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ORIGINAL ARTICLE

Blood Indices and CHA_2DS_2VASC Score in Patients who Underwent Manual Compression Repair for Femoral Artery Pseudoaneurysms

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Abstract

Introduction: Manual compression repair (MCR) for femoral artery pseudoaneurysm (FAP) is an earlier and well-known non-surgical procedure. Relationship with the success of MCR and CHA_2DS_2VASC score, neutrophil to lymphocyte ratio (NLR), platelet to lymphocyte ratio (PLR), mean platelet volume (MPV), and red-cell distribution width (RDW) were unknown.

Methods: We investigated 17,391 catheterization procedures from April 2009 to December 2015. 118 FAPs were suitable for MCR. Age, sex, concomitant vascular disease, and laboratory findings were compared between patients who have non-thrombosed pseudoaneurysm (NTP) and those who have thrombosed pseudoaneurysm (TP) after one or more MCR attempts.

Results: 81 FAPs were successfully sealed after one or more MCR attempts. The success rate was 38.9% at the first attempt and 68.6% at the third attempt. The dual antiplatelet usage rate was high (68.5%) in the study population. FAP dimensions, fistula tract width, or length did not differ between groups. Patients who have sealed pseudoaneurysm have a higher CHA_2DS_2VASC score (2 [1–3.5] vs. 3 [2–4], p=0.019). There is no difference in terms of NLR, PLR, RDW, and MPV. Patients in TP group were found to have a thicker left ventricular posterior wall (PW) on transthoracic echocardiogram (1.0±0.2 vs. 1.1±0.2, p=0.047).

Discussion and Conclusion: MCR may be considered as a therapeutic option for FAPs. It is well-known, a practical procedure without the need for costly equipment. MCR treatment was successful at older ages, high CHA_2DS_2VASC score, and a thicker PW on transthoracic echocardiography. Multiple attempts should be used for clinical success.

Keywords: Femoral artery; manual compression repair; pseudoaneurysm.

The femoral artery pseudoaneurysm (FAP) is a well-known complication of cardiac or endovascular catheterization procedures. The reported incidence of FAP ranges from 0.05% to 2% in diagnostic procedures and 2% to 6% in therapeutic procedures[1]. Manual compression repair (MCR), ultrasound-guided compression repair (UGCR), and ultrasound-guided thrombin injection (UGTI) commonly used as non-surgical procedures. MCR is an earlier technique that is simple and practical.

CHA_2DS_2VASC score is a novel risk predictor of thromboembolic stroke risks in patients with atrial fibrillation[2]. It can also reflect an increased risk for venous thromboembolism, acute stent thrombosis, and mechanical mitral valve thrombosis[3-5]. Its effect on thrombosis of FAP after MCR is unknown. Neutrophil to lymphocyte ratio (NLR) and platelet to lymphocyte ratio (PLR) have investigated in patients with coronary artery disease (CAD), aortic aneurysm, major vascular surgery, and carotid disease[6-10]. Red cell distribu-

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tion width (RDW) and mean platelet volume (MPV) were related to aortic aneurysm and CAD[9,11-15]. These hematological indices may reflect the micro-inflammatory load or tendency to thrombosis. Their effects on thrombosis of FAP are also unknown.

Our purpose is to investigate the relationship between these novel risk factors and the success of MCR for FAP management.

