CARDIVA MEDICAL, INC.

VASCADE MVP® Venous Vascular Closure System (VVCS)

INSTRUCTIONS FOR USE
Model 800-612C

CAUTION – Federal (USA) law restricts this device to sale by or on the order of a physician

DESCRIPTION

The VASCADE MVP Venous Vascular Closure System (VVCS) Model 800-612C is intended to seal the femoral vein access site(s) at the completion of the procedure. The system is designed to deliver a resorbable Collagen Patch, extra-vascularly, at the venotomy site to aid in achieving hemostasis. The device can be used in 6F to 12F inner diameter (15F maximum outer diameter), 12cm[1] introducer sheaths. The system consists of a sterile disposable Vascular Closure Catheter which houses a resorbable Collagen Patch, and the VASCADE MVP Clip (refer to Figure 1). The collagen patch is composed of type I Bovine collagen and is delivered in a compressed form that is approximately 15mm in length. The dry weight of the collagen is 12mg ± 3mg. The patch expands as a result of rehydration in the presence of blood in the tissue tract to provide an extravascular seal. A radiopaque proximal marker band on the Catheter provides means to aid in verifying placement of the patch in the tissue tract adjacent to the femoral venotomy site prior to the release of the patch. A second distal marker band locates the distal tip of the VASCADE MVP Disc. After completion of the procedure, the VASCADE MVP Catheter is inserted through the introducer sheath. The VASCADE MVP Disc is then deployed within the vessel and the introducer sheath is removed over the VASCADE MVP Catheter. After the introducer sheath is removed, the VASCADE MVP Disc is positioned against the intimal aspect of the venotomy, providing both temporary hemostasis and protection from intravascular placement of the Collagen Patch, and the VASCADE MVP Clip is applied at skin level to maintain the position of the Disc. After confirming the position of the Collagen Patch either fluoroscopically or by ultrasound, the Black Sleeve is unlocked and retracted to expose the Collagen Patch to the tissue tract. The system is left in place for a brief dwell period to allow the patch to swell, after which the Disc is collapsed and the VASCADE MVP Catheter is removed from the vein leaving the resorbable, extra-vascular, hemostatic Collagen Patch at the venotomy site providing hemostasis.

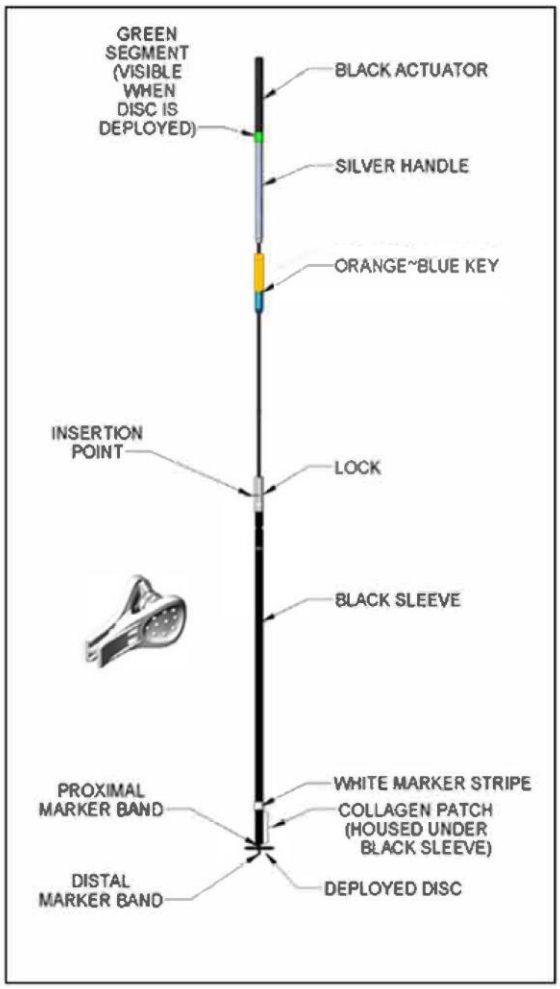


Fig. 1 – VASCADE MVP®
Venous Vascular Closure System (VVCS)

Description of Use for Multi-Access Procedures:

Multi-access site procedures such as cardiac ablations performed by electrophysiologists for the treatment of arrhythmias require the use of several access sites (multi-access), typically placed in the femoral vein of one or both limbs. The AMBULATE Trial (see clinical data section) comprehensively studied these multi-access site procedures by closing multiple venotomies in the same vein, and evaluating the interactions between indwelling procedural sheaths and VASCADE MVP.

[1] *Overall length of the sheath (including the hub) needs to be less than 15cm.*

A multi-access site indication is required for vascular closure devices to provide hemostasis in procedures that require more than one access site in the same vessel such as cardiac ablations. VASCADE MVP Venous Vascular Closure System is indicated for this use

INDICATIONS FOR USE

The VASCADE MVP Venous Vascular Closure System (VVCS) Model 800-612C is indicated for the percutaneous closure of femoral venous access sites while reducing time to ambulation, total post-procedure time, time to hemostasis, and time to discharge eligibility in patients who have undergone catheter-based procedures utilizing 6 – 12F inner diameter (15F maximum outer diameter) procedural sheaths, with single or multiple access sites in one or both limbs.

CONTRAINDICATIONS

The VASCADE MVP VVCS should not be used in patients with a known allergy to bovine derivatives.

WARNINGS

- Do not reuse or re-sterilize. The VASCADE MVP is intended to be used once only for a single patient. Product reuse or re-sterilization, may result in transmission of infectious or blood borne diseases and/or death.
- Do not use if components or packaging appear to be damaged or defective or if any portion of the packaging has been previously opened. Damaged or opened packages may compromise product functionality.
- Do not use if product is beyond the expiration date. Product performance has not been established beyond the labeled shelf life.
- Do not deploy the VASCADE MVP Disc in a stent. Do not pull the deployed VASCADE MVP disc through a stent. Damage to the product may occur.
- Do not use VASCADE MVP if access is through a previously placed permanent closure device such as a metal clip and/or permanent suture. Interference between the two closure devices may result.
- Do not deploy the Collagen Patch if there is a suspicion that the VASCADE MVP Disc is not seated against the intimal aspect of the venotomy site. Partial or complete obstruction of blood flow may result.
- Do not deploy a second collagen patch at the same access site within 30 days. The previously implanted collagen plug may be inadvertently introduced into the femoral vessel.

