Importance of Femoral Access Method in Predicting the Development of Contrast Induced Nephropathy after Transfemoral Transcatheter Aortic Valve Implantation

İlker Gül[1], Mustafa Zungur[1], Ahmet Taştan[1], Muhammed Esad Çekin[1], Ahmet Çağrı Aykan[2], Aysel İslamlı[1], Talat Tavlı[1]

[1] Şifa University Faculty of Medicine, Department of Cardiology, İzmir, Turkey
[2] Ahi Evren Chest Cardiovascular Surgery Training and Research Hospital, Clinic of Cardiology, Trabzon, Turkey

ABSTRACT

Introduction: Transcatheter aortic valve implantation (TAVI) is more reliable than surgical valve replacement for high-risk or inoperable aortic stenosis patients. In this study, we aimed to investigate the effects of different femoral access methods on the development of vascular complications and contrast-induced nephropathy (CIN) after transfemoral (TF)-TAVI.

Patients and Methods: In total, 110 patients (aged 78.9 ± 12.2 years; 55 females) who underwent aortic valve replacement by TF-TAVI between June 2013 and April 2015 were included in the study. CIN was defined as an absolute increase in serum creatinine level of > 0.5 mg/dL or a relative increase of > 25% within 48-72 h after TF-TAVI. The patients were classified into two groups according to the femoral access methods: surgical cut-down (SCD) and vascular closure device (VCD) groups.

Results: The amount of contrast medium (CM; p< 0.001) and the incidence of CIN (p= 0.038) were higher in the VCD group. Baseline glomerular filtration rate (GFR), baseline creatinine, Mehran score and CM were determined as the predictive factors of CIN development. Receiver operating characteristic analysis revealed that CM, which may predict the development of CIN, was determined as 178.5 mL, and GFR, which may predict the development of CIN, was determined as 48.9 mL/dk/1.73 m^2.

Conclusion: It may be preferred to perform the femoral arterial procedure using the SCD method instead of VCD in TAVI patients whose GFR is < 48.9; the use of CM may increase due to various reasons.

Key Words: Contrast induced nephropathy; transcatheter aortic valve implantation; femoral artery; vascular closure device; surgical cut-down

Transfemoral Transkateter Aort Valv İmplantasyonu Sonrası Kontrast Bağımlı Nefropati Gelişiminde Femoral Giriş Yönteminin Önemi

ÖZET

Giriş: Transkateter aort valv implantasyonu (TAVİ) yöntemi cerrahi kapak replasmanı açısından yüksek riskli veya opere edilemeyen ileri aort darlığı hastalarında daha güvenilir bir yöntemdir. Biz bu çalışmada transfemoral (TF)-TAVİ sonrası farklı femoral giriş metodlarının, vasküler komplikasyonlar ve kontrast bağımlı nefropati (KBN) gelişimi üzerine olan etkilerini araştırmayı amaçladık.

Hastalar ve Yöntem: Haziran 2013-Nisan 2015 tarihleri arasında TAVİ yöntemiyle aort valv replasmanı yapılan 110 hasta (yaş= 78.9 ± 12.2 yıl, 55 kadın) çalışmaya dahil edildi. KBN, TF-TAVİ'den 48-72 saat sonra serum kreatinin değerinde > 0.5 mg/dL artış veya başlangıca göre %25'ten daha fazla yükselme olarak tanımlandı. Hastalar vasküler giriş yöntemlerine göre cerrahi cut-down (SCD) ve vasküler kapama cihazı (VCD) olarak iki gruba ayırıldı.

Bulgular: Kontrast madde (KM) miktarı (p< 0.001) ve KBN insidansı (p= 0.038) VCD grubunda fazlaydı. Bazal glomerüler filtrasyon oranı (GFO), bazal kreatinin, Mehran skoru ve KM'nin, KBN gelişiminin belirleyicileri oldukları saptandı. ROC analizleri sonucunda; KBN gelişimini belirleyici KM değerinin 178.5 mL ve GFO'nun 48.9 mL/dakika/1.73 m^2 olduğu belirlendi.

Sonuç: Çeşitli nedenlerle kullanılacak KM miktarı artabilecek, GFO 48.9'un altında olan TAVİ hastalarında femoral arteriyel prosedürler için VCD yerine SCD yöntemi tercih edilebilir.

Anahtar Kelimeler: Kontrast bağımlı nefropati; transkateter aort valv implantasyonu; femoral arter; vasküler kapama cihazı; cerrahi cut-down

Correspondence

İlker Gül

E-mail: drilkergul@gmail.com
Submitted: 10.01.2016
Accepted: 03.02.2016

INTRODUCTION

Degenerative aortic stenosis (AS) is one of the common valvular heart diseases worldwide, and its incidence is continuously increasing[1]. If severe AS is not treated, it can develop into heart valve pathology with high morbidity and mortality rates[2]. Surgical methods or transcatheter procedures can be implemented for AS treatment. Clinical studies have determined that transcatheter aortic valve implantation (TAVI) is more reliable in high-risk or inoperable patients[3-9].

