

Original Investigation

Comparison of Vascular Closure Devices vs Manual Compression After Femoral Artery Puncture

The ISAR-CLOSURE Randomized Clinical Trial

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IMPORTANCE The role of vascular closure devices (VCD) for the achievement of hemostasis in patients undergoing transfemoral coronary angiography remains controversial.

OBJECTIVE To compare outcomes with the use of 2 hemostasis strategies after diagnostic coronary angiography performed via transfemoral access—a VCD-based strategy with 2 types of devices, an intravascular device and an extravascular device, vs standard manual compression. The primary hypothesis to be tested was that femoral hemostasis achieved through VCD is noninferior to manual compression in terms of vascular access-site complications. A secondary objective was the comparison of the 2 types of VCD.

DESIGN, SETTING, AND PARTICIPANTS Randomized, large-scale, multicenter, open-label clinical trial. We enrolled 4524 patients undergoing coronary angiography with a 6 French sheath via the common femoral artery from April 2011 through May 2014 in 4 centers in Germany. Last 30-day follow-up was performed in July 2014.

INTERVENTIONS After angiography of the access site, patients were randomized to hemostasis with an intravascular VCD, extravascular VCD, or manual compression in a 1:1:1 ratio.


MAIN OUTCOMES AND MEASURES Primary end point: the composite of access site-related vascular complications at 30 days after randomization with a 2% noninferiority margin. Secondary end points: time to hemostasis, repeat manual compression, and VCD failure. An α -level of .025 was chosen for primary and secondary comparisons.


RESULTS Of the 4524 enrolled patients, 3015 were randomly assigned to a VCD group (1509 received intravascular VCD and 1506 received extravascular VCD) and 1509 patients were randomly assigned to the manual compression group. Before hospital discharge, duplex sonography of the access site was performed in 4231 (94%) patients. The primary end point was observed in 208 patients (6.9%) assigned to receive a VCD and 119 patients (7.9%) assigned to manual compression (difference, -1.0% [1-sided 97.5% CI, 0.7%]; P for noninferiority $<.001$). Time to hemostasis was significantly shorter in patients with VCD (1 minute [interquartile range {IQR}, 0.5-2.0]), vs manual compression (10 minutes [IQR, 10-15]; $P < .001$). Time to hemostasis was significantly shorter among patients with intravascular VCD (0.5 minute [IQR, 0.2-1.0]), vs extravascular VCD (2.0 minutes [IQR, 1.0-2.0]; $P < .001$) and closure device failure was also significantly lower among those with intravascular vs extravascular VCD (80 patients [5.3%], vs 184 patients [12.2%]; $P < .001$).

CONCLUSIONS AND RELEVANCE In patients undergoing transfemoral coronary angiography, VCDs were noninferior to manual compression in terms of vascular access-site complications and reduced time to hemostasis.

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Percutaneous coronary angiography and interventions have become a cornerstone in the diagnosis and treatment of coronary artery disease. A substantial proportion of the morbidity associated with these procedures is related to access-site complications.¹ The common femoral artery is still the most frequently used access site, especially in the United States. After the procedure, closure of the arteriotomy site is usually achieved by manual compression.² Since the mid-1990s, however, vascular closure devices (VCDs) have been introduced into clinical practice with the aim of improving efficacy and the safety of percutaneous procedures.³ The devices are implanted to close the arteriotomy of the vessel wall by targeted force. Different types of VCDs have been developed, including intravascular and extravascular devices.¹ Increased efficacy, in comparison with manual compression (ie, reduced time to hemostasis and earlier ambulation), has been a consistent finding across different trials of VCDs.^{4,5}

However, concern exists about the safety of VCDs in comparison with manual compression. A number of meta-analyses suggested an increased risk of vascular complications—in particular, groin hematoma and arterial pseudoaneurysm—in comparison with manual compression.^{4,5} Moreover, the size of randomized trials has generally been modest, permitting evaluation of device efficacy but precluding definitive assessment of safety issues. In addition, significant heterogeneity in outcomes has been noted and concerns have been raised regarding a number of methodological issues in trial design.^{1,4} Although it is recognized that a class effect for VCDs likely does not exist, comparative efficacy studies between devices used in contemporary practice remains a scientific gap.