PRECAUTIONS

- The VASCADE MVP should only be used by a trained licensed physician or healthcare professional.
    - Note the training referred to here is previous training for accessing vessels, and positioning and using catheters. The VASCADE MVP device does not require formal training beyond review of the content provided in this IFU.
- Do not use in access sites where there is suspicion of a “backwall” stick. Increased bleeding risk may occur.
- Do not use if venotomy is noted to be a “side stick.” Bleeding risk may increase.
- Do not use if venotomy site is noted to be “high,” above the Inguinal Ligament (cephalad to lower half of the femoral head or the inferior epigastric artery origin from the external iliac artery). This may increase the risk of bleeding.
- Do not use in a vein with suspected intraluminal thrombus, hematoma, pseudoaneurysm, or arteriovenous fistula. These conditions may complicate proper device use and performance.
- Do not use if intra-procedural bleeding around the introducer sheath is noted including hematoma formation (sign of possible multiple wall stick). This may suggest problems with the access site.
- Do not use in a procedural sheath > 12cm in length (or >15cm in overall length) or with a diameter other than 6-12F. This may complicate disk deployment.

SPECIAL PATIENT POPULATIONS

NOTE: The safety and effectiveness of VASCADE MVP have not been evaluated in the following patients who are/have:

- Less than 18 years of age;
- Pregnant and/or lactating women;
- Pre-existing immunodeficiency disorder and/or chronic use of systemic steroids;
- Known significant coagulopathy/bleeding disorder such as thrombocytopenia (platelet count <100,000/mm^3), thrombasthenia, hemophilia, von Willebrand’s disease or anemia (Hemoglobin <10g/dL, Hematocrit <30%);
- Previous vascular grafts or surgery at the target vessel access site;
- Symptomatic ipsilateral lower extremity ischemia;
- Femoral venous lumen less than 6 mm;
- Length of the tissue tract, the distance between the anterior venous wall and skin, is estimated to be less than 2.5cm;
- Fibrinogen level < 150 mg/dl if patient received fibrinolytic agent;
- Extreme morbid obesity (BMI > 45 kg/m2) or underweight (BMI < 20 kg/m^2);

Adverse Events

Complications may occur and may be related to the procedure or the vascular closure. They include, but are not limited to:

- Allergic response
- Vascular occlusion
- Venous thrombus
- Arterio-venous fistula
- Bleeding from the puncture site
- Oozing from the puncture site
- Bruising at the puncture site
- Death
- Device failure/malfunction
- Edema
- Embolization tissue, (thrombus, air, calcific debris, device)
- Pulmonary Embolism
- Hematoma
- Infection
- Inflammatory response
- Intimal tear / dissection
- Laceration of the vessel wall
- Lower extremity ischemia
- Perforation of the vessel wall
- Peripheral nerve injury
- Pseudoaneurysm
- Retroperitoneal bleeding
- Deep vein thrombosis
- Vascular injury
- Vasovagal response
- Wound dehiscence
- Puncture site pain
- Superficial vein thrombosis

AMBULATE CLINICAL TRIAL

VASCADE MVP was evaluated in a prospective, multi-center, randomized (1:1) clinical trial (the AMBULATE Trial) in 13 sites in the United States. The trial involved 204 patients undergoing catheterization procedures, comparing VASCADE MVP (100 patients) to Manual Compression (104 patients). Table 1 and Table 2 summarize the reported major and minor complications in the trial for all patients.

The major complication rate*s* are clinically the same *(0%)* for both VASCADE MVP and Manual Compression.

Table 1: Major Venous Access Site Closure-Related Complications, Number of Limbs with Each Event

Major Venous Access Site Closure-Related Complications at 30 Days by Event	**VASCADE MVP** (N=199)		**Manual Compression** (N=209)	
Any major venous access site closure-related complication	0	0.0%	0	0.0%
Access site-related bleeding requiring transfusion	0	0.0%	0	0.0%
Vascular injury requiring surgical repair	0	0.0%	0	0.0%
Access site-related infection confirmed and requiring intravenous antibiotics and/or extended hospitalization	0	0.0%	0	0.0%
New onset permanent access site-related nerve injury (i.e., persisting for > 30 days)	0	0.0%	0	0.0%
New onset access site-related nerve injury in the ipsilateral lower extremity requiring surgical repair	0	0.0%	0	0.0%
Pulmonary embolism requiring surgical or endovascular intervention and/or resulting in death	0	0.0%	0	0.0%
Pulmonary embolism NOT requiring surgical or endovascular intervention and/or NOT resulting in death	0	0.0%	0	0.0%

The VASCADE MVP minor complication rate is numerically lower than Manual Compression and is clinically similar.

Table 2: Minor Venous Access Site Closure-Related Complications, Reported, Number of Limbs with Each Event

Minor Venous Access Site Closure-Related Complications at 30 Days by Event	**VASCADE MVP** (N=199)		**Manual Compression** (N=209)	
Any Minor Venous Access Site Closure-Related Complication	2	1.0%	5	2.4%
Access site-related bleeding requiring > 30 minutes of continual manual compression to achieve initial venous hemostasis	0	0.0%	0	0.0%
Access site-related hematoma > 6 cm documented by ultrasound	0	0.0%	2	1.0%
Late access site-related bleeding (following hospital discharge)	0	0.0%	0	0.0%
Ipsilateral deep vein thrombosis, confirmed by ultrasound/imaging	0	0.0%	0	0.0%

Minor Venous Access Site Closure-Related Complications at 30 Days by Event	VASCADE MVP (N=199)		Manual Compression (N=209)	
Localized access site infection confirmed and treated with intramuscular or oral antibiotics	1	0.5%	1	0.5%
Arteriovenous fistula requiring treatment	0	0.0%	0	0.0%
Arteriovenous fistula not requiring treatment	0	0.0%	1	0.5%
Pseudoaneurysm requiring thrombin/fibrin adhesive injection or ultrasound-guided compression	1	0.5%	0	0.0%
Pseudoaneurysm not requiring treatment	0	0.0%	0	0.0%
Access site-related vessel laceration	0	0.0%	0	0.0%
Access site-related wound dehiscence	0	0.0%	0	0.0%
Transient access site-related nerve injury	0	0.0%	1	0.5%

VASCADE MVP 6-12F VVCS AMBULATE TRIAL

The AMBULATE Trial was a prospective, randomized, controlled multi-center clinical trial designed to evaluate the safety and effectiveness of the study device in sealing multiple femoral venous access sites and providing reduced times to ambulation compared with manual compression at the completion of catheter-based procedures performed through 6 – 12F inner diameter introducer sheaths. The trial was conducted at 13 sites in the United States and involved 204 patients undergoing catheterization procedures, comparing VASCADE MVP VVCS (100 patients) to Manual Compression (104 patients).

