

Hemostatic Wound Dressing for Postinterventional Hemostasis in Large Femoral Artery Access Sites: An Initial Efficacy and Safety Study

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Abstract

Purpose: To present the results of a prospective single-center study that evaluated the safety and efficacy of a hemostatic dressing following femoral artery access. **Methods:** Within a 9-month period, 80 patients (mean age 68±14 years; 55 men) were treated with a hemostatic dressing patch (Hematrix Active Patch) containing aminocaproic acid, calcium chloride, and thrombin after endovascular procedures via a 6- to 8-F femoral artery access. After removing the sheath, the wound dressing was placed on the puncture site followed by constant manual compression adapted to the sheath size (specified pressure times: 8 minutes for 6-F, 9 minutes for 7-F, and 10 minutes for 8-F). Patients were treated with an additional pressure bandage for 24 hours. Hemostasis was checked clinically and with duplex ultrasound after patch removal and at 24 hours. Patient characteristics [platelets, systolic blood pressure, international normalized ratio (INR), and partial thromboplastin time (PTT)], sheath sizes, and approach direction were compared among patients with successful hemostasis (within specified pressure times) vs those with prolonged compression. **Results:** A total of 39 6-F, 19 7-F, and 22 8-F sheaths were employed. In 73 (91.2%) of 80 patients, hemostasis was reached within the prespecified pressure times (mean 8.8±0.8 minutes). In 7 patients (4 6-F, 1 7-F, 2 8-F) a longer compression time was necessary (mean 34±30 minutes). No serious major complication occurred. Twelve (15.0%) minor and 5 (6.3%) moderate subcutaneous hematomas were observed. Two (2.5%) false aneurysms were treated successfully. Ambulation and discharge was possible within 24 hours in 79 (98.7%) cases. Patients with initial hemostasis and those with prolonged compression did not differ substantially ($p>0.05$) according to sheath size, approach direction, INR (1.09±0.3 vs 1.11±0.3), platelets ($234\pm47\times10^3/\mu\text{L}$ vs $249\pm93\times10^3/\mu\text{L}$), systolic blood pressure (150±26 vs 152±17 mm Hg), or PTT (31±7.9 vs 34.8±10.0 seconds). **Conclusion:** The evaluated wound dressing seems to be safe and effective in reducing time to hemostasis in large arterial access sites. However, a randomized trial with a larger population and an active control group is necessary to confirm these preliminary data. Moreover, additional focus on shortening the time to ambulation is required in future studies.

Keywords

compression, femoral artery access, hematoma, hemostasis, hemostatic dressing patch, pseudoaneurysm, vascular access

Introduction

Achieving safe and quick hemostasis after percutaneous vascular interventions (PVI) is a major concern.^{1,2} Complications following arterial cannulation can be life-threatening. Although severe bleeding rarely occurs, extensive hematoma, arteriovenous fistula (AVF), and false aneurysm are adverse access site complications with incidences ranging from 2.2% to 6.6%; these sequelae can be responsible for delayed hospital discharge and increased mortality.³

In clinical routine, manual compression is still the gold standard for achieving safe hemostasis after PVI, although this procedure is time-consuming and uncomfortable for the

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patient due to extended immobilization and groin pressure.⁴ In this context, traditional manual compression has to be maintained up to 30 minutes depending on the size of the arterial cannulation. In 6-F and larger femoral accesses, compression times between 15 and 30 minutes are required to achieve safe hemostasis. Afterward an additional pressure bandage is usually necessary for up to 24 hours.

Since 1990, several different vascular closure devices have been developed and are increasingly used to obtain quick and safe hemostasis and reduce time to ambulation as well as access site complications. All of them require training prior to application.⁵ Moreover, topical hemostatic patches coated with different procoagulant components are available for the management of bleeding wounds, including vascular access sites.^{4,6–10} There are only a few studies evaluating safety and efficacy of these hemostatic patches in achieving hemostasis after diagnostic or interventional coronary or peripheral PVI.^{6,8–12}

Since 2011, a hemostatic wound dressing (Hematrix Active Patch; Hematrix, Neubiberg, Germany) has been approved for clinical use in cases of traumatic or iatrogenic venous and arterial bleeding. However, little clinical data are available concerning the safety and efficacy of this patch in terms of sealing arterial access sites between 6-F and 8-F.¹² In addition the potential use of such patches in antegrade access sites has not been addressed yet. Therefore, the purpose of this prospective cohort study was to evaluate safety and efficacy of this novel hemostatic patch with special regard to immediate hemostasis at the vascular access site of fully anticoagulated patients after peripheral PVIs.

