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FULL PAPER

Factors associated with pseudoaneurysm development and necessity for reintervention: a single centre study

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Objective: Evaluate the factors associated with pseudoaneurysm development and morphology. Measure ultrasound-guided thrombin injection (UGTI) and surgical treatment outcomes for pseudoaneurysms, and the necessity for post-primary intervention (reintervention)

Methods: Retrospective analysis of ultrasound scans and CT angiography of peripheral pseudoaneurysm interventions from February 2011 to April 2017. 99 patients (61.6% female) were identified; median age 72 years (range 12–89). Multivariate analysis of patient demographics, including pre-intervention anticoagulant and antiplatelet medication was performed.

Results: Primary intervention for peripheral pseudoaneurysms (62.6% common femoral artery) included 93 UGTI and 6 surgical repairs; with 12 reinterventions (9 UGTI and 3 surgical). Pseudoaneurysm incidence for vascular interventional radiology (VIR) was 0.48% (31/6451) and cardiology was 0.24% (60/25,229). Rates for primary success, immediate complications, 30-day mortality and reintervention were measured respectively for UGTI (98.9%, 3.0%, 2.0%, and 11.8%) and surgical repair (100%, 0.0%, 22.2% and 16.7%). Reintervention risk factors included pre-intervention thrombocytopenia ($<150 \times 10^9/L$) ($p = 0.025$) and pseudoaneurysms following vascular surgery

($p = 0.033$). Other positive associations for reintervention (non-significant) included use of a sheath size $> 6Fr$ ($p = 0.108$) or arterial closure device ($p = 0.111$) during the pseudoaneurysm causative procedure. The pre-intervention warfarin subgroup developed a larger mean pseudoaneurysm sac size (4.21 cm, range 0.9–7.6), compared to no treatment ($p = 0.003$), aspirin ($p = 0.005$) and clopidogrel ($p = 0.026$) subgroups. UGTI dosage for thrombosis had a positive correlation with incremental sac size increase ($p < 0.001$).

Conclusion: The main reintervention risk factor was pre-intervention thrombocytopenia, with additional positive associations including pseudoaneurysms caused by surgery, increased sheath size and arterial closure devices. Warfarinized patients developed larger sac-sized pseudoaneurysms compared with other pre-intervention regimens, with positive correlation of higher UGTI dosage required for thrombosis.

Advances in knowledge: Patients with pre-intervention thrombocytopenia and pseudoaneurysms attributed to vascular surgery are subgroups that may benefit from post-intervention imaging surveillance due to significant reintervention risk.

INTRODUCTION

Pseudoaneurysms represent the second most common complication following vascular access procedures, complicating 0.2% of diagnostic angiography procedures¹ and between 0.9 and 4.9% of angioplasty procedures.^{2–4} The incidence of pseudoaneurysms widely varies in the literature and the aetiology is thought to be multifactorial; including more complex and prolonged vascular interventions,⁵ larger sheath sizes,⁶ and the use of antiplatelet and/or anticoagulant therapy.^{7,8}

Ultrasound-guided thrombin injection (UGTI) has become the mainstay treatment for peripheral pseudoaneurysms.^{9–15} Open surgical repair of pseudoaneurysms are reserved for cases where UGTI has failed or is contraindicated; such as actively bleeding pseudoaneurysms, significant risk for distal embolization with a wide pseudoaneurysm neck or concomitant arteriovenous fistula.¹⁶ There is limited evidence for manual compression alone for pseudoaneurysm management, however, it was advocated as a pragmatic first-line approach in centres with limited resources,¹⁷ and for selective cases; where pseudoaneurysms are compressible, small (<2 cm), lack a definable neck,

directly adjacent to vessels, or with concomitant arteriovenous fistula.¹⁸

Although UGTI has a primary success rate >95%,^{9–15} pseudoaneurysms can reoccur and require further interventional management following the primary procedure (reintervention). Stone et al reported the recurrence of pseudoaneurysm following successful UGTI had an incidence rate of only 3.4% (47/1375), questioning the need for routine post-procedural duplex examinations in a cost-containment environment.¹⁹ Despite this low incidence rate, undiagnosed pseudoaneurysms which are left untreated can lead to morbidity and mortality. Therefore, it is essential to determine distinct criteria for post-intervention duplex surveillance, analyzing both patient and procedural factors that may influence pseudoaneurysm recurrence and reintervention rate. To date, both thrombocytopaenia and pseudoaneurysm sac size >2 cm have both been described as independent risk factors for pseudoaneurysm reoccurrence.²⁰

Our primary aim was to evaluate the factors associated with pseudoaneurysm development following procedures by vascular interventional radiology (VIR), cardiology and vascular surgery. Our secondary aim was to analyze the effects of anticoagulant and antiplatelet agents on reintervention and pseudoaneurysm morphology.