All of the randomized patients in the study were patients undergoing interventional electrophysiology procedures for the ablation of cardiac arrhythmias which included atrial fibrillation, atrial flutter, atrial fibrillation-flutter, supraventricular tachycardia, and ventricular tachycardia. Only patients with multiple access sites were enrolled in order to support the desired indication. Randomization was stratified to account for patients with varying numbers of access sites, namely 3 access sites/patient and 4 access sites/patient, in a 1:1 treatment device to control arm ratio to ensure treatment and control arms have the same proportion of access sites/patient, i.e., 3 access sites/patient vs. 4 access sites/patient. Adults age ≥ 18 were eligible if they met the following inclusion criteria: undergoing elective, non-emergent, catheter-based procedures via the common femoral vein(s) using a 6F to 12F inner diameter introducer sheath; minimum of 3 and maximum of 4 femoral venous access sites, and a maximum of 2 access sites per leg. Patients were excluded if they had any of the following: active systemic or cutaneous infection or inflammation in vicinity of the groin; any pre-existing immunodeficiency disorder; chronic use of high dose systemic steroids; history of bleeding diathesis, coagulopathy, hypercoagulability; platelet count < 100,000 cells/mm3; or severe comorbidities with life expectancy less than 12 months in the opinion of the site investigator. Patients were also excluded if they had undergone femoral arteriotomy or venotomy within the past 10 days, experienced previous vascular complications or residual hematoma, had been treated with an intravascular closure device within the previous 30 days, or who were scheduled for femoral venous or arterial access within the next 30 days. Additional exclusion criteria included history of DVT~~,~~ pulmonary embolism~~,~~ thrombophlebitis~~,~~ significant anemia or renal insufficiency; BMI > 45 kg/m2 or < 20 kg/m2; inability to routinely walk at least 20 ft. without assistance; use of low molecular-weight heparin (LMWH) within 8 hours before or after the procedure; and concomitant procedures or conditions that would interfere with an ambulation attempt at 2-3 hours post-procedure. If participants met the eligibility criteria, then they were consented for the study prior to their electrophysiology procedure. At the end of the study, participants were excluded if any of the following occurred during the electrophysiology procedure: any attempt at femoral arterial access; procedural complications that would interfere with routine recovery, ambulation, or discharge times; difficulty with needle puncture or insertion of the introducer sheath; sheath placement cephalad to lower half of the femoral head or the inferior epigastric vein origin from the external iliac vein; obvious intraprocedural bleeding or thrombotic complications; any sheath use < 6 or > 12F inner diameter; or tissue tract < 2.5 cm deep).
All patients were scheduled to return for follow-up examinations at 30 ± 7 days post-procedure. Post-procedure, patients were evaluated for any major or minor complications or adverse event including bleeding, neurological and other potential device or procedure-related adverse effects. Out of 204 enrolled patients, 99% (202) patients were available for analysis at the completion of the study; one patient in each treatment group was lost to follow up and one device patient completed the follow up-visit at 3 days post-procedure. Of the 204 total randomized patients in the study, 192 patients (94.1%) completed a follow-up office visit, with 178 patients (87.3%) completing the 30-day (± 7 days) follow-up visit per protocol. A subset of 50 patients was also enrolled in an Ultrasound Sub-Study, with exams performed at the 30 ± 7-day follow-up visit.

The baseline demographic and clinical characteristics of the 2 treatment groups were very similar. The mean ages in the VASCADE MVP and manual compression groups were 61.5 ± 11.6 years, and 63.4 ± 11.1 years, respectively. The percentage of female

subjects was 33% in the VASCADE MVP group and 38% in the manual compression group. The mean BMI was 29.0 in the VASCADE MVP group and 29.3 in the manual compression group. Pre-procedure anticoagulant / antiplatelet administration within the previous 24 hours was reported in 84% of VASCADE MVP and 85% of manual compression cases. In the randomized cohort, intra-procedural heparin was administered in 85% of VASCADE MVP cases and 90% of manual compression cases. Of those cases, protamine was administered in 92% of VASCADE MVP cases and 91% of manual compression cases. Activated clotting times (ACTs) were collected at the end of the catheterization procedure in subjects receiving unfractionated heparin, with mean ACT for subjects reported as 298.6 seconds vs. 285.9 seconds in the VASCADE MVP and manual compression groups, respectively.

EFFECTIVENESS RESULTS

A total of 204 of the 204 enrolled patients in the AMBULATE Trial were evaluable for effectiveness. Time to Ambulation (TTA), Total Post Procedure Time (TPPT), Time to Hemostasis, Time to Discharge Eligibility (TTDE), Time to Discharge (TTD), and Time to Closure Eligibility (TTCE) are presented in Table 3 below.

The primary effectiveness endpoint was time to ambulation (TTA), defined as elapsed time between removal of the final VASCADE MVP device (treatment arm) or removal of the final sheath (control arm), and time when subject stands and walks 20 feet without evidence of venous re-bleeding from the femoral access sites. Time to Ambulation was reported in hours (h): minutes (mm) as a per-patient analysis. For the primary ANCOVA model adjusting for the stratification factor, i.e. the number of access sites, the VASCADE MVP treatment effect for TTA compared to MC was -3.32 hours, (2.8 ±1.3 hours for VASCADE MVP vs. 6.1 ±1.6 hours for manual compression; p<0.0001), indicating VASCADE MVP superiority. TPPT and TTDE demonstrated superiority over manual compression. TTH was noninferior to manual compression per the pre-specified analysis. Additionally, the TTH results implied superiority over manual compression.