Methods

Study Design and Device

In a prospective, single-center cohort study, 80 patients (mean age 68±14 years; 55 men) were treated with the Hematrix Active Patch hemostatic dressing after endovascular procedures via a 6-F to 8-F common femoral artery access within a 9-month period from January to September 2014. Patients with extreme obesity (BMI >35 kg/m²) or known intolerance to the dressing components were not eligible. The study was in accordance with the Declaration of Helsinki and was approved by the institutional review board. All patients gave written informed consent and were made aware of potential risks.

The Hematrix hemostatic wound dressing contains spongy polyurethane foam impregnated with the coagulant components aminocaproic acid (27 mg), calcium chloride (0.9 mg), and thrombin (8 IU thrombin/cm²). According to the manufacturer's recommendation it has to be centered on the wound/access site for at least 5 to 6 minutes with constant manual pressure in order to support the coagulation process without leaving foreign material at the access site or

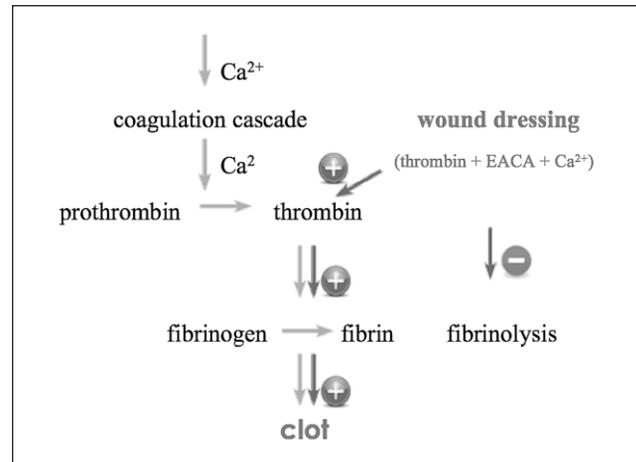


Figure 1. Mechanism of action of the evaluated hemostatic wound dressing. EACA, ϵ -aminocaproic acid.

in the tissue tract. The coagulation process starts retrograde after blood intrusion from the wound dressing toward the punctured vessel wall without proceeding intra-arterially (Figure 1).

PVI and Hemostasis

All patients were on aspirin (100 mg/d) before the procedure, and all had laboratory analyses of platelet count, international normalized ratio (INR), and partial thromboplastin time (PTT) within 24 hours prior to PVI.

The procedure was performed by a board-certified interventional radiologist (18 years of experience) using a single-wall puncture technique. Successful access via the common femoral artery was documented angiographically. Heparin (5000 units) was given intra-arterially after sheath insertion. An antegrade ipsilateral femoral artery approach (n=39) was used for angioplasty of the superficial femoral, popliteal, or crural arteries, while a retrograde ipsilateral approach (n=41) was used for iliac or renal artery angioplasty. A contralateral crossover approach was selected in 8 patients suffering from multilevel disease. Data pertaining to the size and direction of the access sites are given in Table 1. Sheath sizes measured 6-F (n=39), 7-F (n=19), and 8-F (n=22). The activated clotting time was not measured. Calcification at the access site was identified as readily apparent radiopacities within the vascular wall and was graded as none/mild, moderate, and severe based on a modified grading system of Mintz et al.¹³

After the intervention, the sheath was removed and moderate manual occlusive pressure was applied proximal to the puncture site by an experienced resident (3 years of experience). Since some blood intrusion is necessary to promote the coagulation process, a small amount of blood was allowed to reach the skin surface. The wound dressing was

Table 1. Overview of Interventional Procedures.

