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# How should I treat a common femoral arterial haemorrhage and deep vein thrombosis post percutaneous coronary intervention for non-ST-elevation myocardial infarction?

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## CASE SUMMARY

**BACKGROUND:** A 71-year-old Chinese male presented with a non-ST-elevation myocardial infarction and was started on dual antiplatelet therapy. A percutaneous coronary intervention (PCI) via the right femoral artery was complicated by a deep vein thrombosis (DVT) post removal of the access sheath, probably related to prolonged compression and immobility. Subcutaneous enoxaparin was started for the DVT.

**INVESTIGATION:** A computed tomography angiogram (CT-A) of the right lower limb was carried out as there was worsening swelling and bruising over the right groin after starting subcutaneous enoxaparin and bridging warfarin. The CT-A showed a focal arterial blush adjacent to the right common femoral artery.

**DIAGNOSIS:** Common femoral arterial haemorrhage complicating enoxaparin use for the treatment of DVT post PCI.

**MANAGEMENT:** Anticoagulation was stopped but dual antiplatelet therapy was continued. C-clamp compression of the puncture site was performed overnight. A repeat CT-A the next day showed resolution of bleeding with a stable haematoma. Intravenous heparin was subsequently started for the DVT and bridged to subcutaneous enoxaparin and warfarin.

**KEYWORDS:** deep vein thrombosis, femoral arterial haemorrhage, post percutaneous coronary intervention

## PRESENTATION OF THE CASE

A 71-year-old male was admitted for an acute coronary syndrome. The electrocardiogram showed T inversions in V3 and V4 which were associated with a significant rise in cardiac enzymes. He was loaded with aspirin 300 mg and ticagrelor 180 mg and continued on aspirin 100 mg daily, ticagrelor 90 mg twice a day and subcutaneous enoxaparin 60 mg twice a day.

The patient underwent a coronary angiogram via the transradial approach on day four which showed 50% occlusion of the distal left main (LM) coronary artery, 90% occlusion of the mid left anterior descending (LAD) artery and 50% occlusion of the ostial left circumflex artery. The patient refused a coronary artery bypass and thus a percutaneous coronary intervention (PCI) was performed. A transfemoral PCI was performed with drug-eluting stents placed in the mid LAD and distal LM/proximal LAD. The right groin vascular access site was subsequently closed with a collagen plug vascular closure device (Angio-Seal™; St. Jude Medical, St. Paul, MN, USA) and the patient was continued on aspirin and ticagrelor thereafter. Subcutaneous enoxaparin was stopped after PCI.

Extensive bruising and a large haematoma were noted post PCI. Manual haemostasis was initially achieved and a compression bandage was applied. Unfortunately, a right lower limb duplex scan three days after the PCI showed a deep vein thrombosis (DVT) of the distal external iliac and common femoral vein **(Figure 1)**. In view of the DVT, the patient was again started on subcutaneous enoxaparin 50 mg twice a day, and ticagrelor was changed to clopidogrel. Bridging warfarin was started two days after enoxaparin. However, the right groin haematoma expanded. A computed tomography (CT) angiogram of the right lower limb

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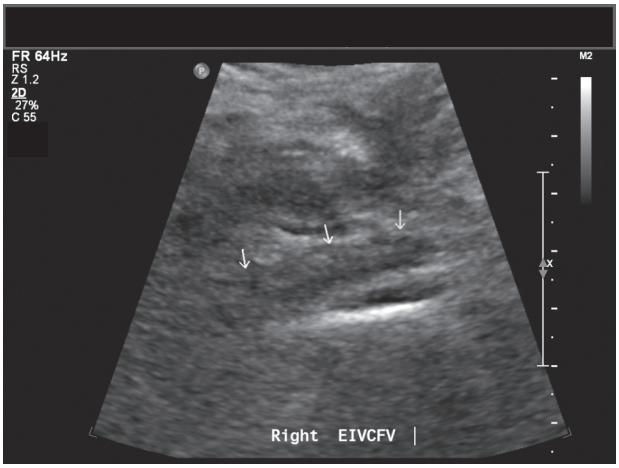


**Figure 1.** *Right lower limb duplex scan. Arrows: right external iliac vein and common femoral vein deep vein thrombosis.*

was carried out three days after starting enoxaparin. This showed a focal arterial blush adjacent to the right common femoral artery which was consistent with an active haemorrhage **(Figure 2, Figure 3)**.

