

ORIGINAL ARTICLE

Comparison of Chitosan-Containing Hemostatic Pad and Manual Compression after Coronary Angiography with Femoral Access

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Abstract

Background: Femoral access remains a common choice in coronary angiography due to its easy accessibility and high success rate. Various techniques exist for achieving hemostasis following femoral artery catheterization.

Objectives: The aim of our study is to compare the methods of chitosan-containing hemostatic pad (HP) and manual compression (MC) in terms of efficacy and safety in patients undergoing percutaneous coronary intervention (PCI) with coronary angiography via femoral access.

Method: A total of 204 patients from 3 centers were included in our study between August 2021 and June 2023. The patients were divided into 2 groups, HP and MC, with 102 patients in each. Patients were evaluated for back and low back pain, complications, and duration of hemostasis immediately after angiography and up to 24 hours. Student's t test and Mann-Whitney U test were used for numerical variables, while chi-square test was used for categorical variables. $P < 0.05$ was considered statistically significant.

Results: Hemostasis time and back and low back pain were significantly lower in the HP group (7.5 ± 1.1 versus 15.1 ± 1.6 , $p < 0.001$ and 2.13 ± 1.29 versus 4.22 ± 1.69 , $p < 0.001$, respectively). While ecchymosis was found to be significantly lower in the HP group (2.9% versus 14.7%, $p = 0.003$), there was no significant difference in terms of other complications.

Conclusion: HP was found to be more advantageous than MC in patients who underwent coronary angiography with femoral access. While ecchymosis and back and low back pain were found to be lower in the HP group, the absence of the need for sandbags also increases patient comfort.

Keywords: Coronary Angiography; Chitosan; Hemostatics.

Introduction

Femoral access is still frequently used in coronary angiography, because it is easily accessible and has a high chance of success.¹ For this purpose, a diagnostic or therapeutic intervention is performed by passing a sheath through the femoral artery.² After the procedure is completed, the sheath is removed, and hemostasis is achieved in the access area. Post-procedure complications such as hematoma, bleeding, ecchymosis,

pseudoaneurysm, and atrioventricular fistula can occur.³ This possibility increases especially in patients who have received intensive anticoagulant and antiaggregant treatment before the procedure.⁴ In addition, the need for long-term bed rest also negatively affects patient comfort.

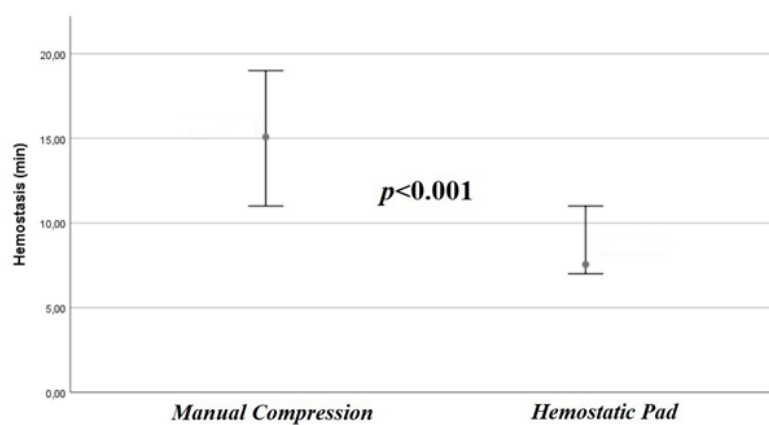
There are various alternative methods, such as manual compression (MC), band pressure, pressure dressing, tourniquet, and vessel closure devices to provide hemostasis in the femoral region. Today, MC is still the most frequently used method.⁵ In the MC method, after the sheath is

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Central Illustration: Comparison of Chitosan-Containing Hemostatic Pad and Manual Compression after Coronary Angiography with Femoral Access

Central Figure

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Comparison of HP and MC in terms of hemostasis time

removed, the femoral region is compressed for 15 to 20 minutes, and a sandbag is subsequently left for about 6 hours.⁶ During this period, patients should lie on their back and avoid moving as much as possible. This method has limitations, such as requiring long-term bed rest, prolonging hospital stay, and adversely affecting patient comfort.⁷

Chitosan-based hemostatic pad (HP) is used as an alternative method to provide hemostasis in the femoral region. Chitosan is a linear aminopolysaccharide obtained by deacetylation of chitin found in shellfish.⁸ As soon as chitosan comes into contact with blood, it pulls the erythrocytes and platelets towards the vessel wall, allowing the rapid formation of fibronogen tissue.⁹ Chitosan was primarily used by the military on battlefields as a local hemostatic agent.¹⁰ Thus, increasing knowledge in rapid control of bleeding has paved the way for the use of chitosan at local puncture sites. The HP is used as a 5.1 × 5.1 cm pad. Regardless of the body's coagulation processes, a clot forms within 30 seconds when it comes into contact with blood. After about 5 to 10 minutes of MC, hemostasis is achieved without the need for a sandbag. After 2 hours of bed rest, the patients are mobilized.