Table 3: Primary and Secondary Efficacy Endpoints (TTA / TPPT / TTH / TTDE / TTD / TTCE)

Outcome	VASCADE MVP			Manual Compression			ANCOVA Analysis	
	Total	3 Access Sites	4 Access Sites	Total	3 Access Sites	4 Access Sites	Parameter Estimate (95% CI)	p-value
TTA, h							-3.32 (-3.71, -2.92)	<0.0001
N	N=100	N=31	N=69	N=104	N=34	N=70		
Mean ± SD	2.8 ± 1.3	2.5 ± 0.8	2.9 ± 1.5	6.1 ± 1.6	5.9 ± 1.2	6.2 ± 1.7		
Median (min, max)	2.2 (2.0, 11.5)	2.2 (2.0, 5.6)	2.3 (2.0, 11.5)	6.1 (3.4, 15.7)	5.3 (4.2, 9.1)	6.2 (3.4, 15.7)		
TPPT, h							-3.69 (-4.10, -3.27)	<0.0001
N	N=100	N=31	N=69	N=104	N=34	N=70		
Mean ± SD	3.1 ± 1.3	2.7 ± 0.8	3.3 ± 1.5	6.8 ± 1.7	6.4 ± 1.3	6.9 ± 1.9		
Median (min, max)	2.6 (2.2, 11.8)	2.4 (2.2, 5.9)	2.7 (2.2, 11.8)	6.4 (4.2, 15.9)	6.2 (4.5, 9.8)	6.6 (4.2, 15.9)		
TTH, min							GEE Model -7.5 (-8.7, -6.3)	<0.0001
N	N=369	N=93	N=276	N=382	N=102	N=280		
Mean ± SD	6.1 ± 3.7	5.4 ± 2.0	6.3 ± 4.1	13.7 ± 6.5	11.4 ± 6.4	14.5 ± 6.4		
Median (min, max)	5.1 (0.4, 33.3)	5.1 (1.3, 23.3)	5.1 (0.4, 33.3)	11.7 (0.6, 37.1)	10.0 (2.9, 32.7)	12.5 (0.6, 37.1)		
TTDE, h							-3.41 (-3.87, -2.96)	<0.0001
N	N=100	N=31	N=69	N=104	N=34	N=70		
Mean ± SD	3.1 ± 1.3	2.7 ± 0.8	3.2 ± 1.5	6.5 ± 1.9	6.2 ± 1.3	6.6 ± 2.2		
Median (min, max)	2.5 (2.3, 11.7)	2.5 (2.3, 5.9)	2.6 (2.3, 11.7)	6.3 (4.3, 21.3)	5.7 (4.6, 9.4)	6.5 (4.3, 21.3)		
TTD, h							-0.04 (-3.25, 3.17)	0.98
N	N=100	N=31	N=69	N=104	N=34	N=70		

Outcome	VASCADE MVP			Manual Compression			ANCOVA Analysis	
	Total	3 Access Sites	4 Access Sites	Total	3 Access Sites	4 Access Sites	Parameter Estimate (95% CI)	p-value
Mean ± SD	21.8 ± 13.4	20.5 ± 10.8	22.3 ± 14.5	21.8 ± 9.5	22.7 ± 10.6	21.4 ± 9.0		
Median (min, max)	22.3 (2.3, 96.1)	22.9 (2.3, 48.2)	22.3 (3.5, 96.1)	22.1 (5.7, 72.9)	22.8 (5.7, 71.5)	21.6 (5.8, 72.9)		
TTCE, min								
N	N=100	N=31	N=69	N=104	N=34	N=70	-27.23 (-33.86, -20.60)	<0.0001
Mean ± SD	10.5 ± 6.0	9.0 ± 4.1	11.1 ± 6.6	37.6 ± 33.2	32.2 ± 27.6	40.3 ± 35.5		
Median (min, max)	10.1 (1.7, 47.5)	9.8 (1.7, 17.5)	10.2 (2.0, 47.5)	25.2 (1.8, 132.3)	21.1 (2.0, 108.9)	27.8 (1.8, 132.3)		

Proportions of subjects achieving TTA at various fixed time points during the AMBULATE Trial are shown in Table 4.

Table 4: Proportion of Patients Achieving Ambulation at Fixed Time Points (per-patient analysis)

Time point	VASCADE MVP (N=100)		Manual Compression (N=104)	
≤ 1 hours	0	0%	0	0%
≤ 2 hours	1	1%	0	0%
≤ 3 hours	78	78%	0	0%
≤ 4 hours	84	84%	1	1%
≤ 5 hours	93	93%	18	17%
≤ 6 hours	98	98%	48	46%
≤ 7 hours	99	99%	87	84%
≤ 8 hours	99	99%	93	89%
≤ 9 hours	99	99%	100	96%
≤ 10 hours	99	99%	103	99%
≤ 12 hours	100	100%	103	99%
≤ 24 hours	100	100%	104	100%

Device Success was defined as the ability to deploy the delivery system, deliver the collagen, and achieve hemostasis with the VASCADE MVP. Device success was achieved in 351 of the 363 access sites in which device deployment was attempted (97%). Table 5 shows the proportion of subjects achieving Device Success. Device issues were limited to known device performance issues based on VASCADE MVP product family such as device pull through, unable to deploy disc, unable to achieve temporary hemostasis, and use error.

Table 5: VASCADE MVP Device Success (Device Arm Only) Per Access Site

Actual Devices Attempted	Number of Access Sites	Successes	Percent
	363	351	97%

Procedure Success was defined as attainment of final hemostasis at all venous access sites and freedom from major venous access site closure-related complications through 30 days (Per-patient analysis, both arms). No major access site-related complications were reported in either randomized group, however there were 2 VASCADE MVP subjects and 1 manual compression subject that did not complete follow-up. Therefore, Procedure Success was achieved in 98% of VASCADE MVP cases and in 99% of manual compression cases. Table 6 shows the proportion of subjects achieving Procedure Success.