A contrast medium (CM) is used for illustration during TAVI. Renal function, which is generally stablised before TAVI, can be disrupted after the surgery. In the case of acute kidney injury (AKI) after invasive interventional surgeries, morbidity and mortality rates increase[10-12]. AKI can also be diagnosed based on serum creatinine and urine output measures (Table 1). Contrast-induced nephropathy (CIN) is one of the reasons for AKI development in hospitals[13]. CIN is defined as an absolute increase in serum creatinine of > 0.5 mg/dL or a relative increase of > 25% within 48-72 h after TAVI[14]. Thus, factors that can lead to the development of CIN after interventional cardiovascular surgeries must be well known. It has been specified that the CM volume used in invasive surgeries is the most important factor causing AKI. CIN occuring in elderly and high-risk TAVI patients can influence the overall condition of the patients. Till date, several studies have been conducted on the factors affecting CIN development in patients with TAVI[15-17].

The common femoral artery is still the most widely used access site and least invasive approach for tranfemoral (TF)-TAVI[8,18]. Femoral artery access for TF-TAVI is achieved either by surgical cut-down (SCD) and surgical closure or through a percutaneous approach with vascular closure devices (VCDs).

Table 1. Acute kidney injury (AKI) classification

Stage 1

- Increase in serum creatinine to 150%-199% (compared with baseline)
- Increase of 0.3 mg/dL (26.4 mmol/L)
- Urine output < 0.5 mL/kg/h for > 6 h but < 12 h

Stage 2

- Increase in serum creatinine to 200%-299% (compared with baseline)
- Urine output < 0.5 mL/kg/h for > 12 h but 24 h

Stage 3+

- Increase in serum creatinine to 300% (compared with baseline)
- Serum creatinine of 4.0 mg/dL (354 mmol/L) with an acute increase of at least 0.5 mg/dL (44 mmol/L)
- Urine output < 0.3 mL/kg/h for 24 h
- Anuria for 12 h

Different types of VCDs have been developed for femoral interventions. VCDs have been successfully used during transcatheter or endovascular interventions[19,20]. Nevertheless, this technique may be associated with complications[21,22]. As a matter of fact, access site complications and adverse events are associated with a higher incidence of renal failure in TAVI patients[23].

However, the importance of the femoral artery closure methods in predicting CIN development has not yet been investigated in detail. The importance of SCD and VCD in the prediction of CIN development in TF-TAVI patients was evaluated in this study.

PATIENTS and METHODS

This prospective observational cohort study was performed between June 2013 and April 2015 in a tertiary cardiovascular centre from Turkey. For this study, 110 patients who underwent aortic valve replacement with TF-TAVI at our centre were evaluated. Patients who were considered appropriate for TF-TAVI by our cardiac team were included in the study because they were inoperable or at a high risk for surgical aortic valve replacement. The operative risks of patients were calculated using the logistic European System for Cardiac Operative Risk Evaluation (Logistic EuroSCORE) and Society of Thoracic Surgeons Predictive Risk of Mortality (STS) scores. Patients with a logistic EuroSCORE > 20% or a STS score > 10% were considered high-risk patients[23]. These cases underwent renal replacement therapy before TF-TAVI, and those with a creatinine value > 2.5 mg/dL were not included in the study.

Vascular access was achieved by surgical cut-down in 36 cases (SCD group) and vascular closure device in 74 cases (VCD group). Clinical data, patient characteristics, echocardiographic data, processual variables and morbidity and mortality rates were prospectively followed-up for 6 months after TF-TAVI. Informed consent was obtained from each subject, and the study was conducted in accordance with the Declaration of Helsinki. The study protocol was approved by the Ethics Committee.

Severe AS was diagnosed using echocardiography. An average aortic gradient > 40 mmHg, an aortic valve area < 1 cm^2 and a valve area index (valve area/body surface area) < 0.6 cm^2 were indicators of severe AS[24]. An Edwards e-sheath for TF and a balloon-expandable Edwards Sapien XT valve (Edwards Lifesciences, Irvine, Calif., USA) were used for TF-TAVI. VCD (ProStar XL; Abbott Laboratories, North Chicago, Ill., USA) was used in eligible patients for femoral artery diameter and anatomical measurements. SCD was applied to patients who were unsuitable for the iliac and femoral artery anatomy for VCD. Clopidogrel (300 mg loading dose and 75 mg/day thereafter for a minimum of 3 months), acetylsalicylic acid (100 mg lifelong) and intravenous antibiotherapy were prescribed to all patients. Before TAVI in hybrid labarotory,

the activated clotting time (ACT) was controlled by the team. A bolus of intravenous heparin was administered at the start of each procedure to achieve an ACT of 250-300 s. Iohexol (Omnipaque; GE Healthcare), a nonionic, low osmolar and monomeric contrast medium was used for angiography. Examinations, such as computed tomography (CT) and coronary angiography that required the administration of CM except for TF-TAVI, were performed at least 72 h prior to the procedure. The daily renal functions of all patients were monitored from admission to discharge (COBAS Integra 400 plus; Roche Diagnostics).