Materials and Methods

Patient Population

We retrospectively analyzed data from 17,391 consecutive patients who had undergone cardiac diagnostic or interventional procedures through femoral artery access between April 2009 and December 2015 in our institution. The hospital records of patients reviewed to gather information for age, sex, type of procedure (diagnostic or interventional), cardiovascular risk factors (presence of hypertension, diabetes, or hyperlipidemia), anticoagulation state, dual antiplatelet usage after the procedure, presence of cerebrovascular or peripheral artery disease, and emergency of the procedure (acute coronary event or elective). Patients with arterial blood pressure above 140 mmHg for systolic and/or 90 mmHg for diastolic at two separate occasions or receiving antihypertensive medication considered to be hypertension. Diabetes mellitus defined as a fasting blood glucose level above 126 mg/dl or treatment with anti-diabetic drugs or insulin. Total cholesterol >200 mg/dl, LDL-cholesterol >130 mg/dl, or receiving lipid-lowering drugs defined as hyperlipidemia. CHA_2DS_2VASC score calculated according to the presence of risk factors. Hypertension, diabetes, congestive heart failure, vascular disease (history of myocardial infarction or peripheric vascular disease), and female sex scored 1 point for each. If the patient's age is 65–74, then 1 point; if the patient's age is 75 or above, then 2 points were added. If there is a history of any previous stroke, transient ischemic attack, or thromboembolism, 2 points added[2]. Cerebrovascular disease, renal and hepatic disease, and chronic obstructive pulmonary disease (COPD) noted.

Laboratory Findings

Blood samples were taken on admission. Hematologic parameters were assessed by automatic blood counter (A Sysmec XE-2100, Symex, Kobe, Japan). Serum creatinine and lipid profiles were measured using an auto-analyzer (Roche Diagnostic Modular Systems, Tokyo, Japan). MPV and RDW values were noted, NLR and PLR values were calculated.

Catheterization Procedures

Different interventional cardiologists carried out the puncture of the femoral artery with sheath sizes of 6 French (F) for diagnostic and 6F or 7F for therapeutic procedures. Patients with an acute coronary syndrome (ACS) were pretreated with a loading dose of 300 mg for non-ST elevation myocardial infarction or 600 mg for ST elevation myocardial infarction clopidogrel and 300 mg acetylsalicylic acid were used if the patient was not in treatment with these antiplatelet agents. A bolus of 100 international units (IU) of heparin (Max:10.000 IU) per kilogram body weight was administered for percutaneous coronary interventions. The arterial sheath was removed immediately, after diagnostic procedures and after 4-h after the procedure after interventional procedures. Manual compression of the puncture site was carried out for ≥10 min or more until hemostasis was achieved. A compression bandage was applied, and the patients had a bed-rest for 6 h. No closure devices were used throughout the study.

Duplex Ultrasound Scannings and Compression Repair Procedure

Patients who diagnosed FAP were assessed for the suitability of MCR. In unstable patients (presence of severe pain, expanding hematoma with or without nerve compression, necrosis of skin, and infection in the groin), surgical repair of FAP was performed. Otherwise, MCR was used. The compression was directed to the area of maximal pulsation and was increased until the femoral thrill or the pathological pulsation of the hematoma disappeared. When precise localization was difficult because of absent clinical signs, compression was directed to the estimated puncture area of the artery. The pressure was applied until femoral bruit or the pulsation of the hematoma had permanently disappeared, but not longer than 60 min. Analgesics were given when needed. Then, a compression bandage was applied for 24 h. After the MCR attempt, a repeat duplex ultrasound was performed the next day. If FAP has thrombosed, the procedure ended. Else, the patient was re-evaluated. If the patient was stable, another attempt of MCR was performed. A maximum of three attempts of MCR was conducted. If the patient became unstable, surgical repair was performed. After all MCR attempts, patients with thrombosed pseudoaneurysm (TP) were considered as one group, non-TP (NTP) was considered as the other one. At the end of the study, all of the NTP patients were referred to surgery for repair.

Statistical Analysis

Statistical analysis performed using SPSS 20.0 for Windows (SPSS, IBM Corp.). Descriptive statistics generated using means, medians, ranges and standard deviations for continuous variables, and percentages were taken for categorical variables. The Chi-square test or Fisher exact tests were used to compare percentages. Independent samples Student's t-test and Mann–Whitney U test were performed for comparing values based on their distribution properties. The Mann–Whitney U test was also used for the comparison of ordinal variables. The logistic regression test was used to find independent predictors. Statistical significance was assessed at the 5% (p=0.05) level.