Against this background, the randomized Instrumental Sealing of ARterial puncture site—CLOSURE device vs manual compression (ISAR-CLOSURE) trial was designed to assess whether VCDs are noninferior to manual compression in terms of access site–related vascular complications in patients undergoing diagnostic coronary angiography via transfemoral access. We compared 2 different types of contemporary VCDs. The intravascular bioabsorbable device uses an inner and an outer plate on the surface of the artery, the 2 of which are pulled together tautly on deployment. The extravascular VCD consists of a bioabsorbable polyglycolic acid plug that is released on the external surface of the artery. After device deployment, some additional compression is required to allow time for the plug to extend and fill the subcutaneous puncture tract.¹ The secondary objective was the comparison between 2 different types of contemporary VCDs, the intravascular VCD and the extravascular VCD.

Methods

Study Design

ISAR-CLOSURE is an investigator-initiated, prospective, randomized, open-label, multicenter trial. Full details of the trial rationale and design have been previously published (Trial Protocol in Supplement 1).⁶

Patient Population

Patients were recruited at the Deutsches Herzzentrum München in Munich, the 1. Medizinische Klinik, Klinikum rechts der Isar in Munich, Krankenhaus der Barmherzigen Brüder in Munich, and Klinikum Landkreis Erding, all in Germany. Patients were eligible for enrollment if they provided written informed consent and were undergoing diagnostic coronary angiography (without subsequent percutaneous coronary intervention) with a 6F sheath through the common femoral artery, which had to have a diameter of greater than 5 mm (proven by angiography). Major exclusion criteria were implantation of a VCD within the last 30 days, symptomatic leg ischemia, prior thromboendarterectomy (TEA) or patch plastic of the common femoral artery, planned invasive diagnostic or interventional procedure in the following 90 days, a heavily calcified vessel, active bleeding or bleeding diathesis, severe arterial hypertension (>220/110 mm Hg), local infection, autoimmune disease, allergy to resorbable suture, and pregnancy. Detailed inclusion and exclusion criteria have previously been published.⁶ The study was approved by the ethics committee at each participating center.

Randomization

Patients were randomly assigned to arteriotomy closure with 1 of the following techniques: the intravascular FemoSeal VCD, the extravascular Exoseal VCD, or manual compression at a 1:1:1 ratio after performance of coronary angiography and femoral angiography of the access site via the 6F sheath. Sealed opaque envelopes containing a computer-generated sequence at a permuted block size of 3, 6, and 9 were used (generated at the data coordinating ISARResearch Center). Randomization was stratified by study center.

Study Treatment

Investigators participating in the trial were trained and certified from the manufacturer of the respective VCD. The VCDs were deployed according to the instructions for use. In patients assigned to receive manual compression, the sheath was removed by a physician and manual compression was applied proximal to the puncture site. Compression was continued for at least 10 minutes or until hemostasis. Hemostasis was defined as no bleeding or only light superficial bleeding and no expanding hematoma. A pressure bandage was applied for 2 hours after VCD implantation and 6 hours after manual compression.

Follow-up

All patients were scheduled to undergo color-coded duplex sonography of the access-site before hospital discharge. At 30 days, patients were not routinely seen in the participating center. Most patients received a structured follow-up letter or were interviewed via a telephone call with trained personnel of the ISARResearch Center about any complaints related to the access site, ie, hematoma, swelling, bleeding, pain, hospital admission, repeat intervention, operation, infection etc. In case of any complaints related to the access site, patients were instructed to seek further clinical and duplex sonographic

follow-up at the outpatient clinic. In patients incurring an adverse event at another hospital, the respective source documents were solicited.