The estimated GFR was calculated using the Modification of Diet in Renal Disease (MDRD) formula. Before TAVI, 1 mL/kg/h of 0.9% NaCl solution was administered for 24 h to patients with a GFR of < 50 mL/min/1.73 m^2; 48-72 h after TAVI, 0.5 mg/dL or a 25% increase compared to the basal creatinine value was defined as CIN[13-17].

Femoral Access Considerations

Aorto-ilio-femoral contrast-enhanced CT examination was performed on all patients to determine the femoral access technique. Patients were evaluated according to the requirements of minimum diameters of vascular sheaths (Edwards-Saphien 16-18-20F e-sheath), which are to be used for TF-TAVI. Femoral access techniques of the patients were determined by the cardiac team. Patients who had a sufficient distance between superficial and deep femoral artery bifurcation or inferior epigastric artery and e-sheath to femoral artery ratio < 1.05 were included in the VCD group. Iliofemoral tortuosity was not found to predict vascular complications[18]. Mostly, the artery straightens out as soon as the stiff wire is advanced through the tortuous part of the artery. Hence, patients who had tortuosity in ilifemoral or aortic vascular tracts were included in the VCD group. The patients who had severe iliofemoral calcification, aortic aneurism or thrombus in the aorta were not included in the VCD group.

The Prostar XL, suture-mediated VCD is composed of a guidewire-compatible hydrophilic sheath, which contains two pairs of nitinol needles that are deployed from inside the arteriotomy, and two braided polyester sutures, a needle guide and a rotating barrel precisely controlling the needles during device deployment. In brief, puncture of the anterior wall of the common femoral artery was ensured by selective angiography. After dilation of the tract to the femoral artery with a dilatator, the Prostar is advanced over a hydrophilic guidewire and deployed. Following valve deployment, the introducer sheath is retracted to the level of the external iliac artery, and selective angiography is performed to assess for iliofemoral complications. Thereafter, the sheath is removed over the extra or super-stiff guidewire and the femoral arteriotomy is sealed by advancing the white suture to the artery with the pusher. The guidewire remains in situ until significant adequate haemostasis is obtained. The guidewire is then gently removed, and the green suture is tightened; a final angiogram is performed to ensure femoral artery closure and assess for vascular complications.

The other femoral access method was surgical cut-down in TF-TAVI cases. In patients who were unsuitable for the VCD technique, the common femoral artery was opened using the SCD method by cadiovascular surgeons over the femoral bone head. After TF-TAVI, the sheath was removed over the stiff guidewire and the surgeons closed the femoral artery puncture site with surgical sutures.

Vascular Acedemic Research Consortium (VARC) consensus, renal and vascular complications after Transcatheter Aortic Valve Implantation

VARC-2 criteria are shown in Tables 1 and 2. In this study, renal and vascular complications were reported according to the VARC-2 consensus document[25].

Statistical Analysis

SPSS 17.0 statistical software (SPSS Inc., Chicago, IL, USA) and MedCalc software program, release 12.3.0.0 (MedCalc Software, Belgium) were used for statistical analysis. To test the distribution pattern, the Kolmogorov-Smirnov method was used. Normally distributed continuous variables were expressed as mean ± standard deviation (SD), non-normally distributed continuous variables were expressed as a median (interquartile range) and categorical variables were expressed as a percentage. To identify the correlations between CIN and the clinical or laboratory parameters, a univariate analysis was performed using an unpaired t-test or Mann-Whitney U test for the continuous variables and the χ^2 test or Fisher's exact test for the categorical variables, respectively. A multivariate logistic regression analysis was used to assess the relation among the parameters, whose statistical significance was demonstrated on a univariate analysis level of $p < 0.10$ and through well-known risk factors. Models were developed with step-wise techniques, for which the results were expressed as odds ratios with 95% confidence intervals (CI). An exploratory evaluation for additional cut-off points of different variables was performed using the receiver operating characteristic (ROC) curve analysis. Significant difference was defined as $p < 0.05$.

