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Prevention of Radial Artery Occlusion—Patent Hemostasis Evaluation Trial (PROPHET Study): A Randomized Comparison of Traditional Versus Patency Documented Hemostasis After Transradial Catheterization

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Objective: The objective of this study was to evaluate the efficacy of hemostasis with patency in avoiding radial artery occlusion after transradial catheterization. Background: Radial artery occlusion is an infrequent but discouraging complication of transradial access. It is related to factors such as sheath to artery ratio and is less common in patients receiving heparin. Despite being clinically silent in most cases, it limits future transradial access. Patients and Methods: Four hundred thirty-six consecutive patients undergoing transradial catheterization were prospectively enrolled in the study. Two hundred nineteen patients were randomized to group I, and underwent conventional pressure application for hemostasis. Two hundred seventeen patients were randomized to group II and underwent pressure application confirming radial artery patency using Barbeau's test. Radial artery patency was studied at 24 hr and 30 days using Barbeau's test. Results: Thirty-eight patients had evidence of radial artery occlusion at 24 hr. Twenty patients had persistent evidence of radial artery occlusion at 1 month. Group II, with documented patency during hemostatic compression, had a statistically and clinically lower incidence of radial artery occlusion (59% decrease at 24 hr and 75% decrease at 30 days, $P < 0.05$), compared with patients in group I. Low body weight patients were at significantly higher risk of radial artery occlusion. No procedural variables were found to be associated with radial artery occlusion. Conclusion: Patent hemostasis is highly effective in reducing radial artery occlusion after radial access and guided compression should be performed to maintain radial artery patency at the time of hemostasis, to prevent future radial artery occlusion. © 2008 Wiley-Liss, Inc.

Key words: transradial cath (TRAD); total occlusions (OCCL); complications adult cath/intervention (COMP)

INTRODUCTION

Transradial access (TRA) for diagnostic and interventional procedures is gaining more popularity in view of data supporting its superior safety from a standpoint of access site complications. This procedure is also readily accepted by patients because of increased comfort by eliminating the need for bed rest. Radial artery occlusion is one of the few postprocedural complications of TRA [1]. It is clinically quiescent in properly selected cases and rarely results in ischemia. It limits future TRA. It also decreases patient confidence in the safety of the procedure despite its clinical quiescence. It is probably related to the size of the introducer sheath [2,3] and more likely related to the ratio of the arterial diameter to the

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Conflict of interest: Nothing to report.

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sheath [4]. Repeated cannulations predispose to occlusion [5]. Heparinization has been found to be effective in reducing the occurrence of radial artery occlusion [6]. Despite heparinization, we have observed a 7–12% radial artery occlusion rate using plethysmography. Different devices have been developed by operators and industries to achieve local compression and have had comparable hemostatic efficacy. They usually allow for mobility of the wrist joint and also are nonobstructive to the veins, hence allowing liberal application of pressure to ensure hemostasis. We have anecdotally observed that manual nonocclusive compression has a lower incidence of radial artery occlusion compared to conventional compression. Our previously reported findings of the occluding "plug" retrieved from occluded radial arteries that were reaccessed, have confirmed thrombosis to be the process leading to early occlusion [7]. These observations provide support to our belief that interruption of the process of thrombus formation at the outset, at the time of hemostasis, by maintaining radial artery flow, at the site of puncture, may decrease radial artery occlusion. Recent observational studies have shown occlusive hold to be a predictor of subsequent radial artery occlusion [8]. In view of these observations we decided to perform a randomized comparison of patent versus conventional compression for hemostasis and its effects on radial artery occlusion.

METHODS

Patient Population

A total of 480 consecutive patients presenting for elective outpatient diagnostic cardiac catheterization were enrolled in the study. Patients on Coumadin therapy ($n = 21$), thrombocytopenia ($n = 4$), and those for an a-priori transfemoral approach ($n = 8$) were excluded from the study. A Barbeau's test was performed at baseline and presence of dual circulation and patency of palmar arch was confirmed. Three patients were excluded due to abnormal Barbeau's test. We were unable to gain radial access in eight patients (1.7%). Four hundred thirty-six patients successfully underwent transradial cardiac catheterization. Patients were randomized once radial artery was successfully accessed. Two hundred nineteen patients were randomized to conventional compression for achieving hemostasis. Two hundred eighteen patients underwent compression with documented patency of radial artery termed as "patent hemostasis." One patient in group II was not available for follow-up. Twenty-four-hour and 30-day follow-up was completed in 219 (100%) patients in group I and 217 (99.5%) patients in group II. The techniques for traditional and "patent hemostasis" are described later. The study was terminated at 436 patients because of a large difference in the observed end point. The study protocol was approved by the institutional review board. All patients provided informed consent.