End Points and Definitions

The primary end point was the incidence of vascular access site complications, ie, the composite of hematoma at least 5 cm in size, pseudoaneurysm, arteriovenous fistula, access site-related major bleeding, acute ipsilateral leg ischemia, need for vascular surgical or interventional treatment, or local infection at 30 days after randomization. Secondary end points were time to hemostasis, repeat manual compression, and VCD failure. Hematoma was defined as palpable mass of at least 5 cm. The diagnosis of a pseudoaneurysm required the ultrasonographic evidence of an aneurysmal neck with periodic flow signal at the artery puncture site. An arteriovenous fistula was diagnosed in case of a discontinuity of the vessel wall with a systolic-diastolic flow profile at the artery puncture site. Definition of access site-related major bleeding was based on REPLACE-2 (Randomized Evaluation in PCI Linking Angiomax to Reduced Clinical Events) criteria⁷ and included a reduction in hemoglobin of at least 3 g/dL with evident bleeding, a reduction in hemoglobin of at least 4 g/dL with or without evident bleeding, or bleeding requiring blood transfusion. Diagnosis of acute ipsilateral leg ischemia required any of the following: missing peripheral pulse, rest pain, cold and pale extremity, or ultrasonographic or computed tomographic angiographic evidence of vessel occlusion. The end point vascular interventional or surgical procedure was met in case of acute ipsilateral leg ischemia or necessity for hematoma evacuation. Local infection was defined as infected skin or soft tissue lesion at the vascular puncture site that requires antibiotic treatment. Time to hemostasis was defined as the elapsed time (minutes) between sheath removal and observed hemostasis. All end point events that were observed during 30 days were counted as end points irrespective of whether they resolved or not during the first 30 days. A more detailed description of the end point definitions has previously been published.⁶ All events were adjudicated and classified by an event adjudication committee in which members were unaware of the assigned treatment. Source data provided to the adjudication group included results of the color-coded duplex sonography, hospital medical records, discharge summary, laboratory values, and if required, additional reports (eg, death certificates, computer tomography reports, etc).

Statistical Considerations

The trial was designed to test the hypothesis that VCDs are noninferior to manual compression in terms of vascular access-site complications in patients undergoing diagnostic coronary angiography. The sample size calculation was based on the following assumptions: 1-sided significance level of 2.5%, a power of 80%, an assumed incidence of the primary end point of 5% with the strategy of manual compression, and a 2% margin of noninferiority. With these assumptions, inclusion of 4195 patients was required. To compensate for potential losses to follow-up, it was planned to enroll a total of 4500 patients. Sample size calculation

was performed using NQuery statistical software, version 7.0. The reported incidence of access site-related vascular complications varies widely.^{1,4} The 5% incidence of the primary end point in the manual compression group was chosen based on the data reported in the literature^{1,4} and on our personal experience in a large number of patients assessed by dedicated surveillance protocols. Considering that the majority of expected complications are not severe in nature, we chose a noninferiority margin that represents 140% of the complication rate assumed for the control group.

The primary comparison was between VCD and manual compression. A secondary comparison was between the 2 vascular closure devices. We accounted for these 2 main comparisons by choosing an α -level of .025 according to the Bonferroni correction. No imputation for missing data was planned according to the protocol. Categorical variables were summarized using frequencies and proportions and compared using the χ^2 test or Fisher exact test, as appropriate. Continuous data were summarized using median (interquartile range [IQR]) and compared using the nonparametric Wilcoxon rank-sum test.

All analyses were performed in a blinded manner regarding the randomly assigned treatment and on an intention-to-treat basis. Noninferiority testing of VCD vs manual compression regarding the primary end point was also performed in a per-protocol population, by including all those patients in whom the randomly assigned hemostasis technique was actually used. EquivTest, version 1.0 (from Statistical solutions) and S-PLUS software, version 4.5 (Insightful) were used for statistical analyses.

