

Pseudoaneurysms: When and How to Treat Them

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Abstract

Pseudoaneurysms are vascular complications increasingly common at a time when the Interventionist Medicine progresses and shows a significant increase of its procedures, whether diagnostic or therapeutic. This review seeks to define this condition appropriately, showing its complications, discussing the various forms of diagnosis (Clinical, US, CT, MRI and Angiography), as well as the various types of treatment proposed (Expectant, Surgical, by Compression, Endovascular, with Injections of Thrombin and Salina); this article, reviewing the various types of treatment, assesses their indications, contraindications and complications, emphasizing the percutaneous treatment with thrombin injection.

Keywords: Aneurysm False/therapy; Aneurysm False/ ultrassonography; Thrombin/administration & dosage; Vascular Diseases/ complications.

Introduction

The increasing progress of interventional medicine caused an increase in the number of post-procedural vascular complications, either diagnostic or therapeutic. Thus, the occurrence of complications after punctures, either arterial or venous, is described with an incidence of 0.7% to 9%¹ with a close relationship not only with the types of procedures performed (increasingly more complex, time consuming, and using larger catheters and introducers), but also with the use of drugs that the patient may be taking (anticoagulants, antiplatelet drugs, glycoprotein Ilb/IIIa inhibitors, etc.), with the patient's biotype (obese patient show more technical difficult in compressing the puncture site), and human error. (Compression performed erroneously or briefly), as shown in Figure 1).

A special thanks to my wife Cristina, for your understanding and cooperation, to me as necessary. A special thanks also to Dr. Nicos Labropoulos, Master of Studies and Vascular Procedures with whom I learned a lot.

The following are pos-procedural vascular complications:

- Bruising
- Pseudoaneurysms (PA)
- Arteriovenous fistulas
- Hemorrhage

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Received on: 15/01/2013; accepted on: 06/06/2013

- Arterial thrombosis
- Dissection
- Ipsilateral nervous or venous compression

Among the vascular complications, except for bruises, which are quite common and most often of little clinical significance, the pseudoaneurysm is the most frequent, accounting for up to 1.5% after angiography and up to 6% after therapeutic procedures¹, followed by arteriovenous fistula, hemorrhage, thrombosis, dissection, neurovascular compression, skin ischemia, among other.

Vascular complications are responsible for increased morbidity, mortality, and duration of hospitalization, with subsequent increased costs. A meta-analysis of the study CAVET I^2 , indicated a complication rate of 6.6%, and of these, 21% required surgical repair.

Pseudoaneurysms can be defined as a pulsatile hematoma that communicates with an artery through an orifice in the arterial wall. This way, a neck is formed that connects the artery to one or more cavities (whose walls are formed by the tissue surrounding the artery), allowing systolic flow towards the cavity and diastolic flow toward the artery (Scheme 1), unlike true aneurysm, whose walls consist of the vessel walls itself³.

The etiologies of PA are:

• Post-procedural (by far the most common)

• Postoperatively of vascular surgery (mainly grafts and arteriovenous fistulas surgery)

Infectious

• Traumatic⁴ (Accidents, injuries from firearm or knife), being less frequent.



Figure 1 - A: Obese patient, post-procedure; B: Manual compression.

The most common location is related to the femoral artery, followed by brachial, radial (the incidence is increasing, since this access route has been widely used), subclavian, and other arteries⁵ (Figures 2, 3, 4, 5, 6 and 7).

Measures are useful in evaluating the pseudoaneurysm (Scheme 2):

- Number of cavities
- Cavity dimensions (anteroposterior and laterolateral)
- Neck dimensions (length and width)

• Distance from the skin to the pseudoaneurysm (vertical and oblique)

Diagnosis

The diagnosis of such entity can be performed by means of:

- Clinic
- Angiography
- CT
- MRI
- Color Doppler Echocardiography

Clinical assessment begins with ectoscopy when, in most cases, we note the presence of a bruising at the suspected site; by palpation we can detect the presence of a fremitus, and by auscultation we identify a systodiastolic murmur (to and from)³ at the site of the pseudoaneurysm.