METHODS AND MATERIALS

The study was designed to evaluate clinical service outcomes within our institution (vascular radiology department, University Hospitals of Leicester NHS Trust), focusing on reintervention rate following pseudoaneurysm intervention. This was approved by our local audit board and did not require any formal ethical approval in accordance with the UK National Research Ethics Service guidelines.

UGTI was the preferred minimally invasive treatment option at our institution. Contraindications for UGTI and primary indications for surgical management included actively bleeding pseudoaneurysms, cases associated with a significant risk of distal embolization or truncal ischaemia; such as pseudoaneurysm neck >3 mm and concomitant arteriovenous fistulae. If a pseudoaneurysm was infected at presentation, surgical washout and repair was indicated. Immediate failure of pseudoaneurysm thrombosis after UGTI failure was an indication for open surgical repair. Manual compression was not routinely used in the management of pseudoaneurysms at our institution.

A retrospective search was performed using the radiology image-reporting software CRIS by Healthcare Solutions Software, of all ultrasound scans and CT angiography (CTA) at our single centre institution between February 2011 and April 2017. Search identifiers included "pseudoaneurysm", "pseudo aneurysm", "false aneurysm", "haematoma", "bleed" and "thrombin". All cases of peripheral pseudoaneurysm intervention were included in the study independent of procedural success. Visceral pseudoaneurysms and their interventions were excluded because of their underlying different aetiology. 99 patients were identified having had UGTI or open surgical repair for pseudoaneurysm

intervention; 61.6% were female and the median age was 72 years (range 12–89).

UGTI imaging reports were used to identify procedural success, pseudoaneurysm location, sac size and dose of thrombin required to thrombose the sac. CTA was reviewed to confirm pseudoaneurysm location and determine sac size where pre-intervention ultrasound imaging was initially not performed. Angiography reports for pseudoaneurysm causative procedures were reviewed to identify the type of vascular closure device used. All ultrasound and CTA imaging were previously reported and/or approved by a consultant radiologist. The ultrasound and CTA imaging for pseudoaneurysms was reviewed again by a vascular radiologist (NK, 6 years of VIR experience). No further repeat revisions were undertaken to verify accuracy of pseudoaneurysm measurements. A separate CRIS search was performed to determine the total number of interventional vascular radiology and cardiology procedures during the study period, to measure incidence for cardiology and VIR subspecialties.

Biochemistry and haematology laboratory data for patients prior to pseudoaneurysm intervention was acquired from iLAB Operations Software by Agilent Technologies. Pre-intervention anticoagulation and antiplatelet drug data were retrieved using a reference report from the Electronic Prescribing and Medicines Administration system by Medchart. This was cross-checked with JAC Medicines Management electronic prescribing system and electronically-stored admission letters via Integrated Clinical Environment Care Coordination Software by Sunquest Laboratory^{TM}. Baseline patient characteristics, including drug regimens prior to pseudoaneurysm intervention and characteristics of the pseudoaneurysm causative procedure are shown in [Tables 1 and 2](#) respectively.

Multivariate analysis of reintervention vs no reintervention cases included odds ratio (OR) and 95% confidence interval (CI); probability values of <0.05 were regarded as statistically significant. *t*-Test for two independent means was calculated for pseudoaneurysm sac size and between pre-intervention anticoagulation and antiplatelet subgroups. Pearson correlation coefficient was calculated to measure strength of linear association between thrombin dosage for primary immediate thrombosis and the pseudoaneurysm sac size.