The study was approved by our Clinical Research Ethics Committee of Bagcilar Training and Research Hospital on August 17, 2017 as a 2017–601 protocol number. Informed consent has been obtained from patients. The study protocol complied with the Declaration of Helsinki.

Results

Between April 2009 and December 2015, a total of 155 FAPs detected. Thirty-seven FAPs (23.9%) of these did not receive MCR. Because 18 of these FAPs, (11.6%) found to be thrombosed with repeat duplex ultrasound at the time of admission just before the compression attempt and 19 of FAPs (12.2%) were in unstable patients. They referred to surgical care without any MCR attempts. One hundred and eighteen FAPs used for the analysis.

Sixty-three FAPs diagnosed in males (53.4%). Hypertension was the most common risk factor (77.1%). Diabetes (22.9%) and hyperlipidemia (41.5%) were less prevalent. Ejection fraction (EF%) on transthoracic echocardiography (TTE) was good (51±11%). Comorbid risk factors, cerebrovascular disease, renal and hepatic disease, and COPD were low.

More than half of FAPs managed with 1-time MCR. Other patients received multiple attempts. The overall success of MCR was 38.9% on the first attempt, 55% at the second attempt, reaching to 68.6% on the third attempt (Table 1).

Table 1. Success rates of MCR attempts

Success of MCR	n (%)	Cumulative success (%)
1. MCR	67 (56.8)	38.9
2. MCR	27 (22.9)	55
3. MCR	24 (20.3)	68.6

MCR: Manual compression repair.

Even in multi-lobar FAPs, 11 (73%) of them thrombosed with MCR in total. The mean largest diameter of FAP was 29±14 mm. Thirteen FAPs (8.3%) had two, 2 FAPs (1.2%) had four lobes. One patient (0.6%) had a concomitant AV fistula. The dual antiplatelet usage ratio of the study population was 68.5%. Five patients (4.2%) were on warfarin therapy, and they had stable CAD. All of them received bridging therapy with enoxaparin preoperatively.

There were 37 patients (19 male [51.4%]; mean age 59.4±12.6 years) in NTP group and 81 patients (44 male [54.3%]; age of 65±13.5 years) in TP group. Patients in the NTP group were younger (p=0.037). However, no gender dominance observed between groups. Cardiac risk factors and FAP characteristics were similar. RDW, MPV, platelet (PLT) count, PLR, and NLR were also not different between groups.

The TP group had a higher CHA_2DS_2VASC (p=0.019) score (Fig 1). Interestingly, this group also has a thicker posterior wall (PW) on TTE (p=0.047) (Table 2). Both these two variables independently predicted thrombosis of FAP in the logistic regression analysis (Table 3) . Using a cutoff level of CHA_2DS_2VASC score >2 has 66.6% sensitivity and 59.4% specificity (area under curve [AUC]: 0.673 [95 %CI: 0.491–0.823, p<0.001]) and PW >0.9 criteria has 86.1% sensitivity and 39.3% specificity for predicting thrombosis of FAP (AUC: 0.700 [95% CI: 0.519–0.844, p<0.001]) in the receiver-operating characteristic analysis (Fig. 2).

Discussion

Risk factors for developing FAP include body mass index (BMI), age, gender, the extent of arterial calcification, pre-procedural platelet counts, emergency of the procedure, diagnostic versus interventional procedure, the localization of the arterial cannulation, the size of the arterial sheath, combined arterial or venous access, procedural antiplatelet, and anticoagulant usage[16]. A low puncture level below the common femoral artery (CFA) is an impor-

