP in open heart surgery patients. There have been developments in the historical process to reduce this syndrome, an important one regarding various filtration methods [2-5]. Among them are the use of anti-inflammatory pharmacological agents in the fight against SIRS and increasing the biological compatibility of the extracorporeal systems. In recent years, CPB systems have been modified as a result of studies to reduce the inflammatory response. The CPB circuit called MECC is an example of this modified system [6, 7]. It reduces the inflammatory response by minimizing the contact of blood with foreign surfaces and air and increasing the biocompatibility of the components that make up the circuit [6-8]. This system consists of a centrifugal pump, a diffuse membrane oxygenator, and a heparin-lined vacuum line, onto which heparin can be added as needed [6]. The venous reservoir found in the conventional CPB system is not found in this circuit [6,8]. This allows a reduction in the prime solution used, hence reducing hemodilution. Hemodilution is also one of the important problems in cardiac surgery and has negative effects on postoperative outcomes [5, 9].
In our study, we aimed to compare the results of our patients who underwent isolated coronary artery bypass graft (CABG) surgery with the minimal extracorporeal circulatory system and the conventional extracorporeal circulation system and contribute to the literature by sharing the results.

2. Materials and Methods

2.1.Study Design and Patient Selection

The study was performed retrospectively on patients who underwent isolated CABG surgery in our clinic between September 1, 2013-December 31, 2018. Before the study, local ethics committee approval was obtained (Kanuni Training and Research Hospital, Health Sciences University Ethics Committee of Clinical Research, 2019/41) and the study was conducted per the Helsinki declaration. The patients were divided into two groups as those in whom the MECC system (Group 1) and the conventional extracorporeal circulatory system (Group 2) were used. The data of the patients were analyzed retrospectively from the patient files and the hospital automation system. Preoperative demographic data, comorbidities, American Society of Anesthesiologists (ASA), European System for Cardiac Operative Risk Evaluation (EUROSCORE), New York Heart Association (NHYA), Canadian Cardiovascular Society (CCS) scores were determined. Intraoperative findings included extracorporeal circulation system used, operation time, amount of priming solution used, activated clotting time (ACT), CBP and aortic cross-clamp time, number of anastomoses performed, amount of blood and blood products transfused, and inotropic infusion support. Postoperative data comprised duration of intubation and stay in the intensive care unit, complications, and mortality. In addition, the groups were investigated and compared in terms of preoperative and postoperative (24th hour) hematocrit, alanine aminotransferase (ALT), aspartate aminotransferase (AST), blood urea nitrogen (BUN), and creatinine values.

2.2.The exclusion criteria:

The following patients were excluded from the study:
- Those under the age of eighteen years
- Those undergoing emergency or redo surgery
- Cases who underwent open heart surgery other than CABG
- Those with renal and hepatic insufficiency
- Those with a EUROSCORE of over 7
- Patients with preoperative inotropic drug use or intra-aortic balloon support
- Patients who underwent additional surgery due to intraoperative complications such as aortic dissection, artery-vein injury, or heart injury.

2.3.Routine anesthesia procedure

The routine anesthesia protocol was followed. After preoperative examinations and preparations, the patients were taken to the operating room. Intravenous vascular access was established, and the patients were sedated with 0.05 mg/kg midazolam. Patient monitoring included SpO2 monitoring with pulse oximetry, D2 and V5 lead monitoring with electrocardiography, invasive systemic arterial pressure monitoring from the radial artery on the nondominant side, and esophageal temperature probes. For induction, sodium thiopental (4-6 mg/kg) (Pental Sodium, Ibrahim Etem Pharmaceuticals, Turkey), midazolam (0.1 mg/kg) (Sedazolam, Monemfarma Pharmaceuticals, Turkey), fentanyl (3-15 μg/kg)

