

ORIGINAL ARTICLE

Medicine Science 2022;11(2):598-602

Evaluation of a sternum dehiscence reconstruction graft on an animal model** Ferit Kasimzade¹,  Fatih Ada²,  Ozhan Karatas³**¹Ankara City Hospital, Department of Cardiovascular Surgery, Ankara, Turkey²Sivas Cumhuriyet University, Faculty of Medicine, Department of Cardiovascular Surgery, Sivas, Turkey³Sivas Cumhuriyet University, Faculty of Veterinary, Department of Pathology, Sivas, Turkey

Received 26 October 2021; Accepted 31 January 2022

Available online 06.03.2022 with doi: 10.5455/medscience.2021.10.356

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**Abstract**

Sternum dehiscence occurring after surgeries requiring median incision of the sternum remains a current problem. New materials are needed to prevent or reduce the risk of developing sternum dehiscence. In this study, the effects of extracellular matrix (ECM)-like sternum dehiscence graft in a rabbit model were investigated. A total of 24 rabbits in three groups were used in the study. There were eight rabbits in each group. The first group was the control group, the second group was the conventional closure method, and the third group was the sternum closure graft group. Median sternotomy was applied to the rabbits in the second and third groups. Animals were sacrificed 4 weeks after surgery and sternum samples were taken. Sternum samples taken from untreated animals had normal histological appearance. Cartilage formation and fibrocyte-fibroblast activity were mild in the conventional surgery group, while moderate in the reconstruction graft group. It has been shown histopathologically that sternum closure graft accelerates bone healing ($P=0.015$). It is obvious that if this graft is used clinically, it will reduce the incidence of sternum dehiscence.

Keywords: Sternum, bone, fracture fixation, grafts, experimental animal models, heart surgery**Introduction**

Sternal dehiscence can be described as a incomplete closure of the sternum after open heart surgery or other operations requiring median sternotomy and displacement of the sternum after each respiration along the midline. There are some known risk factors for sternum dehiscence and these factors are; diabetes, chronic obstructive pulmonary disease (COPD), advanced age, osteoporosis and female gender [1]. In addition to these factors, risks related to surgical techniques and materials used in sternal closure have also been reported [2]. For this reason, many different techniques and sternum closure materials have been developed. However, despite all these developments, sternum dehiscence; It can result in long hospital stay, economic and labor loss, and even mortality. Titanium and Nitinol materials used in sternum closure provide a technical change. Bone cement is also used in advanced

cases, but the results are not satisfactory. This practice can be an obstacle for surgeons in cases where patients need median sternotomy again. In recent years, many materials have been used for surgeries dealing with bone tissue. A wide range of products has begun to come to the fore, from stem cell application to grafts of different structures. The sternum closure graft we used in our study has ECM-like morphology and mechanical properties. The structure of the matrix forming the sternum closure graft; PLGA Poly (L-lactide-co-glycolide), chitosan, Pluronic F-127, and 45S5 bioactive glass granules are composed of nano-fiber materials, and ultimately occurs in the form of a taylor cone-forming structure. In this study, it was aimed to evaluate the effectiveness of the closure graft developed for sternum dehiscence, which is a serious problem after cardiovascular surgery, in a rabbit model and to investigate its effect in complex creatures.

Materials and Methods**Animals and experiment method**

The study was initiated after the ethics committee decision numbered 65202830-050.04.04-424 of Sivas Cumhuriyet University Animal Experiments Local Ethics Committee. The study was conducted on a total of three groups and twenty-four rabbits. There were eight rabbits in each group (New Zeland white

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rabbit 6-8 months old, weighing 3.2-3.5 kg for males, 2.75-3 kg for females). The rabbits were housed in equally sized cages and at a constant temperature of twenty degrees, in a laboratory environment capable of receiving twelve hours of night and twelve hours of daylight. Standard rabbit food was used in all rabbits and their water was changed every other day. 90 mg/kg ketamine subcutaneous and 3 mg/kg xylazine intraperitoneal were given to the animals for anesthesia before surgical applications.

Group 1: No procedure was applied to the animals in this group, which is the control group. At the end of the experiment, samples were taken from the sternum after being sacrificed.

Group 2: Sternotomy was performed, but sternum closure was done with the conventional method. Sternum reconstruction graft was not applied. At the end of the study, samples were taken from the sternum after the animals were sacrificed.

Group 3: Sternotomy was performed and, sternum closure was done with the reconstruction graft. At the end of the study, samples were taken from the sternum after the animals were sacrificed.

