Ultrasound-Guided Percutaneous Thrombin Injection for Post-Catheterization Pseudoaneurysm

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Background: The efficacy and safety of ultrasound-guided thrombin injection (UGTI) for the treatment of post-catheterization femoral and brachial artery pseudoaneuerysms (PSA) is unclear in Japan.

Methods and Results: A retrospective study of 32 consecutive patients undergoing percutaneous UGTI of post-catheterization PSA between February 2011 and February 2014 was performed. There were 23 femoral PSA and 9 brachial PSA treated with UGTI. The prevalence of CAD and smoking history were higher in the brachial PSA patients, but there were no statistically significant differences in other patient demographic factors or in the preprocedural antiplatelet therapy between the femoral and brachial PSA patients. The median dose of thrombin injected was 200 U (range, 100–600 U). The initial success rate, early recurrence rate and surgical conversion rate were 91%, 0% and 4% in the femoral PSA, and 89%, 11% and 11% in the brachial PSA, respectively. There were 2 cases of medial nerve compression in the brachial PSA group, but there were no complications in the femoral PSA group (P=0.0198). On outpatient clinical follow-up in the successfully treated patients, there were no recurrences after an average follow-up of 16 months.

Conclusions: UGTI is a feasible, safe and effective less-invasive treatment for post-catheterization PSA. Brachial PSA, however, might require additional attention because of their tendency toward higher recurrence and complications.

Key Words: Iatrogenic; Incidence; Ultrasound-guided compression
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A 13-6-MHz transducer (part of SonoSite MicroMAXX, FUJIFILM SonoSite, Bothell, WA, USA) was used for diagnostic ultrasound (US) and UGTI. PSA geometry, such as the size, distance from the skin and the position in relation to the artery or vein, were documented before UGTI. Furthermore, blood flow was confirmed on peripheral arterial pulsation, or with Doppler flowmeter if pulsation was not palpable. Liquid sterilized bovine thrombin (1,000 units/ml; Mochida Pharmaceutical, Tokyo, Japan) was drawn into a 1-ml syringe, and the syringe was attached to a 22-G needle. Without local anesthesia, the tip of the needle was placed into the sac of the PSA, a small quantity of blood backflow was confirmed, and 0.1–0.2 ml of thrombin was injected. The flow in the sac was checked on color Doppler US, and if there was persistent flow in the sac, an additional 0.2 ml of thrombin was injected. Final US was performed to confirm the obliteration of flow within the PSA and patent native artery, and the peripheral blood flow was confirmed on pulsation or with Doppler flowmeter. Patients with femoral PSA were kept on bed rest for 6–12 h.

The initial success of PSA repair was defined as complete obliteration of the PSA, as seen at follow-up performed 8–24 h after the initial UGTI, and recurrence of PSA was defined as reperfusion of the PSA sac after initial success. If there was still evidence of blood flow in the PSA sac, additional thrombin was injected, as described. Surgical conversion was performed depending on the failure of PSA obliteration or to manage complications. The following complications associated with UGTI were assessed: thromboembolic complication(s), defined because of the unusual location (above-the-knee popliteal artery). A 13-6-MHz transducer (part of SonoSite MicroMAXX, FUJIFILM SonoSite, Bothell, WA, USA) was used for diagnostic ultrasound (US) and UGTI. PSA geometry, such as the size, distance from the skin and the position in relation to the artery or vein, were documented before UGTI. Furthermore, blood flow was confirmed on peripheral arterial pulsation, or with Doppler flowmeter if pulsation was not palpable. Liquid sterilized bovine thrombin (1,000 units/ml; Mochida Pharmaceutical, Tokyo, Japan) was drawn into a 1-ml syringe, and the syringe was attached to a 22-G needle. Without local anesthesia, the tip of the needle was placed into the sac of the PSA, a small quantity of blood backflow was confirmed, and 0.1–0.2 ml of thrombin was injected. The flow in the sac was checked on color Doppler US, and if there was persistent flow in the sac, an additional 0.2 ml of thrombin was injected. Final US was performed to confirm the obliteration of flow within the PSA and patent native artery, and the peripheral blood flow was confirmed on pulsation or with Doppler flowmeter. Patients with femoral PSA were kept on bed rest for 6–12 h.

