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Comparison of Hemostasis Times with a Chitosan-Based Hemostatic Pad (Clo-Sur^{Plus} Radial™) vs Mechanical Compression (TR Band®) Following Transradial Access: A pilot Study☆,☆☆

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ABSTRACT

Background: Hemostasis following transradial arterial access (TRA) is usually achieved by mechanical compression. This study investigated if use of a chitosan-based hemostatic pad (Clo-Sur^{Plus} Radial™) combined with mechanical compression (TR Band®) could shorten hemostasis time after TRA, compared with a TR Band® alone.
Methods: 40 patients undergoing cardiac catheterization and/or percutaneous coronary intervention were assigned into 4 cohorts post TRA: 10 patients received mechanical compression with a TR Band® alone for 120 min. The other 30 patients received compression with a Clo-Sur^{Plus} Radial™ pad combined with a TR Band® for 60 min, 45 min, and 30 min, respectively ($n = 10$/per cohort). Times to hemostasis and access-site complications were recorded.
Results: There were no differences in patient characteristics, mean dose of heparin, or mean activated clotting time value at the end of procedure among the four cohorts. Median time to hemostasis with the TR Band® alone was 120.5 min versus 60 min, 45 min and 30 min for the 60-min, 45-min, and 30-min Clo-Sur^{Plus} Radial™ pad combined with the TR Band® cohorts, respectively. No radial artery occlusion, late rebleeding nor hematoma was noted in this series of patients.
Conclusions: In this pilot trial, use of a Clo-Sur^{Plus} Radial™ pad in combination with a TR band® significantly shortened hemostasis time, as compared to a TR band® alone, with no increased complications noted.

1. Introduction

Transradial access (TRA) is increasingly being utilized for cardiac catheterization (CC) and/or percutaneous coronary intervention (PCI) due to its proven clinical benefits [1]. Hemostasis of the radial access site is an essential component of a successful TRA procedure. Several mechanical compression hemostatic devices have been developed and introduced into clinical practice, with the aim of aiding radial access site hemostasis and limiting vascular complications [2]. The TR Band® (Terumo Medical) is currently the most widely used compression device in the United States after TRA, typically for a period of 2 to 4 h post procedure [3–5]. The Clo-Sur^{Plus} Radial™ pad (Scion BioMedical, Inc.) is a chitosan-based hemostatic pad designed to more rapidly seal the radial artery access site, thus potentially reducing hemostasis time and vascular complications. This study investigated if use of a Clo-Sur^{Plus} Radial™ pad combined with a TR Band® could shorten hemostasis time post TRA, compared with a TR Band® alone.

2. Methods

2.1. Study population and setting

This study was a prospective, single-center, pilot trial approved by Memorial Healthcare System's Institutional Review Board. 40 patients undergoing transradial CC and/or PCI between September 2017 and December 2017, who signed informed consent to participate in this study, were assigned to receive either a TR Band® alone or a Clo-Sur^{Plus} Radial™ pad combined with a TR band® after TRA. The study design used progressively shorter compression times, if there was successful hemostasis with the previous cohort. The first 10 patients received mechanical compression with a TR Band® alone for a planned 120 min. The subsequent 30 patients then received compression with a Clo-Sur^{Plus}

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Radial™ pad combined with a TR Band® for 60 min, 45 min, and 30 min, respectively ($n = 10$, per cohort).

2.2. Application of hemostatic device

In the TR Band only cohort, a TR Band® was snuggly applied around the wrist and inflated with 10 mL of air, with the sheath then removed under the inflated Band. Additional air was added if needed for hemostasis. The TR Band® was left in place for 60 min, and then weaned over the subsequent 60 min, removing 2 mL at 60 min, 2 mL at 80 min, 3 mL at 100 min, and the remaining air at 120 min [6].