However, it is necessary to use an imaging method not only to confirm the diagnosis, as well as to evaluate the characteristics of the pseudoaneurysm (one or more cavities, their dimensions, presence of thrombi or septa inside it), to identify the artery connected to it, if there is compression of other vascular structure, and to study the arterial tree of the entire member. Angiography (Figure 8) allows confirming the presence of the pseudoaneurysm, evaluating their characteristics, and not only the artery related to it, but the whole arterial tree distal to the pseudoaneurysm. However, it is an invasive method (involves new puncture) and employs potentially nephrotoxic contrast (in a population whose age has a high incidence of atherosclerotic disease, diabetes mellitus, and hypertension, which may be associated with some degree of renal dysfunction); in addition, it has a high cost and cannot be performed at the bedside, being limited and failing to demonstrate the compression of venous vascular structures (new venous puncture would be required to perform phlebography).

MRI (Figure 9) is a noninvasive method that has good accuracy and uses non-nephrotoxic contrast (gadolinium), but it is costly, cannot be performed at the bedside, is not available in every hospital, being of difficult reproducibility, both for following-up its evolution or follow-up after treatment, and may be reserved for studying PAs with more difficult access sites^{6,7}.

Computed tomography (Figure 10) is a test of good accuracy, but also uses nephrotoxic contrast agents, cannot be performed at the bedside, costly, not available in every hospital, has difficult reproducibility, thus, as MRI, may be restricted to specific groups^{7,8}.

The Color Doppler Echocardiography (CDE), as shown in Figures 11, 12 and 13, is undoubtedly the ideal method for the diagnosis of PA, not only in the evaluation of their features, but also of its course; it has low cost, can be performed at bedside, does not use contrast, presents no restriction to reproducibility, has excellent accuracy for both diagnosis and identification and evaluation of complications related to it, and is useful in the study of the distal arterial tree and surrounding vascular structures.



Scheme 1 - Pseudoaneurysm of the superficial femoral artery close to the bifurcation.

Pseudoaneurysms may have complications such as:

- Thromboembolism (more frequent)^{9,10}
- Rupture³
- Neurovascular compression³
- Infection¹¹
- Anemia¹²
- Death

Thromboembolism, and anemia are the most common complications; rupture, which may occur spontaneously or



Figure 2 - Pseudoaneurysm of the superficial femoral artery.

during occlusion attempt by compression maneuver, especially in non-compressible Pas, or compressible only under great force,



Figure 3 - Pseudoaneurysm of the brachial artery.



Figure 4 - Pseudoaneurysm of the radial artery.



Figure 5 - Pseudoaneurysm of the ascending aorta.



Figure 6 - Pseudoaneurysm of the common femoral artery.



Figure 7 - Pseudoaneurysm of the internal carotid artery.







Figure 8 - Pseudoaneurysm of the popliteal artery.

In our experience, we diagnose a large pseudoaneurysm which ruptured after attempted compression, being referred for emergency surgery (Figures 14 and 15); another patient with a bulky pseudoaneurysm of the femoral artery (post-procedure) showed spontaneous rupture, followed by hypovolemic shock and death, with no time for any intervention.

The infection is usually associated with bruises, which serve as a culture medium for opportunistic germs, and can rapidly progress to sepsis (Figure 16).

Thus, important and serious complications as mentioned above can and should be avoided, and the best way to do it is closing early the pseudoaneurysm.

Treatment

With regard to treatment, we can mention six modalities:

- Expectant
- Surgical
 Compression Blind Guided by Ultrasonography (US)
 Saline Injection Guided by Ultrasonography (US) or Angiography
 Endovascular Coated stents Coil embolization
 Thrombin injection Guided by Angiography Guided by Ultrasonography

Expectant treatment

Several studies in the literature report that small APs (< 2 cm in diameter), tend to close through spontaneous thrombosis,^{3,13-15}. However, we cannot fail to mention that in our study, a PA with about 2.0 cm in diameter, formed

from the superficial femoral artery, caused embolism and occlusion of the popliteal artery, leading the patient to emergency surgery.

The group of Dr. Kreskowik et al.¹³ followed-up 7 patients with PAs with diameters ranging from 1.3 cm to 3.5 cm, have found that all closed spontaneously within 4 weeks without complications.

We must, however, point out that there is currently no specific report on the natural history of PAs in patients taking antiplatelet drugs or anticoagulants.

Surgical Treatment

The first proposed treatment was surgery; traditional surgery is usually effective, relatively safe (low morbidity and mortality), but it is expensive, invasive, requires a longer period of hospitalization, and may become aesthetically unpleasant (Figure 17), being currently reserved for cases where PA presents rupture, compression of adjacent neurovascular structures, skin ischemia, patients with severe pain, and rapid growth.