RESULTS

Factors associated with pseudoaneurysm development

Pseudoaneurysm vessel location

The majority of peripheral pseudoaneurysms occurred in the common femoral artery ($n = 62$, 62.6%), followed by the superficial femoral ($n = 17$, 17.2%), radial ($n = 6$, 6.1%), brachial ($n = 4$, 4.0%) and external iliac ($n = 4$, 4.0%) arteries. The remaining cases ($n = 6$, 6.1%) involved miscellaneous arteries, as shown in [Table 3](#). Arterial sites for pseudoaneurysms undergoing open surgical repair comprised of the common femoral artery ($n = 8$) and the external iliac artery ($n = 1$).

Table 1. Patient characteristics and drug regimens prior to pseudoaneurysm intervention

Patient characteristics	Median (range)
Age (years)	72 (12–89)
Female	61 (61.6%)
<i>Pre-intervention blood tests</i>	
Haemoglobin (g/L)	108 (70–152)
Platelet count ($\times 10^9/L$)	247 (70–629)
International normalized ratio (INR)	1.1 (0.9–8)
<i>Pre-intervention antiplatelet and anticoagulation agents</i>	
	n = 99 (%)
No treatment	15 (15.2%)
Aspirin	50 (50.5%)
Clopidogrel	36 (36.4%)
Ticagrelor	10 (10.1%)
Prasugrel	1 (1.0%)
Warfarin	23 (23.2%)
Dalteparin (long-term)	4 (4.0%)
Apixaban	2 (2.0%)
Rivaroxaban	1 (1.0%)
<i>Pre-intervention regimen</i>	
Antiplatelet mono-therapy	26 (26.3%)
Antiplatelet dual-therapy	30 (30.3%)
Anticoagulant mono-therapy	21 (21.1%)
Anticoagulant + mono-antiplatelet	4 (4.0%)
Anticoagulant + dual-antiplatelet	3 (3.0%)

Causative procedure

60 (60.6%) of the 99 cases of peripheral pseudoaneurysms were cardiology referrals secondary to cardiac catheterization procedures; 38 (63.3%) sited at the common femoral artery. 27 (45.0%) followed emergency percutaneous coronary intervention (PCI), 20 (33.3%) involved other cardiac interventional procedures (Table 3), and the remaining 13 (21.7%) resulted from purely diagnostic coronary angiography cases. VIR procedures were associated with 31 (31.3%) peripheral pseudoaneurysm cases; 27 (87.1%) secondary to interventional procedures (Table 3), and 4 (12.9%) cases from diagnostic angiography. 4 (4.0%) peripheral pseudoaneurysms were attributed to vascular surgery, and the remaining 4 (4.0%) cases had miscellaneous causes (Table 3). The incidence of pseudoaneurysms following cardiology interventions was 0.24% (60/25,229), and for VIR interventions it was 0.47% (30/6,451 procedures).

Table 2. Procedure characteristics for pseudoaneurysm intervention

Characteristics for pseudoaneurysm causative procedure	
<i>Specialty performing procedure</i>	n = 99 (%)
Cardiology	60 (60.6 %)
VIR	31 (31.3 %)
Vascular surgery	4 (4.0 %)
Unknown	4 (4.0 %)
<i>Sheath size</i>	
	n = 91 (%)
4 Fr (4.19 mm)	3 (3.3 %)
5 Fr (5.24 mm)	8 (8.8 %)
6 Fr (6.28 mm)	40 (44.0 %)
7 Fr (7.33 mm)	15 (16.5 %)
8 Fr (8.34 mm)	13 (14.3 %)
Unknown	12 (13.2 %)
<i>Arterial closure technique for VIR</i>	
	n = 31 (%)
ACD	10 (32.3 %)
Manual compression alone	20 (64.5 %)
Unknown	1 (3.2 %)
<i>Arterial closure technique for cardiology</i>	
	n = 60 (%)
ACD	5 (8.3 %)
Manual compression alone	53 (88.3 %)
Unknown	2 (3.3 %)
Pseudoaneurysm management	
<i>Primary intervention</i>	n = 99 (%)
UGTI	93 (93.6 %)
Open surgical repair	6 (6.1 %)
<i>Reintervention (post-primary intervention)</i>	
	n = 12 (%)
UGTI	9 (67.7 %)
Open surgical repair	3 (33.3 %)

ACD, arterial closure device; UGTI, ultrasound-guided thrombin injection; VIR, vascular interventional radiology.