In the Clo-Sur cohorts, a Clo-Sur^{Plus} Radial™ pad was applied over the radial access site with the sheath still in place, and then covered with a dry gauze pad the same size as the Clo-Sur^{Plus} Radial™ pad. A TR Band® was then applied over the gauze/Clo-Sur^{Plus} Radial™ pad. The sheath was removed before the TR Band® was inflated, to allow blood from the radial access site to partially saturate the Clo-Sur^{Plus} Radial™ pad, to initiate the hemostatic reaction between chitosan and blood. The TR Band® was then inflated with 10 mL of air. Additional air was added if needed for hemostasis (Fig. 1). After 10 min, 3 mL of air was removed, and then 2 mL was removed after another 10 min. The TR Band® was then removed after another 40, 25, or 10 min of compression for a total planned compression time of 60, 45, and 30 min in the Clo-Sur 60-min, 45-min and 30-min cohorts, respectively. The Clo-Sur^{Plus} Radial™ pad was left in place after removal of the TR Band®, and covered with a clear dressing, to be removed the following morning.

2.3. Postoperative access-site outcomes

Clinical parameters including time to hemostasis, hematoma and bleeding at the access site were recorded and evaluated from upon device placement to one hour after device removal, with a 24-h post procedure follow up. Radial artery patency and pain/discomfort were evaluated 1 h after TR Band® removal/hemostasis by the reverse Barbeau's test [5] and a numeric rating pain scale (0 for no pain, through 10 for the worst pain), respectively. *Initial hemostasis* was defined as completion of the above described TR Band® and Clo-Sur^{Plus} Radial™ weaning protocols without having to recompress the radial arteriotomy site because of bleeding from the radial puncture site or expanding hematoma of the forearm. *Time to hemostasis* was defined as the total time between sheath removal and removal of the TR Band®, including the initial protocol defined compression and weaning times and any subsequent compression time needed to obtain successful hemostasis.

2.4. Statistical analysis

Continuous parametric variables are presented as mean ± standard deviation unless otherwise noted. Categorical variables are presented as counts and percentages and compared with the chi-square or Fisher's exact test. Difference among the four cohorts was tested by two-way ANOVA, followed by Tukey's multiple comparison tests using GraphPad Prism software 7.0. A two-tailed *P*-value of <0.05 was considered statistically significant.

3. Results

The 40 patients enrolled in the study were assigned to four equal cohorts. There were no differences in the baseline clinical characteristics (Table 1). Diagnostic coronary angiography was performed in all cases, of which 14 (35%) had ad hoc PCI (Table 2). Access was obtained via the right radial artery in 70% of cases. A 6 Fr sheath was used in 38 patients, a 5 Fr sheath in 1 patient, and a 7 Fr sheath in 1 patient. Heparin was used for all procedures, and 5 patients in the Clo-Sur cohorts received eptifibatide. There was no statistical difference in the amount of heparin used and the end-procedural ACT values between the TR Band® and Clo-Sur cohorts ($p > 0.05$). Blood pressure was measured when the sheath was pulled, and no differences were found between