(Talinate, Ibrahim Etem Pharmaceuticals, Turkey), and rocuronium (0.6 mg/kg) (Myocron, Vem Pharmaceuticals, Turkey) were administered. After anesthesia induction, endotracheal intubation was performed, and the patients were ventilated with a tidal volume of 8-10 ml/kg, a FiO2 of 0.5, a frequency of 10-12/minute and a PEEP of 5 cmH2O. Central venous pressure (CVP) was monitored with the help of a catheter directed to the right atrium from the internal jugular vein using the Seldinger technique, and urine output, with a Foley urinary catheter. Anesthesia was maintained with 0.1-0.3 mg/kg rocuronium, 0.02 mg/kg midazolam, and analgesic doses of fentanyl. Sevoflurane (Sevorane, Abbott, Turkey) was administered as an inhalation anesthetic, with a minimum alveolar concentration (MAC) between 0.5 and 2, depending on the hemodynamic status of the patient. The perioperative hemodynamic findings of the patients and the drugs administered were recorded in the anesthesia follow-up chart. At the end of the operation, the patients were transferred to the intensive care unit, intubated.

2.5.Routine cardiopulmonary bypass procedure and surgical technique

Perfusion during cardiopulmonary bypass was provided with a centrifugal pump (Maquet Jostra AG Group, Germany) in Group 1, and a roller pump (Terumo Medical Corporation, Germany) in Group 2. A heparin-coated membrane oxygenator (Quadrox-i Adult, Jostra AG, Germany) was used in Group 1, while a hollow-fiber membrane oxygenator (Quadrox7100, MaquetJostra AG Group, Germany) and an arterial filter (integrated) were used in Group 2. In Group 1, the prime volume was between 450-600 ml, while it was 1000-1500 ml in Group 2. Cardiopulmonary bypass with non-pulsatile flow was performed in both groups.

All operations were performed with a standard median sternotomy. After the pericardium was opened and suspended, 100-150 U/kg and 300U/kg heparin sodium (Koparin vial, Koçak Pharmaceuticals, Turkey) were administered in Groups 1 and 2, respectively, with ACTs of 250-300 seconds in Group 1 and >400 seconds in Group 2 during cardiopulmonary bypass. If necessary, an additional dose of heparin was administered. Arterial flow to the patient was provided by an aortic cannula placed in the ascending aorta, and venous return was provided by a venous cannula placed in the right atrium. After placing the cannula for cardioplegia and a vent in the ascending aorta, cardiopulmonary bypass was initiated. A cross-clamp was placed on the ascending aorta. Postoperatively, the heart rhythm was returned to normal sinus with the removal of the cross-clamp, either spontaneously or with the help of defibrillation. Cardiopulmonary bypass was terminated when the esophageal temperature reached 37 degrees and cardiac data were at optimal levels. Heparin neutralization was performed with protamine (promin, Vem Pharmaceuticals, Turkey) at a dose of 100-150 U/kg in Group 1 and 300-350 U/kg in Group 2. Following hemostasis, mediastinal and thorax drains were placed, the sternum was closed with a steel wire, the subcutaneous tissue and the skin were closed with vicryl sutures, and the operation was terminated. At the end of the operation, the intubated patient was monitored and transferred to the intensive care unit. When hemodynamic parameters were stable, the patient was extubated by weaning.

2.6.Statistical methods

IBM SPSS 25 program was used in the analysis of the data. For group comparisons, continuous variables were analyzed with the independent sample t-test, and frequency data were analyzed with the Chi-square test.**3.**

3. Results and Discussion

3.1.Results

The study was conducted on a total of 140 patients, 71 patients using the MECC (Group 1) and 69 patients using the conventional extracorporeal circulatory systems (Group 2). The demographic and preoperative risk factors of the patients are compared in Table 1. The groups did not differ significantly in terms of gender, height, weight, EUROSCORE, CCS, and rates of hypertension, diabetes mellitus, cerebrovascular disease, and peripheral arterial disease ($p>0.05$ for all) (Table 1). On the other hand, the mean age, ASA and NHYA scores and rates of Chronic Obstructive Pulmonary Disease (COPD) were higher in patients in whom MECC was used, while the mean ejection fraction (EF) was lower compared to those in which the conventional extracorporeal circulatory system was used ($p<0.05$ for all) (Table 1).

