The experience with the Epiclose®-T vascular access closure device: a human study

Epiclose®-T vasküler giriş kapatma cihazi ile tecrübemiz: Bir insan çalışması

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ABSTRACT

Objective: The Epiclose®-T, a novel closure device for arterial access sites, is designed as a double-balloon device that applies direct pressure on the arteriotomy site, allowing natural coagulation and leaving no artificial material behind. We assessed prospectively the initial safety and efficacy of the Epiclose®-T after diagnostic cardiac catheterization, and evaluated patient comfort.
Methods: In our randomized, controlled, prospective study, the study group consisted of 32 patients (17 male, mean age 52.8±11.0 years) treated with Epiclose®-T device. The control group included 39 patients (20 male, mean age 55.5±11.0 years) treated with manual compression.
Results: Hemostasis was achieved successfully in 90.6% of the study group. For the 30-day follow-up, there were no statistically significant differences between the groups in the rate of major and minor complications. No bleeding requiring transfusion was seen in both groups. However, the number of major complications, including large hematoma (0 vs. 1 patient-2.6%) and pseudoaneursym (0 vs. 1 patient-2.6%), occurred more often in the control group. The number of small hematomas was 3 (7.7%) in the compression group and 2 (6.9%) in the Epiclose®-T group. In the failure group (3 patients), body-mass-index was somewhat lower than that of the success group (median - 26 (25-33) kg/m^2 vs. 27 (24-32) kg/m^2, p=0.07). Most patients were satisfied by the Epiclose®-T closure device and grade it as excellent or good.
Conclusion: Hemostasis can be easily and safely achieved by Epiclose®-T device with no significant minor and major complications with patients' total satisfaction. *(Anadolu Kardiyol Derg 2008; 8: 38-42)*
Key words: Arteriotomy, closure device, Epiclose®-T, cardiac catheterization, hemostasis, manual compression

ÖZET

Amaç: Arteryel giriş bölgeleri için yeni bir kapatma cihazı olan Epiclose®-T, arteriyotomi üzerine direk bası uygulayarak geride herhangi yabancı bir madde bırakmaksızın doğal şekilde koagülasyon sağlayacak çift-balonlu bir sistem olarak dizayn edilmiştir. Tanısal kardiyak kateterizasyon sonrası prospektif olarak Epiclose®-T'nin güvenilirliğini, etkinliğini ve hasta konforunu değerlendirdik.
Yöntemler: Randomize, kontrollü, prospektif çalışmamızda, Epiclose®-T ile kanama kontrolü yapılan 32 hasta (17 erkek, ortalama yaş 52.8±11.0 yıl) çalışma grubunu, elle kompresyonla tedavi sağlanan 39 hasta (20 erkek, ortalama yaş 55.5±11.0 yıl) ise kontrol grubunu oluşturdu.
Bulgular: Çalışma grubundaki hastaların %90.6'sında başarılı şekilde hemostaz sağlandı. Otuz günlük takip süresince her iki grup arasında büyük majör ve minör komplikasyonlar açısından istatistiksel olarak bir fark bulunmadı. Her iki grupta da transfüzyonu gerektirecek kanama meydana gelmedi. Bununla beraber, kontrol grubunda hematom (0'a karşılık 1 hasta-%2.6) ve psödoanevrizmayı (0'a karşılık 1 hasta-%2.6) içeren majör komplikasyonlar daha sıklıkla görüldü. Cihazın başarısız olduğu hasta grubunda (3 hasta) vücut-kitle indeksi başarılı gruba göre daha düşüktü (mediyan 26 (25-33) kg/m^2 karşılık 27 (24-32) kg/m^2, p=0.07). Çoğu hasta, cihazı iyi veya mükemmel olarak tanımladılar.
Sonuç: Epiclose®-T, önemli oranda majör veya minör komplikasyona yol açmadan hemostazı kolaylıkla ve güvenli şekilde sağlayan ve hasta memnuniyeti tam olan bir cihazdır. *(Anadolu Kardiyol Derg 2008; 8: 38-42)*
Anahtar kelimeler: Kapatma cihazı, Epiclose®-T, kardiyak kateterizasyon, hemostazis, elle kompresyon