Standard median sternotomy was performed under general anesthesia for each group except the main control group (Table 1). After the rabbits were given general anesthesia, the chest area was shaved. After shaving, sterile staining, dressing and standard monitoring were applied. After surgical sterilization, the skin and subcutaneous tissues were passed and reached to the sternum. After reaching the sternum, it was divided into two part with surgical scissors from the midline. During this time, care was taken not to open the pleura. The pleura was not opened in any rabbit. After the sternum was separated from the midline, the 2nd group was fixed with 3.0 prolene sutures without any procedure. In group 3, thin fabric reconstruction material (Mavera Medical Devices Inc.) was placed on the midline of the sternotomy and then fixed with 3.0 prolene sutures (Figure 1). Each operation was performed by the

same surgeon to avoid surgical differences during the procedure. After the surgical procedure, the skin and subcutaneous tissues were closed with absorbable rapid sutures. Daily dressing was performed until the wounds were completely healed. All animals were sacrificed with high-dose anesthetic to evaluate sternum healing 4 weeks after the procedure. All sampling procedures were carried out in accordance with ethical rules. Samples were taken by the same person so that there was no difference in sampling. After the animals were sacrificed, the samples were taken for histological and histopathological evaluation and comparisons were made for each group.

Table 1. Study groups

Groups	Surgical Model	Sample Timing	Use of Sternum Closure Graft
Group 1	-	4 th week	-
Group 2	Standard median sternotomy	4 th week	-
Group 3	Standard median sternotomy	4 th week	+

Histopathological method

After the animals were sacrificed, sternum tissues were fixed in 10% neutral formalin solution. It was then kept for 48 hours in a 1% HNO₃ solution. After decalcification was achieved, the tissues were taken into paraffin blocks after routine alcohol-xylol follow-up procedures. 5 μ sections taken on slides with poly-lysine were stained with hematoxylin-eosin (HE) and Masson trichrome (MST) then it was evaluated in terms of cartilage tissue formation and fibrocyte-fibroblast activity as none (0), mild (1), moderate (2) and severe (3) under light microscope (Table 2). Cartilage tissue formation was evaluated similarly to the study of Papparella et al (23). Fibrocyte-fibroblast activity was classified by measuring the thickness of the fibrous tissue formed in staining with Masson's Trichrome (Table 3).