Results

Patients and Procedures

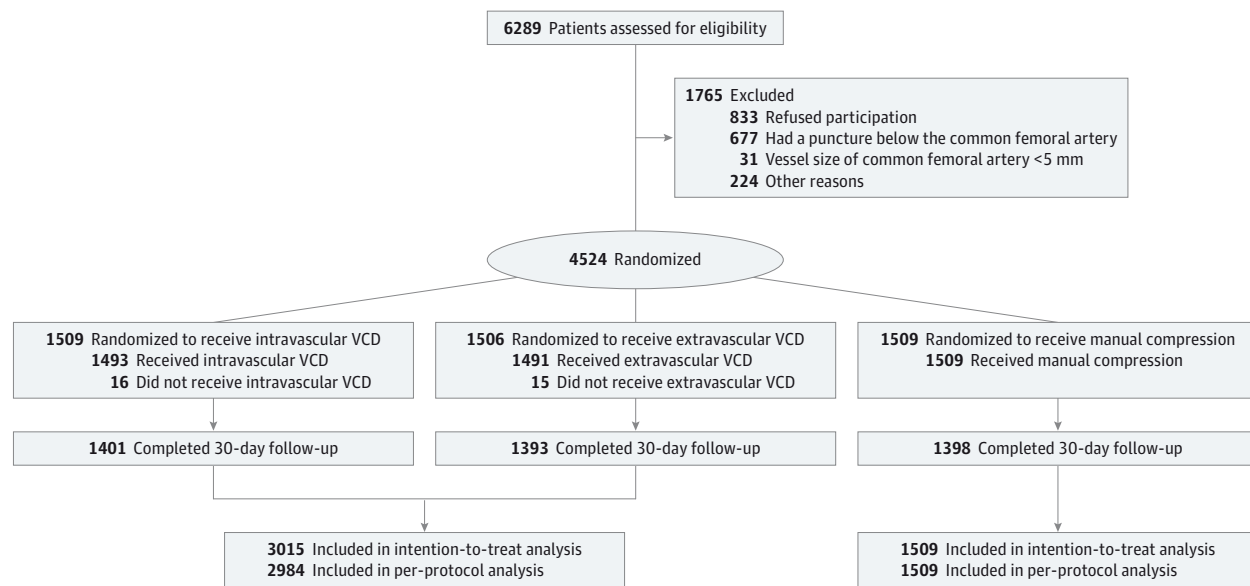
From April 2011 until May 2014, a total of 4524 patients were enrolled in the trial, 3015 patients were randomly assigned to receive a VCD (1509 patients to the intravascular VCD group and 1506 patients to the extravascular VCD group) and 1509 patients to receive manual compression. The **Figure** summarizes the study flow. Duplex sonography of the access site was performed in 4231 of 4524 patients (94%) before hospital discharge, and 4192 of 4524 patients (93%) underwent 30-day clinical follow-up. Patients were lost to follow-up due to the inability to reach them at the prespecified time.

Table 1 summarizes the baseline clinical and demographic characteristics according to treatment allocation to VCD or manual compression. A total of 141 patients (4.7%) assigned to VCD and 58 patients (3.8%) assigned to manual compression underwent diagnostic coronary angiography for an acute coronary syndrome. Antithrombotic medication on admission is depicted in **Table 2**. Sixty-eight percent of the patients were on aspirin, almost 40% were on an ADP receptor antagonist, and 13% were on oral anticoagulation. **Table 3** shows the angiographic and procedural characteristics.

Clinical Outcomes

At 30 days, 5 patients had died. None of the deaths were procedure related. One patient assigned to receive intravas-

Figure. Study Flow Diagram of Patient Randomization to Receive a Vascular Closure Device or Manual Compression



VCD indicates vascular closure device. Patients who did not complete 30-day follow-up could not be contacted at the prespecified time. Patients in the intravascular VCD group and patients in the extravascular VCD group were

combined in both the intention-to-treat analysis and the per-protocol analysis for the primary comparison of VCD vs manual compression.

cular VCD died of malignancy. Of the 3 patients assigned to receive extravascular VCD, 1 died of sudden cardiac causes, 1 death was related to surgery for implantation of a cardiac-assist device for terminal heart failure, and 1 patient died of renal failure in the presence of severe comorbid conditions. One patient randomized to receive manual compression died of renal failure.

Primary Comparison

VCD vs Manual Compression

Clinical outcomes according to treatment allocation to VCD or manual compression are reported in Table 4. The composite primary end point of access site-related vascular complications was observed in 208 patients (6.9%) assigned to receive a VCD vs 119 patients (7.9%) assigned to receive manual compression (difference of proportions, −1.0% [1-sided 97.5% CI, 0.7%]; P value for noninferiority <.001; P value for superiority = .23). Results were consistent in a per-protocol analysis (eTable 1 in Supplement 2). Among 332 patients with incomplete follow-up, the primary end point was observed in 34 patients (10.2%).