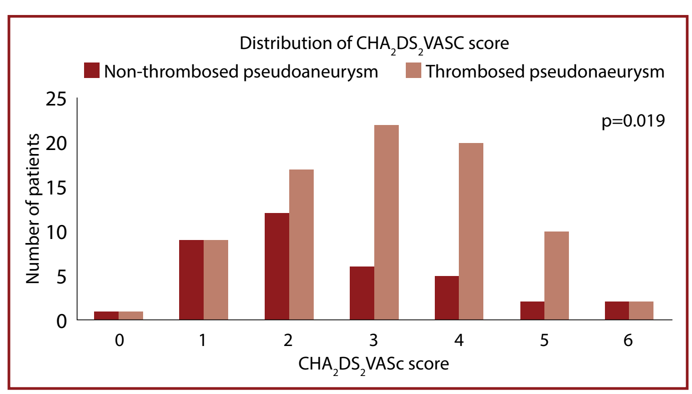

Figure 1. CHA_2DS_2VASc scores of groups.

Table 2. Group characteristics

	NTP group (n=37)	TP group (n=81)	p
Age (years)	59±13	65±14	0.037
Gender	19 male (51.4%)	44 male (54.3%)	0.765
Hypertension	27 (78.4%)	58 (76.5%)	0.826
Diabetes	11 (29.7%)	16 (19.8%)	0.246
Hyperlipidemia	12 (35.1%)	32 (44.4%)	0.422
History of CAD	2 (5.4%)	16 (19.8%)	0.054
COPD	6 (16.2%)	11 (13.6%)	0.705
Renal disease (MDRD < 60 cc/min)	10 (27%)	25 (30.9%)	0.672
Ischemic cerebrovascular disease	1 (2.7%)	6 (7.4%)	0.316
Coronary artery disease			
STEMI	7 (18.9%)	19 (23.5%)	0.970
ACS/NSTEMI	14 (37.8%)	24 (29.6%)	
Stable CAD	16 (43.3%)	38 (46.9%)	
Treatment for CAD			
Medical	19 (51.4%)	37 (45.7%)	0.596
PCI	15 (40.5%)	37 (45.7%)	
CABG	3 (8.1%)	7 (8.6%)	
EF (%)	51±11	51±12	0.743
IVS (cm)	1.1±0.2	1.2±0.2	0.341
PW (cm)	1.0±0.2	1.1±0.2	0.047
Warfarin usage	3 (8.1%)	2 (2.4%)	0.305
DAPT usage	25 (67.6%)	49 (60.5%)	0.283
Days to FAP diagnosis	6±7	5±6	0.819
Width of fistula tract (mm)*	6 (3.5 –12)	14 (6.65–24.5)	0.131
Length of fistula tract (mm)*	3.5 (2.75 –4)	3 (2–3.38)	0.199
Max. Diam. of the FAP (mm)*	25 (18–39.5)	27.5 (17–36)	0.932
Creatinine (mg/dL)	1.07±0.8	1.16 ±0.8	0.384
MDRD GFR (ml/min)	82.8±33.8	74.8±28.7	0.118
Hemoglobin (gr/dL)	12.7±2.0	12.8±2.2	0.761
WBC ($10^3/mm^3$)	8.71±3.36	9.31±2.91	0.178
NEU ($10^3/mm^3$)	5.98±2.91	6.12±2.64	0.843
LYM ($10^3/mm^3$)	1.93±1.03	2.2±0.9	0.071
PLT ($10^3/mm^3$)	275±150	253±80	0.290
RDW (%)	13.9±1.5	13.9±1.9	0.922
MPV (fL)	8.6±1.9	8.6±1.6	0.836
NLR*	3.11 (2.06–4.1)	2.81 (2.05–3.65)	0.590
PLR*	131.21 (110.5–182.9)	116 (88.3–173.43)	0.092
CHA_2DS_2VASc*	2 (1–3.5)	3 (2–4)	0.019