Table 6: Proportion of Procedure Success

Procedure Success	VASCADE MVP (N=100)		Manual Compression (N=104)	
Yes	98	98%	103**	99%
Unknown*	2	2%	1	1%

** VASCADE MVP: subject 03-001 had an office follow-up at 3 days post-procedure and did not return for a later visit; subject 11-007 was lost to follow-up within study period*

***MC: subject 03-002 lost to follow-up within study period*

Patient Satisfaction was evaluated for all subjects. Patients were given a Patient Experience Survey to complete after successful TTA, at the time of TTDE to characterize their comfort experience while on bedrest post-procedure. The completed Survey was collected at the time of completion. The surveys were comprised of comparative study questions regarding patient actual experience (Table 7), as well as questions for scenarios with hypothetically longer (device patients) or shorter (MC patients) bedrest periods (Table 8). In all cases, patient satisfaction scores favored device over manual compression.

Table 7: Patient Experience Survey – Comparative Experience

Bedrest Experience		VASCADE MVP	Manual Compression	% Difference (MVP-MC)/MC
Patient Reported Satisfaction Scores Scale 0-10 with 0 as 'very dissatisfied' and 10 as 'very satisfied	All Patients, current procedure bedrest experience			
	N	100	102	
	Duration	8.3 ± 2.4	5.1 ± 3.4	63%
	Discomfort	7.2 ± 3.1	5.3 ± 3.1	36%
	Pain	7.5 ± 3.2	6.0 ± 3.4	25%
	Patients with a previous ablation procedure, comparison to previous experience			
	N	30	39	
	Duration	7.9 ± 2.3	5.6 ± 3.0	41%
	Discomfort	7.5 ± 2.1	5.4 ± 2.8	39%
	Pain	7.7 ± 2.8	5.5 ± 2.9 (N=38)	40%

Table 8: Patient Experience Survey Summary – Patient preference for hypothetically longer or shorter bedrest durations

Bedrest Experience		VASCADE MVP	Manual Compression
Patient Reported Satisfaction Scores Scale 0-10 with 0 as 'very dissatisfied' and 10 as 'very satisfied'	Patients Randomized to VASCADE MVP, score if bedrest were **hypothetically 2-3 hours longer**		
	N	98	-
	Duration	2.6 ± 3.1	-
	Discomfort	2.7 ± 2.9	-
	Pain	3.2 ± 3.4	-
	Patients Randomized to Manual Compression, score if bedrest were **hypothetically 2-3 hours shorter**		
	Duration (N)	-	9.1 ± 1.7 (102)
	Discomfort (N)	-	8.4 ± 2.2 (101)
	Pain (N)	-	8.2 ± 2.5 (100)

Pain medication administration during bedrest was measured as a secondary factor of patient satisfaction. Medication administered for pain or anxiety while the subject was on initial bedrest (i.e., post-procedure through successful TTA) was recorded for all subjects. Medication was administered for pain in 24% of the VASCADE MVP subjects, and in 49% of the manual compression subjects. Medication was administered for anxiety in 4.0% of the VVCS subjects, and in 2.0% of the manual compression subjects. In an ad-hoc analysis, it was found that there was a reduction in the usage of pain medications for the treatment arm (see Table).

Table 9. Pain Medication Usage

Pain Medication Usage	VASCADE MVP (N=100)		Manual Compression (N=104)		% Improvement
Yes	24	24%	51	49%	51%
No	76	76%	53	51%	

CONCLUSIONS

The results from the AMBULATE Trial demonstrate that patients who underwent catheter-based procedures utilizing 6 – 12F inner diameter (15F maximum outer diameter) procedural sheaths, with single or multiple access sites in one or both limbs, and who were treated with the Cardiva VASCADE MVP Venous Vascular Closure System (VVCS) have had statistically and clinically significant decreased time to ambulation, total post-procedure time, and time to discharge eligibility when compared to patients treated with manual compression. Additionally, time to hemostasis for VASCADE MVP compared to manual compression results were noninferior and statistically imply superiority.

In addition, the trial demonstrated that the rates of total combined major complications were clinically the same (0%) between the VASCADE MVP VVCS and manual compression patients, and that the rates of total combined minor complications were clinically similar between the VASCADE MVP VVCS and manual compression patients (1.0% VVCS vs. 2.4% manual compression).

Also, the procedure success rate for patients treated with the Cardiva VASCADE MVP VVCS was similar to patients treated with standard manual compression (98% VVCS vs. 99% manual compression). Patient satisfaction scores favored the device and pain medication use was lower in the device group compared to the manual compression group.

DEVICE PREPARATION AND PROCEDURE

Access is gained at the beginning of the index procedure for initial procedure sheath placement. Ultrasound-guided access is recommended to limit potential access site issues, such as multiple sticks, backwall stick, high stick, side stick, through-and-though, or unintentionally nicking a nearby vein or artery. During access, where more than one hole is unintentionally made in a vessel or more than one vessel is perforated at a single access site, a closure device should not be used as it may result in a hematoma. For high stick, retroperitoneal bleed may result.

If more than one sheath is planned to be placed in the same vein, the distance between the access sites should be kept at a minimum of 6 mm. Keep the stick separation at the skin level at a minimum of 6 mm and drive the needles to the vein at the same angle to keep the separation between the adjacent venotomies at a minimum of 6 mm. Imaging techniques such as ultrasound can be used to confirm the separation is as recommended.

At the time of initial introducer sheath placement, patient body habitus should be evaluated to provide reasonable assurance that the distance between the femoral venotomy and the skin surface is greater than 2.5cm. After introducer sheath placement, an anterior oblique fluoroscopic image with contrast or an ultrasound image may be digitally recorded and stored, so that the venotomy site location can be estimated and compared to the position of the proximal radiopaque marker just prior to Collagen Patch release. The proximal radiopaque marker is located immediately distal to the Collagen Patch. If more than one sheath is used in the same vein, it is recommended to close the proximal venotomy first to facilitate device placement and imaging prior to Collagen Patch release.

CAUTION: During access care should be taken so that the tissue tract is not pushed laterally or medially prior to accessing the vessel. This is to avoid misalignment of the tissue tract and the Collagen Patch relative to the venotomy site once the device is removed from the vessel, which may result in prolonged time to hemostasis.
If more than one access is made in the vein, keep a minimum of 6 mm separation between the access sites. This is to allow the disc to track back to the vessel wall. Temporary hemostasis may not be achieved if the venotomies are too close to each other.
Not achieving temporary hemostasis may be an indication that the disc is not against the vessel wall. Releasing the collagen patch may result in all or a portion of the patch to be deployed in the vessel.