Introduction

Arterial puncture sites after catheterizations may be problematic because of bleeding, hematomas, pseudoaneurysms, and various other complications. Such complications do not only cause discomfort for the patients, but also longer hospital stay, and bleeding requiring blood transfusion. Sometimes, the patients can undergo vascular surgery. According to published various reports, the incidence of vascular access site complications may be as high as 10% with manual compression (1, 2). To facilitate the occlusion of the arterial access site using catheterization procedures, to prevent vascular complications related to manual

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compression, to allow earlier ambulation and discharge, and finally to improve patient's comfort, several types of closure devices have been invented and developed (3, 4). Most devices used for closure of the arterial puncture site involve biological glues or stitches that remain in the patient's body after the procedure is over. In this study, we evaluated the safety and efficacy of the Epiclose®-T closure device, which leaves no artificial material behind.

Methods

Study Population. Patients scheduled for diagnostic cardiac catheterization were eligible for inclusion in our randomized, controlled, prospective study. Exclusion criteria were age <18 years, the sizes greater or smaller than 6 F, several attempts for vascular access, preexisting large hematoma, patients with uncontrolled hypertension (<180 mmHg) and severe peripheral vascular disease. At the end of each diagnostic cardiac catheterization procedure, if the patients did not meet any of the exclusion criteria, the patients were randomized consecutively to the two groups: the Epiclose®-T group – 32 patients (17 male, mean age 52.8±11.0 years) and manual compression group (control group) – 39 patients (20 male, mean age 55.5±11.0 years).

The study protocol was approved by Institutional Ethic Committee. All patients gave written informed consent.

Baseline demographic characteristics of two groups are listed in Table 1.

Device Description and Procedure: In this study, we used the Epiclose®-T (CardioDex Ltd., Tirat HaCarmel, Israel). The Epiclose®-T is a double balloon closure device that applies direct pressure on the arteriotomy allowing natural coagulation to occur leaving no artificial material behind (Fig. 1). The Epiclose®-T was used to close the femoral artery puncture site after completion of diagnostic catheterization using 6 Fr introducer sheaths via the femoral artery.

The angiography through femoral arteriotomy was performed to visualize the femoral artery of the patients. Subsequently, the device was deployed into the artery through the introducer sheath. It's distal end was positioned near the internal puncture site by an anchor balloon. Once localized, the hemostasis balloon was inflated directly external to the vessel wall. The final availability and positions of inflated balloons was evaluated in two angiographic views (Fig. 2). At this stage, the patient was transferred from the Cath-Lab bed to the post-catheterization follow-up unit bed. Thereafter, the physician deflated the anchor balloon and pulled it back into the distal end of the shaft, while the hemostasis balloon remained pressing against the puncture site. At the end of the hemostasis-waiting period, the hemostasis balloon was slowly deflated and the Epiclose®-T was carefully removed from the patients' groin (Fig. 3). But, if any oozing occurs just after deflation of the hemostasis balloon it was inflated again for the period of additional 10 minutes. In all the cases, elastic pressure bandage was applied on the groin area after the Epiclose®-T removal.

In the manual compression group, hemostatic control of arterial puncture sites was achieved with manual compression performed in the catheterization laboratory holding area by cardiology fellows. After stopping the bleeding, elastic pressure bandage was applied on the groin area. A sand bag weighted 2 kg was placed over the access site for two hours. The patients were asked to remain immobile under close observation for several hours after the procedure.

The patients in both groups were discharged on the procedure day.

The physicians who planned to place Epiclose®-T into the femoral artery had gained experience on the artificial designed device mimicking a groin area with femoral artery. After getting experience to place the new device, the physicians went through to perform Epiclose®-T to the patients.

Data Acquisition: Patients were followed up during in-hospital period for: (1) presence of active bleeding, (2) need for additional manual compression, if any, (3) hematoma diameter in centimeters, (4) presence of a bruit or a pulsatile mass, (5) post-deployment pain, (6) examination of arterial pulses, including femoral artery, popliteal artery and posterior tibial artery (7) time to ambulation. Additionally, patient satisfaction was evaluated by a questionnaire using a scale grading from 1 to 6 (1=insufficient, 6=excellent) prior to the discharge.