The objectives of our study were to compare the methods of traditional MC and HP for hemostasis in patients undergoing percutaneous coronary intervention (PCI) with femoral access and to evaluate the safety and effectiveness of the HP method.

Methods

Study design

A total of 204 consecutive patients who underwent PCI via femoral access from 3 centers between August 2021 and June 2023 were included in our study. After the procedure, the patients were divided into 2 groups. While HP was applied to 102 patients, MC was applied to 102 patients. Written informed consent was obtained from all patients. Study approval was obtained by the local ethics committee (date and number: 30/12/2022-292). The study was conducted in accordance with the 2013 Declaration of Helsinki.

The inclusion criteria were as follows: elective angiography, right femoral artery access, patients over 18 years of age, use of a 6-Fr catheter sheath, blood pressure within normal limits, and normal coagulation tests (international normalized ratio, partial thromboplastin time, prothrombin time). The exclusion criteria were as follows: patients with coagulation disorder, hemophilia, anticoagulant drug use, pregnancy or lactation (in female patients), and myocardial infarction.

Definitions

Hematoma: The situation where blood moves away from the vessel and collects in a different tissue due to damage to the vessel wall is called hematoma. It tends to cause a painful mass in the femoral region, which usually

disappears within 1 to 2 weeks, as blood slowly spreads and absorbs into the soft tissue.

Ecchymosis: Ecchymosis is the accumulation of blood under the skin as a result of trauma. Capillaries become damaged; blood leaks and collects in nearby tissues. Ecchymosis may appear as a large red, blue, or purple area on the skin. It usually heals on its own within 2 to 3 weeks.

Pseudoaneurysm: Pseudoaneurysms are localized pulsatile mass structures formed by blood flowing out of the arterial lumen due to deterioration in the arterial wall and at the same time communicating with the lumen. Since the area around the sac does not consist of the triple layer of arterial structures (intima, media, adventitia), it differs from a true arterial aneurysm in this respect. Vascular damage occurring after cardiac catheterization often requires surgical intervention.

Arteriovenous fistula: This occurs as a result of ongoing bleeding from the femoral artery puncture site draining to the adjacent venous puncture site to relieve pressure. It is recognized by hearing a continuous murmur over the puncture site. Approximately one third of the cases close spontaneously within 1 year, while the rest are referred to surgery.

Coronary angiography and post-procedure follow-up

Experienced interventional cardiologists performed coronary angiography via femoral access. After 10 ml of 2% lidocaine local anesthetic was applied to the femoral region, femoral artery puncture was performed using the Seldinger technique, and a 6-Fr sheath was placed. All patients were given 100 u/kg unfractionated heparin during the procedure. The femoral sheath was removed 4 hours after the procedure. In the MC group, hemostasis was achieved with 10 to 20 minutes of MC after sheath removal. Subsequently, a 5-kg sandbag was placed on the sheath area for 6 hours. After the sandbag was removed, the sheath location was checked, and the patient was mobilized. In the HP group, MC was applied to the femoral artery proximal to the sheath, and the sheath was withdrawn. Afterwards, the compression was loosened slightly and blood supply was provided to the surface. The HP was adhered to the sheath area by making contact with blood. MC was applied to both the HP and proximal for 5 minutes. The proximal compression was then removed. Compression was applied on the HP for 2 more minutes and checked. If hemostasis was achieved, the compression was removed; if not, it was continued for 2

more minutes. The patients were mobilized 2 hours later.

A visual analog scale (VAS) was used to evaluate patients' low back and back pain.¹¹ VAS is a vertical line between 0 and 10 cm. 0 represents no pain and 10 represents the highest pain intensity. This scale was administered immediately after the patients ended their absolute bed rest.

The time between removal of the femoral artery sheath and complete control of bleeding was considered as hemostasis time. Patients were closely monitored for complications immediately and up to 24 hours after angiography. Early complications such as local ecchymosis, hematoma, pseudoaneurysm, and arteriovenous fistula were evaluated by physical examination. Doppler ultrasonography was performed in patients deemed necessary.