Sheath size used during pseudoaneurysm causative procedure

Sheath size (French, Fr) was recorded in 78 of 91 (85.7%) of primary pseudoaneurysm causative procedures, detailed in Table 2. 6 Fr was the most common sheath size used within our study cohort (44.0%), followed by sizes 7 Fr (16.5%), 8 Fr (14.3%), 5 Fr (8.8%) and 4 Fr (3.3%).

Table 3. Pseudoaneurysm prevalence according to interventional procedure and arterial site

	<i>n</i> = 99 (%)
Causative procedure	
<i>Cardiology</i>	
Coronary angioplasty with stent insertion	27 (27.3%)
Coronary angiography (no intervention)	13 (13.1%)
Endocardial ablation	9 (9.1%)
Transcatheter aortic valve implantation	3 (3.0%)
Septoplasty	2 (2.0%)
Intra aortic balloon pump insertion	2 (2.0%)
Pacemaker insertion	1 (1.0%)
Valvuloplasty	1 (1.0%)
Atrioventricular node embolization	1 (1.0%)
Cardiac tissue biopsy	1 (1.0%)
<i>Vascular interventional radiology</i>	
Angioplasty (any vessel)	22 (22.2%)
Angiography (any vessel)	4 (4.0%)
Embolization (any vessel)	4 (4.0%)
Stent insertion (any vessel)	1 (1.0%)
<i>Vascular surgery</i>	
Transcatheter endovascular aneurysm repair	2 (2.0%)
Radio-cephalic fistula formation	1 (1.0%)
Femoro-femoral bypass graft	1 (1.0%)
<i>Miscellaneous</i>	
Failed dialysis access	2 (2.0%)
Spontaneous (high dose anticoagulation)	1 (1.0%)
Spontaneous (cause unknown)	1 (1.0%)
Arterial site of pseudoaneurysm	
Common femoral	62 (62.6%)
Superficial femoral	17 (17.2%)
Radial	6 (6.1%)
Brachial	4 (4.0%)
External iliac	4 (4.0%)
Profunda femoris	2 (2.0%)
Popliteal	1 (1.0%)
Femoro-femoral bypass	1 (1.0%)
Brachio-cephalic fistula	1 (1.0%)
Unknown	1 (1.0%)

Arterial closure device (ACD) usage following pseudoaneurysm causative procedure

The arterial closure technique following VIR procedures leading to pseudoaneurysm formation comprised of 10 (26.3%) uses of ACD (7 AngioSeal™, 3 Exoseal™) and 20 (64.5%) cases of manual compression alone. The closure technique was unavailable in 1 (3.2%) case, where the causative VIR procedure had been performed external to our study centre. Cardiology used an ACD in 5 (8.3%) cases (all AngioSeal™) and manual compression alone in 53 (88.3%) procedures. 2 (3.3%) cardiology cases were performed externally, and arterial closure technique unavailable. Manual compression alone was used in 80.2% of all pseudoaneurysm causative interventions.

PROCEDURAL OUTCOMES FOR PSEUDOANEURYSM INTERVENTION

Type of intervention

99 patient cases were identified from the institutional database that received a combined total of 102 UGTI and 9 open surgical repairs for peripheral pseudoaneurysm management. 93 cases had UGTI as the primary intervention and 6 cases had primary open surgical repair. Requirement for further pseudoaneurysm management (reintervention) contributed an additional nine UGTI and three open surgical repairs to the overall total.

PRIMARY SUCCESS

Primary immediate procedural success for UGTI (immediate sac thrombosis) was achieved in 92 of 93 (98.9%) pseudoaneurysm cases, while open surgical repair was initially successful in 6 of 6 (100%) cases. [Figure 1 \(A,B,C, D\)](#) demonstrates two examples of successful pseudoaneurysm thrombosis with UGTI. [Figure 1 \(E, F\)](#) shows the single UGTI treatment failure, a large superficial femoral artery pseudoaneurysm (Sac >7 cm, short neck 4 mm) that developed after emergency PCI, failing to thrombose after 1000 international units (IU) of thrombin were administered. [Figure 2](#) is a CTA depicting an actively bleeding common femoral artery pseudoaneurysm, developing after failed renal angioplasty, managed with primary open surgical repair.