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There were no statistically significant differences between the femoral and brachial PSA patients in any other demographics or in the preprocedural antiplatelet therapy. The mean maximum PSA diameter was 3.0 cm (range, 1.1–4.0 cm) for femoral PSA and 3.7 cm (range, 1.0–6.6 cm) for brachial PSA, and the median dose of thrombin injected was 200 U (range, 100–600 U) in femoral PSA and 200 U (range, 100–500 U) in brachial PSA.

UGTI was primarily successful in 29 (91%) of all patients: in 21 (91%) of the femoral PSA patients, and in 8 (89%) of the brachial PSA patients. Small PSA flow near the neck remained, however, in the other 3 patients, and there was early PSA recurrence within 3 days in 1 brachial PSA patient. In 2 of the 4 patients with a remaining PSA, additional UGTI was successful, while the 2 remaining patients underwent surgical PSA repair because of medial nerve compression and increasing pain. The primary success rate, recurrence rate and surgical conversion rate were therefore 91%, 0% and 4% in femoral PSA, and were 89%, 11% and 11% in brachial PSA, respectively; there were no statistically significant differences between the groups. Although there were no complications in the femoral PSA patients, there were 2 cases of medial nerve compression in the brachial PSA patients (P=0.0198). These 2 patients, in whom the PSA size was 20×66 mm and 11×26 mm, respectively, as direct visualization of a thrombus within the lumen of the feeding femoral or brachial artery; disappearance of pulsation in the anterior or posterior tibial artery in femoral PSA or the disappearance of the radial or ulnar artery in brachial PSA; infection or an allergic reaction.

Color Doppler US was performed 1–3 days after successful repair of the PSA, and the extent of thrombosis in the PSA sac and the patency of the feeding artery were examined again. During the follow-up period, we also documented any symptoms reported by the patients, including local pain, signs of inflammation and new occurrence or aggravation of claudication symptoms.

Statistical Analysis
Statistical analysis was done with Fisher’s exact test for categorical variables and Student’s t-test for continuous variables, using JMP 10 (SAS Institute, Cary, NC, USA).

Results
Between February 2011 and February 2014, there were 23 femoral PSA and 9 brachial PSA treated with UGTI. Table 1 summarizes the demographics and cardiovascular risk factors, which were typical for patients with atherosclerotic disease. The prevalence of coronary artery disease and smoking history were greater in the brachial PSA than in the femoral PSA patients. There were no statistically significant differences between the femoral and brachial PSA patients in any other demographics or in the preprocedural antiplatelet therapy. The mean maximum PSA diameter was 3.0 cm (range, 1.1–4.0 cm) for femoral PSA and 3.7 cm (range, 1.0–6.6 cm) for brachial PSA, and the median dose of thrombin injected was 200 U (range, 100–600 U) in femoral PSA and 200 U (range, 100–500 U) in brachial PSA.

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had local pain, but no neuralgia in the hand prior to UGTI. Thereafter, medial nerve compression developed and progressed in association with PSA recurrence and enlargement. There were no complications, such as thromboembolic, allergic or infectious events related to UGTI. In the successfully treated patients there were no recurrences after an average follow-up of 16 months (range, 1–40 months).