Sheath Size, F	n	Target	n	Side	n	Direction	n
6	39	EIA/CIA	36	Right	50	Antegrade	39
7	19	CFA/SFA/POP	36	Left	30	Retrograde	41
8	22	ATA/ATP/FA	6				
		Renal artery	2				

Abbreviations: ATA, anterior tibial artery; ATP, posterior tibial artery; CFA, common femoral artery; CIA, common iliac artery; EIA, external iliac artery; FA, fibular artery; POP, popliteal artery; SFA, superficial femoral artery.

then centered with moderate pressure on this initial blood discharge, and the access site was completely covered. Manual pressure was held for a prescribed period of time (without intermittent removal) based on sheath size: 8 minutes for 6-F, 9 minutes for 7-F, and 10 minutes for 8-F.

After the prescribed pressure time, the hemostatic wound dressing was removed, and the puncture site was checked clinically for hemostasis. A transparent medical strip (OPSITE; Smith & Nephew Medical Limited, Hull, England) was fixed on the access site, and the resident performed color-coded duplex ultrasound to rule out any complication and to observe the surrounding soft tissue in the area of the puncture site. If hemostasis failed after the prescribed pressure time, conventional manual compression was conducted until hemostasis. The time from sheath removal to hemostasis was recorded. Afterward, according to a standardized institutional protocol, all patients were treated with an additional pressure bandage and bed rest for 24 hours. During this time, the nursing staff monitored the access site. Hemoglobin levels were not recorded during the observation period.

After the intervention, aspirin was continued in all patients lifelong. Patients receiving stents ($n=49$) had clopidogrel (75 mg/d) prescribed for 4 weeks. All patients had a clinical and color-coded duplex ultrasound follow-up examination after removing the pressure bandage at 24 hours.

Outcome Measures

Procedural success was defined as complete hemostasis within the prescribed pressure time; the time to hemostasis was measured from sheath removal. Clinical success was defined as ambulation and hospital discharge after 24 hours. The safety endpoint was the occurrence of complications, which were classified on the basis of outcome according to the reporting standards of the Society of Interventional Radiology.¹⁴ Minor complications were inconsequential and required no or nominal therapy, including overnight admission for observation only. Major complications were those requiring therapy or minor hospitalization (<48 hours); those requiring major therapy, an unplanned increase in the level of care, or prolonged hospitalization (>48 hours); those resulting in permanent adverse sequelae; and

those resulting in death. Complications were further subdivided as puncture-related [rebleeding, minor (<5 cm) or moderate (>5 cm) hematomas, false aneurysms, and AVFs] or device-related (eg, wound infections and allergic skin reactions). Statistical analysis was performed using the Mann-Whitney *U* test; $p<0.05$ was considered statistically significant.

Results

Efficacy

Successful hemostasis was achieved within the dedicated pressure times (mean 8.8 ± 0.8 minutes) in 73 (91.2%) of 80 patients. Seven (8.7%) patients (4 6-F, 1 7-F, and 2 8-F sheaths) required a longer compression time (mean 34 ± 30 minutes). In total, the mean time to hemostasis (including additional compression) was 10.9 ± 10.6 minutes (range 8–95). No or mild access site calcification was observed in 76 patients and moderate calcification in 4 patients. Ambulation and hospital discharge was possible in 79 (98.7%) patients within 24 hours. One patient was discharged after an additional 24-hour pressure bandage due to a pseudoaneurysm detected in the follow-up duplex scan (see below).

In the subgroup comparison of initial hemostasis and prolonged compression (Figure 2), the patients did not differ significantly in terms of INR level (1.1 ± 0.3 vs 1.1 ± 0.3 ; $p=0.70$), platelet count ($234\pm 47\times 10^3/\mu\text{L}$ vs $249\pm 93\times 10^3/\mu\text{L}$; $p=0.69$), systolic blood pressure during compression (150 ± 26 vs 152 ± 17 mm Hg; $p=0.82$), or PTT (31 ± 7.9 vs 34.8 ± 10.0 seconds; $p=0.48$). Moreover, there was no significant difference in successful hemostasis after the prescribed pressure time in different sheath sizes (Table 2) or different directions of approach.