IMMEDIATE COMPLICATIONS

A total of three (3.0%) patients receiving UGTI experienced immediate post-procedural complications, including thrombus extension to the brachial artery and two separate cases of hand and thigh transient ischaemia. There were no immediate complications in all open surgical repair cases.

30-DAY MORTALITY

30-day mortality rate for UGTI was 2.0% (2/102) and 22.2% (2/9) for open surgical repair. Three of the four 30-day mortality cases were receiving clopidogrel monotherapy and one patient was on warfarin monotherapy prior to intervention. The mortality in the UGTI cases was not related to the pseudoaneurysm or procedure, and instead secondary to respiratory tract infection. Surgical 30-day mortality cases were pseudoaneurysm-related, both re-presenting with extensive thigh and retroperitoneal haemorrhage, and disseminated intravascular coagulopathy secondary to clotting dysfunction and haemodynamic compromise.

Figure 1. Ultrasound images of therapeutic success and failure following UGTI intervention. (a) 3.6 × 1.7 cm pseudoaneurysm of the left superficial femoral artery with 2 mm wide neck and active flow, 2 days following coronary angiography. (b) The neck and sac was injected with 250 IU of thrombin with immediate thrombosis of both. (c) A larger partially thrombosed pseudoaneurysm arising from the right common femoral artery 7 days post-coronary angiography. (d) 200 IU of thrombin were injected into neck and area of flow within the pseudoaneurysm under ultrasound guidance with immediate flow cessation. (e) Pseudoaneurysm of the left common femoral artery (sac size >7 cm and short 4 mm neck) post-emergency percutaneous coronary intervention and stent insertion. 500 IU of thrombin was injected under ultrasound-guidance without success. (f) Bidirectional flow persisted within the neck of the pseudoaneurysm despite a total dose of 1000 IU of thrombin injection, with only partially thrombosed sac, resulting in procedural failure. The pseudoaneurysm consequently underwent a successful open surgical exploration and repair. IU, international unit; UGTI, ultrasound-guided thrombin injection.

REINTERVENTION

The primary UGTI intervention group ($n = 93$) had 11 cases of reintervention (11.8%), comprising of 9 UGTI and 2 open surgical repairs, with a median interval of 26 days. The open surgical repair group ($n = 6$) had a single case of reintervention (16.7%) with an interval of 2 days, involving an extensive external iliac arterial bleed and intramuscular haematoma ($11 \times 7 \times 12$ cm) requiring reexploration and repair. A multivariate analysis was performed to identify risk factors in patients requiring pseudoaneurysm reintervention. Pre-procedural platelet count $<150 \times 10^9/L$ was associated with an increased risk for requiring reintervention [OR 5.01, CI 95% (1.23–20.51), $p = 0.025$]. Pseudoaneurysms that arose after a vascular surgical procedure were more likely to require a future reintervention [OR 9.56, CI 95% (1.20–76.24), $p = 0.033$]. Both a sheath size >6 Fr [OR 3.48, CI 95% (0.76–15.83), $p = 0.108$] and ACD usage [OR 3.55, CI 95%

(0.75–16.84), $p = 0.111$] during the pseudoaneurysm causative procedure, had positive associations with the requirement for reintervention. No other associations for reintervention were found from patient factors (gender, age, pre-intervention laboratory tests and drug regimen) or pseudoaneurysm factors (location and sac size); Table 4.

PSEUDOANEURYSM MORPHOLOGY

Sac size and pre-intervention drug regimen

Pseudoaneurysm sac sizes were recorded from ultrasound and/or CTA reports in 77 (75.5%) of the 102 UGTI procedural reports. Imaging in all open surgical repairs did not discern the true pseudoaneurysm sac size due to extensive extravasation and associated haematoma formation; therefore we could not include these cases. A mean sac size was measured for patients on no treatment prior to UGTI (2.65 cm, range 1.3–4.5), and for those

Figure 2. CTA of actively bleeding pseudoaneurysm that was successfully treated with surgery CTA of a patient with renal artery stenosis that had a failed left renal angioplasty and developed a right common femoral artery pseudoaneurysm. The arterial phase images demonstrate an ill-defined blush of contrast in keeping with active haemorrhage. There is haematoma in the right groin which tracked up into the right retroperitoneum. The patient underwent emergency open surgical repair with a successful outcome. CTA, CT angiography.

on aspirin (2.91 cm, range 0.6–8.3), clopidogrel (3.07 cm, range 1.0–8.3) and warfarin (4.21 cm, range 0.9–7.6); represented in Figure 3. There was a statistically significant association between increasing pseudoaneurysm sac size and pre-UGTI warfarin treatment (as monotherapy or drug combination), in comparison to patients on no treatment ($p = 0.003$), or aspirin ($p = 0.005$) and clopidogrel ($p = 0.026$); as either mono- or dual-agent regimens.