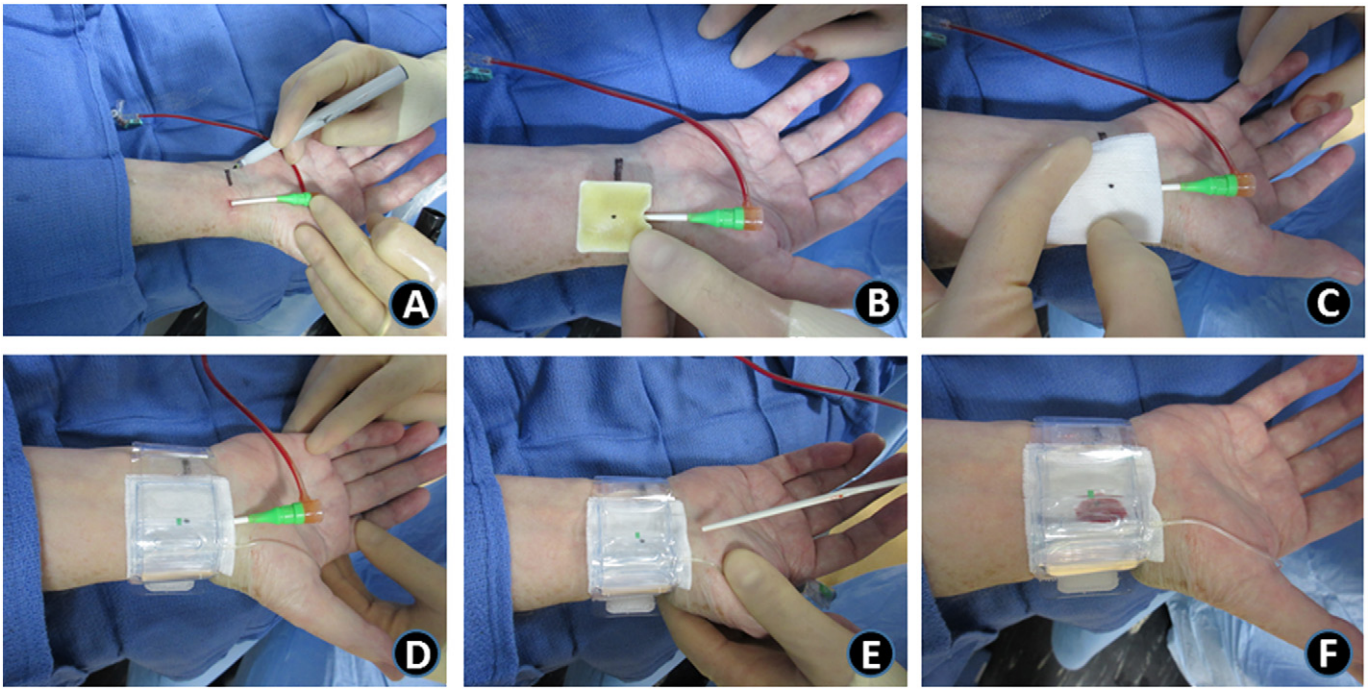

Fig. 1. Application of a Clo-Sur^{Plus} Radial™ pad for transradial access site hemostasis. (A) The level of the access site was marked on the lateral side of the palmar surface of the wrist with a sterile marking pen. (B) The center of the Clo-Sur^{Plus} RADIAL™ pad was marked, and applied directly over the access site, with the sheath still in place, but pulled back 4 cm. (C) The center of a dry 2 × 2 in. gauze pad was then marked, and placed over the Clo-Sur^{Plus} RADIAL™ pad, aligning the marked center dot with the skin entrance site. (D) A TR Band® was snuggly applied over the 2 × 2 in. gauze, with the small green square 2–3 mm proximal to the previously marked center of the 2 × 2 gauze and Clo-Sur^{Plus} RADIAL™ pad. (E) The sheath was removed, allowing a small amount of blood to soak the Clo-Sur^{Plus} RADIAL™ pad to initiate the clotting cascade. (F) The TR Band® was then inflated with 10 cc's of air and removed per protocols (see details in Methods).

Table 1
Baseline characteristics of study patients.

	TR band	Clo-Sur Pad/TR band		
	n = 10	60-min (*n* = 10)	45-min (n = 10)	30-min (n = 10)
Age	67.3 ± 17.9	60.8 ± 11.9	66.2 ± 9.8	58.7 ± 17.2
Sex, male (%)	8 (80%)	9 (90%)	7 (70%)	5 (50%)
BMI (kg/m^2)	30.2 ± 9.1	29.9 ± 5.3	27.5 ± 4.7	28.6 ± 3.0
Hypertension	9 (90%)	8 (80%)	6 (60%)	9 (90%)
Diabetes	2 (20%)	2 (20%)	4 (40%)	4 (40%)
Dyslipidemia	5 (50%)	6 (60%)	6 (60%)	7 (70%)
Tobacco use				
Current smoker	5 (50%)	3 (30%)	3 (30%)	0
Former smoker	0	3 (30%)	2 (20%)	3 (30%)
Never smoker	5 (50%)	4 (40%)	5 (50%)	7 (70%)
Medications				
Aspirin	8 (80%)	10 (100%)	8 (80%)	8 (80%)
P2Y12 inhibitors	5 (50%)	6 (60%)	4 (40%)	5 (50%)
Family history of CAD	0	0	0	0

Data given as mean ± standard deviation or n (%).
BMI = body mass index; CAD = coronary artery disease.

the TR Band® and Clo-Sur cohorts. Procedure time was calculated as sheath insertion until sheath removal, and no differences were found among the cohorts (Table 2).