Complications

No serious major complication occurred. The initial ultrasound examination found 12 (15.0%) minor and 5 (6.3%) moderate subcutaneous hematomas at the access site; none increased within 24 hours, and no specific treatment was necessary. The moderate hematomas were all seen in cases of prolonged compression (Table 3). There were 3 (4%)

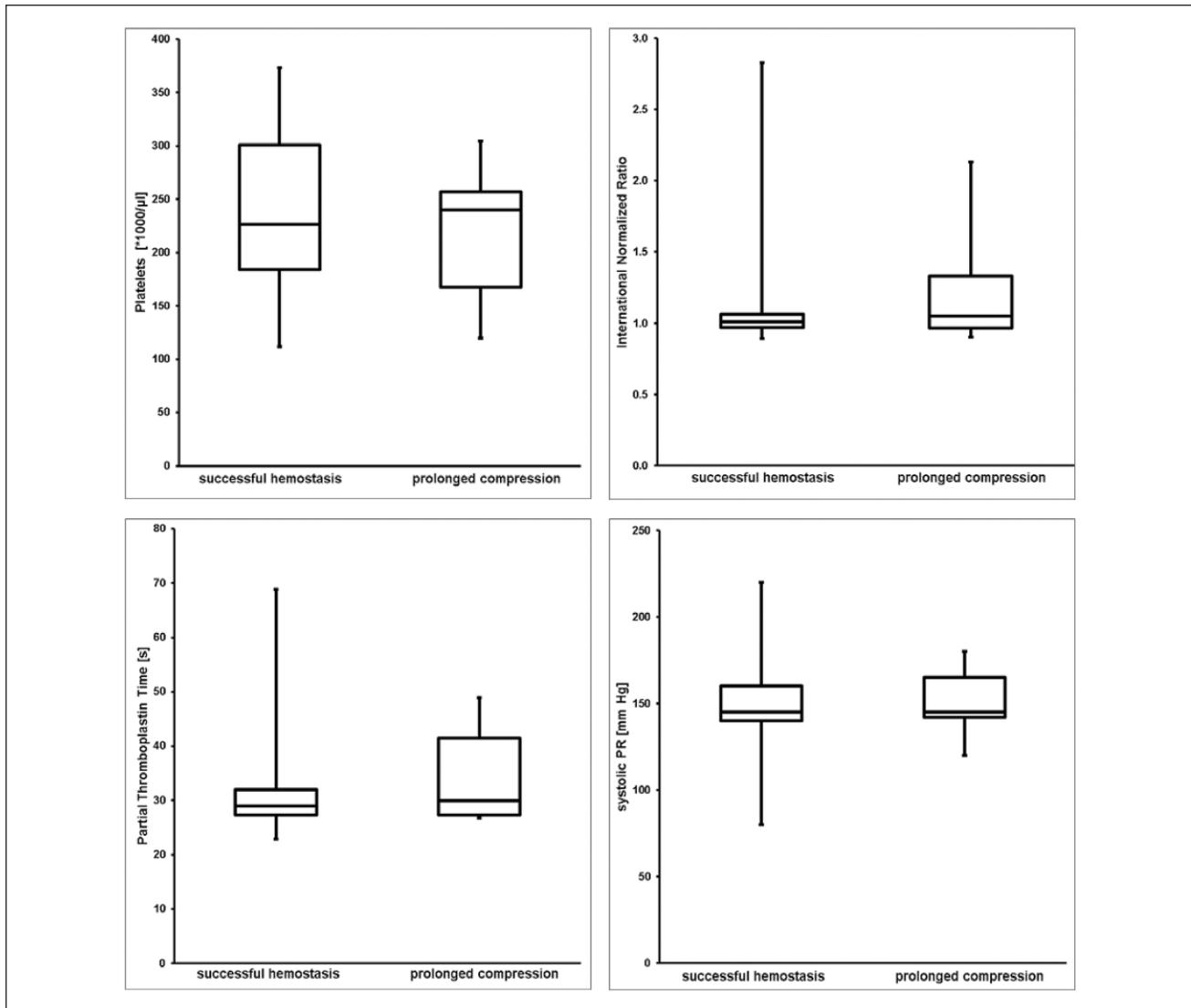


Figure 2. Comparison of partial thromboplastin time, systolic blood pressure (PR), platelets, and international normalized ratio in cases of successful hemostasis vs prolonged compression (procedural failure).