Sac size and UGTI dosage

The exact thrombin dose was recorded in 82 (80.4%) of 102 UGTI procedural reports. The increase in pseudoaneurysm sac size and thrombin dosage (IU) required to cause complete thrombosis were positively correlated (Figure 4), with a Pearson correlation coefficient of 0.483 ($p < 0.001$). Mean therapeutic thrombin dosage was calculated pre-UGTI for patients on no

treatment (367 IU, range 50–750), mono- or dual-antiplatelet therapy without anticoagulant (367 IU, range 50–2000), and any anticoagulant agent with or without antiplatelet agent (410 IU, range 100–1000). No significant difference was found when comparing the subgroup with the highest thrombin dosage (anti-coagulation $\pm$ antiplatelet), with the no treatment subgroup ($p = 0.288$) or with mono- or dual-antiplatelet therapy without anticoagulant ($p = 0.287$).

DISCUSSION

The primary success rate of UGTI for peripheral pseudoaneurysm intervention at our institution was in line with current published research, estimated as $>95\%$ from a range of studies.^{9–15} The single UGTI failure from our study (Figure 1, E and F), involving a large superficial femoral artery pseudoaneurysm

Table 4. Multivariate analysis of patient and pseudoaneurysm factors for reintervention

Variable	Odds ratio (95% Confidence interval), <i>p</i> -value
Patient factors	
<i>Female</i>	5.1724 (0.6319–42.3399), 0.1255
<i>Age (years)</i>	
≤50	3.0370 (0.5320–17.3387), 0.2114
51–65	1.4400 (0.3874–5.3527), 0.5862
66–75	0.6667 (0.1337–3.3232), 0.6208
76–85	0.1933 (0.0236–1.5826), 0.1255
>85	3.6889 (0.6232–21.8368), 0.1502
Pre-intervention blood tests	
Haemoglobin <130 g/L (female) or <120 g/L (male)	2.9231 (0.3515–24.3104), 0.3210
Platelet count <150 × 10 ⁹ /L	5.0159 (1.2261–20.5198), 0.0249^a
INR >1.2	0.7135 (0.1417–3.5922), 0.6822
Pre-intervention drug regimen	
Antiplatelet mono-therapy	0.2826 (0.0343–2.3309), 0.2404
Antiplatelet dual-therapy	1.1048 (0.2995–4.0747), 0.8811
Anticoagulant (any)	2.5000 (0.6943–9.0022), 0.1610
Pseudoaneurysm morphology	
<i>Arterial site</i>	
Common femoral	0.5093 (0.1440–1.8014), 0.2952
Superficial femoral	3.2527 (0.8327–12.7061), 0.0898
<i>Sac size</i>	
≥2 cm	2.2619 (0.2470–20.7098), 0.4700
≥3 cm	0.8485 (0.1585–4.5421), 0.8478
≥4 cm	1.9048 (0.3531–10.2738), 0.4536
Causative specialty	
Cardiology	0.7556 (0.2139–2.6691), 0.6633
VIR	0.4521 (0.0917–2.2290), 0.3294
Vascular surgery	9.5556 (1.1976–76.2431), 0.0332^a
Sheath size and arterial closure device used in causative procedure	
>5 Fr	0.4355 (0.0759–2.4970), 0.3508
>6 Fr	3.4783 (0.7644–15.8277), 0.1069
>7 Fr	1.8182 (0.3241–10.2008), 0.4969
Arterial closure device usage	3.5500 (0.7485–16.8370), 0.1107

INR, international normalized ratio; VIR, vascular interventional radiology.