Statistical analysis

Statistical analysis was performed using SPSS 25.0 (Armonk, NY: IBM Corp.). The Kolmogorov-Smirnov test was used to determine whether the variables were normally distributed. Unpaired Student's t-test was used for normally distributed variables, and Mann-Whitney U test was used for abnormally distributed variables. Normally distributed variables were expressed as mean \pm standard deviation. If data showed abnormal distribution, they were expressed as median (interquartile range). Chi-square test was used to compare categorical variables. The categorical variables were expressed as absolute and relative frequencies. A value of $p < 0.05$ was considered statistically significant.

Result

A total of 204 patients, 102 from each group, were included in the study. While the mean age of the patients was 62.6 ± 9.2 in the HP group, it was 61.2 ± 12.5 in the MC group. The total number of men was 138 (67.6%), and there was no difference between the groups. The patient groups were similar to each other in terms of demographic and clinical characteristics (Table 1). When the groups were compared in terms of hemostasis time, it was found to be significantly lower in the HP group (7.5 ± 1.1 versus 15.1 ± 1.6 , $p < 0.001$, respectively) (Central Illustration).

The patient groups were similar in terms of activated partial thromboplastin time, prothrombin time, and international normalized ratio. There was no significant

Table 1 – Baseline characteristics and complications of the study population

	HP (n = 102)	MC (n = 102)	P value
Sex (male), n(%)	70(68.6)	68(66.7)	0.765
Age, (years)	62.6±9.2	61.2±12.5	0.345
HT, n(%)	31(30.4)	37(36.3)	0.373
DM, n(%)	35(34.3)	28(27.5)	0.289
HPL, n(%)	25(24.5)	27(26.5)	0.748
Smoker, n(%)	25(24.5)	29(28.4)	0.526
CRF, n(%)	15(14.7)	11(10.8)	0.401
EF, (%)	49.4±10.2	47.5±11.5	0.210
Systolic Blood Pressure (mmHg)	130±15	128±16	0.517
Diastolic Blood Pressure (mmHg)	80±10	79±10	0.369
Heart rate (per minute)	82±16	84±13	0.224
Body mass index (kg/m ²)	28.6±3.1	29.1±4.2	0.379
Processing time (min)	53.5±8.7	52.1±7.6	0.235
Hemostasis time(min)	7.5±1.1	15.1±1.6	<0.001
Hematoma, n(%)	1(1)	4(3.9)	0.174
Ecchymosis, n(%)	3(2.9)	15(14.7)	0.003
Pseudoaneurysm, n(%)	0(0)	1(1)	N/A
A-V fistula, n(%)	0(0)	0(0)	N/A

A-V: arteriovenous; CRF: chronic renal failure; DM: diabetes mellitus; EF: ejection fraction; HPL: hyperlipidemia; HT: hypertension; HP: hemostatic pad; MC: manual compression.

difference in platelet count between the groups. The laboratory findings of the patients are given in Table 2.

Low back and back pain measured by VAS were found to be significantly lower in the HP group (2.13 ± 1.29 versus 4.22 ± 1.69 , $p < 0.001$, respectively) (Figure 1).

When the groups were compared in terms of complications, ecchymosis was found to be significantly lower in the HP group. There were 1 hematoma in the HP group and 4 hematomas in the MC group. Pseudoaneurysm developed in only 1 patient in the MC group. Atrioventricular fistula was not detected in any patient.

Discussion

In our study, we compared MP and HP in terms of efficacy and safety in patients who underwent PCI with femoral access. Hemostasis was achieved in a shorter time

in the HP group, and the patients were mobilized earlier. After absolute bed rest, low back and back pain were found to be lower in the HP group. In addition, ecchymosis was less frequent in the HP group, and there was no significant difference in terms of other complications.