As shown in Table 3, successful initial hemostasis was achieved in 100% of patients in the 60-min and 45-min cohorts using the Clo-Sur^{Plus} Radial™ pad combined with a TR Band®. 30% of patients in the TR Band® alone cohort and 20% of the 30-min Clo-Sur cohort did not achieved initial hemostasis. This "failure" was oozing/bleeding when the TR Band® was initially weaned by removing 2 mL or 3 mL of air, requiring protocol driven recompression for an additional 10 min in the Clo-Sur cohort and 20 min in the TR Band® alone cohort. Median total time to hemostasis for the TR Band® alone cohort was 120.5 min versus 60 min, 45 min and 30 min for the 60-min, 45-min, and 30-min Clo-Sur cohorts, respectively. Mean total time to hemostasis with the TR Band® alone was 219 min versus 63.8 min, 45.5 min and 33.9 min for the 60-min, 45-min, and 30-min Clo-Sur cohorts, respectively. One patient in the TR Band® alone cohort took an unexpected 945 min to achieve hemostasis due to multiple unanticipated events, including alcohol withdrawal/delirium tremens. This single outlier significantly skewed the mean compression time in this cohort. One patient in the 60-min Clo-Sur cohort achieved initial hemostasis per protocol, however, the TR Band® was removed 25 min later due to waiting for the physician to check the patient so the total hemostasis time took 85 min. One patient in the 30-min cohort complained of pain (score 4) at the access site while the Clo-Sur^{Plus} Radial™ pad and TR Band® were still in place, but completed the 30 min for hemostasis. There was no radial artery occlusion in any subject, assessed at 1 h post hemostasis by the reverse Barbeau's test. No recurrent bleeding, hematoma, or other immediate or delayed complications occurred in any other case.

Table 3
Hemostasis outcomes.

	TR band	Clo-Sur Pad/TR band		
	n = 10	60-min (n = 10)	45-min (n = 10)	30-min (*n* = 10)
Successful initial hemostasis	7 (70%)	10 (100%)	10 (100%)	8 (80%)
Total compression time (min.)				
Range (Min–Max)	120–945	60–85	45–50	30–56
Median	120.5	60	45	30
Mean ± SEM	219 ± 81.5	63.8 ± 2.7	45.5 ± 0.5	33.9 ± 2.7
Pain/discomfort	0	0	0	1 (10%)
Radial artery occlusion	0	0	0	0
Hematoma/oozing	0	0	0	0

Data given as median, mean ± SEM or n (%).

4. Discussion

In this small pilot trial, hemostasis times after TRA were significantly shorter using a Clo-Sur^{Plus} Radial™ pad combined with a TR band®, compared to a TR Band® alone. There were no RAOs or other complications noted. There was 100% initial successful hemostasis in both the 60- and 45-min cohorts with the use of the Clo-Sur^{Plus} Radial™ pad. The two initial hemostasis failures in the 30-min cohort all occurred with the initial weaning of 3 mL of air from the TR Band®, which was the same weaning protocol used with the 60- and 45-min cohorts. These two initial failures may have occurred by chance. Two patients in the 30-min cohort received eptifibatide, as did 3 patients in the other Clo-Sur cohorts. Only one of the five patients that received eptifibatide bled on initial weaning, that one being in the Clo-Sur 30-min cohort. Whether 10 min was too short of a period to initiate weaning of air with a Clo-

Table 2
Procedural characteristics of study patients.