Transradial Catheterization Procedure

After sterile preparation and injection of 2% lidocaine at the puncture site, a 20-gauge Teflon catheter was used to enter the radial artery 6–8 cm above the crease of the wrist, using Seldinger technique, with through-and-through puncture. The stylet was removed and Terumo 0.021″ guidewire was placed in the hub of the cannula, and the system was gradually withdrawn. Upon appearance of pulsatile flow the guidewire was advanced into the radial artery lumen. The radiofocus glide sheath was then advanced over the guidewire into the radial artery. A "radial cocktail" consisting of 200 mcg of nitroglycerin, 5 mg of Diltiazem, and 50 units/kg of unfractionated heparin (maximal dose of 5,000 units) was administered diluted in a 20-ml syringe, intraarterially. The procedure was completed using 4-french diagnostic coronary catheters.

Conventional Hemostasis Procedure

All introducer sheaths were immediately removed. The sheath was pulled out 4–5 cm and a Hemoband™ plastic band was placed around the wrist. A composite of a needle cap covered with a 4×4 gauze piece rolled around the needle cap was placed under the hemoband at the sheath entry site, and the band was tightened after which the sheath was pulled out. The band was left in place for 2 hr, then slowly removed, and a light dressing was applied to the site. After application of hemoband, Barbeau's test was performed to assess radial artery patency status. Patients in this group who had interruption of radial artery flow during hemostatic compression were recorded to have "occlusive hold." The operators were blinded to these data at that time and hence no alterations were made.

"Patent Hemostasis" Procedure

The sheath was pulled out 4–5 cm and a plastic band "hemoband" was placed around the forearm at the site of entry. The needle cap and gauze composite was placed over the site of entry. A pulse oximeter sensor was placed over the index finger, the hemoband was tightened, and the sheath was removed. Ipsilateral ulnar artery was occluded and the hemoband was loosened till plethysmographic signal returned (confirming radial artery patency) or bleeding occurred. If bleeding occurred at the pressure required to maintain patency, manual compression was used ($n = 8$, 3.6%). If radial artery patency could be maintained and hemostasis

TABLE I. Demographic and Procedural Data

Variable	Group I (traditional hold)	Group II (patent hold)	*P* value
Age (years)	65.91 + 12.7	63.52 + 12.9	<0.05
BSA (m^2)	1.95 + 0.23	1.95 + 0.22	>0.05
Height (cm)	166.99 + 8.9	166.92 + 9	>0.05
Weight (kg)	87.15 + 20.6	87.58 + 20.4	>0.05
Fluoro time (min)	6.056 + 5.7	6.135 + 6	>0.05
Procedure time (min)	18.78 + 5.4	19.52 + 5.1	>0.05
Creatinine (mg/dl)	1.069 + 0.47	1.007 + 0.29	>0.05
Cigarette smoking (%)	21 (10)	17 (8)	>0.05
Diabetes (%)	59 (27)	44 (20)	>0.05
Gender (females %)	97 (44)	120 (55)	>0.05
Hypertension (%)	204 (93)	206 (95)	>0.05

Continuous variables listed as mean + standard deviation.

was achieved, the bands were left in place for 2 hr. The patency of the radial artery was checked at least once every hour.

Assessment of Radial Artery Patency

Radial artery patency was assessed using Barbeau's test. A pulse oximeter sensor was placed over the index finger. A plethysmographic signal was observed and both radial and ulnar arteries were compressed to observe loss of plethysmographic signal. Then the radial artery was released and the return of plethysmographic signal was observed. Return of signal confirmed radial artery flow and hence patency. Absence of return of signal was interpreted as radial artery occlusion. The ulnar artery was then released to observe return of signal, confirming proper functioning of the equipment. This test was performed at 24 hr and 1 month after the procedure.

RESULTS

Clinical Data

Baseline clinical data for group I and group II are presented in Table I. No significant difference was found in the distribution of gender, body surface area, weight, and creatinine as well as prevalence of diabetes mellitus, hypertension, and procedure duration. An independent *t* test comparing the mean age of group I and group II found a significant difference. Group I patients were statistically significantly older (65.9 ± 12.7 years) than group II patients (63.5 ± 12.9 years), although the difference was clinically insignificant.

A 5-french introducer was used in all patients. All patients received weight-based heparin. All patients received aspirin 81 mg orally, before the procedure.