Data given as mean±standard deviation, or %. Data marked with an *(asterisks) given as median and interquartile range. CAD: Coronary artery disease, COPD: Chronic obstructive pulmonary disease, PCI: Percutaneous coronary intervention, CABG: Coronary artery bypass graft, FAP: Femoral artery pseudoaneurysm, DAPT: Dual antiplatelet therapy, PLT: Platelet count, MDRD: Modification of diet in renal disease, GFR: Glomerular filtration rate, EF: Ejection fraction, IVS: Interventricular septum, LYM: Lymphocytes, Max. Diam. of the FAP: Maximum diameter of the femoral pseudoaneurysm, NEU: Neutrophil count, NLR: Neutrophil to lymphocyte rate, NTP: Non-thrombosed pseudoaneurysm, RDW: Red cell distribution width, MPV: Mean platelet volume, PLR: Platelet to lymphocyte rate, PW: Posterior wall thickness, TP: Thrombosed pseudoaneurysm, WBC: White blood cell count.

tant risk factor for developing FAP[17]. The presence of pulsatile mass is a very helpful finding for clinical diagnosis of FAP[16,18]. The best modality to diagnose FAP is duplex ultrasound imaging.

An early study by Kresowick et al.[19] found all FAPs to be spontaneously thrombosed after 4 weeks of observation in percutaneous transluminal coronary angioplasty patients. FAP cavity size ranges were 1.3–3.5 cm, and that study

Table 3. Logistic regression analysis

	B	Sig.	Exp(B)	95.0% C.I.for EXP(B)	
				Lower	Upper
PW	3.38	0.039	2.95	1.17	7.93
CHA_2DS_2VASc	0.53	0.012	1.70	1.12	2.55

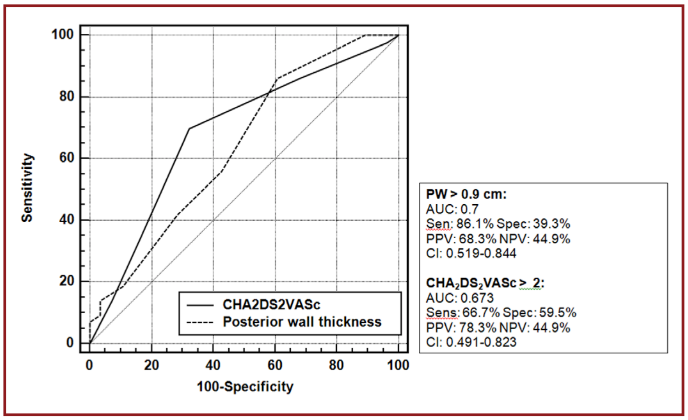

Figure 2. ROC curve.

included only seven patients. A study with a FAP size of <3 cm, closure rate was reported as 87% at a mean of 23 days[20]. Failure of spontaneous thrombosis found to be related closely with the use of anticoagulation status and antiplatelet medication[21]. One recent study found that 44% of patients on dual antiplatelet therapy who were initially treated by observation only ended up needing the other therapy[2].

Low volume of flow to pseudoaneurysm, neck length of FAP (>0.9 mm), or increased flow velocity on the communicative tract after compression are good prognostic signs. However, these findings were observed in very small-scale studies[17,22]. Another study that included 147 FAP patients showed that the spontaneous closure rate of FAPs was 86% with a mean of 23 days from diagnosis. No MCR or UGCR was performed. However, this study excluded patients who needed anticoagulation and who had FAPs greater than 3 cm[23]. The depth of arterial break and the size of FAP predicted success in a study with UGCR treatment compression. The success rate of UGCR was 81%[24]. UGCR and MCR were compared in another study with 168 patients. After a total of three attempts of compression, only one patient in each group needed surgery. The reason for the high success rate could be the reduced use of anticoagulants. They stated that MCR allows a less fatiguing and more comfortable posture for the operator and can be performed in any condition without the prolonged use of expensive equipment[25]. Theiss et al.[26] studied MCR success rates in 86 patients. MCR was succeeded in 74 patients (87%). Of these, 74% were treated at the first attempt, while 16% were cured at the second and 10% were cured at the third attempt. The success rate was lower with aspirin and antithrombotic medication usage. No major complications were observed. In a study that contained FAPs developed after 6–8F catheters usage, the success rate of UGCR was 63%[27]. However, only the usage of compression bandage had a 32% success rate[28]. MCR and UGCR were used in a study with 168 FAPs. Failure was twice as likely with UGCR in comparison to a standard compression (4.7% vs. 9.4%)[25]. Ultrasound-guided hematoma aspiration and UGCR were studied in 32 patients and reached a 96.9% success rate. All patients were on anticoagulation or at least one antiplatelet before aspiration. The only failure was in a patient with a coexisting arteriovenous (AV) fistula[29].