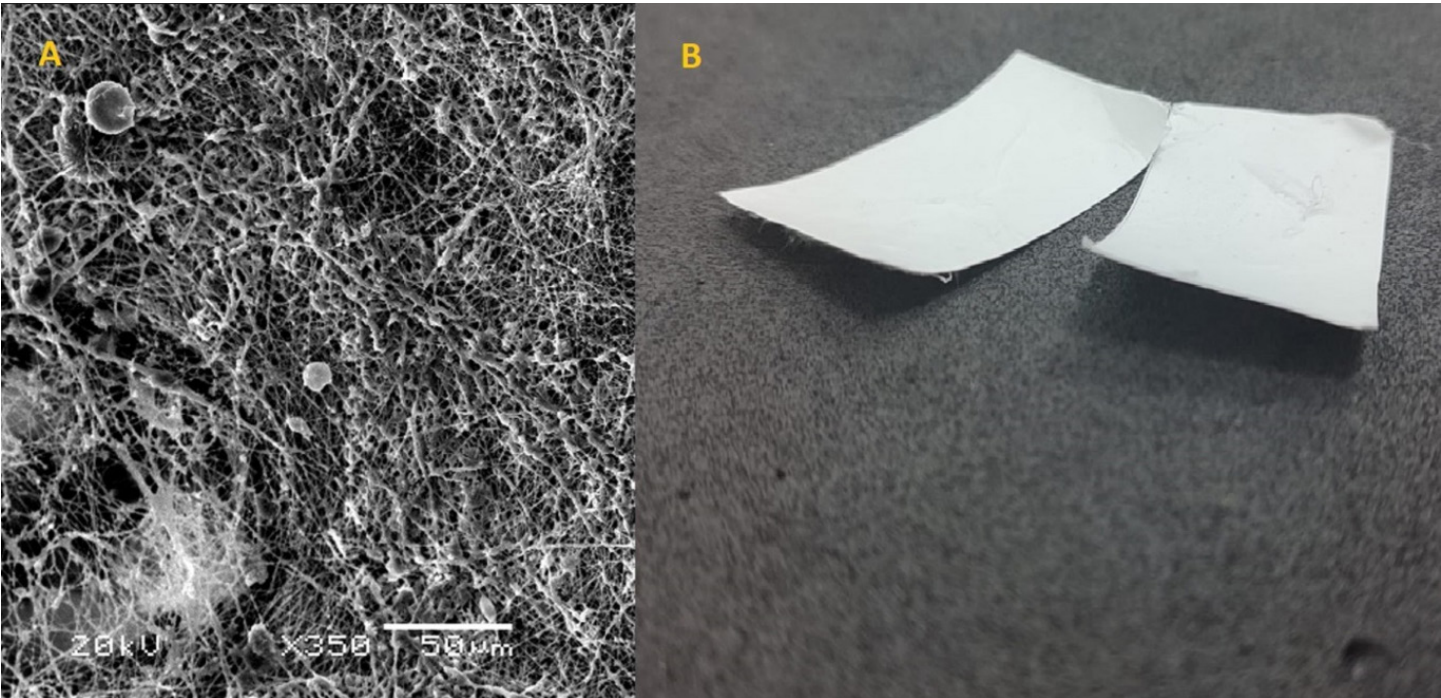


Figure 1. A: SEM image of the sternum closure graft, (SEM: Scanning Electron Microscope) B: Sternum closure graft

Table 2. Histopathological evaluation results. a,b,c refers to the differences between groups in the same column (p <0.05)

Groups	Cartilage formation	Fibrocyte-Fibroblast activity
Group 1 (Control Group)	2.83±0.40 ^a	2.83±0.40 ^a
Group 2 (Conventional Surgery)	1.33±0.40 ^b	1.33±0.40 ^b
Group 3 (Sternum Closure Graft)	2.16±0.40 ^c	2.16±0.40 ^c
Statistical Significance	(p <0.05)	(p <0.05)

^a: It shows the difference of the control group from the conventional closure group (p=0.002) and the sternum closure graft group (p=0.015). ^b: It shows the difference of the conventional closure group from the control group (P=0.002) and the sternum closure graft group (P=0.015). ^c: It shows the difference of the sternum closure graft group from the control group (P=0.015) and the conventional closure group (P=0.015).

Statistical analysis

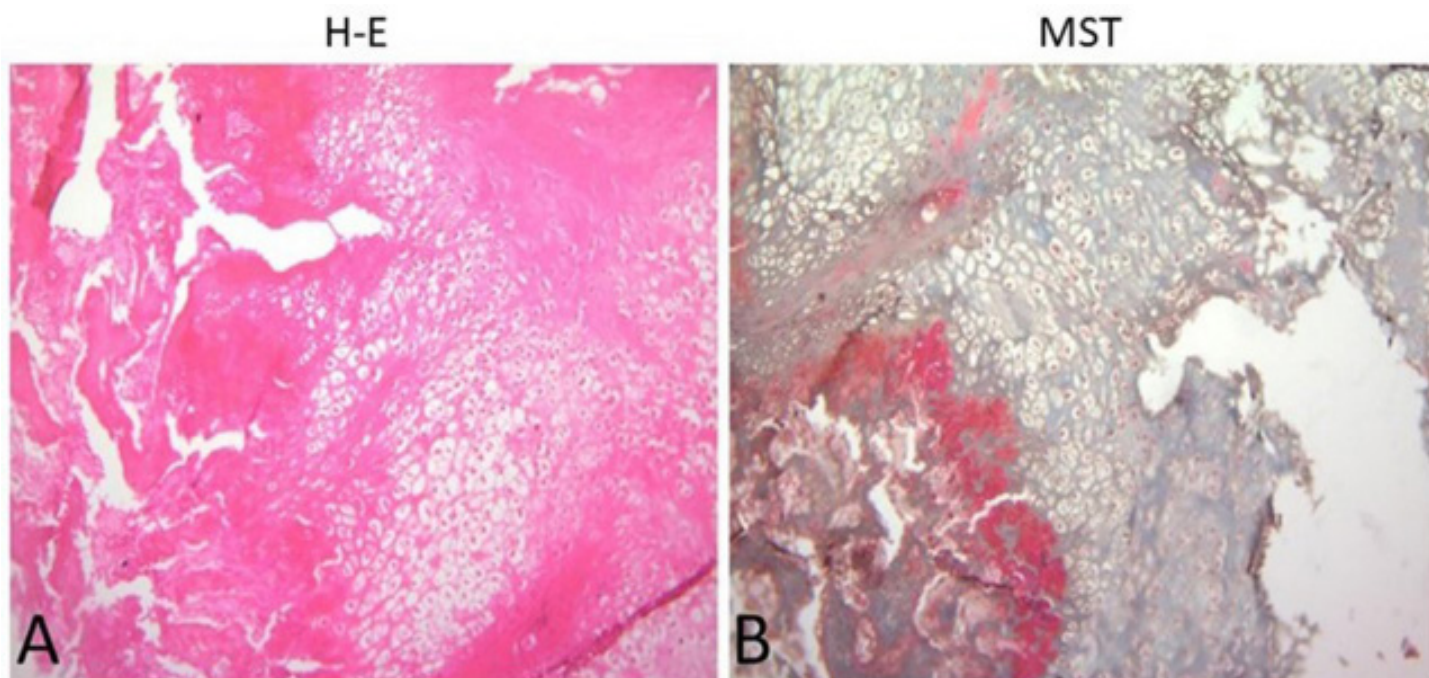
The data obtained were analyzed with the SPSS 20.00 program (StataCorp LP, College Station, TX, USA). The difference between the groups was determined by Kruskal Wallis, one of the nonparametric tests, and the group that made the difference with the Mann Whitney U test. P-value <0.05 was considered statistically significant.