The intraoperative findings of the patient groups are compared in Table 2. The two groups were similar in terms of operation, CPB, and aortic cross-clamp time, the number of grafts, and inotropic infusion therapy ($p>0.05$ for all). The ACT duration, the amounts of priming solution, erythrocyte transfusion, and fresh frozen plasma transfusion were higher in the patient group in which the conventional extracorporeal circulatory system was used ($p<0.05$ for all).

Table 3 shows the comparison of the preoperative and postoperative biochemical values of the patient groups. The ALT (preoperative and postoperative), AST (preoperative and postoperative), postoperative BUN, and postoperative creatinine values were similar between the two groups ($p>0.05$). The preoperative hematocrit value of the patient group in which the MECC system was used was significantly lower, while the postoperative hematocrit value was significantly higher compared to the conventional extracorporeal circulatory system group ($p<0.05$). Preoperative BUN and creatinine values of the patients in which the MECC system was used were significantly higher than the conventional extracorporeal circulatory system group ($p<0.05$).

Table 1. A comparison of demographical data and preoperative risk factors

	Group 1 (MECC) (n=71)	Group 2 (Conventional) (n=69)	P
Age (mean ± SD)	68.41 (± 10,52)	61.98 ± 8.73	**,000***
Female n (%)	11(15.49 %)	8(11.59 %)	,500
Male n (%)	60(84.51 %)	61(88.41 %)	
Height (cm) (mean ± SD)	167.18±7.76	168.01±6.61	,497
Weight (kg) (mean ± SD)	78.79±10.16	79.54±9.81	,659
ASA (mean ± SD)	3.48±0.50	3.25±0.43	**,004***
CCS (mean ± SD)	2.94±0.71	2.77±0.59	,118
NHYA (mean ± SD)	2.93±0.74	2.71±0.54	**,045***
EUROSKORE (mean ± SD)	4.61±1.73	3.94±1.92	,064
EF (mean ± SD)	49.41±9.23	54.27±9.48	**,003***
Hypertension n (%)	57(80.28 %)	53(76.81%)	,703
Diabetes Mellitus n (%)	31(43.66 %)	28(40.58 %)	,712
Cerebrovascular Disease n (%)	8(11.27 %)	5(7.25 %)	,412
COPD n (%)	29(40.84 %)	10(14.49 %)	**,001***
Peripheral Artery Disease n (%)	4(5.79%)	11(15.49 %)	,064

P<0.05: Significance Level, SD: Standard Deviation, ASA: American Society of Anesthesiologists, CCS: Canadian Cardiovascular Society NYHA: New York Heart Association, EUROSCORE: European System for Cardiac Operative Risk Evaluation, EF: Ejection fraction, COPD: Chronic Obstructive Pulmonary Disease

Table 2. Comparison of intraoperative findings

	Group 1 (MECC) (n=71)	Group 2 (Conventional) (n=69)	P
Operation duration (min) (mean ± SD)	206.96±12.75	207.22±12.15	,553
Cardiopulmonary bypass duration (min) (mean ± SD)	95.16±32.27	98.74±32.01	,512
Aorta cross-clamp duration (min) (mean ± SD)	61.77±20.12	67.68±19.02	,066
Number of anastomoses (Graft) (mean ± SD)	3.14±0.81	3.29±0.71	,251
ACT (s) (mean ± SD)	287.31±20.78	486.35±60.26	**,000***
Priming solution (ml) (mean ± SD)	507.03±30.81	1150.43±98.61	**,000***
Inotrope Infusion therapy, n (%)	31 (%43.66)	35 (%50.72)	,403
Erythrocyte transfusion (unit) (mean ± SD)	1.03±1.09	1.88±1.51	**,000***
FFP transfusion (unit) (mean ± SD)	1.08±0.91	1.64±1.01	**,001***

P<0.05: Significance Level, SD: Standard Deviation, ACT: Activated Coagulation Time, FFP: Fresh Frozen Plasma

