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Treatment of Postcatheterisation False Aneurysms: Ultrasound-guided Compression vs Ultrasound-guided Thrombin Injection

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Objectives: *to compare the efficacy and cost-effectiveness of ultrasound-guided compression (UGC) with ultrasound-guided thrombin injection (UGTI) for treatment of postcatheterisation arterial false aneurysms (cFA).*
Design: *prospective clinical study using historical controls.*
Materials and Methods: *we prospectively collected data on 33 consecutive patients diagnosed with cFA larger than 1.5 cm in diameter. These were treated with UGTI. We performed a retrospective review of data on a former group of 33 consecutive historical control patients that were treated by UGC.*
Results: *the groups were similar in respect of demographic and clinical variables. Thirty patients were suitable for UGC and 33 patients were suitable for UGTI. The success rate for UGC was 26/30 (87%) compared to 33/33 (100%) for UGTI ($p<0.05$). Thrombosis was achieved during the first treatment session in 7/26 patients treated by UGC, compared to 26/33 in the UGTI group ($p<0.0001$). Four patients that failed UGC and two patients that were unsuitable for UGC required surgical repair. UGTI as compared to UGC was shorter in duration (25 vs 75 min) and required no sedation. No thromboembolic or systemic complications occurred in either group. Cost analysis revealed savings of $US 517 for each patient treated by UGTI as compared with UGC.*
Conclusions: *in our study, UGTI is superior to UGC, and we suggest that UGTI should become the procedure of choice for the treatment of cFA.*

Key Words: False aneurysm; Catheterisation; Compression; Thrombin.

Introduction

Postcatheterisation false aneurysms (cFA) occur in less than 1% of cases.[1] Poor puncture-site selection, use of large-bore needles and sleeves, interventional procedures, periprocedural use of anticoagulant and antithrombotic agents, poor control of the puncture-site bleeding upon retrieval of the catheter as well as calcified arteries are all associated with an increased rate of this complication. cFA was treated surgically until 1991 when ultrasound-guided compression-closure (UGC) was introduced.[2] UGC rapidly replaced surgery as the treatment modality of first choice, although the success rate was only about 75% and it had several limitations, including significant local discomfort and a significant rate of recurrence. In 1986 Cope *et al*. reported percutaneous injection of thrombin to treat false aneurysms, with occlusion of the feeding vessel.[3] In 1997 Liau *et al*. published a series of 5 patients with cFA treated with ultrasound-guided percutaneous injection of thrombin.[4] This report was quickly followed by several similar publications.[5–10] Subsequently, various concerns have been raised regarding possible complications of this treatment, e.g. thromboembolic or allergic reactions.[11,12] We reviewed our experience with both treatment modalities and evaluated the efficacy and cost efficiency of UGC vs UGTI.

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Materials and Methods

All patients with suspected cFA were evaluated by diagnostic duplex scan in our noninvasive vascular laboratory with an ultrasound scanner (Synergy, General Electric, U.S.A.), utilising a 5-MHz linear array transducer. We recorded the luminal diameter of the cFA and the status of the peripheral pulses and arterial blood flow of all extremities. All patients with cFA

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with a luminal diameter larger than 1.5 cm were considered for non-invasive treatment. Patients with smaller cFA were followed by repeat duplex scans till spontaneous obliteration of the aneurysm and were excluded from this study.

Between July 1999 and February 2001 we prospectively collected data on 33 consecutive patients diagnosed with cFA that were treated by UGTI. This group included 6 patients from other hospitals referred for UGTI in our institution. We compared this group to a historic control group of 33 consecutive patients with cFA that were treated with UGC between June 1997 and June 1999. We reviewed the charts, non-invasive vascular laboratory findings and outpatient follow-up records of all patients.

UGC was performed in a routine fashion under continuous ultrasonographic guidance as previously described by Fellmeth *et al.*[2] Briefly, compression of the aneurysmal neck to arrest flow in the cFA sac was applied for 15 min, up to 3 times in sequence, during one treatment session. If obliteration of the cFA was not achieved the same procedure was repeated the following day, up to a maximum of three sessions. Analgesics and sedative premedication were routinely required to ease the discomfort during the procedure and enable effective compression. Anticoagulant and anti-platelet treatments were regularly discontinued to facilitate successful thrombosis of the aneurysms. Patients rendered unsuitable for UGC and patients that failed UGC were operated.