Radial Artery Occlusion Data

An independent chi-square analysis was calculated comparing group I versus group II for the frequency of occlusion at 24 hr and at 30 days. Twenty-seven (12%) patients in group I developed plethysmographic evidence of radial artery occlusion at 24-hr follow-up, compared with 11 (5%) in group II. This represented a 59% reduction in radial artery occlusion by using patent hemostasis, which was statistically significant ($X^2(1) = 7.22$, $P < 0.05$).

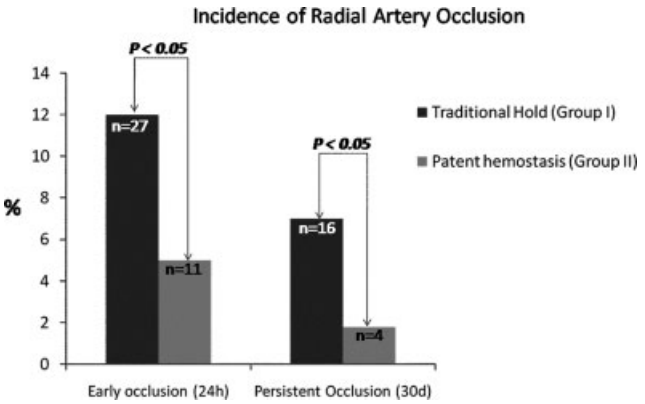

Fig. 1. Patent hemostasis leads to a significant decrease in the incidence of radial artery occlusion at 24-hr and 30-day follow-up.

Sixteen (7%) patients in group I developed plethysmographic evidence of radial artery occlusion at 30-day follow-up, compared with four (1.8%) in group II. This represents a 75% reduction in radial artery occlusion by using patent hemostasis which was statistically significant ($X^2(1) = 7.43$, $P < 0.05$). These results are shown in Fig. 1.

A separate analysis was performed on group I patients (our control group) by dividing the population into those who developed radial artery occlusion at 30 days versus those who did not. This was done to evaluate associations between commonly available demographic and procedural variables and radial artery occlusion. Univariate analysis was performed on all variables for the entire population. An independent *t* test

TABLE II. Results of Univariate Comparison of Patients With or Without Radial Artery Occlusion at 30 Days for Group I

Variable	No occlusion 30 days (n = 203)	Occlusion 30 days (n = 16)	P value
Age (years)	65.3 + 12.6	73.3 + 12.4	<0.05*
Female gender (%)	101 (87.1)	15 (12.9)	<0.05*
Diabetes mellitus (%)	52 (88.1)	7 (11.9)	>0.05
Hypertension (%)	191 (93.6)	13 (6.4)	>0.05
Weight (kg)	88.6 + 20.3	68.6 + 15.7	<0.05*
Procedure time (min)	18.7 + 5.4	19.5 + 5.6	>0.05
Creatinine (mg/dl)	1.08 + 0.48	0.95 +.0.29	>0.05
Smoking (%)	183 (92.4)	15 (7.6)	>0.05
Patency (%)	123 (99.2)	1 (0.8)	<0.05*

*Significant.

was used for continuous variables and an independent chi-square test was used for categorical variables.

Age was significantly different between patients who were occluded and those who were not ($t(217) = -2.445$, $P < 0.05$). Patients who were not occluded at 30 days were significantly younger (65.3 ± 12.6 years) than patients who were occluded (73.3 ± 12.4 years). Fifteen (12.9%) female patients developed plethysmographic evidence of radial artery occlusion at 30-day follow-up, compared with one (1%) male. A significant interaction was found ($X^2(1) = 11.52$, $P < 0.05$).

A significant difference in body weight was found between patients who were occluded at 30 days and those who were not ($t(217) = 3.849$, $P < 0.05$). Patients who were not occluded were significantly heavier (88.61 ± 20.33 kg) than patients who were occluded (68.58 ± 15.70 kg).

Ninety-five (43.4%) of group I patients had an "occlusive hold," i.e. absence of forward radial artery flow during hemostatic compression. A significant association was found between "occlusive hold" as defined earlier, during traditional hemostasis, and development of radial artery occlusion at 30 days. Hundred twenty-three (99.2%) of group 1 who were reported with patency during the conventional procedure were still not occluded at 30-day follow-up, and one (0.1%) patient with patency during the conventional procedure was occluded at 30 days ($X^2(1) = 17.83$, $P < 0.05$). This represents that 99.1% of patients who were able to maintain radial patency at the time of traditional hemostasis were able to maintain patency after 30 days.

No significant difference was found in diabetes mellitus, hypertension, procedure duration, or creatinine. These findings are shown in Table II.