Table 3. Comparison of laboratory parameters

		Group 1 (MECC) (n=71)	Group 2 (Conventional) (n=69)	P
Hematocrit (%) (mean ± SD)	Preoperative	37.11±3.27	38.61±4.36	**,023***
	Postoperative (24th hour)	31.94±3.12	28.17±2.15	**,000***
ALT (IU/L) (mean ± SD))	Preoperative	22.61±13.43	21.87±11.65	,730
	Postoperative (24th hour)	23.46±12.02	26.19±12.48	,191
AST (IU/L) (mean ± SD)	Preoperative	32.55±14.42	31.56±14.94	,692
	Postoperative (24th hour)	37.82±13.63	41.87±17.96	,134
BUN (mg/dl) (mean ± SD)	Preoperative	40.62±11.42	35.07±11.89	**,006***
	Postoperative (24th hour)	42.46±12.59	45.72±12.16	,122
Creatinine (mg/dl) (mean ± SD	Preoperative	1.04±0.34	0.93±0.31	**,046***
	Postoperative (24th hour)	1.07±0.37	1.16±0.35	,159

P<0.05:Significance Level, SD:Standard Deviation, ALT:Alanine Aminotransferase, AST:Aspartate Aminotransferase, BUN: Blood Urea Nitrogen

Postoperative findings and complications of the patient groups are compared in Table 4. There was no significant difference between the two groups in terms of CPAP requirement, arrhythmia, neurological complications, pneumonia, bleeding revision, and mortality (p>0.05 for all). On the other hand, the time until extubation, and intensive care unit stay were significantly shorter and drainage amounts of the patients in the MECC group were significantly lower than those in the conventional extracorporeal circulation system group (p<0.05 for all).

Table 4. Comparison of the groups' postoperative findings and complications

	Group 1 (MECC) (n=71	Group 2 (Conventional) (n=69)	P
Duration of intubation (hours) (mean ± SD)	7.69 ±4.71	10.19±5.72	**,005***
Intensive care stay (hours) (mean ± SD)	25.15±6.42	42.07±7.36	**,000***
Drainage (ml) (mean ± SD)	480.28±217.37	898.55±415.06	**,000***
Re-intubation / CPAP requirement, n (%)	3(4.22 %)	3(4.35 %)	,971
Arrhythmia n (%)	19(26.76 %)	25(36.23 %)	,227
Neurological complications n (%)	1 (1.41%)	2(2.89 %)	,543
Pneumonia, n (%)	4(5.63 %)	5(7.25%)	,697
Revision due to hemorrhage, n (%)	3(4.22 %)	5(7.25 %)	,441
Mortality, n (%)	2(2.82 %)	2(2.89 %)	,977

P <0.05= Significance level. CPAP: Continuous Positive Airway Pressure

3.2.Discussion

CBP is an important element of coronary artery bypass graft surgery; however, off-pump CABG operations are also performed without the use of CPB, and studies comparing the operations performed with these two methods are found in the literature [10]. The MECC system has emerged as a result of novel research. It is stated that it can be an alternative to conventional extracorporeal circulation system and off-pump coronary revascularization [11]. Assad H. et al. compared the results of CABG operations performed with the MECC and the conventional extracorporeal circulatory systems in 244 high-risk patients and reported that the MECC system is a safe alternative for CABG surgery, especially in high-risk patients [8].

In our study, the patients in the MECC group were older and had significantly higher ASA and NHYA scores ($p<0.05$ for both) and insignificantly higher EUROSCORE and CCS scores ($p>0.05$ for both) compared to the patients in the conventional extracorporeal circulatory system group (Table 1). The number of patients with COPD was also higher in the MECC group ($p<0.05$), while the mean ejection fraction of the patients was lower ($p<0.05$) (Table 1). These results show that being high-risk is an important parameter in the preference of the MECC system in our center. The mean CPB and aortic cross-clamp time were similar between the two groups ($p>0.05$) (Table 2), which may be due to the absence of a significant difference between the number of bypass grafts ($p>0.05$) (Table 2).

In a prospective study evaluating the hemodynamics and regional tissue perfusion with the MECC system, MECC and conventional CPB circuits were compared for mean arterial pressure, systemic vascular resistance, and vasoactive drug needs among 40 patients undergoing coronary bypass surgery [12]. The mean arterial pressure was significantly higher, and norepinephrine use was lower in the MECC [12]. In our study, the use of inotropic infusions was insignificantly lower in the MECC group ($p>0.05$) (Table 2).