Among 4192 patients with complete follow-up, the primary end point was observed in 293 patients (7.0%); only 16 of the 293 events (5.5%) were recorded after hospital discharge. The incidence of hematoma was lower in patients assigned to VCD compared with manual compression (145 patients [4.8%] vs 102 patients [6.8%]; P = .006). No patient required interventional treatment or vascular surgery for acute ipsilateral leg ischemia or hematoma evacuation. There was 1 case of access-site infection within 30 days in a patient randomized to receive intravascular VCD. One patient assigned to receive manual compression incurred retroperitoneal bleeding.

Regarding the secondary end points, time to hemostasis was shorter in patients assigned to receive VCD compared with those assigned to receive manual compression (1 minute [IQR, 0.5-2.0], vs 10 minutes [IQR, 10-15]; P < .001). However, repeat manual compression after initial hemostasis was more frequent in the VCD group (53 patients [1.8%], vs 10 patients [0.7%]; P = .003).

Secondary Comparison Between VCDs

Intravascular vs Extravascular

eTable 2 in Supplement 2 summarizes the baseline clinical and demographic characteristics according to treatment allocation to receive intravascular VCD or extravascular VCD. Antithrombotic medication on admission is depicted in eTable 3 in Supplement 2. eTable 4 in Supplement 2 shows angiographic and procedural characteristics.

Clinical outcomes according to treatment allocation to the intravascular VCD or extravascular VCD are reported in eTable 5 in Supplement 2. Time to hemostasis (0.5 minute [0.2-1.0], vs 2.0 minutes [1.0-2.0]; P < .001) and closure device failure (80 patients [5.3%] vs 184 patients [12.2%]; P < .001) were lower with the intravascular VCD group, compared with the extravascular VCD group.

Discussion

In this large-scale, multicenter, randomized clinical trial of patients undergoing diagnostic coronary angiography via transfemoral access, we compared a strategy of arteriotomy closure with VCD with a strategy of manual compression. The main findings are the following: the use of VCD was

Table 1. Baseline Clinical and Demographic Characteristics

	No. (%) of Patients ^a	
	Vascular Closure Device (n = 3015)	Manual Compression (n = 1509)
Age, median (IQR), y	67.4 (58.4-74.7)	68.4 (59.5-74.8)
Women	917 (30.4)	478 (31.7)
Arterial hypertension	2599 (86.2)	1319 (87.4)
Hypercholesterolemia	1942 (64.4)	997 (66.1)
Diabetes mellitus	584 (19.4)	321 (21.3)
Insulin-requiring	142 (4.7)	65 (4.3)
Family history of premature coronary artery disease	944 (31.3)	471 (31.2)
Active or former smoker	1249 (41.4)	602 (39.9)
Prior myocardial infarction	813 (27.0)	393 (26.0)
Prior percutaneous coronary intervention	1785 (59.3)	882 (58.4)
Prior coronary artery bypass graft	255 (8.5)	135 (8.9)
Body mass index, median (IQR) ^b	27.1 (24.5-29.8)	27.0 (24.5-30.2)
Renal failure		
Not dialysis dependent	312 (10.3)	161 (10.7)
Dialysis dependent	11 (0.4)	3 (0.2)
Platelet count, median (IQR), $\times 10^9/L$	208 (176-245)	206 (174-246)

Abbreviation: IQR, interquartile range.

^a Data are reported as No. (%) unless otherwise indicated.

^b Calculated as weight in kilograms divided by height in meters squared.

noninferior to manual compression in terms of vascular access-site complications; time to hemostasis was significantly shorter with VCD compared with manual compression; time to hemostasis was shorter with intravascular VCD vs extravascular VCD; and device deployment failures were less frequent with intravascular VCD vs extravascular VCD.