How should this acute haemorrhage be managed, given that the patient has a provoked DVT with a recent PCI (for which the patient is also on dual antiplatelet therapy)?

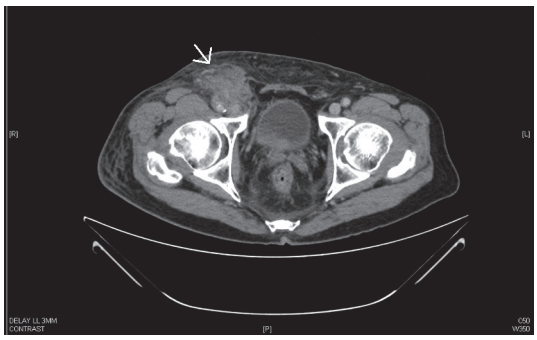

**Figure 2.** *Computed tomography (CT) angiogram of the right lower limb. Arrow: right groin haematoma.*

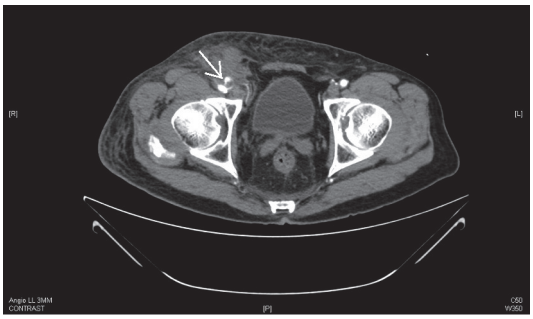

**Figure 3.** *Computed tomography (CT) angiogram of the right lower limb. Arrow: right groin focal arterial blush adjacent to the common femoral artery.*

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# How would I treat?

**THE INVITED EXPERT'S OPINION**

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A collagen plug-based vascular closure device (VCD) is commonly used to achieve haemostasis after percutaneous coronary intervention with femoral artery access. Compared with mechanical compression of the femoral artery access site, it has been shown to reduce time to haemostasis, and to allow early ambulation with improved patient satisfaction. However, VCD failure is not rare (~3%), and is associated with significantly higher vascular complications as compared to VCD success[1]. Vascular complications may include thigh haematoma, retroperitoneal haematoma, pseudoaneurysm, arteriovenous fistula, and arterial occlusion, increasing morbidity, mortality, and medical costs. In the present case, a femoral artery pseudoaneurysm seemed to arise due to incomplete haemostasis of an arterial puncture site by VCD, leading to arterial blood oozing into the surrounding tissues and forming a pulsating encapsulated haematoma. Computed tomography angiography of the lower extremities revealed arterial blood flow into the pseudoaneurysm. Duplex ultrasound scanning can definitely confirm the pseudoaneurysm sac with a swirling colour flow and the neck of the pseudoaneurysm with a "to and fro" flow pattern.

A number of therapeutic modalities have been developed to treat femoral artery pseudoaneurysms. Although open surgical repair is still considered the gold standard, less invasive treatment strategies, including ultrasound-guided probe compression, ultrasound-guided thrombin injection, and insertion of covered stents, are available[2]. However, each modality has its own advantages and disadvantages.

My approach is to destroy the neck of the pseudoaneurysm using a guidewire, and then briefly compress the arterial access site. The neck of the pseudoaneurysm is the narrow track of blood flow between the femoral artery and the pseudoaneurysm sac. Once the fistula track is mature, it is hard to close the track by mechanical compression only. I propose the following treatment. The pseudoaneurysm sac should be punctured before the next enoxaparin dose, and a 5 Fr femoral sheath should be inserted into the pseudoaneurysm sac. An angiogram via a femoral sheath should be obtained to visualise the femoral artery, neck, and pseudoaneurysm. Under fluoroscopic guidance, the pseudoaneurysm neck should be mechanically destroyed and disconnected from the feeding femoral artery using the guidewire via the femoral sheath. Once the pseudoaneurysm neck is destroyed, the bleeding usually stops immediately with clotting of blood within the pseudoaneurysm sac. Brief manual compression of the puncture site is often needed to complete haemostasis. The remaining haematoma will be absorbed over several weeks. Before this procedure, I usually wait five to seven days for maturation of the pseudoaneurysm sac. If the procedure is performed too early, it is technically difficult to puncture into a poorly encapsulated pseudoaneurysm. In addition, considering the high risk of bleeding complications, clopidogrel plus warfarin will be used until deep vein thrombosis resolves.