The follow-up period evaluation for safety and effectiveness was performed just prior to patient ambulation, at patient discharge, 48 hours post discharge, and after 7 and 30 days. The ambulation and discharge follow-up involved examination of the access site and peripheral pulse; the 48 hours and 7 days follow-ups were performed with a telephone interview. Moreover, the 30 days follow-up included physical examination

Table 1. Baseline demographic characteristics for two groups

Variables	Manual compression group (n=39)	Epiclose®-T group (n=32)	p *
Male, n (%)	20 (51)	17 (53)	NS
Female, n (%)	19 (49)	15 (47)	NS
Age, years	55.5 ± 11.0	52.8 ± 11.0	NS
Body mass index, kg/m^2	28.0 ± 1.4	28.4 ± 1.6	NS
Antiplatelet treatment, n (%)	24 (62)	20 (63)	NS
Hypertension, n (%)	25 (64)	20(63)	NS
Femoral artery diameter, cm	11.3 ± 2.0	11.1 ± 2.0	NS
Catheterization time, min	8.1 ± 3.0	8.3 ± 3.0	NS

Data are represented as proportions, percentages and mean±SD values
*- Chi-square test and unpaired t test
NS - non-significant

with palpation and assessment of the access site and peripheral pulses, and late complications such as false aneurysm and arteriovenous fistula.

Study Endpoints and Definitions: The primary endpoints were successful technical deployment of the device and achievement of hemostasis. Successful vascular device closure was defined as complete arterial hemostasis without bleeding after placement of closure device and no need for additional manual compression. If bleeding occurs after deployment, it was defined as failure. Therefore, the study group was divided into the subgroups as success and failure.

The secondary endpoints were major and minor complications during the hospitalization period and 30-days after the procedure.

The following concepts were defined according with previously published studies (5, 6). Major complications are defined as large hematoma, pseudoaneurysm, major bleeding requiring transfusion, any vascular surgery, loss of distal pulses, and groin infections. Large hematoma is defined as accumulation of subcutaneous blood >2 cm in diameter according to subcutaneous induration. Pseudoaneurysm is defined as a communication between an extraluminary cavity and the femoral artery with a back-and-forth flow pattern demonstrated by color Doppler imaging. Infection is defined as erythema and pain around the arterial puncture site associated with fever and elevated white blood cell count requiring intravenous antibiotic treatment. Minor complications are defined as small hematoma. Finally, small hematoma is defined as accumulation of subcutaneous blood <2 cm in diameter according to subcutaneous induration.

Statistical Analysis: Statistical tests were performed using SPSS for Windows version 10.0 software, (Chicago, IL, USA). Continuous variables are presented as means ± SD and categorical variables as numbers and percentages. Comparisons between continuous variables were made using the non-paired student's t-test and Mann Whitney U test. The Chi-square test was used to compare categorical variables. Statistical significance was defined as $p < 0.05$.

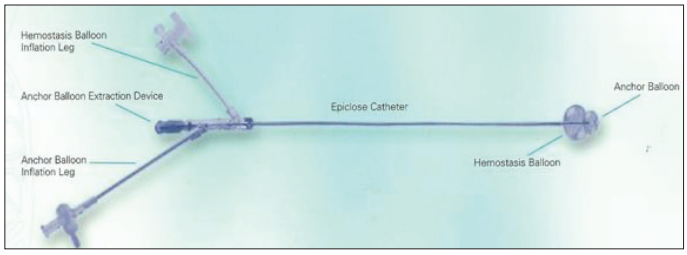

Figure 1. Epiclose®-T design (Images provided by CardioDex Ltd., Tirat HaCarmel, Israel)

Results

Demographics for the two patient groups were comparable (Table 1). There were no statistical differences in terms of gender, age, body mass index, comorbidities, and duration of procedure. Femoral angiograms of all cases showed that there was no peripheral arterial disease and puncture points were proximal to femoral artery bifurcation but distal to inguinal ligament. There was no significant difference in terms of average femoral artery diameter between the two groups. Successful hemostasis was achieved in 29 of 32 patients (90.6%) for Epiclose®-T group. Deployment failure occurred in two patients due to unavailable position of hemostasis balloon and in one patient due to hemostasis balloon burst. As a result, in all three patients (9.4%), hemostasis was achieved by additional manual compression without any complication. Baseline characteristics for Epiclose®-T cases with success or failure are shown in Table 2.