Regarding the surgical technique, the surgeon often prefers to enter directly into the cavity of the PA and repairs the artery, always with digital angiographic control. Some believe that acute blood loss during such action may be poorly tolerated by patients with limited cardiac supply; they prefer to obtain a blood flow control in the distal external iliac artery by means of transverse incision in the inferolateral abdominal wall, after which they proceed to repair the PA³.

Rarely, a more extensive surgery with arterial reconstruction by using grafts of prosthetic material or saphenous vein may be necessary.

The surgery can have complications, namely bleeding, infection, arterial injury, forcing the patient to hospitalization and more prolonged immobilization, which in itself predisposes not only to other complications³, but also new interventions.



Figure 9 - Pseudoaneurysm of the superficial femoral artery.



Figure 10 - Pseudoaneurysm of the brachial artery.



Figure 11 - CDE of PA of the superficial femoral artery.



Figure 12 - CDE showing PA where: A - cavity and neck; B - systodiastolic flow.



Figure 13 - Large PA with thrombi inside it.



Figures 14 and 15 - Large PA with thrombi inside it and showing rupture followed by hypovolemic shock after attempted compression 4 days after the diagnosis.



Figure 16 - Infection and abscess of pseudoaneurysm of the superficial femoral artery.



Figure 17 - Post-operatory of surgery to repair pseudoaneurysm of the right common femoral artery.

Compression treatment

For closing the pseudoaneurysm by means of compression, it is necessary that during this maneuver we are able to compress the neck of the pseudoaneurysm, preventing the artery flow into the cavity and thus, hopefully causing thrombosis in the PA.

The compression treatment has two ways of being performed. The simplest, more practical, but less effective and with a higher incidence of complications (although being the most often used) is blind, i.e., during the procedure no monitoring is performed by ultrasonography, to check if the compression really interrupted the flow to PA or the distal flows are satisfactory.

The other one, compression treatment guided by ultrasonography, is a technique that originated in the early 1990. In his pioneering study, Fellmeth et al.¹⁴ studied by ECD 39 injuries in femoral arteries (35 PAs and 14 arteriovenous fistulas)

diagnosed in a period of 6 hours to 14 days after catheterization. Contraindications to compression were identified in 10 cases of PAs (spontaneous thrombosis in 4, anatomy not suitable in 3, infection in 1, skin ischemia in 1, and excessive discomfort in 1). Of 29 PAs who underwent US guided compression, 27 were successfully obliterated (93%), with no evidence of recurrence or immediate or late complications.

Steinsapir et al.¹⁶ showed similar success in their study (90%), referring to a case of thromboembolic complication, which responded promptly to thrombolysis. In other series, similar success has been described, but reports emerged on the compression stop due to pain in the patient during the procedure and great variability in the compression time.

The compression can be performed manually or with mechanical devices such as the C-clamp; the compression time may vary, according to the study described by Fellmeth

et al.¹⁴, ranging from 10 to 120 min, and from 60 to 240 min in study by Agarwal et al.¹⁷ (Figure 18).

By this technique it is possible to view the PA, the flow inside and its interruption when we compress the neck of the pseudoaneurysm, leading to thrombosis and obliteration of the cavity, being observable the flow in the artery during the entire procedure; flow monitoring in the arterial segment distal to the PA being compressed is very important because it can avoid the occurrence of ischemia or even arterial occlusion in patients who often already exhibit marked impairment of the arterial tree (Figure 19).

The compression has a variable success rate ranging from 47% to $100\%^{18}$ in some series and from 60% to 90% in others^{19,20}

Some patients complain of severe pain and require analgesics, and in some cases even sedation; patients receiving anticoagulants require a longer compression and have a higher rate of recurrence.

Contraindications to the treatment by compression³:

• Non-compressible PA or compressible with arterial occlusion or marked reduction in distal flow

- Location above the inguinal ligament
- Presence of infection
- Venous thrombosis
- Limb or skin ischemia
- Neurovascular compression²¹
- Compartment syndrome
- Prosthetic graft.
- Complications resulting from compression treatment:

• Thromboembolism, which does not respond to anticoagulation or thrombolysis, in most cases has indication for surgical treatment.

• Deep vein thrombosis, which usually responds well to medical treatment.

• Arterial occlusion, a severe condition often requiring immediate intervention.

Thus, the US guided compression is a non-invasive, effective, and relatively safe therapeutic approach for the treatment of selected cases of PAs.

Treatment with saline injection

Percutaneous treatment of pseudoaneurysm with saline injection can be guided by US 22 or angiography, and is always associated with compression maneuver.