UGTI was performed according to the method previously described by Kang *et al.*[5] Bovine thrombin solution (GENTRAC Inc., Middleton, WI, U.S.A.), at a concentration of 1000 u/m after reconstitution of thrombin powder in sterile normal saline, was drawn into a 2-millilitre syringe attached to a 21 or 22-gauge spinal needle. The skin was prepped with chlorhexidine gluconate 0.5% in alcohol 70% solution and the needle was inserted into the cFA under continuous sonographic guidance with the color-flow turned off. With the tip of the needle inside the aneurysmal lumen and the color-flow turned on, thrombin solution was gently injected, resulting in a visible acoustic noise on the screen. Obliteration of the cFA was detected by complete disappearance of the color-flow signal inside the cFA, usually within a few seconds, and the needle was removed. If obliteration of the cFA lumen failed, 1–2 similar doses of thrombin were repeatedly injected. We did not apply any local compression and remarkably none of the patients required any analgesic or sedative treatment. Anticoagulant and anti-platelet medication was not modified in this group. All patients were kept in bed for 4 h and were re-examined the next morning to confirm complete obliteration. In a few cases of obese patients or huge haematomas we experienced exceptionally poor visualisation of the needle tip by duplex. Subsequently we used specially designed needles with echogenic tips (Echotip, 21-gauge 10-centimetre long needle, Cook, Bloomington, IN, U.S.A.) that enabled more reliable confirmation of proper positioning of the needle tip inside the aneurysmal sac.

Results

Comparison of the treatment groups

The UGC and UGTI groups were similar with regard to age (66 vs 65 years) and male to female distribution (15:18 vs 14:19, respectively). There were no significant differences between the treatment groups regarding underlying medical conditions, e.g. ischaemic or rheumatic heart disease, hypertension, cigarette smoking and hyperlipidaemia. The groups were comparable regarding the ratio of interventional vs diagnostic procedures, and cardiac vs peripheral catheterisations. All cFA were of the femoral artery, except 2 cases of brachial artery cFA in the UGTI group. The median diameter of the cFA was 2.37 cm (range: 1.50–5.25 cm) in the UGC group and 2.25 cm (range: 1.50–4.53 cm) in the UGTI group.

Ultrasound-guided compression

Treatment by UGC was considered in 33 consecutive patients (Table 1). One patient died prior to treatment and in 2 patients UGC could not be performed due to underlying medical conditions, e.g. severe obesity and unstable cardiac condition. In 26/30 (87%) UGC was successful, though in 19/30 (63%) more than one session of compression was required. No systemic complications have been reported, though the vast majority of the patients had large groin hematomas that resolved spontaneously. One out of 6 patients that required surgery had a prolonged hospitalisation due to a severe operative wound infection. No late failures were revealed.

Ultrasound-guided thrombin injection

Thirty-three consecutive patients with cFA were offered UGTI as the first treatment modality (Table

Table 1. Results. Comparison of the procedure-related outcome of patients allocated for treatment by UGC and UGTI.

	UGC	UGTI
Pre-treatment mortality	1 (3%)	0
Patients unsuitable for treatment modality	2	0
Catheterisation-treatment interval (days)	2 (1–30)	3 (1–30)
Thrombin (units/injection)	n/a	300 (100–3000)
Patients available for non-surgical treatment	30	33
successful obliteration	26 (87%)	33 (100%)
on-table obliteration, 1st session	7 (23%)	26 (79%)
on-table obliteration, 2nd session	11 (37%)	6 (18%)
delayed spontaneous obliteration	8 (27%)	1 (3%)
failure of treatment	4 (13%)	0 (0%)
noninvasive vascular lab stay (min/pt)	75 (15–120)	25 (15–60)
procedure-related hospital stay (days/pt)	2 (1–5)	1 (1–2)
complications: superficial skin infection	2 (7%)	1 (3%)
patients treated surgically	6 (20%)	0 (0%)
operating room time (h/case)	1.5 (1–2)	n/a
post-operative hospital stay (days/pt)	3 (2–24)	n/a
complications: surgical wound infection	1	n/a

Values represent number of patients, except when otherwise noted. Average values are presented as median and range, in parentheses. (UGC – ultrasound-guided compression therapy, UGTI – ultrasound-guided thrombin injection, pt – patient, n/a – not appicable).

1). UGTI was applicable and resulted in complete obliteration of the cFA in all patients (100%). In 26/33 (79%) the cFA thrombosed completely during the initial treatment session and only 6/33 (18%) required a second session of UGTI. In addition, one patient with a brachial cFA that completely obliterated initially was found with a patent cFA on next day evaluation and required repeated UGTI. One patient with superficial skin infection in the groin required treatment with oral antibiotics. No adverse reactions of immunologic origin or any other systemic complications have occurred. Two patients reported transient pain of a few seconds' duration distal to the injection site immediately following thrombin injection. Careful examination of the peripheral pulses and doppler studies of the extremities did not detect any objective signs of embolisation. Unlike in the UGC group, this procedure was associated with minimal discomfort of the 21-gauge needle stick and resulted in a uniform pattern of patient satisfaction. No late failures were revealed.

Statistical analysis

We compared the proportion of successful treatment among the two study groups, using Fisher's exact test. This test is appropriate due to the relatively small size of the study and the small expected frequency. The overall success rate of UGTI reached statistical difference compared to UGC ($p = 0.0460$). The difference in favor of UGTI in achieving fast cure during the first treatment session was highly significant ($p<0.0001$).