In summary, a femoral artery pseudoaneurysm is not a rare complication after VCD failure. Mechanical destruction of the pseudoaneurysm neck, followed by brief compression of the arterial access site, is a simple and effective method to treat this troublesome complication.

## Conflict of interest statement

The author has no conflicts of interest to declare.

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# How would I treat?

## THE INVITED EXPERTS' OPINION

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This is a troublesome case that requires treatment for both thrombosis and active bleeding. The main discussion points in treating this troublesome case consist of the following three issues: a) medication therapy, the necessity of dual antiplatelet therapy (DAPT) post implantation of a drug-eluting stent (DES) and anticoagulant therapy for deep vein thrombosis (DVT); b) how to repair an expanding right groin haematoma; and c) the pros and cons of invasive intervention for DVT.

In general, DAPT should be continued for at least 12 months after PCI to prevent stent thrombosis (ST)[3]. However, the effect of discontinuing DAPT within one month after DES implantation for acute coronary syndrome is unknown. In this particular case, although right groin haematoma with active arterial bleeding has expanded, the most critical issue should be to avoid ST, and treatment for the pseudoaneurysm should be considered subsequently. DVT would be less important for this patient as long as severe pulmonary embolism has not occurred.

We would therefore continue DAPT and stop anticoagulant therapy immediately after inferior vena cava (IVC) filter implantation to prevent pulmonary embolism in the first instance.

The next step would be to consider how to repair the right groin haematoma. The puncture hole of the right common femoral artery (CFA) must have caused the haematoma. Therefore, to occlude the bleeding point will lead to recovery of the pseudoaneurysm.

Since manual haemostasis and a compression band were not successful, but rather caused the DVT, additional, invasive treatment for the pseudoaneurysm should be conducted. We would try ultrasound-guided thrombin injection into the pseudoaneurysm first. This therapy has been developed as a less invasive and highly successful treatment for a femoral pseudoaneurysm and was originally reported by Liau in 1997[4]; however, this therapy has the risk of thrombin contamination to the artery[5]. Therefore, we would perform thrombin injection with balloon occlusion for the right CFA (which was approached by the contralateral CFA) to prevent thrombin contamination to the right CFA. If complete occlusion with thrombi of the pseudoaneurysm is not achieved, surgical repair would be required. Even if surgical treatment were to be performed, we do not recommend stopping antiplatelet therapy during the perioperative period.

After repair of the pseudoaneurysm, we would start anticoagulation therapy for DVT and implant an IVC filter. We would stop aspirin (that is, single antiplatelet therapy with clopidogrel alone), based on the results of the WOEST trial which showed increasing bleeding events in DAPT and anticoagulant therapy compared to single antiplatelet therapy (clopidgrel) with an anticoagulant[6]. A month later, if contrast computed tomography shows complete disappearance of the DVT, we would actively retrieve the IVC filter and change anticoagulant therapy to DAPT.

## Conflict of interest statement

The authors have no conflicts of interest to declare.

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# How did I treat?

## ACTUAL TREATMENT AND MANAGEMENT OF THE CASE

As the haemorrhage site was deemed compressible, the patient had manual compression with a C-clamp and haemostasis was achieved. Enoxaparin and warfarin were stopped but dual antiplatelet therapy was continued. A repeat CT angiogram the next day showed resolution of bleeding with a stable haematoma. A vascular surgeon was consulted and the patient was started on intravenous heparin for the DVT. This was subsequently bridged to subcutaneous enoxaparin with re-initiation of warfarin one day later. The patient was subsequently discharged well 18 days after admission with plans for dual antiplatelet therapy for one year with concomitant warfarin for three months.

Dual antiplatelet therapy (DAPT) with aspirin and a $P2Y_{12}$ inhibitor is the therapy recommended by both the American Heart Association and the European Society of Cardiology to reduce stent thrombosis post PCI. Premature discontinuation of therapy has been associated with an increased risk of stent thrombosis[7]. However, this is not adequate for the treatment of venous thromboembolism. Oral anticoagulation therapy with a Vitamin K antagonist, such as warfarin, is indicated for the treatment of venous thromboembolism[8]. It is believed that the different mechanisms behind the thrombosis process necessitate treatment via different inhibitory pathways to achieve the desired antithrombotic effect.