As previously stated, for closing the pseudoaneurysm by compression, it is necessary that during this maneuver we are able to compress the neck of PA, preventing the artery flow into the cavity and, therefore, hopefully causing thrombosis in the PA. The injection of saline is always followed by short manual compression. Thus, the injection of saline (35 to 30 ml of saline) was made very close to the neck, with the purpose of causing swelling in that region, which facilitate the neck occlusion after the compression (Scheme 3).

The authors reported a success rate in this method of 92% (59 of 64) without any complication; the 5 PAs, which could not be closed, were treated with thrombin injection²².

In our service, we had the opportunity to perform this procedure in a single patient with PA of radial artery, occurring closure without complications.

We believe that this treatment should be reserved for those APs that are located closest to the skin, which would facilitate the puncture and location of a suitable site for the injection of saline. The contraindications are the same as the compression treatment, and patients should be sedated in case of great pain during compression.

Endovascular Treatment

Endovascular treatment can be performed by placing coated stents or coil embolization (small metallic devices with thrombogenic capacity, widely used for the occlusion treatment of cerebral aneurysms).

The treatment by using stents is an alternative to occlude pseudoaneurysm, but is not suitable when the pseudoaneurysm affects the bifurcation of the common femoral artery due to occlusion risk of the deep femoral artery; in addition, the insertion of an endoprosthesis at that site contraindicates new arterial punctures in this segment, thus losing the function of vascular access route.

Thus, to access a PA originated in the femoral artery, the placement of stent involves contralateral puncture, and through aortoiliac bifurcation we reach the femoral artery in which the stent is to be positioned at the origin of the pseudoaneurysm neck (Figure 20).

We believe that this type of treatment has its main indication in complex lesions such as pseudoaneurysms associated with arteriovenous fistulas²³ or patients who have contraindications or unwilling to undergo surgical treatment.

Coil embolization can be performed in two ways: by directly accessing the cavity of the PA (percutaneously), where several coils are inserted, with thrombogenic capacity, thus leading to obliteration and subsequent thrombosis of the pseudoaneurysm.



Figure 18 - Examples of compressions. A - Manual; B and C - Devices for mechanical and mixed compression; D - guided compression performed with the US probe itself.



Figure 19 - Schematic showing compression erroneously performed where arterial occlusion occurs.

The other way is through artery catheterization and insertion of coils in the PA neck, thus determining the thrombosis not only in the neck but also in the cavity²⁴ (Figure 21). Disadvantages of this method are the persistence of flow in the pseudoaneurysm after the procedure, which may lead to pain and skin necrosis when the coils are implanted near to the skin^{25,26}.

Eventually, in special situations, it may be necessary to use a combination of both techniques in order to obtain a final solution⁴.

The following are contraindications to endovascular treatment:

• Femoral bifurcation (risk of occlusion of the deep femoral artery)



Scheme 3 - Needle positioning for injection close to the neck.



Figure 20 - Sequences of stent placement for PA treatment.



Figure 21 - Insertion of coils in the PA neck.

- Loss of future access route due to risk of stent perforation
- Infection of the skin at the segment to be punctured
- High costs (relative)
- Renal failure (relative)

Whatever the form of endovascular treatment adopted, it is always invasive, costly, time-consuming, uses potentially nephrotoxic contrast, and thus subject not only to complications inherent to the procedure itself, but also the establishment or progression of pre-existing renal failure.

Treatment with thrombin injection

Percutaneous treatment of pseudoaneurysms with thrombin injection can be guided by ultrasonography²⁷, as well as guided by angiography¹; the method using angiography can apply protection by positioning the balloon catheter (angioplasty) in the artery at the level of pseudoaneurysm neck to occlude the fistula in the arterial wall during the injection of thrombin, trying to prevent thromboembolic complications, which not always can be prevented²⁸.

The method guided by ultrasonography was first described in 1986 by Cope and Zeit²⁷ and subsequently developed and published by Liau et al.²⁹, in 1997, and Kang et al.³⁰ in 1998. It consists in puncturing the PA cavity guided by ultrasonography, where the injection of thrombin is performed (Figure 4A and B). Initial studies used bovine thrombin at large doses (about 1,000 to 1.500UI), which determined the appearance of some cases of allergic reactions (persistent hives³¹, anaphylaxis (use of bovine thrombin)³², and thromboembolism^{33,34}.

Currently low doses of thrombin are employed; almost always homologous human thrombin is used, although in the literature already exist studies with autologous thrombin³⁵ for this procedure.