Multivariate Predictors of Radial Artery Occlusion

Logistic regression was then used to predict the probability of radial artery occlusion at 30 days in group I (control group). The predictor variables used included sex, age, weight, and patency at the time of hemostasis. Employing a 0.05 criterion of statistical significance, weight and patency had significant effects. The odds ratio for weight was 0.944, $P < 0.05$. A one-unit (kg) increase in weight would decrease the probability of being occluded by 5.6%. The odds ratio for patency is 0.052, $P < 0.05$. The probability of being occluded, with patency during the traditional hemostasis, would decrease by 94.8%. The overall success rate of this model is 83.6%. About 83.6% of the time we can correctly determine the category a patient will be in, occluded or not occluded at 30 days, by using these variables.

Hemostatic Efficacy

Bleeding complication was defined as blood loss from the access site leading to hemodynamic instability, transfusion, or death. Hematomas greater than 3 cm in diameter were considered significant. Access site was auscultated for bruit, and if bruit was present it was evaluated by ultrasonography.

None of the patients developed a bleeding complication. Eight patients in group II (3.6%) needed a manual hold for 20 min, because of inability to obtain hemostasis without maintaining patency of the radial artery.

DISCUSSION

Radial artery occlusion, although largely clinically silent, creates limitations for future TRA. Early (24 hr) occlusion is more frequent and some of these patients will recanalize, hence lowering the incidence of radial artery occlusion observed at 1 month after the index procedure. Previous data imply that radial artery occlusion is a very rare event. Compared with the initial reports, the TRA technique has changed. Hydrophilic introducers and lower profile equipment probably help lower the incidence of radial artery occlusion, although wider application of TRA to a more heterogeneous subset of patients may well increase the incidence of

radial artery occlusion. The radial pulse is frequently present even after the access site develops occlusion. The occluded radial artery distal stump has been found to have up to 70% of mean arterial pressure because of macrocollateral circulation from the palmar arches [9], leading to a palpable pulse. Hence palpation of radial pulse does not imply radial artery patency. Plethysmographic evaluation of palmar circulation with Barbeau's test has provided a rapidly available and very accurate means to detect radial artery occlusion. It has shown equivalent diagnostic accuracy in the diagnosis of radial artery occlusion, with extremely high correlation with duplex Doppler ultrasonography (unpublished data). Recent data [8] indicate a higher prevalence of radial artery occlusion after TRA, ~10%, when all patients are evaluated at follow-up, using plethysmographic technique.

The pathophysiology of radial artery occlusion was always contemplated to be related to either spasm or thrombus formation. In our previously described report [7] of a technique to reaccess radial artery after occlusion, we described histopathology of the occlusion "plug" retrieved from reaccessed occluded radial arteries. It has consistently been indicative of rapidly organizing thrombus. Radial artery occlusion after TRA appears to be a complex interplay of processes such as local trauma, more a factor in smaller radial arteries, associated with formation of occlusive thrombus formation, leading to occlusion. Once this has occurred, if the local milieu favors recanalization, it "spontaneously" recanalizes, otherwise organizes into a chronic fibrotic occlusion.

We did not measure radial artery diameter in this study, although our univariate clinical variables significantly associated with occlusion at 30 days, such as older age, female gender, and low body weight are all associated with smaller caliber radial arteries.

In our control group population, body weight was the only clinical variable that was a significant multivariate predictor of radial artery occlusion. This probably again is related to the fact that heavier patients have larger caliber radial arteries.

Absence of patency at the time of the conventional procedure was the strongest multivariate predictor of occlusion at 30 days in group I. Patients who were able to maintain patency with the conventional hemostasis were able to remain patent at 30 days. We speculate that patients who achieved hemostasis without loosing radial artery patency, did not develop occlusive thrombus and hence did not occlude while being compressed and certainly not after removal of compression at 30 days.

No other clinical or procedural variable was found to be independently related to risk of occlusion.

Our data highlight the strong association between radial artery patency during hemostasis and development of subsequent radial artery occlusion. We have also demonstrated in a prospective randomized fashion that guided hemostasis strategy, with careful prevention of interruption of radial artery flow during hemostatic compression, is highly effective in decreasing radial artery occlusion after transradial catheterization.