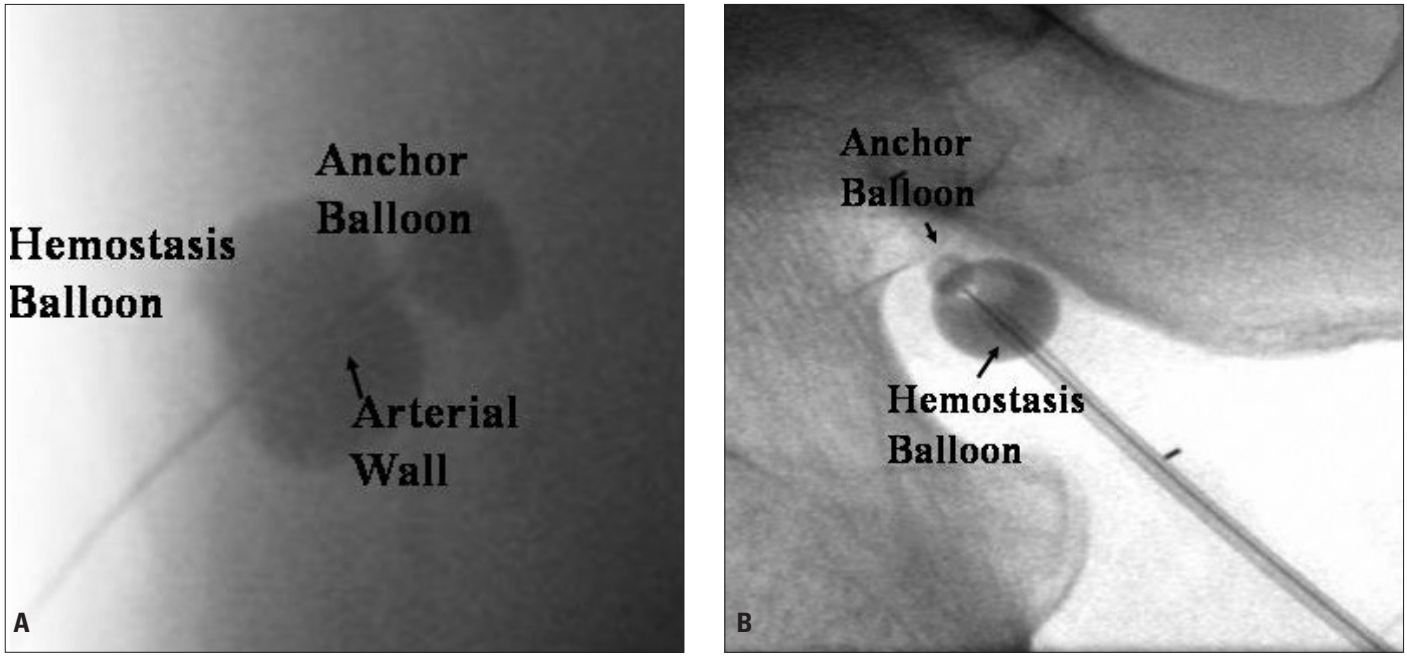

Figure 2. (a) Anchor and hemostasis balloons viewed at postero-anterior projections at the access site. (b) Lateral projection was also viewed for the alignment of the balloons to check whether the balloons were placed in the correct position or not.