Although VCDs have been used in clinical practice for approximately 20 years, a degree of controversy has continued to surround their use. The principal reasons for using these devices, which are associated with additional costs compared with manual compression, are to reduce time to hemostasis, facilitate earlier mobilization after sheath removal, and enhance patient comfort.¹ Initial randomized controlled trials that included consideration of these principal reasons consistently showed benefit to VCD use when compared with manual compression. However, the scale of these trials was modest—typically 100 to 500 patients—and the studies were not powered for safety end points such as access-site bleeding, pseudoaneurysm formation, or other vascular complications. In fact, a meta-analysis of 30 trials enrolling approximately 4000 patients concluded that the methodological quality of the available evidence with VCD use was poor and that existing evidence suggested an unfavorable safety profile in comparison with manual compression.⁴ A more recent systematic review similarly failed to dispel safety concerns.⁵

Against this background, the results of this trial may represent an important development for the clinical use of these

Table 2. Antithrombotic Medication on Admission

	No. (%) of Patients	
	Vascular Closure Device (n = 3015)	Manual Compression (n = 1509)
Acetylsalicylic acid	2072 (67)	1025 (68)
ADP-receptor blocker		
Clopidogrel	1058 (35.1)	503 (33.3)
Prasugrel	131 (4.3)	48 (3.2)
Ticagrelor	29 (1.0)	16 (1.1)
Oral anticoagulation		
Warfarins	330 (10.9)	175 (11.6)
Rivaroxaban	42 (1.4)	33 (2.2)
Dabigatran	14 (0.5)	6 (0.4)
Apixaban	2 (0.1)	2 (0.1)

Abbreviation: ADP, adenosine diphosphate.

devices. By enrolling more than 4500 patients, ISAR-CLOSURE represents the largest randomized clinical trial of VCD to date. The trial was specifically powered for a primary safety end point—the composite of vascular complications at 30 days—and the test hypothesis was that VCD use would be noninferior to standard manual compression. The null hypothesis could be rejected with a high degree of certainty and noninferiority is highly likely (primary end point rate for VCD, 6.9% vs 7.9% for manual compression; *P* value for noninferiority <.001). In fact, the incidence of large hematoma was significantly reduced with VCD use. Moreover, in line with expectations, metrics of efficacy, such as time to hemostasis, were clearly in favor of VCD use. Overall, the increase in efficacy of VCD use, with no trade-off in safety, provides a sound rationale for the use of VCD over manual compression in daily routine.

The results of our study are broadly in line with recently published results from the CLOSE-UP study (CLOSure DEvices Used in everyday Practice). In CLOSE-UP, the primary end point of large groin hematoma was significantly lower with the extravascular Femoseal VCD compared with manual compression (2.2% vs 6.7%; *P* = .002).⁸ In our trial, we also observed a reduction in large hematoma, although the magnitude was more modest (4.8% vs 6.8%; *P* = .006). The reasons for the difference in the magnitude of effect are unclear but may be due to the differences in immobilization protocols. In the CLOSE-UP study, recommendations for bedrest were the same in both groups; in our study we allowed earlier mobilization after VCD vs after manual compression (2 vs 6 hours) and the rate of need for repeat compression was higher in the VCD group (1.8% vs 0.7%; *P* = .003). In addition, in ISAR-CLOSURE we systematically assessed for pseudoaneurysm and arteriovenous fistula with duplex ultrasound assessment of the groin prior to hospital discharge and found no significant differences between the VCD use and manual compression. Taken together, these findings are important as it was the end points of groin hematoma and pseudoaneurysm that caused concern in previous meta-analyses.^{4,5}

A further important limitation of existing literature with VCD use is the lack of direct comparative efficacy studies

between different devices in contemporary use. In this respect, in ISAR-CLOSURE we also undertook a randomized comparison between 2 devices: an intravascular VCD and an extravascular VCD. The main finding was that vascular access site complications were numerically lower, although not statistically significantly lower, in patients assigned to the intravascular VCD group compared with the extravascular VCD (6.0% vs 7.8%; $P = .04$). In addition, both time to hemostasis and closure device failure were lower with the intravascular VCD. The observed trend toward more favorable outcomes with the intravascular VCD, as compared with the extravascular VCD, might be explained by the different mechanisms by which they achieve hemostasis. It could be speculated that the intravascular positioning of the intravascular VCD provides more tension, therefore a tighter fit and improved hemostasis.