In recent years, triple antithrombotic therapy (TAT) with both DAPT and an oral anticoagulant has been used increasingly for patients with atrial fibrillation (AF)/venous thromboembolism post PCI. However, a meta-analysis by Andrade et al[9] evaluating the risk of bleeding while on triple antithrombotic therapy post PCI showed that triple antithrombotic therapy (which was commonly indicated for AF and prosthetic heart valves) is associated with a significant risk of major bleeding events with an odds ratio of more than two at both 30 days and six months post PCI compared to DAPT alone. Some guidance was provided by the European Society of Cardiology in 2010[10] and the American College of Chest Physicians in 2012[8] for patients with atrial fibrillation who require triple therapy. Both recommend triple antithrombotic therapy post PCI for AF depending on the stent placed – one month for a bare metal stent, and three to six months for a drug-eluting stent. This is followed by a single antiplatelet agent with warfarin up to one year, with lifelong warfarin thereafter. Unfortunately, these guidelines were largely based on limited evidence from small, single-centre and retrospectively analysed cohorts, with most of the data available being for triple antithrombotic therapy post PCI in patients with concurrent AF.

More recent studies may shed new light on possible therapies. In an open-label, randomised controlled trial by the WOEST study group[6] in 2013 of patients on oral anticoagulant therapy, the use of clopidogrel with oral anticoagulant therapy (dual therapy) was compared with TAT in patients undergoing PCI. The use of dual therapy was associated with a significant reduction in bleeding complications (hazard ratio [HR] 0.36, 95% confidence interval [CI] 0.26 to 0.5) as compared with TAT. Further analysis of the severity of the bleeding episodes (using surrogates of number of bleeding events, need for transfusions and bleeding classifications) also suggested that those in the dual therapy group had less severe episodes compared to those in the TAT group. The use of dual therapy was not associated with an increased incidence of secondary endpoint markers that included death, myocardial infarction and stent thrombosis (although the study was not powered to detect the differences in occurrences). Barring the limitations of the study, the data would suggest that the use of clopidogrel with an oral anticoagulant alone would be a safe option for patients who require an oral anticoagulant and who have undergone PCI. The latest findings of the ISAR-TRIPLE trial, which was recently presented at the Transcatheter Cardiovascular Therapeutics scientific symposium 2014 (TCT 2014) in September 2014, also suggest that prolonged TAT may not be as necessary as was previously thought. In the open-label, randomised controlled trial, patients who had drug-eluting stents implanted were randomised into two groups, with one group started on six weeks of clopidogrel, and the other group six months of clopidogrel together with aspirin and an oral anticoagulant. A variety of primary endpoints (including death, stent thrombosis and TIMI major bleeding) and secondary endpoints (including the composite ischaemic endpoint and bleeding complications) was assessed. The group on the shortened duration of TAT did not demonstrate a significant difference in the primary or secondary endpoints compared to the group on the longer duration of TAT. The findings would suggest that physicians need to consider carefully the ischaemic and bleeding risks when choosing a longer or shorter duration of TAT.

Moreover, there is limited knowledge with regard to the use of newer $P2Y_{12}$ inhibitors, such as prasugrel or ticagrelor, as a component of triple antithrombotic therapy, although a recently published observational study by Sarafoff et al[11] seems to suggest a higher incidence of TIMI bleeding incidents when prasugrel is used instead of clopidogrel as part of triple antithrombotic therapy.

Bleeding is a common non-cardiac complication post PCI. Risk factors for bleeding include increased age, female gender and renal impairment[7,12]. Various scores[12] have been proposed for predicting bleeding post PCI but none has been prospectively validated as yet. When bleeding occurs post PCI, it is often difficult to manage because such patients are often on dual antiplatelet agents after stent placement. Interestingly, data extrapolated from the GRACE registry suggest that patients who had major bleeding episodes (defined as life-threatening bleeding requiring ≥2 U of packed red blood cells, resulting in a decrease in haematocrit of ≥10%, occurring intracerebrally, or resulting in stroke or death) had higher mortality rates if aspirin or $P2Y_{12}$ inhibitors were stopped compared to those whose DAPT was continued[13]. This suggests that one should persist with DAPT while managing bleeding complications to avoid preventable mortality.

It is unfortunate that our patient developed both a DVT and an arterial bleeding event after PCI. When treating both events concurrently, it is important to consider the severity of the bleeding, the extent of the venous thromboembolism and the nature of the PCI performed. These factors will help guide the therapy choices, which include local haemostatic control, the subsequent use of suitable antiplatelet and antithrombotic therapy, as well as the duration of therapy.

## Conflict of interest statement

The authors have no conflicts of interest to declare.

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