Femoral access is generally preferred in coronary angiography due to its ease and high success.¹² In order to provide hemostasis in the femoral artery after the procedure, a sandbag is placed on the groin area after MC, and absolute bed rest is required. Especially in patients who receive intensive antiaggregant and anticoagulant treatment after PCI, MC takes longer, and this is a time-consuming and troublesome situation for healthcare professionals. Long-term absolute bed rest after the procedure disrupts the comfort of the patients and causes low back and back pain. Elderly patients especially have greater difficulty tolerating sandbags and prolonged bed rest. Oral or intravenous

Table 2 – Laboratory findings of the study population

	HP (n = 102)	MC (n = 102)	P value
WBC ($\times 10^3/\mu\text{l}$)	9.5 \pm 3.6	9.6 \pm 3.3	0.772
Hgb (g/dl)	13.6 \pm 2.1	13.6 \pm 1.6	0.798
Hct (%)	42.0 \pm 6.0	41.0 \pm 4.5	0.173
Plt ($\times 10^3/\mu\text{l}$)	251 \pm 69	238 \pm 75	0.200
GFR (ml/min)	89(74-97)	90(69-102)	0.456
Glucose(mg/dl)	120(97-209)	117(100-173)	0.895
Bun (mg/dl)	43.6 \pm 17.5	40.6 \pm 17.8	0.226
Creatinine(mg/dl)	0.86(0.73-1.04)	0.87(0.77-1.02)	0.613
aPTT(sec)	34.2 \pm 1.8	33.8 \pm 1.8	0.137
PT(sec)	12.2 \pm 0.9	12.0 \pm 0.8	0.225
INR	0.93 \pm 0.08	0.92 \pm 0.08	0.346

aPTT: activated partial thromboplastin time; BUN: blood urea nitrogen; GFR: glomerular filtration rate; Hct: hematocrit; Hgb: hemoglobin; INR: international normalized ratio; Plt: platelets; PT: prothrombin time; WBC: white blood cell; HP: hemostatic pad; MC: manual compression.

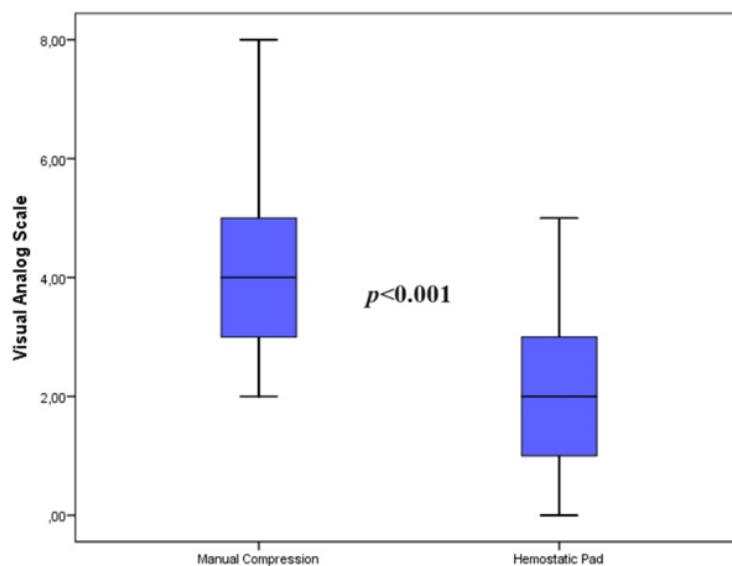


Figure 1 – Comparison of HP and MC in terms of back and low back pain using VAS

hydration is applied to the patients in order to remove the contrast agent used during the procedure from the body and to prevent nephrotoxicity. This situation increases the patients' need to urinate and creates a major problem for patients who cannot insert a catheter.

Chitosan-containing hemostatic powders were approved by the FDA in 2006. Early studies have shown that dressing containing chitosan provides hemostasis faster than standard gauze and reduces mortality.¹³ Chitosan was first used in military areas to provide wound hemostasis in

emergencies.¹⁴ Today, it is also used in elective conditions. Previously, chitosan was produced in granular form, roll gauze, and cylindrical applicators, but it is also currently available in the form of pads.

In a 2013 study, dressings impregnated with 2 g chitosan powder in patients with coronary angiography provided faster hemostasis than normal dressings, and no significant difference was found between complications.¹⁵ In another study, chitosan-containing dressing and normal dressing were compared in pediatric patient groups. In this study, while venous hemostasis was found to be significantly shorter, no difference was found in arterial hemostasis.¹⁶ In hemodialysis patients, dressing made with 0.5 and 1 g chitosan powder in the vascular access area provided hemostasis in a shorter time than conventional dressing. Therefore, its use is recommended in patients with prolonged vascular access hemostasis.¹⁷ In a study in pigs whose femoral arteries were cut and left to bleed for 3 minutes, chitosan-containing dressings were found to improve bleeding control and survival.⁹

In our study, patients' back and low back pain were measured with VAS just before mobilization. As expected, lower pain level was detected in the HP group. In the HP group, patients were able to move more easily during bed rest, since no sandbags were placed. In addition, absolute bed rest with sandbags for at least 6 hours was required in the MC group, while the patients in the HP group were mobilized after 2 hours. All these reasons may explain why patients in the HP group felt less pain. This not only increases patient comfort, but also reduces the need for painkillers.