Clinicians working in the field of open heart surgery sought solutions to reduce the rate of blood transfusion [13], which reduces long-term survival rates [14,15]. The MECC system was developed based on this research since it allows lower prime volumes [16]. In their study, Ohata et al. evaluated the hematocrit values during and after CPB and showed a significant elevation in the MECC group [17]. Another study found that postoperative hematocrit values were high and the need for transfusion was significantly reduced in patients in whom the MECC system was used [18].

In our study, the amount of prime solution and the need for erythrocyte and FFP transfusion were significantly higher in the conventional CPB group than in the MECC group ($p<0.05$ for all) (Table 2). In addition, we think that significantly lower ACT values (Table 2) reduce the need for transfusion due to the low amount of heparin used. The hematocrit value was also significantly higher in the MECC group ($p<0.05$) (Table 3).

The systemic inflammatory response resulting from the contact of blood with non-endothelial surfaces after cardiopulmonary bypass can cause severe multiorgan dysfunction that can result in mortality [19]. Studies are reporting that anemia due to hemodilution also causes organ dysfunction [20-21]. Remadi et al. prospectively compared 100 patients who underwent aortic valve replacement in 2004 using the conventional CPB and the MECC systems and found that renal functions were better, and the rate of neurological adverse events was lower in the MECC group postoperatively [22]. In a prospective randomized study of 400 patients comparing the MECC system with the conventional CPB extracorporeal system, urea and creatine were significantly higher in patients in which the conventional CPB extracorporeal system was used [23]. Liebold et al. compared the liver perfusions of 40 CABG patients who were prospectively operated on with the standard and the MECC systems in 2004 and found that liver perfusion was higher in the MECC group postoperatively [24]. In their study in which they compared the conventional extracorporeal system and the MECC system in CABG operations, Immer et al. showed a lower incidence of AF and a faster recovery, hence stating that MECC was a safe perfusion method for CABG, similar to off-pump and conventional CPB [25].

Aminotransferases (ALT and AST) are found in the hepatocytes and elevated in liver injury [26]. In our study, we evaluated liver functions with preoperative and postoperative ALT and AST results. Although the preoperative ALT and AST values were insignificantly higher in the MECC group, they were postoperatively insignificantly higher among patients in which the conventional extracorporeal system was used, as was the case with creatinine value ($p>0.05$) (Table 3). We also found that in the MECC group, although the preoperative BUN value was significantly higher ($p<0.05$), it was insignificantly lower postoperatively (Table 3). Arrhythmia and neurologic complication rates were insignificantly lower, and the drainage amount and the need for revision due to hemorrhage were significantly lower in the MECC group (Table 4). We think that lower heparin dose, shorter ACT value, and factors such as hemodilution are effective in this result.

Intubation and intensive care unit length of stay were also investigated in studies [25, 27]. Immer et al. prospectively compared patients in which the conventional and MECC systems were used and found that the duration of intubation and intensive care unit stay were significantly shorter in the MECC group [25]. A different study reported no difference between the two groups regarding these two parameters [27]. COPD is a common comorbid disease in patients undergoing

coronary artery bypass graft surgery [28]. In our study, COPD was more common in the MECC group. Despite this, ventilation and intensive care hospitalization times were found to be shorter ($p<0.05$) (Table 4). No significant difference was found in terms of mortality rates; however, studies are reporting lower mortality rates in those operated on with the MECC system than in those in whom standard CPB was used [23].

The single-center, retrospective nature of our study and the low number of patients were the two main limitations of our study.

4. Conclusion

We can report that the MECC system is a safe and useful extracorporeal circulatory system. Relatively low-risk patients with normal preoperative ejection fractions, EUROSCORE values below 7, and normal kidney and liver functions were included in our study. Considering that mortality and morbidity rates may be lower in these patients, we think that more valuable results can be obtained with multicenter prospective studies with a larger number of high-risk patients.

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