1. Use the Cardiva VASCADE MVP VVCS only as described below:

Device	Model	Sheath Size Compatibility (French)		Sheath Length	Disc Size	Collagen Patch Length	Device Working Length	Maximum OD (with collapsed Disc)
		Inner Diameter	Max Outer Diameter (approx)					
Cardiva VASCADE MVP VVCS	800-612C	6F – 12F	15F	up to 12 cm	7.7 mm	15 mm	15 cm	2.1 mm

Note: The Collagen implant is a biological material compatible with Magnetic Resonance Imaging (MRI).

2. Inspect the package for damage (breaks, tears, open seals, water damage, etc.) and verify that expiration date has not passed.

3. Using standard sterile technique[2], remove the tray containing the VASCADE MVP VVCS Catheter and Clip from the foil pouch. Carefully remove VASCADE MVP VVCS Catheter and Clip from the tray. Examine the device by first verifying that the Black Sleeve is locked in position and the Collagen Patch is not exposed. Also verify that the Orange-Blue Key **(Figure 2)** is not engaged in the Lock (the Lock is located at the proximal aspect of the Black Sleeve), and the Orange-Blue Key is located at the proximal end of the Catheter Shaft. Inspect the Catheter further by examining the deployed VASCADE MVP VVCS Disc. To deploy the Disc, hold the Silver Handle firmly and pull back on the Black Actuator until it locks in place. When the Disc is locked in the deployed position, the Green Segment will become visible as shown in Figure 3. Examine the Disc, which should appear circular and symmetrical with an intact membrane. **Figure 4** shows the deployed and collapsed Disc. After examination, collapse the Disc by pressing the Black Actuator tip down **(Figure 5)**. The tip of the VASCADE MVP VVCS Catheter should return to its original profile.

[2] See Aseptic Presentation Section for additional information.

Fig. 2 – Verify Orange-Blue Key is not engaged in the Lock and Black Sleeve is locked in position

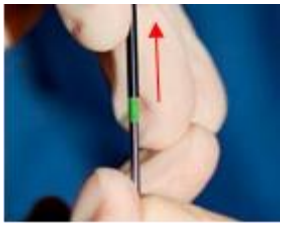


Fig. 3 – Pull back on Black Actuator Tip to deploy the Disc

Fig. 4 – Deployed & Collapsed Disc

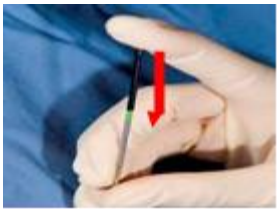


Fig. 5 – Collapse Disc by pressing Black Actuator Tip like a ballpoint pen

4. Verify that the sheath is not positioned in a tortuous vessel, by examining the sheath placement images obtained earlier. If required, retract the sheath slightly to a non-tortuous location. Verify that the sheath is still positioned within the vein. If more than one sheath is in the vein, retract the most proximal sheath (top sheath) so that the distal opening of that sheath is proximal to the distal opening of other sheaths by 3-4 cm. This is to eliminate interference of a deployed Disc with other indwelling sheaths during device deployment. **Care must be taken not to lose vessel access**. Deploy VASCADE MVP VVCS and obtain hemostasis in the most proximal sheath first (as per steps outlined below). Then move distally to repeat the steps to obtain closure for the other sheaths.

WARNING: Verify there is no vessel tortuosity or side branches within 3-4 cm from the distal opening of the sheath and the end of the sheath is not resting against the vessel wall. This is to prevent any vascular injury as a result of advancing the catheter. If required, retract the sheath slightly to a non-tortuous location, being careful not to lose vessel access.

5. Flush the sheath with sterile saline solution prior to insertion of the device.
6. Prior to insertion of device in the introducer sheath, momentarily insert the tip of the VVCS Catheter in saline solution up to the White Marker Stripe and quickly remove.

CAUTION: Do not soak the VASCADE MVP VVCS Catheter in saline. Momentarily insert only the Catheter tip in saline solution immediately before use to avoid over-hydration of the patch, which may result in difficulty of retracting the sleeve and causing Catheter pull through during the sleeve retraction step.

7. Gently insert the VASCADE MVP VVCS Catheter (with disc collapsed) into the introducer sheath hub as shown in **Figure 6**. Use short strokes to insert the device.
8. Insert the VASCADE MVP VVCS Catheter such that approximately half of the Lock is visible. Make certain that the Lock is NOT fully inserted into the sheath. See **Figure 7** for correct placement.

CAUTION: Do not advance VASCADE MVP VVCS Catheter into the patient if resistance is felt due to risk of vascular damage.

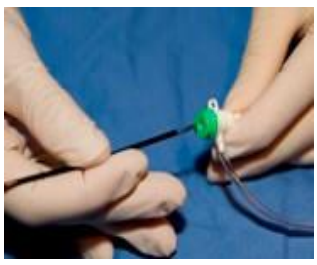


Fig. 6 – Insert device into hub of introducer sheath

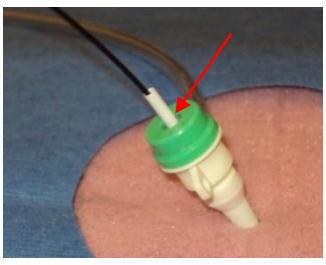


Fig. 7 – Insert device half way of the Lock

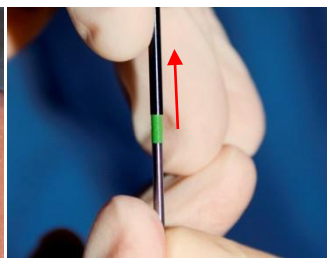


Fig. 8 – Pull back on Black Actuator Tip to deploy the VASCADE MVP VVCS Disc

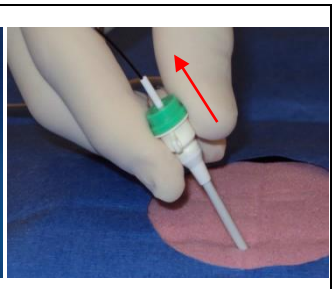


Fig. 9 – Grasp hub of sheath and remove over catheter

9. Deploy the Disc by holding the Silver Handle and pulling back the Black Actuator until it locks in place as shown in **Figure 8.**

CAUTION: Do **not** continue to pull on the Black Actuator once it is locked in place as this may damage the device.