Strategies to prevent complications of TRA should start from patient selection, with avoidance of TRA in patients with absence of palmar collateralization. Hemorrhagic complications are very effectively reduced using TRA compared with femoral access [10]. Prevention of radial artery occlusion will make TRA virtually complication free. Strategies using the lowest profile access in subsets at a higher risk, such as patients with low body weight, would be ideal, although the needs of the interventional procedure usually dominate the selection of equipment profile. Heparinization, when safe, is important to utilize and probably aids recanalization after an occlusive hold, by making the local environment less thrombotic. Once the procedure is completed, the only variable that appears to lower the incidence of radial artery occlusion is a hemostatic strategy that maintains patency immediately after sheath removal. It appears to be the most potent variable influencing occurrence of radial artery occlusion. It also is the most universally applicable, not limited by any other systemic comorbidity. As opposed to an intervention such as heparinization that usually causes systemic anticoagulation, this approach is free of systemic risks. It also does not affect the rest of the procedure.

As no increase in bleeding complications was noted in our population, there appears to be no drawback of a lower pressure hemostatic approach as opposed to the tolerated but higher pressure approach used conventionally. It is presumably more advantageous to use devices that progressively "loosen" over time, further ensuring nonocclusive or patent hold. Hemostatic devices allowing application of measured pressure titrated to a value less than patient's systolic blood pressure that provides local hemostasis may be ideal. Frequent access site evaluation and application of the shortest duration of compression needed to achieve hemostasis may presumably also be of help in reducing the occurrence of radial artery occlusion.

Limitations

The only limitation of a "patent hemostasis" approach is the necessity of a manual hold in a few patients (3.6%), decreasing staff and patient freedom immediately after the procedure. As most patients with coronary artery disease will need more than one cathe-

ter-based procedure in their lifetime, harmless strategies to prevent occlusion at the occasional expense of extra staff time appear to be worthwhile, to repeatedly enjoy the safety and comfort of TRA.

For the purposes of identifying the predictors of radial artery occlusion after traditional transradial procedure, we used our control group (group I). Group II patients were not entered in this analysis as the hemostasis procedure in this group was not traditional.

Patients undergoing ad-hoc coronary intervention were not included in the study due to inherent uncontrollable procedural variables including variations in antithrombotic therapy usage, and differences in size of access, which may affect the end-point, making it difficult to isolate the effect of our ''patent hemostasis'' approach.

CONCLUSION

Patent hemostasis is successful in significantly lowering the incidence of radial artery occlusion after TRA, without compromising hemostatic efficacy.

REFERENCES

1. Stella PR, Kiemeneij F, Laarman GJ, Odekerken D, Slagboom T, van der Wieken R. Incidence and outcome of radial artery occlusion following transradial artery coronary angioplasty. Cathet Cardiovasc Diagn 1997;40:156–158.
2. Dahm JB, Vogelgesang D, Hummel A, Staudt A, Volzke H, Felix SB. A randomized trial of 5 vs. 6 French transradial percutaneous coronary interventions. Catheter Cardiovasc Interv 2002; 57:172–176.
3. Wu SS, Galani RJ, Bahro A, Moore JA, Burket MW, Cooper CJ. 8 French transradial coronary interventions: clinical outcome and late effects on the radial artery and hand function. J Invasive Cardiol 2000;12:605–609.
4. Saito S, Ikei H, Hosokawa G, Tanaka S. Influence of the ratio between radial artery inner diameter and sheath outer diameter on radial artery flow after transradial coronary intervention. Catheter Cardiovasc Interv 1999;46:173–178.
5. Sakai H, Ikeda S, Harada T, Yonashiro S, Ozumi K, Ohe H, Ochiai M, Miyahara Y, Kohno S. Limitations of successive transradial approach in the same arm: The Japanese experience. Catheter Cardiovasc Interv 2001;54:204–208.
6. Lefevre T, Thebault B, Spaulding C, Funck F, Chaveau M, Guillard N, Chalet Y, Bellorini M, Guerin F. Radial artery patency after percutaneous left radial artery approach for coronary angiography. The role of heparin. Eur Heart J 1995;16:293.
7. Pancholy SB. Transradial access in an occluded radial artery: New technique. J Invasive Cardiol 2007;19:541–544.
8. Sanmartin M, Gomez M, Ramon JR, et al. Interruption of blood flow during compression and radial artery occlusion after transradial catheterization. Catheter Cardiovasc Interv 2007;70:185–189.
9. Kerawala CJ, Martin IC, Palmar arch backflow following radial forearm free flap harvest. Br J Oral Maxillofac Surg 2003;41: 157–160.
10. Agostoni P, Biondi-Zoccai GG, de Benedictis ML, Rigattieri S, Turri M, Anselmi M, Vassanelli C, Zardini P, Louvard Y, Hamon M. Radial versus femoral approach for percutaneous coronary diagnostic and interventional procedures: Systematic overview and meta-analysis of randomized trials. J Am Coll Cardiol 2004;44:349–356.