Cost analysis

We performed a limited cost analysis based on local charges (expressed in US$) for non-invasive vascular laboratory, operating room, hospitalisation and thrombin, but excluding other charges, e.g. surgeons' fee. Time utilisation of the noninvasive vascular laboratory was more than twice in the UGC group compared to the UGTI group. Failure to obliterate most of the cFA by UGC on the first session required an additional day of hospitalisation for those patients. Six patients in the UGC group required surgery (average 1.5 h operating room per case) that was followed by an average post-operative hospital stay of 6.7 days per patient, a relatively prolonged period that resulted from a significant operative wound infection in one of the patients. The success in obliterating most cFA by UGTI on the first session and the fact that none of the patients in the UGTI group required surgery translated to significant cost savings in this group, about US$517/patient, or 45% relative cost reduction (Table 2).

Discussion

UGC has been judged to be effective with a success rate of up to 88% in a recent study.[14] Nevertheless, surgical intervention is still required in failed cases. UGC is often associated with considerable discomfort to the patient, it requires repeat duplex studies and

Table 2. Expenses. The expenses are calculated as average for one treated patient, based on local costs expressed in US$.

	UGC	UGTI
Noninvasive vascular lab utilisation ($90/h)		
diagnostic study (15 min/study)	22	22
treatment session (75 min/UGC, 25 min/UGTI)	114	39
completion study (15 min/study)	22	22
follow-up study (15 min/study)	22	22
Thrombin solution ($96/vial)	0	96
Post-procedure hospitalisation ($360/day)	792	432
Operating room utilisation (1.5 h/case)	98	0
Post-operative hospitalisation ($360/day)	80	0
Total	1150	633

(UGC – ultrasound-guided compression therapy, UGTI – ultrasound-guided thrombin injection, $ – US$).

relatively prolonged noninvasive vascular laboratory utilisation.

The initially published series on UGTI revealed its excellent success rate but failed to deal convincingly with the concerns of thromboembolic or other systemic complications, e.g. allergic reactions. A report on a thromboembolic complication of UGTI for a brachial artery cFA[11] and a report on a case of extensive femoral artery thrombosis following UGTI of a femoral cFA (unpublished communication) further emphasised the significance of those concerns.

We compared the results of UGTI in a prospective consecutive series of patients to the results of UGC in a historic control group of consecutive patients treated previously in our hospital. Unlike in prospective randomised trials a selection bias can not be completely excluded in this study, yet the results are in agreement with those previously published in the literature. We feel that the importance of those results in a new treatment modality outweight the shortcomings of the study design.

At the initiation of UGTI in our institution we carefully monitored each procedure with particular attention to possible thromboembolic complications. Precise visualisation of the tip of the injecting needle inside the lumen of the cFA was an absolute condition before injection of thrombin. Thrombin was very gently injected to avoid from a possible jet of the solution to reach the lumen of the native artery.

All patients were screened for history of allergy, or exposure to thrombin during former cardiovascular surgery. We also prepared ourselves to treat possible systemic reactions, as recently suggested.[12] Two of our patients reported on sudden pain of a few seconds' duration in their legs, just distal to the injection site. Although no objective evidence for possible arterial embolisation could be detected by physical examination or doppler studies, we speculated that those symptoms could have been caused by possible microemboli that rapidly lysed due to normal thrombolytic reactions in the circulation.

We were also puzzled by the case of a patient with a brachial cFA that "recanalised" on repeat duplex 24 h following successful UGTI, without evidence of re-bleeding or embolisation. A second attempt of UGTI resulted in complete obliteration of the cFA. We speculated that a factor such as the size of the needle-hole, the configuration of the aneurysm and its neck, or an undetected coagulation abnormality could have contributed to this outcome. Because lack of any objective evidence of detectable arterial embolisation, we did not alter our approach and continue to offer UGTI as the first treatment modality for patients with cFA. Nevertheless, we initiated a study to elucidate the haemodynamic and pharmacologic mechanisms involved in this novel procedure.

There was a significant variability in the amount of thrombin required to achieve obliteration of the cFA, partially due to inter-operator variation. According to the experience of the senior author (EEW) 100–200 units of thrombin are usually sufficient to induce thrombosis, though occasionally a second injection is required, particularly when there is more than one "loculation" of the cFA.

Taylor *et al.*[7] compared UGTI to UGC and demonstrated significant reduction in cost for this procedure, yet the hospital charges were not influenced significantly because their patients required continued hospitalisation due to their severe illnesses. In our study significant cost savings resulted from the fact that none of the patients in the UGTI group required surgery and post-operative hospitalisation. Gaining

confidence in this procedure and given the low rate of "recurrence" we feel that further reduction in cost may be achieved by selective same-day discharge of patients with uncomplicated small or medium size cFA that are easily treated by UGTI.

The comparison of the two treatment groups unequivocally shows the superiority of UGTI over UGC for the treatment of cFA. UGTI is relatively simple, requires a short learning curve, is safe and convenient for the patient and is applicable in most cases with a near-100% success rate. Though the number of cases treated by this method is still in the range of a few hundreds worldwide, the reproducibility of previously published results is encouraging. Further studies to elucidate the pharmacologic and haemodynamic mechanisms of this treatment modality are warranted. Given the satisfactory results that have been achieved by various groups it appears that UGTI is an effective, cost-efficient and safe procedure that should become the procedure of choice to treat cFA.

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