RESULTS

General Characteristics of Patients

In total, 110 patients (aged 78.9 ± 12.2 years; 55 females) were included in our study. No significant differences between the study groups in terms of baseline demographic, laboratory and echocardiographic characteristics were observed. There were no differences between groups according to the permanent pacemaker implantation, logistic EuroSCORE, STS score, major bleeding and blood transfusion (≥ 2 units). When the risk factors were evaluated, a difference between the groups in terms of coronary artery disease (CAD), diabetes mellitus, hypertension, chronic obstructive pulmonary disease and peripheral arterial disease (PAD) was not ascertained. CM,

Table 2. Vascular access site and access-related complications

Major vascular complications

- Any aortic dissection, aortic rupture, annulus rupture, left ventricle perforation or new apical aneurysm/pseudoaneurysm.
- Access site or access-related vascular injury (dissection, stenosis, perforation, rupture, arteriovenous fistula, pseudoaneurysm, haematoma, irreversible nerve injury, compartment syndrome and/or percutaneous closure device failure) leading to death, life-threatening or major bleeding,* visceral ischaemia or neurological impairment.
- Distal embolization (noncerebral) from a vascular source requiring surgery or resulting in amputation or irreversible end-organ damage.
- Use of unplanned endovascular or surgical intervention associated with death, major bleeding, visceral ischaemia or neurological impairment.
- Any new ipsilateral lower extremity ischaemia documented by patient symptoms, physical exam and/or decreased or absent blood flow on lower extremity angiogram.
- Surgery for access site-related nerve injury.
- Permanent access site-related nerve injury.

Minor vascular complications

- Access site or access-related vascular injury (dissection, stenosis, perforation, rupture, arteriovenous fistula, pseudoaneuysms, haematomas and/or percutaneous closure device failure) not leading to death, life-threatening or major bleeding, visceral ischaemia or neurological impairment.
- Distal embolization treated with embolectomy and/or thrombectomy and not resulting in amputation or irreversible end-organ damage.
- Any unplanned endovascular stenting or unplanned surgical intervention not meeting the criteria for a major vascular complication.
- Vascular repair or the need for vascular repair (via surgery, ultrasoundguided compression, transcatheter embolization or stent-graft).

Percutaneous closure device failure

- Failure of a closure device to achieve haemostasis at the arteriotomy site leading to alternative treatment (other than manual compression or adjunctive endovascular ballooning).

CIN, total vascular injury and urgent peripheral intervention rates were higher in the VCD group. Post-procedural infection, lymph drainage and re-hospitalization rates were higher in the SCD group. Total surgery time and total hospital stay were longer in the SCD group (Table 3,4).

Procedure

The balloon-expandable aortic valve via transfemoral access was implanted in all patients. The average radiation time was 8.1 ± 3.3 min. The average CM and average extubation times were 171.1 ± 35.2 mL and 211 ± 58.1 min, respectively. The length of stay in the intensive care unit and the length of stay at the hospital were 1.5 ± 0.7 and 4.5 ± 2.8 days, respectively.

CIN after TF-TAVI was observed in a total of 29 (26.4%) patients. The length of intensive care unit and hospital stay in the CIN group was 1.7 ± 1.2 and 4.8 ± 1.5 days, respectively. After TF-TAVI, three of the patients needed permanent pacemaker implantation due to atrioventricular conduction block (2.7%). Vascular complications occurred in 18 patients; nine of these patients were in the CIN positive group (p= 0.012). These complications were access-related vascular injury. Urgent peripheral intervention was required for nine patients with vascular complications (8.2%). Five of them were in the CIN positive group (p= 0.038). CM volume increased in patients who had vascular injury (248.8 ± 41.3 mL vs. 168.9 ± 24.3 mL; p< 0.001). A differentiation between the groups in terms of stroke and bleeding complications was not ascertained. The amount of applied CM was higher in the CIN positive group (p< 0.001) and the GFR was decreased in the CIN positive group (p= 0.005). Seven of the patients died during the study period (SCD group, two patients; VCD group, five patients) (Table 5).

CIN Predictors

In univariate analysis, which was conducted to determine CIN predictors after TF-TAVI, it had been ascertained that statistically significant p values of CAD, PAD, baseline creatinine, baseline GFR, CM, blood transfusion > 2 units, VCD and Mehran score were < 0.10. Multivariate regression analysis was performed using these variables. According to the multivariate analysis, baseline GFR, baseline creatinine, CM and MS were associated with CIN development (Table 6). ROC analyses of the variables determined as significant with multivariate regression analysis was performed. As a result of these ROC analyses, the contrast medium volume, which may predict the development of CIN, was determined as 178.5 [area under the curve (AUC), 0.810; 95% CI, 0.704-0.928; sensitivity, 78% and specificity, 76%] and baseline GFR, which may predict the development of CIN, was determined as 48.9 (AUC, 0.692; 95% CI, 0.546-0.828; sensitivity, 66% and specificity, 72%] (Table 7).