Although the complication rates in the femoral access area have decreased with increasing experience, complications such as ecchymosis and hematoma are still an important problem, especially in patients receiving intensive antiaggregants and anticoagulants.¹⁸ In previous studies, the frequency of ecchymosis was 20% to 22%, and hematoma was 3% to 4%.^{19,20} In our study, the frequency of ecchymosis was found to be significantly lower in the HP group. Some patients in the MC group move when they should be lying absolutely still on their back. In addition, elderly patients especially are mobilized early because they cannot tolerate sandbags for a long time. These conditions may explain the more frequent ecchymosis in the MC group. Although the incidence of hematoma was numerically lower in the HP group, it was not statistically significant. The incidence of pseudoaneurysm in the femoral artery is reported to be 2% to 9% in the literature.¹⁸ In our study, it was detected in only 1 patient in the MC group.

Limitations

The pain level of the patients was measured subjectively. The difference in pain threshold between patients may have affected the pain score. Routine Doppler ultrasonography was not performed in all patients. Long-term patient outcomes were not followed up. The number of patients was relatively low. Some puncture-related complications should not be ignored.

Conclusion

In our study, HP appears to be a more advantageous method than traditional MC in patients undergoing coronary angiography with femoral access. Shorter hemostasis time and faster mobilization were detected in patients in the HP group. The absence of the need for sandbags was a situation that increased patient comfort. In addition, in the HP patient group, ecchymosis was detected less frequently, and the severity of low back and back pain was also lower.

Author Contributions

Conception and design of the research: Kiliç R; acquisition of data: Kiliç R, Güzel T; analysis and interpretation of the data: Kiliç R, Güzel T, Kaya AF; statistical analysis and writing of the manuscript: Kiliç R, Aktan A; critical revision of the manuscript for intellectual content: Güzel T, Kaya AF.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Sources of Funding

There were no external funding sources for this study.

Study Association

This study is not associated with any thesis or dissertation work.

Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee of the Diyarbakır Gazi Yaşargil Training and Research Hospital Ethics Committee under the protocol number 292. All the procedures in this study were in accordance with the 1975 Helsinki Declaration, updated in 2013. Informed consent was obtained from all participants included in the study.