NOTE: When the Disc is properly deployed, the Green Segment will become visible distal to the Black Actuator. If the catheter is not properly locked in place, the Black Actuator will slide back to its original position and the Green Segment will disappear indicating that the Disc is not properly deployed. In this case repeat the step for deploying the Disc by pulling the Black Actuator more firmly until it locks in place.

10. Gently remove sheath, without applying any compression at the access site or holding the VASCADE MVP VVCS Catheter**,** as shown in **Figure 9**. As the sheath slides over the VASCADE MVP VVCS Catheter, grasp the Catheter as the sheath exits the body. Continue sliding the sheath over the VASCADE MVP VVCS Catheter and discard sheath.

CAUTION: Compressing the access site during sheath removal may not allow the Disc to track back to the venotomy and may cause Disc deformation. This may lead to inability to achieve temporary hemostasis.

11. Apply gentle tension on the Black Actuator until temporary hemostasis is achieved. Note whether any portion of the White Marker Stripe, which is located near the distal aspect of the Black Sleeve, is visible above the skin. If it is, then the length of the tissue tract is less than 2.5 cm, indicating the tissue tract may not be long enough for the Collagen Patch.

WARNING: If any portion of the White Marker Stripe is showing DO NOT RELEASE the Collagen Patch as this may increase the risk of infection.

NOTE: If any portion of the White Marker Stripe is showing and the collagen patch is not to be deployed, the VASCADE MVP VVCS Catheter should be removed by collapsing the Disc and manual compression should be applied per institutional protocol.

12. Once temporary hemostasis is achieved, apply the Clip to the Black Sleeve at skin level as shown in **Figure 10.** Verify that deployed Disc is positioned against the intimal surface of the vessel at the venotomy site, either by fluoroscopy (to verify that the more proximal radiopaque marker is positioned at the venotomy), or by ultrasound. The Collagen Patch is located immediately proximal to the Proximal Marker Band. The Distal Marker Band locates the distal end of the Disc.

CAUTION: Applying too much upward tension on the Silver Handle may cause Disc to pull out of vessel. Should this occur, convert to your **institution's manual compression protocol.**
WARNING: It is important to ensure that the Disc is in contact with the intimal aspect of the venotomy before deploying the extra-vascular Collagen Patch to avoid releasing the Collagen Patch in the vessel**. This is indicated by having temporary hemostasis and further verified by either** fluoroscopy **(Figure 11a) or ultrasound imaging (Figure 11b)**.

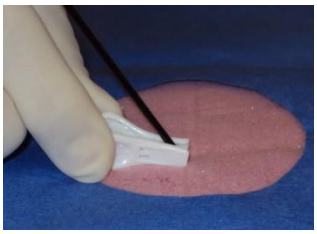


Fig. 10 – Apply Clip to Black Sleeve at skin level

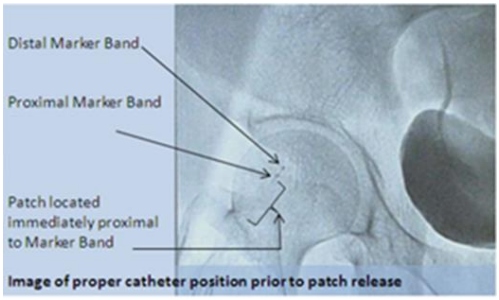


Fig. 11a – Fluoroscopic image demonstrating proper position of Disc

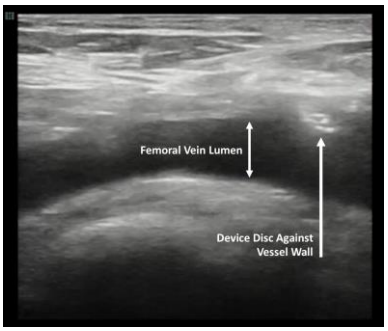


Figure 11b Ultrasound image demonstrating proper position of Disc

EXTRA-VASCULAR COLLAGEN PATCH DEPLOYMENT AND DEVICE REMOVAL

13. Once the Disc location is verified, expose the extra-vascular resorbable Collagen Patch by unlocking the Black Sleeve. This is done by grasping the Lock with the left hand, between the thumb and the index finger, and grasping the Orange-Blue Key with the right hand and then sliding the Orange-Blue Key into the Lock until no blue color is visible, as shown in **Figure 12**. Once the Sleeve is unlocked and while still holding on to the Lock, remove the Clip with the right hand, and gently slide the

Lock back along the angle of entry to retract the Black Sleeve as shown in **Figure 13**. The Black Sleeve will move freely after some initial resistance. A second resistance point may be felt after the sleeve is moved approximately 1.6 cm (0.6 inch).

Proceed to fully retract the Black Sleeve proximally to the Silver Handle. This action exposes the Collagen Patch extra-vascularly, which will swell at the venotomy site. The Collagen Patch may be allowed to swell for up to 30 seconds prior to removal of the VASCADE MVP VVCS Catheter. The Clip may be reapplied during the Collagen Patch swell period with minimal tension on the Catheter **(Figure 14)**.

NOTE: If the Black Sleeve does not retract easily, recheck that the blue end of the Orange-Blue Key is fully engaged in the Lock.

NOTE: If the Collagen Patch is removed during sleeve retraction, collapse the Disc, remove the Catheter and apply manual compression, per institutional protocol.