DISCUSSION

According to the results of our study, the rate of vascular access complications and CIN were higher in patients whose femoral arteries were processed with VCD. It was determined that the main reason for this situation was the increase in the use

Table 3. Demographic and surgical characteristics of the patients

Variables	SCD (n= 36)	VCD (n= 74)	p value
Age (years)[A]	79.1 (± 5.4)	77.3 (± 8.0)	0.250
Female (%)	19 (52.8%)	36 (48.6%)	0.420
Body mass index (kg/m^2)[A]	27.7 (± 6.6)	26.8 (± 3.4)	0.489
Previous coronary surgery (%)	5 (13.9%)	8 (10.9%)	0.622
Previous PCI (%)	6 (16.7%)	14 (18.9%)	0.498
Coronary artery disease (%)	21 (58.3%)	38 (51.4%)	0.314
Permanent pacemaker (%)	1 (3.4%)	2 (2.4%)	0.964
Diabetes mellitus (%)	10 (27.8%)	21 (28.4%)	0.568
PAD (TASC ≥ B patients) (%)	8 (22.2%)	12 (16.2)	0.443
STS score (%)[B]	13.2 (9.9-15.1)	12.1 (9.2-13.5)	0.696
Logistic euroscore (%)[B]	33.8 (27.5-39.1)	35.9 (30.1-40.1)	0.422
Contrast-induced nephropathy (%)	5 (13.9%)	24 (32.4%)	0.038
CM (mL)[A]	146.7 (± 36.8)	183.0 (± 48.1)	< 0.001
Mortality (in hospital) (%)	1 (2.8%)	3 (4.1%)	0.737
Mortality (6 months after TAVI) (%)	2 (5.6%)	5 (6.8%)	0.808
Total vascular injury (%)	2 (5.6%)	16 (21.6%)	0.032
Major vascular complications (%)	1 (2.8%)	8 (10.8%)	0.205
Minor vascular complications (%)	2 (5.6%)	7 (9.5%)	0.483
Percutaneous transluminal angioplasty (%)	0	8 (10.8%)	0.043
Surgical repair (%)	1 (2.8%)	3 (4.1%)	0.737
Graft stent implantation (%)	0	4 (5.4%)	0.155
Major bleeding (%)	1 (2.8%)	8 (10.8%)	0.205
Minor bleeding (%)	8 (22.2%)	21 (28.4%)	0.491
Blood transfusion ≥ 2 units	2 (5.6%)	9 (12.2%)	0.265
Hypotension after TAVI	6 (16.7%)	16 (21.6%)	0.542
Lymph drainage (%)	8 (22.2%)	3 (4.1%)	0.002
Post-procedural infection (%)	8 (22.2%)	1 (1.4%)	< 0.001
Re-hospitalization (%)	6 (16.7%)	1 (1.4%)	0.002
Total operation time (min)[A]	122.9 (± 25.7)	104.2 (± 38.3)	0.010
Intensive care unit stay (days)[A]	1.6 (± 0.6)	1.4 (± 0.9)	0.155
Hospital stay (days)[A]	4.7 (± 1.2)	4.2 (± 1.6)	0.048

[A] values reported as mean ± SD.
[B] values reported as median (25th and 75th percentiles).
CM: Contrast medium, GFR: Glomerulkar filtration rate, PAD: Peripheral arterial disease, PCI: Percutaneous coronary intervention, SCD: Surgical cut-down, STS: Society of thoracic surgeons, VCD: Vascular closure device.

of opaque substance in patients in whom the femoral procedure was performed using VCD.

There is a prognostic significance of the level of kidney functions after cardiovascular interventions. Development of AKI after the interventional procedures increases the rates of morbidity and mortality. CIN is one of the most important causes leading to AKI. It was shown that prognosis was negatively affected by the occurrence of CIN subsequent to TAVI[10-13]. CIN rates subsequent to TAVI were reported to be 10%-30% in various studies[26-28]. CIN occurred in 29 patients in our study (26.4%). This rate was in agreement with that of previous studies. Five (13.9%) of these patients were in the SCD group, and 24 (32.4%) of them were in the VCD group (p = 0.038). Bagur et al. reported that the mortality rate was 15.0% and 7.0% in patients developing CIN subsequent to TAVI and in those not developing CIN, respectively[29]. In our study, while the in-hospital mortality rate in CIN positive and CIN negative patients was similar (6.9% vs. 2.4%, p= 0.274), the mortality rate in the first 6 months subsequent to TAVI increased in CIN positive patients (17.2% vs. 2.4%, p= 0.005). In the analyses