Results

Sternum samples taken from animals in the control group (Group 1) that had not undergone any procedures had a normal histological appearance (Figure 2). Cartilage formation and fibrocyte-fibroblast activity were slightly higher in the conventional closure group (Group 2), which is one of the treatment groups (Table 2). On the other hand, cartilage formation and fibrocyte-fibroblast activity were observed to be moderately high in the group that underwent sternal closure graft (Group 3) (Figure 3).

Table 3. Cartilage tissue formation and fibrocyte-fibroblast activation scoring system

Cartilage tissue scores	
No changes	Absent (-)
Less than 10%	Mild (+)
Between 10 and 40 %	Moderate (++)
Fibrocyte-Fibroblast activity scores	
Less than 20 µm	Absent (-)
20-80 µm	Mild (+)
80-160 µm	Moderate (++)
More than 160 µm	Severe (+++)

**Figure 2.** (A-B) Control group. Normal histological appearance. (H-E ve MST) x10. (H-E: Hematoxylin-Eosin, MST: Masson Trichrome)

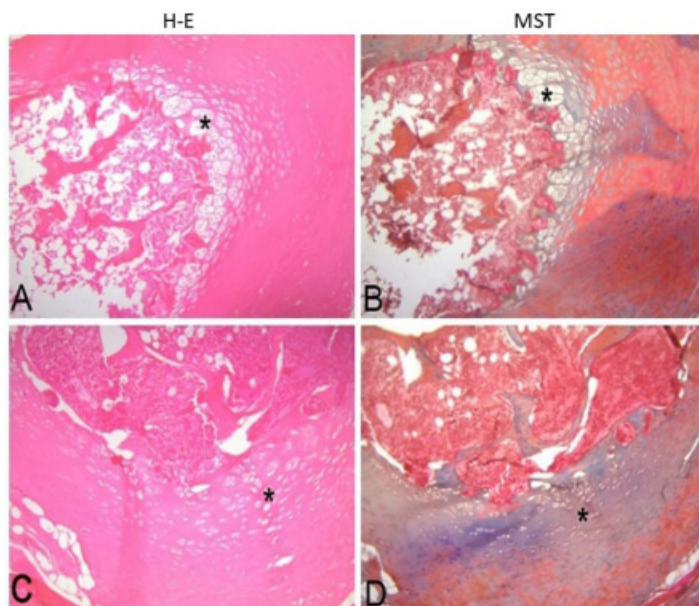


Figure 3. (A-B) Conventional closure group. Mild cartilage formation and mild fibrocyte-fibroblast activity (*), (C-D) Sternum closure graft group. Moderate cartilage tissue formation and moderate fibrocyte-fibroblast activity (*) (H-E ve MST)x20. (H-E: Hematoxylin–Eosin, MST: Masson Trichrome)

Discussion

Dehiscence of the sternum; It is the incomplete closure of the sternotomy line after surgeries requiring median sternotomy. The incidence of dehiscence after all surgeries requiring sternotomy has been reported as 0.2-6.46% [3,4]. There are many factors that affect sternum dehiscence and are known to increase predisposition. High body mass index, diabetes, COPD, re-exploration, beta-blocker use, advanced age, female gender, osteoporosis, peripheral artery disease, history of immunosuppressive therapy, renal failure, use of bilateral internal mammarian artery, postoperative intensive care delirium, high amount blood transfusions are known risk factors for sternum dehiscence [4-6]. In addition to many identified risk factors, there are also dehiscence factors related to intraoperative techniques and the used materials. One of them is bone wax applied to the sternum medulla [7]. In addition to mediastinitis and respiratory dysfunction, spontaneous right ventricular rupture has also been reported as a mortal complication of sternum dehiscence [8].