Other techniques for the management of FAP were duplex-guided thrombin injection (DGTI), saline injection, covered stent implantation, and coil placement[17]. DGTI is a high success rate procedure, but it has limited value on FAPs which smaller than 2.5 cm and short necks[30]. Large hematomas with skin necrosis, expanding FAPs, infected FAPs, nerve compression, and severe pain with neuropraxia are requires surgical decompression of hematoma and repair.

In our study group, lower rates of success for FAP thrombosis were seen. A couple of factors can affect this result. First, the usage of dual antiplatelet medications after the procedure was high. Second, despite there was no difference between groups, the mean FAP diameter was high in both study groups. Third, because the compression procedure was not visually guided like the UGCR, this factor could have also contributed to the lower success rates. The size of FAP, length, and thickness of the fistula tract were not different between the groups. Hence, the days of diagnosis and the urgency of catheterization (i.e., stable angina vs. ACS) were similar between groups. When compared with one attempt of MCR, the success rate of three attempts of MCR has much better. This finding showed that repeated attempts of MCR were important (Table 1).

The success of MCR was better in elderly patients. Patients with a higher CHA_2DS_2VASC score had a favorable outcome for FAP thrombosis. The left ventricular PW was thicker on echocardiogram in the TP group (1.03±0.18 cm vs 1.13±0.20 cm). Relative wall thickness (RWT) is an indicator of left ventricular hypertrophy and calculated from PW measurement. In a study, LV hypertrophy defined by RWT has been associated with low arterial shear stress[31]. Low shear stress may play a role in thrombosis of FAP. However, no clinical studies were performed to confirm this finding. Higher NLR was assumed to be the microinflammation marker[32,33]. It was similar between the groups. Besides, platelet count, PLR, MPV, and RDW values were not different between the groups even if only stable CAD patients were compared. These findings point out that platelet reactivity does not have an impact on the thrombosis of FAP.

Moderate correlations with the CHA_2DS_2VASC scores displayed that high values can be indicators of the thrombosis of FAP. Echocardiographic increased PW thickness was the novel finding of the thrombosed FAPs. Further studies on a large scale are needed to confirm these findings.

Limitations

There are a few limitations in our study that needs to take into consideration. The BMI of patients not included in our study. Since obesity is known to facilitate developing FAP, we cannot predict its effects on the success of MCR. In addition, we could not include information about the level of FAPs as to whether they localized on the CFA or lower. It expected to produce lower MCR success rates with the lower function of the femoral artery (i.e., superficial femoral artery). Furthermore, the hemodynamic status of patients during MCR (i.e., high blood pressure) not closely monitored.

Conclusions

Even in high-risk patients who have large FAPs and ongoing therapy with antiplatelet drugs, MCR may be a therapeutic option as a conservative approach. Patients with higher CHA_2DS_2VASC score or thicker PW are more likely to get benefit from MCR treatment. Repeated MCR attempts should be used to increase the success rate of the procedure. Further studies on a large scale are needed to confirm these findings.

Ethics Committee Approval: The study was approved by our Clinical Research Ethics Committee of Bagcilar Training and Research Hospital on August 17, 2017 as a 2017–601 protocol number.

Peer-review: Externally peer-reviewed.

Authorship Contributions: Concept: S.V., Design: S.V., F.K.; Data Collection or Processing: S.V., F.K., G.K.; Analysis or Interpretion: S.V., F.K., S.K., E.O.; Literature Search: S.V., G.K.

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