References

1. Merriweather N, Sulzbach-Hoke LM. Managing Risk of Complications at Femoral Vascular Access Sites in Percutaneous Coronary Intervention. *Crit Care Nurse*. 2012;32(5):16-29. doi: 10.4037/ccn2012123.
2. Walter J, Vogl M, Holderried M, Becker C, Brandes A, Sinner MF, et al. Manual Compression versus Vascular Closing Device for Closing Access Puncture Site in Femoral Left-Heart Catheterization and Percutaneous Coronary Interventions: A Retrospective Cross-Sectional Comparison of Costs and Effects in Inpatient Care. *Value Health*. 2017;20(6):769-76. doi: 10.1016/j.jval.2016.05.004.
3. Bhatti S, Cooke R, Shetty R, Jovin IS. Femoral Vascular Access-site Complications in the Cardiac Catheterization Laboratory: Diagnosis and Management. *Interv Cardiol*. 2011;3(4):503-14. doi: 10.2217/ica.11.49.
4. Choussat R, Black A, Bossi I, Fajadet J, Marco J. Vascular Complications and Clinical Outcome after Coronary Angioplasty with Platelet IIb/IIIa Receptor Blockade. Comparison of Transradial vs Transfemoral Arterial Access. *Eur Heart J*. 2000;21(8):662-7. doi: 10.1053/euhj.1999.1945.
5. Abando A, Hood D, Weaver F, Katz S. The Use of the Angioseal Device for Femoral Artery Closure. *J Vasc Surg*. 2004;40(2):287-90. doi: 10.1016/j.jvs.2004.05.007.
6. Robertson L, Andras A, Colgan F, Jackson R. Vascular Closure Devices for Femoral Arterial Puncture Site Haemostasis. *Cochrane Database Syst Rev*. 2016;3(3):CD009541. doi: 10.1002/14651858.CD009541.pub2.
7. Pieper CC, Thomas D, Nadal J, Willinek WA, Schild HH, Meyer C. Patient Satisfaction after Femoral Arterial Access Site Closure Using the ExoSeal® Vascular Closure Device Compared to Manual Compression: A Prospective Intra-individual Comparative Study. *Cardiovasc Intervent Radiol*. 2016;39(1):21-7. doi: 10.1007/s00270-015-1204-2.
8. Arnaud F, Teranishi K, Tomori T, Carr W, McCarron R. Comparison of 10 Hemostatic Dressings in a Groin Puncture Model in Swine. *J Vasc Surg*. 2009;50(3):632-9. doi: 10.1016/j.jvs.2009.06.010.
9. Kozen BG, Kircher SJ, Henao J, Godinez FS, Johnson AS. An Alternative Hemostatic Dressing: Comparison of CELOX, HemCon, and QuikClot. *Acad Emerg Med*. 2008;15(1):74-81. doi: 10.1111/j.1553-2712.2007.00009.x.
10. Morrison JJ, Mountain AJ, Galbraith KA, Clasper JC. Penetrating Pelvic Battlefield Trauma: Internal Use of Chitosan-based Haemostatic Dressings. *Injury*. 2010;41(2):239-41. doi: 10.1016/j.injury.2009.10.023.
11. Waterfield J, Sim J. Clinical Assessment of Pain by the Visual Analogue Scale. *Brit J Ther Rehabil*. 1996;3(2):94-7. doi: 10.12968/bjtr.1996.3.2.14869.
12. Babu SC, Piccorelli GO, Shah PM, Stein JH, Clauss RH. Incidence and Results of Arterial Complications Among 16,350 Patients Undergoing Cardiac Catheterization. *J Vasc Surg*. 1989;10(2):113-6. doi: 10.1067/mva.1989.0100113.
13. Pogorielov M, Kalinkevich O, Deineka V, Garbuzova V, Solodovnik A, Kalinkevich A, et al. Haemostatic Chitosan Coated Gauze: In Vitro Interaction with Human Blood and In-vivo Effectiveness. *Biomater Res*. 2015;19:22. doi: 10.1186/s40824-015-0044-0.
14. Pozza M, Millner RW. Celox (Chitosan) for Haemostasis in Massive Traumatic Bleeding: Experience in Afghanistan. *Eur J Emerg Med*. 2011;18(1):31-3. doi: 10.1097/MEJ.0b013e32833a5ee4.
15. Hejazi F, Hosseinzadeh F, Rad, LI, Bagheri AR, Vahedian M, Damanpak V. Effectiveness of Celox Powder and Standard Dressing in Control of Angiography Location Bleeding. *J Babol Univ Med Sciences*. 2013;15(4):30-6. doi: 10.13140/2.1.1013.8248.
16. Amoozgar H, Abtahi S, Edraki MR, Mohammadi H, Ajami GH., Mehdizadegan N, et al. Effect of Celox® Powder on Initial Hemostasis after Cardiac Catheterization in Pediatric Patients with Congenital Heart Disease: A Prospective Study. *Iran J Pediatr*. 2020;30(4):1-9. doi: 10.5812/ijp.95784.
17. Chamanzari H, Choubdar M, Sharifipour F, Gholami H, Daneshvari F. Comparison of Celox Powder and Conventional Dressing on Hemostasis of Vascular Access Site in Hemodialysis Patients. *Evid Base Care*. 2015;4(4):25-34. doi: 10.22038/EBCJ.2014.3657.
18. Tavakol M, Ashraf S, Brenner SJ. Risks and Complications of Coronary Angiography: A Comprehensive Review. *Glob J Health Sci*. 2012;4(1):65-93. doi: 10.5539/gjhs.v4n1p65.
19. Bektaş O. Femoral Arter Yoluyula Yapılan Koroner Anjiyografi Sonrası Girişim Yerinin Geleneksel Kum Torbası ve Kapama Cihazı Kullanılarak Kapatılmasının Karşılaştırılması. *Aile Hekimliği*. 2017;9(5):1-5.
20. Ercan SL, Karşlı VM, Davutoğlu V, Huraibat A, Oylumlu M, Inanç IH, et al. Comparison of Controlled Pressure Belt -allowing Mobility to Sandbags after Percutaneous Coronary Intervention: Pilot Study. *Turk Kardiyol Dern Ars*. 2013;41(8):699-704. doi: 10.5543/tkda.2013.04742.