In addition to the physical examination findings, it is important to evaluate the posterior-anterior chest X-ray for the identification of dehiscence. In the diagnosis of sternum dehiscence, 3 wire positions in the form of displacement, rotation and disruption have been defined for the traditional closure method in chest radiography [9]. The most common of these has been reported as displacement.

The Robicsek technique has been shown to reduce dehiscence, especially in COPD patients, in surgery with classical sternal closure materials [10]. The new parasternal wire closure technique developed by Sharma et al., which is a modified version of the Robicsek technique, has also been shown to reduce dehiscence and mediastinitis [11]. It was reported by John that closure performed directly through the sternum may also reduce dehiscence [12]. In addition, it has been observed that weaved closure in sternum closure made with traditional materials is effective in reducing dehiscence in patients with high dehiscence risk [13]. Treatment

of dehiscence by surgery of transposition of the greater omentum to the sternum has also been reported [14].

Many materials such as titanium plates, cables and cannulated screws have been developed for complicated sternum dehiscence [15]. Titanium plates, one of the many techniques developed, were found to be more advantageous than traditional closure methods in terms of sternal dehiscence and mediastinitis [16]. This feature of titanium plates has been found to be superior not only in preventing dehiscence but also in treatment [17]. It has been observed that thermoactive nitinol clips are effective both in preventing and treatment dehiscence [18,19]. Polydioxanone sutures have been reported to be prevent in patients with high dehiscence risk [20]. In addition, sternum corsets used to prevent dehiscence in the postoperative period [21,22].

However, none of the listed methods has a factor that increases the rate and amount of bone formation in the sternum medulla. In fact, almost all of the methods listed are aimed at providing the physical unity of the sternum. The sternum closure graft used in our study served as the ideal bone with its morphology and mechanical properties similar to the ECM. The structure of the matrix consists of a nano-fiber structure consisting of PLGA Poly(L-lactide-co-glycolide), chitosan, pluronic F-127 and 45S5 bioactive glass granules and forming a taylor cone.

The matrix applied in our study gains antibacterial properties thanks to the bioactive glass granule and the inorganic part of the bone and chitosan, and supports osteogenic differentiation by promoting cell migration into the bone tissue. In addition, it provides the necessary mechanical stability at the interface by establishing a bond between the matrix and the main tissue surrounding it. The structural and chemical properties of the matrix affect cell activities such as adhesion, migration and proliferation of cells. The results in the samples taken 4 weeks after the start of the experiment showed that it contributed to bone formation, increased the number and activity of fibroblasts, and increased cartilage formation. In addition to other methods in sternum closure, bone formation can be accelerated with the material used in our study to be placed on the sternotomy line. As a result of the findings, cartilage formation, fibrocyte activity, and fibroblast activity were found to be statistically significantly higher in the sternum closure reconstruction graft group compared to the conventional surgical closure group. These findings suggest that sternal closure reconstruction graft can be successfully applied to prevent sternum dehiscence. On the other hand, it is obvious that clinical studies including long-term follow-up are needed.

Limitations

There are several limitations in our study. The first of these is that only two of the sternotomy methods have been compared. In addition, the study being an animal experiment limited the chance of long-term follow-up. In addition, it is obvious that clinical studies including long-term follow-ups are needed.

Conflict of interests

The authors declare that they have no competing interests.

Financial Disclosure

This study was supported by TÜBİTAK 1507 program with project number 7191000.

Ethical approval

The study was initiated after the ethics committee decision numbered 65202830-050.04.04-424 of Sivas Cumhuriyet University Animal Experiments Local Ethics Committee.