Procedural time for Epiclose®-T took less than 5 minutes in cardiac catheterization laboratory, including femoral angiography. Average deployment time, the time interval between anchor balloon deflation time and time interval when hemostasis balloon remained inflated, was measured as 62±32 min. Time to ambulation was 3.17±0.24 hours for the Epiclose®-T group and 3.21±0.24 hours for the compression group. Time to discharge was 4.44±0.45 hours for the Epiclose®-T group, and 4.41±0.43 hours for the manual compression group. There was no statistically significant differences between two groups in the time to ambulation and time to discharge (p>0.05 for both).

No infection and bleeding requiring transfusion were seen in both groups. No patient underwent vascular surgery. The number of large hematomas, and pseudoaneurysms occurred more often in the manual compression group than that of the Epiclose®-T group: 1 (2.6%) in the compression group, 0 (0%) in the Epiclose®-T group for both large hematoma and pseudoaneurysm. Of the minor complications, the number of small hematomas was 3 (7.7%) in the compression group and 2 (6.9%) in the Epiclose®-T group.

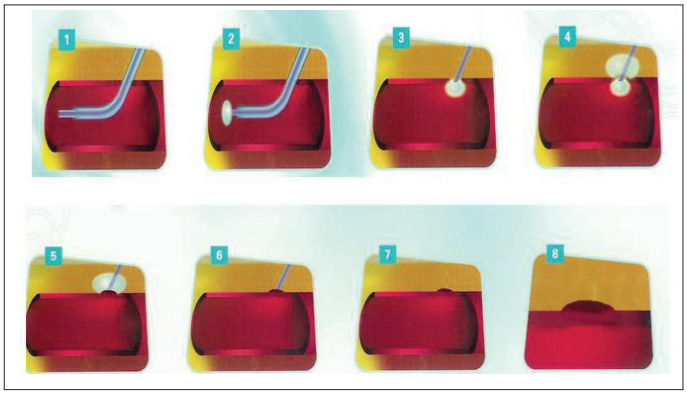

Figure 3. Epiclose®-T application scheme (1) Epiclose is inserted into the artery via the existing introducer sheath. 2. Anchor balloon is inflated inside the artery (3) and withdrawn to inner puncture site, forming a block (Introducer sheath is removed). 4. Hemostasis balloon is inflated directly on outer puncture. 5. Anchor balloon is deflated and removed, stimulating coagulation on the outer puncture. 6. Hemostasis balloon is deflated upon achieving closure. 7. Epiclose®-T is retracted from body. 8. Artery is sealed naturally.
(Images provided by CardioDex Ltd., Tirat HaCarmel, Israel)

Table 2. Comparison between failure and success subgroups of patients treated with Epiclose®-T device

Variables	Success (n=29)	Failure (n=3)	P*
Male, n(%)	16 (55.2)	2 (66.6)	NS
Female, n(%)	13 (44.8)	1 (33.4)	NS
Antiplatelet therapy, n(%)	19 (65.5)	2 (66.6)	NS
Platelet count (x1000)	235 (210-260)	230 (215-275)	NS
Prothrombin time, sec	13.0 (13-16)	13.5 (13.5-16.5)	NS
Systolic blood pressure, mmHg	138 (135-155)	140 (130-160)	NS
Body mass index, kg/m²	27 (24-32)	26 (25-33)	0.07

Data are represented as proportions, percentages and median, minimum-maximum values
*- Chi-square test and Mann - Whitney U test
NS- non-significant

Comparisons of success and failure subgroups (Table 2) showed that body-mass-index of the failure group was somewhat lower than that of the success group (median 26 (25-33) kg/m² vs. 27 (24-32) kg/m², p=0.07).

Of 29 patients on whom successful deployment was performed, 22 (75.9%) patients evaluated the procedure as excellent (score 6) and 5 (17.2%) patients as good (score 5). Hence, the number of patients reported total satisfaction was 27 (93.1 %).

Discussion

In this study, the results have shown that the Epiclose®-T closure device is safe and efficient, and its application is easy.