Table 4. Laboratory data and echocardiographic findings

Variables	SCD (n= 36)	VCD (n= 74)	p value
Baseline creatinine (mg/dL)[A]	1.18 (± 1.2)	1.12 (± 0.4)	0.662
Baseline GFR (mL/min/1.73 m^2)[B]	57.3 (17.9-88.2)	60.7 (21.8-96.1)	0.120
Baseline potassium (mEq/L)[A]	4.37 (2.96-5.12)	4.39 (3.12-5.02)	0.716
Baseline brain natriuretic peptide (pg/mL)[A]	4880.6 (1436.6-8780.4)	5044.8 (2918.1-9123.1)	0.085
Baseline high sensitive troponine-T (ng/dL)[B]	37.8 (± 14.8)	40.6 (± 18.9)	0.120
Low density lipoprotein (mg/dL)[A]	102.3 (86.3-137.2)	103.3 (75.2-133.1)	0.126
Haemoglobin (g/dL)[B]	11.1 (± 1.89)	11.6 (± 1.92)	0.832
Platelet (× 10^3)[A]	217.2 (174.6-239.1)	235.9 (185.6-276.1)	0.129
White blood cell (× 10^3)[B]	6.9 (± 1.9)	7.4 (± 4.4)	0.257
C-reactive protein (mg/dL)[A]	3.4 (2.4-5.1)	2.7 (2.0-4.1)	0.657
Left ventricle ejection fraction (%)[B]	43.1 (± 9.2)	42.2 (± 10.2)	0.226
Aortic valve area (cm^2) (before TAVI)[B]	0.61 (± 0.11)	0.66 (± 0.13)	0.968
Aortic valve area (cm^2) (six months after TAVI)[B]	1.78 (± 0.18)	1.86 (± 0.42)	0.762
Mean aortic gradient (mmHg) (before TAVI)[A]	50.0 (39.6-57.2)	50.9 (41.0-55.5)	0.604
Mean aortic gradient (mmHg) (six months after TAVI)[A]	8.7 (6.2-9.5)	7.8 (5.8-9.2)	0.425
Post-aortic regurgitation ≥ grade 2	2 (%5.6)	6 (%8.1)	0.987
sPAP (mmHg) (before TAVI)[B]	46.5 (± 11.2)	44.8 (± 9.6)	0.248

[A] values reported as median (25^{th} and 75^{th} percentiles).
[B] values reported as mean ± SD.
GFR: Glomerular filtration rate, SCD: Surgical cut-down, sPAP: Systolic pulmonary artery pressure, TAVI: Transcatheter aortic valve implantation, VCD: Vascular closure device.

Table 5. Demographic and surgical characteristics of the CIN (+) and CIN (-) patients

Variables	CIN (+) (n= 29)	CIN (–) (n= 81)	p value
Age (years)[A]	78.6 (± 9.4)	77.3 (± 8.3)	0.657
Female gender (%)	18 (62.1%)	37 (45.7%)	0.097
Body mass index (kg/m^2)[A]	28.5 (± 7.9)	28.4 (± 7.1)	0.339
Previous coronary surgery (%)	2 (6.9%)	11 (%13.6)	0.086
Previous PCI (%)	2 (6.9%)	18 (22.2%)	0.132
Permanent pacemaker (%)	1 (3.4%)	2 (2.4%)	0.686
Diabetes mellitus (%)	8 (28.7%)	23 (28.4%)	0.569
PAD (TASC ≥ B patients) (%)	9 (22.2%)	11 (16.2)	0.036
Ejection fraction (%)[A]	41.8 (± 8.2)	43.1 (± 6.8)	0.243
Logistic EuroSCORE (%)[B]	33.1 (27.8-37.2)	32.5 (26.8-35.6)	0.813
STS score (%)[B]	13.1 (11.8-15.9)	12.6 (10.9-15.1)	0.175
Baseline creatinine (mg/dL)[B]	1.14 (0.88-1.27)	1.02 (0.87-1.16)	0.032
Baseline GFR (mL/min/1.73 m^2)[A]	47.1 (± 13.6)	54.8 (± 20.4)	0.005
CM (mL)[A]	193.7 (± 42.6)	161.2 (± 33.6)	< 0.001
Intensive care unit stay (days)[A]	1.7 (± 1.2)	1.3 (± 0.7)	0.120
Total hospital stay (days)[A]	4.8 (± 1.5)	4.1 (± 1.7)	0.170
Mortality (in hospital)	2 (6.9%)	2 (2.4%)	0.274
Mortality (six months after TAVI) (%)	5 (17.2%)	2 (2.4%)	0.005

[A] values reported as median (25^{th} and 75^{th} percentiles).
[B] values reported as mean ± SD.
CIN: Contrast induced nephropathy, CM: Contrast medium, GFR: Glomerular filtration rate, PAD: Peripheral arterial disease, PCI: Percutaneous coronary intervention, sPAP: Systolic pulmonary artery pressure, STS: Society of Thoracic Surgeons, TAVI: Transcatheter aortic valve implantation.