^aSignificantly different (*p* < 0.05)

(Sac <7 cm, neck 4 mm) following emergency PCI, failed to thrombose after 1000 IU of thrombin and the pseudoaneurysm subsequently underwent active extravasation. In our institution, surgery is considered over UGTI in pseudoaneurysm management in the following circumstances: evidence of active bleeding and risk factors for distal embolization; wide neck >3 mm and concomitant arteriovenous fistulae. Pseudoaneurysm sac complexity through number of locules and size are not complete contraindications for UGTI utilization and will depend on the

aforementioned factors. However, sac size >2 cm has been shown to increase the odds of pseudoaneurysm recurrence by 229% compared to <2 cm sacs, while number of locules has no effect on UGTI outcome or recurrence.²⁰

Our data suggest that neither anticoagulant nor antiplatelet therapy influenced the primary success rate of pseudoaneurysm intervention and requirement for reintervention. Similar studies have demonstrated UGTI procedural success ranging between

Figure 3. Effect of pre-UGTI patient drug regimen on mean pseudoaneurysm sac size (with range). UGTI, ultrasound-guided thrombin injection.

94 and 100%, where 26.7–31.4% of patients were receiving pre-intervention anticoagulant therapy.^{21,22} In our study cohort, there was no significant influence of pre-intervention anticoagulant and antiplatelet regimens on immediate pseudoaneurysm intervention outcomes. However, with two surgical pseudoaneurysm-related 30-day mortality cases resulting from uncontrolled blood loss and haemodynamic compromise, whilst on anticoagulant and antiplatelet regimens, we suggest careful consideration still needs to be employed with regards to pre-intervention anticoagulation and its immediate reversal when a pseudoaneurysm is detected. Preceding elective intervention cases at our institution, oral anticoagulation is held for at least 5 days with a bridging plan of low molecular weight heparin therapy. We speculate that anticoagulant reversal may be suboptimal in the emergency setting, where intervention is required immediately. This is supported by the large proportion of pseudoaneurysms that occur following emergency PCI in our cohort.

Figure 4. Correlation between pseudoaneurysm sac size and thrombin dosage causing sac thrombosis. IU, international unit.

Our study demonstrated that pseudoaneurysms were most prevalent in the common femoral artery; shown in literature to be the most frequent site to develop post-catheterization.^{9–15} Cardiac catheterization was associated with the highest number of referrals for common femoral artery pseudoaneurysm interventions, corroborating existing research.^{2,23,24} The incidence of pseudoaneurysms secondary to vascular access procedures by VIR (0.47%) and cardiology (0.24%) falls between the reported rates of 0.02–4.5%.^{25–27} The difference between incidences is multifactorial and not comparable between specialties, with cardiac angiography having dominance for radial artery vascular access site and a higher procedural volume.

The requirement for further pseudoaneurysm reintervention was higher in patients with a platelet count $<150 \times 10^9/L$. There is a known association between a pre-procedural platelet count $<200 \times 10^9/L$ and the occurrence of pseudoaneurysms after arterial puncture, acknowledged as a risk factor for pseudoaneurysm formation after PCI.^{8,28} Esterson et al also showed that thrombocytopenia was an independent predictor of pseudoaneurysm recurrence, recommending follow-up imaging in this subgroup.²⁰ The reason for the association for low platelet count and reintervention in this subgroup is unknown. One theory is that patients with a lower platelet count prior to primary intervention may achieve initial immediate thrombosis via UGTI, however, the clot lattice is platelet poor and therefore recanalization of the pseudoaneurysm occurs. Vascular surgical cut down procedures were additionally identified as a potential risk factor for pseudoaneurysm reintervention. However, a low number of surgical cases within our cohort may pose invalidity to the statistically significant association, and needs to be corroborated by further research. The pathophysiological cause behind this association is unknown but may be related to the fibrous tissue that forms around a surgical wound that can allow recanalization of the pseudoaneurysm to occur. At our institution, it is not routine practice to follow-up patients after UGTI, as post-procedural clinical assessment is usually adequate to confirm therapeutic success. In those patients who have a persistent pulsatile groin swelling post-UGTI, ultrasound follow-up is performed within the 30-day interval. Our results suggest that it may be beneficial for patients with a pre-intervention platelet count $<150 \times 10^9/L$ or pseudoaneurysm attributed to vascular surgery procedures to be routinely followed up within the 30-day interval.