The most frustrating period after cardiac catheterization for both patient and physician can be accepted as manual compression period (7). Several types of closure devices were developed in order to eliminate the discomfort and complications of this frustrating period. Principal purpose of closure devices is to manage hemostasis efficiently. In the present study, we achieved hemostasis control by Epiclose®-T with a success rate of 90.6%. This is a highly acceptable rate. Moreover, in the failure cases, hemostasis was achieved immediately by manual compression with a light manual compression less than 3 minutes; and no complication occurred in those cases. In our study, time to ambulation and time to discharge were similar for the two groups. However, the patients in the device group did not feel pain as much as in manual compression group, and defined the closure procedure as excellent or good. Moreover, easy deployment of the device let the patients to be transferred to their beds. This easy deployment prevented the personnel from spending a lot of time for one patient. During the deployment time, the patients remained in their rooms with no stress and one person was able to follow up many patients.

One of the major problematic issues in the closure device applications is the length of learning curve (8). Even though, Epiclose®-T application is markedly easy; only after physician's learning curve reached the best lend with several attempts on artificial device, physicians operated on the patients.

Current closure devices leave behind artificial materials after application, such as sutures, collagen, and thrombin in the femoral artery of the patient (9-12). The most important advantage of this device is that there left no artificial material behind. After anchor balloon is deflated, little amount of blood comes into the special area under hemostasis balloon and this process led the natural coagulation cascade stop the bleeding. After pulling out the device, no foreign material was left in the body. However, current devices, which leave artificial material behind, can lead to several complications related to this property. Femoral artery stenosis and groin infection can be observed in patients treated with suture-mediated closure device; thrombin-based closure device can cause rises in serum C-reactive protein and amyloid-A levels (13-16). We consider that these kinds of complications do not occur after Epiclose®-T procedure because of absence of remaining material behind after pulling it out.

Recent trials did not show clearly whether closure devices could decrease local vascular complications (17, 18). Moreover, in a study by Kahn et al. (6), more local vascular complications occurred in patients treated with closure device than in those treated with manual compression. In our study, we did not notice

any significant difference in the rate of local vascular complication between the device group and manual compression group. Of the patients receiving manual compression, one patient had large hematoma and another one had pseudoaneursym. Pseudoaneurysm was managed with ultrasound guidance. No pseudoaneurysmal complication was observed in the device group. Large trials related to Epiclose®-T will allow to reach better results in a conclusion about complications.

Subgroup analysis in the patients treated with Epiclose®-T revealed that there were no differences between the failure and success subgroups in gender, antiplatelet therapy, platelet number, prothrombin time, systolic blood pressure, and body mass index. However, body mass index was lower in the failure group than that of the success group. This can be explained by the fact that hemostasis balloon needs enough soft tissue in the groin for pressing the femoral artery efficiently and achieving hemostasis successfully. Hemostasis balloon can lose its correct position if there is not enough tissue for supporting the balloon. Hence, the balloon cannot achieve hemostasis. Current data suggests that Epiclose®-T is advantageous in the patient group for whom there can be a difficulty for manual compression because of higher body mass index.

Study Limitations

The number of patients included in this study was low. This prevents us to reach conclusive results. We included only the patients undergoing diagnostic coronary angiography with 6 F sheath. Hence, it is necessary to conduct another study with larger sheath in the patients undergoing coronary interventions. According to our hospital policy, we do not use heparin in diagnostic procedures. Since we did not use heparin in both groups, this prevents us from evaluating the complication rate exactly and also to reach an exact conclusion. It is not clear if this study can be a reference for the institutes in which heparin is being routinely used in diagnostic angiography.

Conclusion

As a conclusion, Epiclose®-T is a safe and effective closure device, which can be easily applied through the sheath during coronary angiography without any bleeding. One can consider that Epiclose®-T device can be a comfortable and safe alternative to manual compression; and also it does not leave material behind in the body. In our study, the success group had higher body mass index than the failure group. This result came from the adipose tissue for the need of hemostasis balloon. Epiclose®-T can be useful in the patients with higher body mass index, the general problematic group for the hemostasis after procedure compression.