Table 3. Angiographic and Procedural Characteristics

	Vascular Closure Device (n = 3015)	Manual Compression (n = 1509)
Ejection fraction, median (IQR), % ^a	60 (52-62)	60 (52-62)
Diseased vessels, No. (%)		
1	522 (17.3)	269 (17.8)
2	567 (18.8)	272 (18.0)
3	930 (30.8)	452 (30.0)
No obstructive coronary artery disease	996 (33.0)	516 (34.2)
Multivessel disease, No. (%)	1497 (49.7)	724 (48.0)
Arterial blood pressure, median (IQR), mm Hg		
Systolic	140 (129-160)	140 (128-160)
Diastolic	75 (65-80)	75 (65-80)

Abbreviation: IQR, interquartile range.

^a Data were available for 3872 patients.

Limitations

Our trial has a number of important limitations. First, due to the different study procedures used to achieve hemostasis, blinding of treatment allocation to patients and treating physicians was not feasible. However, we tried to minimize the bias introduced by the open-label design by end point analysis according to precise criteria for end point assessment, use of core laboratories, blinded adjudication by event adjudication committee members, and analysis according to intention-to-treat measures. Despite these measures, we cannot fully exclude the influence of bias inherent to a study with open-label design.

Second, we enrolled only patients undergoing diagnostic coronary angiography and excluded those undergoing percutaneous coronary intervention. The reason for this decision was the variability in the use of periprocedural antithrombotic therapy in patients undergoing intervention, which makes assessment of the relative contribution of the different arteriotomy closure methods difficult to interpret. In addition, a previous meta-analysis of VCD use documented significant heterogeneity in outcomes according to whether patients underwent diagnostic or therapeutic procedures.⁹ However, the results of our study provide a useful basis for the investigation of VCD use in patients undergoing coronary intervention as well as in procedures with sheath size greater than 6 French.

Third, patients at high risk for vascular complications, including those with heavy vascular calcification, previous TEA or patch plastic of the common femoral artery, or symptomatic leg ischemia were excluded.

Fourth, 30-day follow-up was complete in 93% of the patients. Had we excluded patients with incomplete 30-day follow-up from the analysis, the power of the study would have decreased from 80% to 79%. However, the overwhelming majority of the end point events occurred during hospital stay and only 22 of the 332 patients with incomplete 30-day follow-up did not have a duplex sonographic examination before discharge. Thus the number of events that we

Table 4. Outcomes at 30 Days

	No. (%) of Patients		Difference in Proportions, % (95% CI)	P Value
	Vascular Closure Device (n = 3015)	Manual Compression (n = 1509)		
Vascular access site complications (primary end point) ^a	208 (6.9)	119 (7.9)	-1 (-2.7 to 0.7)	<.001 ^b
Hematoma ≥5 cm	145 (4.8)	102 (6.8)	-2 (-3.4 to -0.4)	.006
Pseudoaneurysm	53 (1.8)	23 (1.5)	0.3 (-0.5 to 1.1)	.56
Arteriovenous fistula	12 (0.4)	2 (0.1)	0.3 (-0.1 to 0.6)	.13
Access site-related major bleeding ^c	3 (0.1)	3 (0.2)	-0.1 (-0.4 to 0.2)	.39
Acute ipsilateral leg ischemia	0	0		
Need for vascular surgical or interventional treatment	0	0		
Local infection	1	0		.48
Secondary end points				
Time to hemostasis, median (IQR), min	1 (0.5 to 2.0)	10 (10 to 15)		<.001
Repeat manual compression	53 (1.8)	10 (0.7)		.003

Abbreviation: IQR, interquartile range.

^a Primary end point defined as the composite of hematoma at least 5 cm in size, pseudoaneurysm, arteriovenous fistula, access site-related major bleeding, acute ipsilateral leg ischemia, need for vascular surgical or interventional treatment, or local infection.

^b P value from the noninferiority analysis.

^c Based on criteria from REPLACE-2 (Randomized Evaluation in PCI Linking Angiomax to Reduced Clinical Events).

might have missed among patients without a complete 30-day follow-up is unlikely to be relevant. Finally, catheterization via the radial artery approach is another method investigated for reducing access-site complications, although comparison against this strategy was beyond the scope of the current trial.^{1,10}

Conclusions

In patients undergoing transfemoral coronary angiography, VCDs were noninferior to manual compression in terms of vascular access site complications and reduced time to hemostasis.

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The Instrumental Sealing of Arterial puncture site—CLOSURE device vs manual compression (ISAR-CLOSURE) Trial Investigators

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