Table 5. Demographic and surgical characteristics of the CIN (+) and CIN (-) patients (continuation)

Variables	CIN (+) (n= 29)	CIN (–) (n= 81)	p value
Major stroke (%)	0	0	Ns
Major bleeding (%)	4 (13.8%)	5 (%6.2)	0.048
Minor bleeding (%)	7 (24.1%)	22 (%27.2%)	0.561
Blood transfusion ≥ 2 units	7 (24.1%)	4 (4.9%)	0.003
Hypotension after TAVI, %	8 (27.6 %)	14 (17.3%)	0.233
Total vascular injury (n= 18; %)	9 (31.0%)	9 (%11.1)	0.012
Major vascular complication (n= 9; 8.2%)	5 (17.2%)	4 (4.9%)	0.038
Access-related vascular injury (n= 8; 7.3%)	5 (17.2%)	3 (3.7%)	0.015
Minor vascular complication (n= 9; 8.2%)	4 (13.8%)	5 (6.2%)	0.048
Access-related vascular injury (n= 9; 8.2%)	4 (13.8%)	5 (6.2%)	0.048
Urgent peripheral intervention (n= 9; 8.2%)	5 (17.3%)	4 (4.9%)	0.038
Total operation time (min)[A]	113.2 (± 19.4)	111.5 (±15.3)	0.334

[A] values reported as median (25th and 75th percentiles).
[B] values reported as mean ± SD.
CIN: Contrast induced nephropathy, CM: Contrast medium, GFR: Glomerular filtration rate, PAD: Peripheral arterial disease, PCI: Percutaneous coronary intervention, sPAP: Systolic pulmonary artery pressure, STS: Society of Thoracic Surgeons, TAVI: Transcatheter aortic valve implantation.

Table 6. Univariate and multivariate analysis of risk factors determining contrast induced nephropathy

	Univariate analysis		Multivariate analysis	
Variables	**OR (95% CI)**	**p value**	**OR (95% CI)**	**p value**
Age	1.0 (0.5-1.4)	0.510	-	-
Diabetes mellitus	1.6 (0.8-2.6)	0.122	-	-
Coronary artery disease	1.8 (0.8-3.5)	0.062	0.9 (0.4-1.2)	0.542
Peripheral arterial disease (TASC ≥ B)	1.6 (0.9-2.8)	0.045	1.3 (0.8-2.4)	0.102
STS score	0.6 (0.2-1.0)	0.875	-	-
Logistic euroscore	0.9 (0.6-1.2)	0.606	-	-
Ejection fraction	1.0 (0.8-1.3)	0.154	-	-
Baseline creatinine	1.7 (1.1-2.6)	0.022	3.2 (0.7-2.1)	0.007
Baseline GFR	3.4 (1.5-5.2)	< 0.001	4.3 (1.4-8.8)	< 0.001
CM	4.6 (1.7-6.9)	< 0.001	2.9 (1.5-3.9)	0.014
VCD	1.9 (1.1-2.7)	0.006	0.8 (0.8-1.9)	0.771
Mehran score	2.9 (1.1-5.2)	0.014	4.1 (1.1-7.4)	< 0.001
Haemoglobin	0.6 (0.2-1.1)	0.519	-	-
Major bleeding	1.1 (0.6-1.8)	0.198	-	-
Blood transfusion ≥ 2 units	1.3 (0.7-2.1)	0.048	1.0 (0.6-1.7)	0.337
Hypotension	0.8 (0.5-1.2)	0.702	-	-

CM: Contrast medium, GFR: Glomerular filtration rate, STS: Society of Thoracic Surgeons, VCD: Vascular closure device.

Table 7. ROC results for the prediction of CIN using baseline creatinine, baseline glomerular filtration rate, Mehran score and contrast volume

	Cut-off	AUC	Sensitivity (%)	Specificity (%)	95% CI
Contrast medium volume	178.5	0.810	78	76	0.704-0.928
Glomerular filtration rate	48.9	0.692	66	72	0.546-0.828
Mehran score	15.6	0.678	62	68	0.514-0.836

AUC: Area under the curve, CI: Confidence interval, CIN: Contrast induced nephropathy, ROC: Receiver operating characteristic.

performed according to the study groups, in-hospital mortality rates (VCD; 4.1% vs. SCD; 2.8%, p= 0.737) and mortality rates subsequent to TAVI were similar in the first 6 months (VCD; 6.8% vs. SCD; 5.6%, p= 0.808). The reason for this situation was thought to be the low mortality rate occurring during the study. As the following period takes longer, the gap between them may become clear.