Variables	TR band	Clo-Sur Pad/TR band		
	n = 10	60-min (n = 10)	45-min (n = 10)	30-min (n = 10)
Diagnostic only	7 (70%)	5 (50%)	6 (60%)	8 (80%)
Diagnostic + PCI	3 (30%)	5 (50%)	4 (40%)	2 (20%)
Vascular approach				
Left	3 (30%)	6 (60%)	3 (30%)	0
Right	7 (70%)	4 (40%)	7 (70%)	10 (100%)
Sheath size				
5 Fr	1 (10%)	0	0	0
6 Fr	8 (80%)	10 (100%)	10 (100%)	10 (100%)
7 Fr	1 (10%)	0	0	0
Sheath in-out time (min)	70.2 ± 64.3	40.5 ± 22.8	69.1 ± 54.8	44.2 ± 28.9
GP IIb/IIIa inhibitors	0	2 (20%)	1 (10%)	2 (20%)
Radial cocktail				
Verapamil	10 (100%)	10 (100%)	10 (100%)	10 (100%0
Nitroglycerin	10 (100%)	10 (100%)	10 (100%)	10 (100%)
Total heparin dose (IU)	8850 ± 6018	6550 ± 1950	6400 ± 2458	6000 ± 1155
ACT at the end of procedure (Sec)	222.3 ± 40.5	228.1 ± 96.7	214.2 ± 46	227.5 ± 48.9
Vital status				
SBP (mm Hg)	137.5 ± 18.1	128.2 ± 30.9	134.9 ± 20.5	136.5 ± 16.1
DBP (mm Hg)	70.9 ± 8.9	70.7 ± 14.1	70.6 ± 10.1	73.7 ± 9.1

Data given as mean ± standard deviation or n (%).
PCI = percutaneous coronary intervention; ACT = activated clotting time.

Sur^{Plus} Radial™ pad under a TR Band® cannot be answered in this small pilot trial.

With mechanical compression with a TR band®, the lower limit of compression/wean time for successful hemostasis post PCI appears to be 2 to 3 h [2–4]. There are several recent reports of "hemostasis pads" significantly shortening TRA hemostasis times. A recent study showed a reduced time to hemostasis with use of a StatSeal Advanced Disc (potassium ferrate based) in conjunction with a TR Band® compared with a TR Band® alone, with no difference in bleeding or RAO [7]. Another recent study showed reduced time to hemostasis after TRA with use of a QuikClot Radial pad (kaolin based) with an elastic compression bandage [6]. Chitosan-based pads have been reported to accelerate hemostasis in patients undergoing percutaneous vascular procedures involving femoral arterial access [8]. Chitosan is a procoagulant consisting of positively charged molecules that attract red blood cells and platelets, thereby promoting hemostasis. Kang et al. [9] reported that a combination of a chitosan-based pad with a rotatory compression device significantly reduced time to hemostasis after TRA. We found that the Clo-Sur^{Plus} Radial™ pad combined with a TR band® significantly reduced time to hemostasis after TRA, compared to a TR Band® alone.

Shortening the duration of compression time to achieve hemostasis post TRA may have several potential benefits. Shorter compression times with the TR band® alone have been shown to reduce the rate of RAO [10,11]. A recent meta-analysis of 31,345 TRA patients showed that shorter compression times and higher doses of heparin were associated with a lower risk of RAO [12]. The shorter duration of compression achieved using hemostasis pads, as opposed to only a mechanical compression bracelet, may then further reduce RAO after TRA. A shorter duration of compression may also help to reduce patient discomfort caused by a tight band around their wrist. Shorter hemostasis times may also help to reduce healthcare system costs, by allowing outpatient CCs to be discharged home more quickly [7], and allowing inpatient CC/PCIs to be more quickly transferred from the cath lab recovering area back to their room, thereby improving efficiencies in the cath lab.

4.1. Study limitations

This pilot study has several limitations. Firstly and most important, the sample size was small and underpowered, making it difficult to adequately compare the four cohorts, or to draw any definitive conclusions regarding efficacy of the Clo-Sur^{Plus} Radial™ pad. Secondly, the compression and weaning times in the Clo-Sur cohorts were empiric. Possibly the initial weaning was too early, and later or no weaning may be more effective and efficient. Thirdly, this was an open label study, it could not reasonably be blinded.

5. Conclusions

This small pilot trial suggests that hemostasis can be achieved more quickly after TRA using the combination of a Clo-Sur^{Plus} Radial™ pad and a TR band®, with no increase in access site complications, as compared to a TR band® alone. Potential benefits include less RAO, improved patient comfort, and less resource utilization post TRA. Future larger, adequately powered studies will be needed to assess the true efficacy and safety of this combination of a Clo-Sur^{Plus} Radial™ pad and a TR band® for radial hemostasis.

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