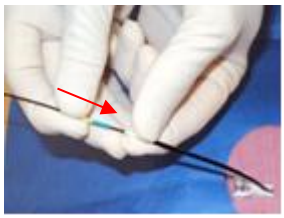


Fig. 12 – Unlock the Black Sleeve by sliding Orange-Blue Key into the Lock

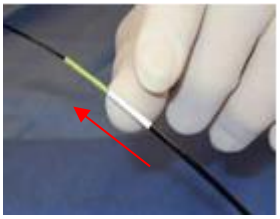


Fig. 13 – Retract the Black Sleeve by grasping the Lock and applying gentle upward tension toward the Silver Handle

Fig. 14 – Reapply Clip during the Collagen Patch swell period

Fig. 15 – Grasp Green Tube prior to collapsing the Disc

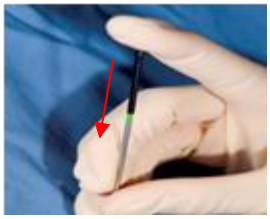


Fig. 16 – Collapse the Disc by pressing on the Black Actuator Tip

14. AFTER 15-30 seconds of patch swell time and PRIOR TO collapsing the Disc, remove the Clip. Rest the palm of the hand on the patient and grasp the green tube between the thumb and the index finger as shown in **Figure 15.** Push the green tube in the proximal direction approximately 1.5 cm while gently pulling back on the VASCADE MVP VVCS Catheter to maintain Disc position against vessel wall. The green tube may be slid back and forth 2-3 times in order to assure release of the Collagen patch from device. Upon completion of this step, leave the green tube in the forward position. Apply gentle compression at the site and collapse the Disc by pressing on the Black Actuator Tip as shown in **Figure 16**. Apply gentle manual compression at the site as the VASCADE MVP VVCS Catheter is removed. Continue to apply manual compression.

15. Observe for complete hemostasis. Manual compression can be used to decrease or stop any tract ooze until full hemostasis is achieved.

NOTE: Prior to the VASCADE MVP VVCS Catheter removal confirm that the Disc is completely collapsed by verifying that the Green Segment on the handle is no longer visible. Care should be taken not to compress too firmly over the VVCS catheter during the removal step of the device so that the catheter can be easily removed and without displacement of Collagen Patch.

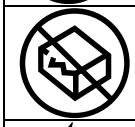
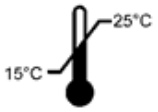
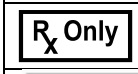
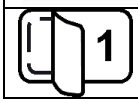
16. Apply sterile dressing to site per institution protocol. Maintain bed rest and periodically check site until patient is ready to ambulate.
17. Complete information on Patient Implant Card and provide to the patient.

Device Disposal:
After use, dispose of the contaminated device and/or packaging materials using standard hospital procedures and universally accepted practices for bio-hazardous wastes.

Additional Information for Step #3 Regarding Aseptic Presentation Steps to Follow:

- Inspect the product packaging. Observe for any breaks, holes, or openings that would compromise the integrity and sterility of the product.
- Read the label. Check the expiration date and verify correct product/size is used.
- Position near the sterile field. Be sure the scrubbed person receiving the product is prepared and ready to receive it with a clear space in the field.
    - All packaging for sterile products has a designated side to open from. Locate this side and slowly peel the package open.
    - Open the packaging with arms extended to avoid accidental contact with the product or the sterile field. Be sure the secondary sterile packaging containing the product does not come in contact with the edges of the external packaging as they are not considered sterile. Create a large enough opening in the package to remove the interior packaging containing the product without touching the non-sterile areas.
- Present the product to the scrubbed person.
- Discard packaging following facility protocol.

GRAPHICAL SYMBOLS ON THE VASCADE MVP VVCS PACKAGING

Symbol	Standard / Regulation*	Standard Reference No. / Symbol Title	Definition
	ISO 15223-1	5.1.1 / Manufacturer	medical device manufacturer
	ISO 15223-1	5.1.2 / Authorized representative in the European Community	authorized representative in the European Community
	ISO 15223-1	5.1.4 / Use-By Date	date after which the medical device is not to be used.
	ISO 15223-1	5.1.5 / Batch Code	manufacturer's batch code so that the batch or lot can be identified.
	ISO 15223-1	5.1.6 / Catalogue number	manufacturer's catalogue number so that the medical device can be identified.
	ISO 15223-1	5.2.4 / Sterilized using irradiation	medical device that has been sterilized using irradiation.
	ISO 15223-1	5.2.6 / Do not resterilize	medical device that is not to be re-sterilized.
	ISO 15223-1	5.2.8 / Do not use if package is damaged	medical device that should not be used if the package has been damaged or opened.
	ISO 15223-1	5.3.4 / Keep dry	medical device that needs to be protected from moisture.
	ISO 15223-1	5.3.7 / Temperature limit	temperature limits to which the medical device can be safely exposed.
	ISO 15223-1	5.4.2 / Do not re-use	medical device that is intended for one use, or for use on a single patient during a single procedure.
	ISO 15223-1	5.4.4 / Caution	Indicates the need for the user to consult the instructions for use for important cautionary information such as warnings and precautions that cannot, for a variety of reasons, be presented on the medical device itself.
	ISO 15223-1	5.4.5 / Contains or presence of natural rubber latex B.2 / Negation Symbol	Indicates that there is no presence of natural rubber or dry natural rubber latex as a material of construction within the medical device or the packaging of a medical device.
	21 CFR 801.109	Prescription Device	product is a medical device and Federal Law (USA) restricts this device to sale by or on the order of a physician
	N/A	Package quantity	quantity of systems in package
	ISO 11607-1	Sterile barrier packaging	Identifies the sterile barrier packaging

**Standards and Regulations:*

ISO 15223-1: *Medical devices-Symbols to be used with medical device labels, labelling and information to be supplied*

US FDA Title 21 CFR 801.109*: Prescription Devices*

ISO 11607-1*: Packaging for terminally sterilized medical devices — Part 1: Requirements for materials, sterile barrier systems and packaging systems*

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LIMITED WARRANTY

Cardiva Medical, Inc. warrants that each VASCADE MVP Venous Vascular Closure System (VVCS) is free from defects in workmanship and material under normal use and service, and provided it is used prior to the stated expiration date. Cardiva Medical, Inc. will not be liable for any incidental, special or consequential loss, damage or expense direct or indirect from the use of its product. Liability under this warranty is limited to refund or replacement of any device that has been found by Cardiva Medical, Inc. to be defective at the time of shipment. Damage to the device through misuse, alteration, improper storage or improper handling shall void this limited warranty. The remedies set forth in this warranty and limitation shall be the exclusive remedy available to any person. No employee, agent or distributor of Cardiva Medical, Inc. has any authority to alter or amend this limited warranty, or assume or bind Cardiva Medical, Inc. to any additional liability or responsibility with respect to this device. There is no express or implied warranty, including any implied warranty of merchantability or fitness for a particular purpose, on the Cardiva Medical, Inc. product(s) described herein.