Table 2. Outcomes and Complications According to Sheath Size and Approach Direction.

	Successful Hemostasis	Prolonged Compression	Minor Bleeding	Moderate Bleeding	False Aneurysm
Sheath size, F					
6	34	5	7	3	2
7	18	1	1	1	0
8	21	1	4	1	0
Approach					
Antegrade	37	3	7	3	1
Retrograde	36	4	5	2	1

patients in whom vessel puncture was too low (in the profunda femoris artery); however, repuncture was successful after appropriate manual compression. No complications occurred in those cases.

Two false aneurysms were observed, also in the prolonged compression subgroup. The first (3 cm) was detected at the initial ultrasound in an obese 59-year-old man after 3 puncture attempts during treatment of an

Table 3. Complications in the Study Cohort and by Outcome.

Complications	Study Cohort (n=80)	Successful Hemostasis (n=73)	Prolonged Compression (n=7)
Minor bleeding	12	12	0
Moderate bleeding	5	0	5
False aneurysm	2	0	2
Severe rebleeding	0	0	0
Arteriovenous fistula	0	0	0
Local allergic reaction	0	0	0

iliac artery stenosis. Immediate ultrasound-guided manual compression was successful. A 3.5-cm pseudoaneurysm was identified 24 hours after sheath removal in a case involving an antegrade approach for superficial femoral artery disease; ultrasound-guided manual compression and 24 hours of additional pressure bandage were necessary.

There were 7 cases of minor bleeding in the antegrade accesses and 5 among the retrograde accesses (Table 3). Moderate bleeding was seen in 3 cases of antegrade and in 2 cases of retrograde access. No severe rebleeding, AVF, or device-related complications occurred in the study cohort. No surgical repair or groin-related transfusion was necessary.

Discussion

Achieving safe and quick hemostasis after peripheral PVI is a major concern. Compared with gold standard conventional manual compression times, such as 19.3 ± 7.8 minutes in 6-F percutaneous coronary interventions¹⁰ and 44.7 ± 27.4 minutes in neurointerventional procedures¹⁵ using 6- to 8-F femoral sheaths, the mean 8.8 ± 0.8 minutes in 91% of the patients treated in our study with the hemostatic patch is impressive.

We found no difference in patients with initial hemostasis and those needing prolonged compression. It is our subjective impression that calcification at the access site seems to be negligible, since prolonged compression in our patients was mainly necessary in cases of none or mild calcification. Two of the 7 patients having prolonged compression (23 and 95 minutes, respectively) were on phenprocoumon bridging (INR 1.61 and 2.13), which could have been a reason for delayed hemostasis. Another possible reason could be an insufficient retrograde coagulation process from the wound dressing toward the punctured vessel. Moreover, inadequate pressure during patch application could be the cause, even though this was performed by 2 experienced residents.

The Hematrix dressing seems to be a safe, effective, and easy to use device for sealing arterial access sites with comparable complication rates to current clip-, collagen-, or suture-based closure systems.^{4-6,16} For example, in a prospective multicenter study on access-related vascular complications after employing intravascular and extravascular

closure systems in 3014 patients, Schulz-Schüpke et al¹⁶ observed moderate hematomas in 4.8% and false aneurysm in 1.8%, rates that are similar to ours. Advantageously, the Hematrix requires no training, and no foreign material or sutures are left at the puncture site, making immediate repuncture feasible. Additionally, it can be used in any size access artery and arteriosclerotic situation.