References

1. Olbrecht VA, Barreiro CJ, Bonde PN, et al. Clinical outcomes of noninfectious sternal dehiscence after median sternotomy. *Ann Thorac Surg.* 2006;82:902-7.
2. Alhalawani AM, Towler MR. A review of sternal closure techniques. *J Biomater Appl.* 2013;28:483-97.
3. Listewnik MJ, Jędrzejczak T, Majer K, et al. Complications in cardiac surgery: An analysis of factors contributing to sternal dehiscence in patients who underwent surgery between 2010 and 2014 and a comparison with the 1990-2009 cohort. *Adv Clin Exp Med.* 2019;28:913-22.
4. Molina JE, Lew RSL, Hyland KJ. Postoperative sternal dehiscence in obese patients: incidence and prevention. *Ann Thorac Surg.* 2004;78:912-7.
5. Schimmer C, Reents W, Berneder S, et al. Prevention of sternal dehiscence and infection in high-risk patients: a prospective randomized multicenter trial. *Ann Thorac Surg.* 2008;86:1897-904.
6. Reyna GC, Baca GGA, Concebida LEM, et al. Risk factors for mediastinitis and sternal dehiscence after cardiac surgery. *Rev Esp Cardiol.* 2006;59:130-5.
7. Alhan C, Arıturk C, Senay S, et al. Use of bone wax is related to increased postoperative sternal dehiscence. *Kardiochir Torakochirurgia Pol.* 2014;11:385-90.
8. Arbulu A, Gursel E, Camero LG, et al. Spontaneous right ventricular rupture after sternal dehiscence: a preventable complication?. *Eur J Cardiothorac Surg.* 1996;10:110-115.
9. Boiselle PM, Mansilla AV, Fisher MS, et al. Wandering wires: frequency of sternal wire abnormalities in patients with sternal dehiscence. *AJR Am J Roentgenol.* 1999;173:777-80.
10. Celik S, Kirbas A, Gurer O, et al. Sternal dehiscence in patients with moderate and severe chronic obstructive pulmonary disease undergoing cardiac surgery: the value of supportive thorax vests. *J Thorac Cardiovasc Surg.* 2011;141:1398-402.
11. Sharma R, Puri D, Panigrahi BP, et al. A modified parasternal wire technique for prevention and treatment of sternal dehiscence. *Ann Thorac Surg.* 2004;77:210-3.
12. John LC. Modified closure technique for reducing sternal dehiscence; a clinical and in vitro assessment. *Eur J Cardiothorac Surg.* 2008;33:769-73.
13. Narang S, Banerjee A, Satsangi DK, et al. Sternal weave in high-risk patients to prevent noninfective sternal dehiscence. *Asian Cardiovasc Thorac Ann.* 2009;17:167-70.
14. Ceresa F, Casablanca G, Patané F. Complicated sternal dehiscence treated with the strasbourg thoracic osteosyntheses system (STRATOS) and the transposition of greater omentum: a case report. *J Cardiothorac Surg.* 2010;5:1-3.
15. Voss B, Bauernschmitt R, Brockmann G, et al. Complicated sternal dehiscence: reconstruction with plates, cables, and cannulated screws. *Ann Thorac Surg.* 2009;87:1304-6.
16. Vos RJ, Jongbloed L, Sonker U, et al. Titanium plate fixation versus conventional closure for sternal dehiscence after cardiac surgery. *Thorac Cardiovasc Surg.* 2017;65:338-42.
17. Voss B, Bauernschmitt R, Will A, et al. Sternal reconstruction with titanium plates in complicated sternal dehiscence. *Eur J Cardiothorac Surg.* 2008;34:139-45.
18. Gucu A, Toktas F, Eris C, et al. Nitinol thermoreactive clips for secondary sternal closure in cases of noninfective sternal dehiscence. *Tex Heart Inst J.* 2012;39:513-6.
19. Negri A, Manfredi J, Terrini A, et al. Prospective evaluation of a new sternal closure method with thermoreactive clips. *Eur J Cardiothorac Surg.* 2002;22:571-5.
20. Luciani N, Anselmi A, Gandolfo F, et al. Polydioxanone sternal sutures for prevention of sternal dehiscence. *J Card Surg.* 2006;21:580-4.
21. Tewarie LS, Menon AK, Hatam N, et al. Prevention of sternal dehiscence with the Sternum External Fixation (Stern-E-Fix) corset—a randomized trial in 750 patients. *J Cardiothorac Surg.* 2012;7:1-8.
22. Cakir H, Yurekli I, Donmez K, et al. Risk models for patients undergoing robotic surgery, minimal invasive heart surgery and open-heart surgery. *Medicine Science Int Med J.* 2018;7:959-6.
23. Papparella A, Nino F, Coppola S, et al. Peritoneal morphological changes due to pneumoperitoneum: the effect of intra-abdominal pressure. *Eur J Pediatr Surg.* 2014;24:322-7.