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Disclosure

Authors (HK, Aİ, CB, TÇ, SK, BA, EI) declare no financial conflict of interest with the firm, producer and vendor of the device

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References

1. Nasser TK, Mohler ER III, Wilesky RL, Hathaway DR. Peripheral vascular complications following coronary interventional procedures. Clin Cardiol 1995; 18: 609-14.
2. Skillman JJ, Kim D, Baim DS. Vascular complications of percutaneous femoral cardiac interventions: incidence and operative repair. Arch Surg 1988; 123: 1207-12.
3. Kussmaul WG, Buchbinder M, Whitlow P, Aker UT, Heuser RR, King SB, et al. Rapid arterial hemostasis after cardiac catheterization and percutaneous transluminal angioplasty: results of a randomized trial of a novel homeostatic device. J Am Coll Cardiol 1995; 25: 1685-92.
4. Sanborn TA, Gibbs HH, Brinker JA, Knopf WD, Kosinski EJ, Roubin GS. A multicenter randomized trial comparing a percutaneous collagen hemostasis device with conventional manual compression after diagnostic angiography and angioplasty. J Am Coll Cardiol 1993; 22: 1272-9.
5. Eggebrecht H, Haude M, von Birgelen C, Woertgen U, Schmermund A, Baumgart D, et al. Early experience with the 6 French Angia-SealTM: Immediate closure of femoral puncture sites after diagnostic and interventional coronary procedures. Cathet Cardiovasc Intervent 2001; 53: 437-42.
6. Kahn ZM, Kumar M, Hollander G, Frankel R. Safety and efficacy of the Perclose suture-mediated closure device after diagnostic and interventional catheterizations in a large consecutive population. Cathet Cardiovasc Intervent 2002; 55: 8-13.
7. Di Mario C. Closure devices: Case closed? Cathet Cardiovasc Intervent 2002; 55: 14-15.
8. Turi ZG. It's time to seal every artery but …comparing apples and oranges in the vascular sealing literature. Cathet Cardiovasc Intervent 2001; 53: 443-4.
9. Kapadia SR, Raymond R, Knopf WD, Jenkins S, Chapekis A, Ansel G, et al. The 6 Fr AngioSeal arterial closure device: results from a multicenter prospective registry. Am J Cardiol 2001; 87: 789-91.
10. Baim DS, Knopf WD, Hinohara T, Schwarten DE, Schatz RA, Pinkerton CA, et al. Suture-mediated closure of the femoral access site after cardiac catheterization: results of the suture to ambulate and discharge (STAND I and STAND II) trials. Am J Cardiol 2000; 85: 864-9.
11. Mooney MR, Ellis SG, Gershony G, Yehyawi KJ, Kummer B, Lowrie M. Immediate –sealing of arterial puncture sites after cardiac catheterization and coronary interventions: initial U.S. feasibility trial using the Duett vascular closure device. Cathet Cardiovasc Intervent 2000; 50: 96-102.
12. Carere RG, Webb JG, Ahmed T, Dodek AA. Initial experience using Prostar: a new device for percutaneous suture-mediated closure of arterial puncture sites. Cathet Cardiovasc Diagn 1996; 37: 367-72.
13. Gemmete JJ, Dasika N, Forauer AR, Cho K, Williams DM. Successful angioplasty of a superficial femoral artery stenosis caused by a suture-mediated device. Cardiovasc Intervent Radiol 2003; 26: 410-2.
14. Yamamoto N, Koyano K, Azuma M, Ochiai H, Kashiwabara T. Groin infection caused by a percutaneous femoral artery closure device: Report of a case. Surg Today 2003; 33: 801-4.
15. Whitton Hollis H Jr, Rehring TF. Femoral endarteritis associated with percutaneous suture closure: new technology, challenging complications. J Vasc Surg 2003; 38: 83-7.
16. Saleh N, Olausson A, Nilsson T, Hansson LO, Tornvall P. Comparison of effects of a thrombin-based femoral artery closure device with those of a mechanical compression device on serum C-reactive protein and amyloid A after percutaneous coronary intervention. Am J Cardiol 2003; 92: 324-327.
17. Silber S. Hemostasis success rates and local complications with collagen after femoral access for cardiac catheterization: analysis of 6007 published cases. Am Heart J 1998; 135: 152-6.
18. Shrake KL. Comparison of major complication rates associated with four methods of arterial closure. Am J Cardiol 2000; 85: 1024-5.