We observed a 9% procedural failure rate using a sheath size-adjusted pressure time, which was based on the manufacturer's recommendation of at least 5 to 6 minutes of constant manual pressure on the access site. Unfortunately, there were no further recommendations on pressure times relative to sheath sizes. In this context, we were guided by the results published by Antoni et al¹² concerning 6-F access sites, as well as by our own experiences in daily clinical routine prior to initiating this study. For safety reasons, we added extra compression time per sheath size [2 minutes (33%) for 6-F, 3 minutes (50%) for 7-F, and 4 minutes (66%) for 8-F]. As regards other topical hemostatic pads, our failure rate is more or less comparable to data for the Clo-Sur PAD (Medtronic Vascular, Santa Rosa, CA, USA) published by Balzer et al,⁶ who described a failure rate of 5% after a mean time to hemostasis of 10.15 ± 1.96 minutes in sheath sizes from 5-F to 7-F in 60 patients. Cases in that study also required a conversion to conventional manual compression technique. Nyguen et al¹⁰ described a 23% failure rate with a mean time to hemostasis of 16 ± 5.3 minutes in sheath sizes from 4-F to 8-F with the Clo-Sure PAD; Mlekusch et al⁸ had a 19% failure rate with a mean time to hemostasis of 13.6 ± 3.6 minute in 6-F sheaths. In their comparative study, Nguyen et al¹⁰ reported a 21% failure rate for the Chito-Seal hemostasis pad (Abbott Vascular Devices, Galway, Ireland), with a mean of 16.2 ± 4.9 minutes to hemostasis in 4-F to 8-F sheaths.

Hallak et al⁷ described a very low 2.1% failure rate with a mean time to hemostasis of 7.8 ± 3 minutes for D-STAT Dry hemostatic bandage (Vascular Solutions, Inc, Minneapolis, MN, USA) in a multicenter study with 187 patients undergoing a 4-F to 6-F approach. The differences between our data and those for D-STAT Dry hemostatic bandage likely arise from the different outcome definitions and larger sheath sizes used in the present study. Comparing our results with those for Clo-Sur PAD^{6,8,10} or Chito-Seal hemostasis pad,¹⁰ our mean time to hemostasis seems to be equal or shorter in 6-F to 8-F sheaths.

In the only other report on the Hematrix Active Patch, Antoni et al¹² reported successful hemostasis in 93 of 100 patients after a 5-minute prescribed pressure time in retrograde 6-F accesses in elective diagnostic heart catheterization. Seven cases required at least 5 additional minutes of compression. No severe rebleeding, pseudoaneurysm, or AVF was observed. One case of questionable local allergic reaction to the patch was described. Although the present study evaluated antegrade and retrograde femoral accesses using 6-F to 8-F sheaths in PVI, our procedural success rate was comparable. However, we did encounter 2 false aneurysms.

Limitations

Major limitations of this prospective single-center study are the lack of randomization and an active control group in which post-PVI hemostasis was performed with a conventional manual compression technique. Moreover, hemostasis is a dynamic process and therefore evaluating the exact time to hemostasis was not possible using the tested wound dressing, which should not be intermittently removed during compression. Given the need to use predefined compression times in this study, it is quite likely that a shorter time to hemostasis would be feasible and should be addressed in future studies.

All described minor hematomas were irregularly confined and located subcutaneously without any capsulation; most occurred in low-lying femoral arteries. Presumably they arose during initial blood intrusion into the wound dressing, which is necessary to accelerate the coagulation process. All patients received a pressure dressing and overnight bed rest. One may argue that these minor bleedings could have grown bigger with shorter dressing application or bed rest. In our experience, though, these bleedings are already coagulated after patch compression.

Furthermore, in the present study, clinical success with only a fixed time of 24 hours was evaluated; for safety reasons, no shorter time to ambulation was allowed in this initial study. Finally, cost-effectiveness was not addressed. Despite the obvious advantages of the tested wound dressing, further analysis is warranted to evaluate whether the 93 euro cost of a wound dressing can achieve savings in nursing and catheterization laboratory resources.

Conclusion

The Hematrix hemostatic patch seems to be safe and effective for postinterventional management of large arterial access sites. Moreover, time to hemostasis as well as the procedural failure rate seem to be equal or lower compared with other current topical closure systems. Minor complications were few and did not differ significantly in antegrade and retrograde accesses or by sheath size. Randomized trials

with larger patient populations are necessary to confirm these preliminary data and to evaluate potential shorter times to ambulation compared to manual compression.

Declaration of Conflicting Interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: Ralph Kickuth is a consultant for Abbott Vascular. Thorsten Bley is a consultant for GlaxoSmithKline and Merck, Sharp & Dohme GmbH; is on the speakers' bureau of Bayer, Bracco, GE, Guerbet, HeartFlow, and Siemens; and receives research funding from Deutsche Forschungsgesellschaft (DFG: BL 1132/1-2) and research cooperation from Siemens, Noras, and Rapid.

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