### Discussion

Pseudoaneurysms are one of the most major complications at the puncture site after catheterization. At Kokura Memorial Hospital, PSA occurred in 0.08% of the diagnostic angiography cases and in 0.54% of the therapeutic intervention cases during the study period, which involved >30,000 procedures. Limiting the observation to a period from February 2011 to January 2012, the rate of detection of femoral PSA using 4-, 5-, 6-, 7- and 8-Fr sheaths was 0.24%, 0.60%, 1.29%, 2.91% and 5.41%, respectively, and the rate of detection of brachial PSA using 4-, 5-, 6- and 7-Fr sheaths was 0%, 0.37%, 0.87% and 0%, respectively; there were statistically significant differences between the rates of detection of femoral and brachial PSA as the size of the sheath increased. These frequencies are similar to the findings of previous reports, namely 0.2% of diagnostic angiography procedures and 0.9–4.9% of angioplasty procedures. Although small PSA can be obliterated spontaneously, large PSA need to be treated because they can cause severe complications, such as neuropathy, deep vein thrombosis or skin necrosis. Surgical repair had been the primary recommended treatment for PSA until the 1990s. Subsequently, less-invasive treatments, such as UGC or UGTI, have been reported and recommended as first-line therapy for iatrogenic femoral PSA. Few data on the safety and efficacy of UGTI for the treatment of these PSA in East Asia, exist, however, other than a few case reports and small case series with short-term follow-up. There are marked differences between Japanese and Western patients in terms of the thrombotic and thrombolytic status, with Japanese patients having a less prothrombotic and less endogenous thrombolytic profile, and in fact, the relative proportion of hemorrhagic strokes is higher in Japan than in Western countries, with intracerebral or subarachnoid hemorrhage accounting for up to 33% of strokes in Japan, compared to only 10–15% of strokes in the USA. Moreover, Japan has the lowest incidence of acute myocardial infarction among industrialized countries, and the incidence of venous thromboembolism is lower in individuals in East Asia than in Western countries. Therefore, it is necessary to review our experience with UGTI for iatrogenic PSA to evaluate its safety and efficacy in Japan.

UGTI is associated with a high frequency of PSA obliteration, low recurrence and rare complications, and is recommended as the initial treatment in patients with large and/or symptomatic femoral artery PSA. In the present study, UGTI was primarily successful in 21 (91%) of the femoral PSA patients and in 8 (89%) of the brachial PSA patients (Table 2). The success rates reported in previous studies have approached 95%, so the present success rate is lower than that in many of the past reports. In contrast, the present PSA recurrence rate was 1 (3%) for the total patient group; similar to that in previous reports. Although these results could be related to the less prothrombotic and less thrombolytic status of Japanese subjects, they might depend on technical problems or patient selection; it has been reported that the success rate tends to be lower in relatively smaller series of <60 PSA than in larger series of >200 PSA. There were no complications in the femoral PSA patients, but there were 2 cases of medial nerve compression in the brachial PSA patients. These both occurred in failed cases of PSA thrombosis by UGTI, and they might have been prevented by additional treatment at an appropriate time.

There are limited data on the safety and efficacy of UGTI for the treatment of brachial PSA, and the previous reports concerning UGTI for the upper extremity PSA are listed in Table 3. Although the present study was small in size, it is the second largest study concerning UGTI for the upper extremity PSA. The present findings and those of previous reports suggest that there might be higher recurrence or complications after UGTI for the upper extremity PSA than for...
femoral PSA. These observations may be supported by the Babu et al study, which showed that the brachial approach has a greater complication rate than the femoral approach: that is, surgical intervention for complications was necessary in 60 (0.57%) of brachial approach patients and in 14 (0.23%) of femoral approach patients. In contrast, at Kokura Memorial Hospital, the incidence of brachial PSA was lower than that of femoral PSA. This may be because the incidence of PSA is possibly influenced by the difference in hemostatic methods used after removing the sheath, for example, manual compression of the femoral artery vs. a Tometa-Kun compression device in the brachial artery. These complications might be related to the anatomical features of the brachial artery, which is in close association with the medial nerve and runs within the medial brachial fascial compartment. Furthermore, the small diameter of the brachial artery may make it more prone to thrombosis. Although the present results for brachial PSA were limited by the small study size, we believe that the present study adds some valuable knowledge for clinicians treating upper extremity PSA.

Conclusions

For PCPSA that failed to be obliterated on UGC, UGTTi was safe and effective as an initial treatment in Japan, as it is in Western countries. Brachial PSA, however, might require special attention because of their apparent tendency toward higher recurrence and complications.

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Disclosures

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References