Although various methods are available to perform aortic valve replacement with TAVI, TF access is the most commonly used method amongst them[23,30]. To perform TF-TAVI, femoral artery anatomy is required to be suitable for this procedure. In patients whose TF access is suitable for TAVI, surgical or percutaneous opening of the arterial access and repair of the artery by suturing after the surgery are required. SCD and VCD can be used for femoral access. More reliable femoral access can be achieved using SCD and repair can be made after the procedure. However, in our study, it was detected that procedure and hospitalization periods extended with this method. Femoral infections were more frequently encountered after SCD and rehospitalization rates increased. Unlike SCD, procedure and hospitalization periods were shorter with VCD and rehospitalization rates decreased after discharge. Despite these advantages, vascular complications increase with VCDs as shown in previous studies. These complications most frequently occur in the iliofemoral region. In previous studies, TAVI-induced vascular complication rates were reported to be 1.9%-17.3%[21,22,31]. In our study, however, vascular complication occurred in a total of 18 (16.4%) patients. This rate was in agreement with the other studies.

The most common cause of CIN development after interventional procedures is the increase in the use of CM. Especially during the placement of VCDs into the femoral artery and closure, extra CM use is required. Many literature studies have examined CIN and renal failure development subsequent to TAVI[16,17,32]. However, a study that examines CIN development by vascular closure techniques is not available. In our study, it was determined that the amount of CM used in the VCD group was increased compared with the SCD group (183.0 ± 48.1 mL vs. 146.7 ± 36.8 mL p< 0.001). Two reasons became prominent for the increase in the amount of CM. The first reason was the use of extra CM for VCD implantation and the closure of the artery after the procedure. Second, vascular complications were observed more frequently in the VCD group. For the repair of vascular complications, percutaneous balloon and, if needed, graft stent implantation were required. Angiographic imaging was performed with extra CM injection to the arteries with lesion for all these procedures. During the study, PROSTAR XL was used as VCD for TF-TAVI. In various studies, unsuccessful vascular closure rates with PROSTAR XL device subsequent to TAVI were reported to be 3.6%-10%[21, 22]. In our study, PROSTAR XL failure occurred in five (6.8%) patients. In a study by Hayashida et al, major vascular complication (MVC) rate and minor vascular complication rate were 8.6% and 11.6%, respectively, during TAVI[31]. Out of 18 vascular complications that occurred in our study, nine were major (8.2%) and nine were minor (8.2%) complications. In the SCD group, vascular complication occurred in two patients (5.6%), whereas in the VCD group, vascular complication was detected in 16 patients (21.6%) (p= 0.032). The most important cause of the MVC was that PROSTAR XL sutures could not completely close the femoral artery. Percutaneous transluminal angioplasty (PTA) was applied urgently to eight patients after MVC development. As PTA could not eliminate the vascular pathologies, peripheral stent implantation was performed in the four of these eight patients. Extra imaging was performed and CM was used due to these additional procedures. It was determined that CIN development increased in the VCD group in the evaluations made 48-72 h after the additional imaging and invasive procedures. CM amount, Mehran score, baseline creatinine and baseline GFR were identified as predictors of CIN development in the univariate and multivariate regression analyses conducted.

Study Limitations

The basic limitations to our study are the low number of patients and that the study was performedat a single centre. Therefore, although the number of patients in the CIN positive group who experience complications is huge, it may not have statistical significance. The main reasons (radiotoxic, nephrotoxic and ischaemic) of CIN development were not put forth in depth because renal biopsy was not performed. Balloon-expandable ES-XT valve was used in our study. These results may vary in the self-expandable aortic valves or newly developed 14-F femoral sheats with less requirement of opaque substance.

CONCLUSION

In conclusion, there are various advantages and disadvantages of intervening into the femoral artery using SCD and VCD. In our study, it was found that CIN development increased subsequent to femoral procedure with VCD in TF-TAVI patients. The most important reason of this situation was the increased amount of CM required in VCD patients. Vascular complication rates were higher in the VCD group compared with the SCD group. However, this rate was similar to that observed in previous studies. For vascular repair, PTA or peripheral stent implantation were performed. Performing extra imaging and using extra CM were required for these invasive procedures. It is determined that in cases where CM amount > 178.5 mL, nephropathy development will significantly increase for patients with GFR < 48 according to the results of the ROC analyses performed in patients developing CIN. Due to these reasons, it may be preferred to perform the femoral arterial procedure with SCD instead of VCD in TF-TAVI patients whose GFR is < 48 because the use of CM may increase because of various reasons.

CONFLICT of INTEREST

The authors reported no conflict of interest related to this article.

AUTHORSHIP CONTRIBUTIONS

Concept/Design: İG, MZ, TT
Analysis/Interpretation: İG, AT, MEÇ, Aİ
Data Acquisition: İG, MZ, AT, MEÇ, Aİ
Writing: İG, AÇA
Critical Revision: İG, MZ, TT
Final Approval: All of authors

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