ACD use had a positive association with the need for pseudoaneurysm reintervention; although not statistically significant, there was a relative high OR of 3.6. Korney et al reported ACDs may increase the risk of haematoma formation and pseudoaneurysms from a 30-study meta-analysis.²⁹ Nilosky et al demonstrated mechanical compression was favourable to ACDs in patients undergoing PCI in respect to vascular complication rate.³⁰ It is theoretically possible that an ACD could maintain the opening of the pseudoaneurysm neck, hence increasing the risk of pseudoaneurysm recurrence rates and the need for reintervention. Catheter sheath sizes > 6 Fr additionally had a positive but non-significant association with reintervention requirement. In the literature, larger circumference arterial punctures have been shown to increase pseudoaneurysm incidence, compared to

smaller-sized punctures used in purely diagnostic angiography.⁶ We can only speculate that larger sheath sizes may increase pseudoaneurysm recurrence and reintervention rates; however, a larger study would be needed to demonstrate this effect first.

Patients who previously received anticoagulation with warfarin prior to pseudoaneurysm formation and intervention developed a significantly larger sac size when compared to other drug treatment subgroups. On a pharmacological basis, warfarin inhibits vitamin K-dependent synthesis of active forms of the calcium-dependent clotting factors, II, VII, IX, X, and regulatory factors, protein C, S and Z.^{31,32} Deficiency in factor IX has been associated with pseudoaneurysm formation in a number of case reports.^{33–35} Additionally, both protein C and S deficiency have been mapped at higher levels in patients who develop aortic aneurysms.³⁶ The synthetic reduction of these vitamin K-dependent clotting and regulatory factors suggestively affects pseudoaneurysm morphology, whereby drivers of haemostasis are inhibited, causing increased arterial pooling within the sac and the impairment of physiological thrombus formation.

Pseudoaneurysm sac size had a positive correlation with the dose of thrombin required to achieve initial sac thrombosis through UGTI. At our institution, thrombin is normally injected at dosage intervals of 250 IU to assess therapeutic response under Doppler ultrasound guidance. A larger pseudoaneurysm sac volume may dilute the thrombogenic effect from injected thrombin, and could explain why patients with larger sac diameters require higher thrombin dosages to achieve effective thrombosis. The higher thrombin dose used in UGTI to thrombose larger sac-sized pseudoaneurysms has the potential to increase the rate of distal emboli and peripheral ischaemia; Kurawski et al demonstrating an increased complication rate associated with repeated thrombin injections.³⁷ With an immediate complication rate of 3.0%, our study was too small for subgroup analysis of thrombin-related complications.

We accept that there were several limitations to our study. As this was a retrospective study, there was incomplete data from UGTI procedural reports in respect to the pseudoaneurysm

sac size (24.5%), location (1.0%), catheter size (13.2%), arterial closure technique (3.3%) and total thrombin dosage used (19.6%). CTA usage for pseudoaneurysm measurements in patients without pre-intervention ultrasound may have introduced inconsistencies related to cross-modality assessment. Sac dimensions could not be accurately ascertained from CTA prior to surgical repair cases due to excessive haematoma in all cases. Direct comparisons between mono-antiplatelet or anticoagulant therapies were not performed due to small patient numbers (45.8% on combinational regimens), so we were unable to establish individual mono-therapy effect on procedural outcomes. Ultrasound follow-up after UGTI or open surgical repair was not routine practice at our institution, which may have detected pseudoaneurysm recurrence post-treatment for asymptomatic recurrent cases; potentially influencing both success and reintervention rates.

CONCLUSION

UGTI primary success rate was high and in accordance with published studies. The main risk factor for reintervention included pre-intervention thrombocytopaenia; representing a subgroup that may benefit from post-intervention imaging surveillance. Other potential reintervention risk factors included pseudoaneurysms caused by surgery, increased sheath size and arterial closure devices, which require further research. Warfarinized patients developed larger sac-sized pseudoaneurysms compared with other pre-intervention regimens, with positive correlation of higher UGTI dosage required for thrombosis.

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ETHICS APPROVAL

Did not require any formal ethical approval in accordance with the UK National Research Ethics Service guidelines

DISCLOSURE

There are no conflicts of interest or financial ties to disclose

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