The technique used by our group involves performing CDE to evaluate the characteristics of the PA and the entire arterial tree related to it; a quite extensive asepsis is performed in the segment at which the PA is located, then a sterile drape is placed; the probe is coated with a sterile transparent cover for arthroscopy; local anesthesia is performed, after which the PA is visualized and the puncture is guided for injection of thrombin (Figure 22).

Thus, the dilution solution of thrombin in the syringe is slowly injected, and in few seconds the thrombosis of the pseudoaneurysm occurs; very important is the visualization of the needle tip, since it must remain inside the cavity, but the farthest possible from the neck of the pseudoaneurysm, aiming to prevent thromboembolic phenomena (Figure 23).

Our experience at the moment, with this treatment, consists of 69 cases, 4 of external iliac arteries, 54 of common femoral arteries, 8 of superficial femoral arteries, 2 of deep femoral arteries, and only 1 of common carotid artery, all after diagnostic or interventional procedures, being noted 2 cavities in 6 and 3 cavities in 4; all taking antiplatelet drugs, 2 in use of full anticoagulation. There were changes in the anteroposterior cavity diameters from 2.0 to 4.8 cm; laterolateral from 1.3 to 5.5 cm; necks with width from 2 to 3 mm, and length from 3 to 27 mm.

Always using homologous human thrombin at a dilution of 100 IU / ml, in the first two patients were used 300 IU to 250 IU; in ten we used 100 IU, and in the last two we used only 50 IU and 25 IU. In all patients we obtained complete





Scheme 4 A - Needle positioning.

thrombosis of the PA cavity and neck, except in 4 cases, and in 1 PA with 2 cavities we used 2 injections; in others, which had 3 cavities, in 1 we closed 2 of them with 2 injections, and in another with only one injection, using on both the compression of the neck to close the 3rd cavity; in the other case, after closing two cavities, as the 3rd one was small and with a very short neck (1mm), we opted for expectant management and spontaneous closure of this last cavity occurred in 15 days.

We had one case of recurrence after 24 hours, which was promptly resolved with a 2nd injection. We did not record complications in our series.

Dr. Nicos Labropoulos in its Conference in 2002, Rio de Janeiro, outlined determining factors of good outcome³⁶:

- Age of the pseudoaneurysm
- Number of cavities
- Cavity size
- Neck dimensions
- Use of anticoagulant drug.

Thus, earlier PAs with only a cavity, of small dimensions, narrow and long neck, without taking anticoagulant drugs, would have a better prognosis for this procedure.

Several authors have published series with excellent outcomes and low complication rates^{5,17}.

Scheme 4 B - PA thrombosed after injection.

In your experience at Loyola University (Chicago-USA), Drs Steven Kang and Nicos Labropoulos, in the period from February 1996 to September 2003, treating 207 PAs, 192 of femoral arteries (most after catheterization), 7 of brachial arteries (3 post-catheterization, 2 of trauma by firearm, and 2 by removing graft of AV fistula), 3 of radial arteries (2 AV fistula and 1 installation of BPM), 2 in iliac arteries, 1 in subclavian artery (error in puncture for installing CVP monitoring), 1 in posterior tibial artery (accident) and 1 in distal superficial femoral artery (trauma), with ages ranging from 1 to 159 days, cavity diameters ranging from 1 cm to 13.5 cm, neck width and length ranging from 2 to 12mm, and 0 to 33 mm, respectively; achieved total success in 201 (97%), having as complication only 1 case of distal thrombosis of the brachial artery that resolved spontaneously (Figure 24).

Dr. Wolfgang Pfeil presented at the Congress of the European Society of Cardiology, 2002, Berlin-Germany³⁷, a sample of 175 pseudoaneurysm treated with thrombin injection, with 100% success; As complication there was one case of bleeding and 2 cases of patients taken to surgery for thrombectomy due to neurovascular compression by the thrombosed cavity of the PA. In the literature, we have found references to few thromboembolic and allergic complications^{28, 33, 34} (with the use of bovine thrombin)^{31,32}.



Figure 22 - The method used in this procedure implies skin asepsis on the segment containing the pseudoaneurysm, placement of sterile drape, covering the transducer with sterile transparent plastic, and then local anesthesia followed by visualization of the pseudoaneurysm and injection of thrombin in the cavity.

By facing a thromboembolic complication, before taking the patient to surgery we must consider the possibility of treatment by using anticoagulation, thrombolytic drug or glycoprotein IIb/IIIa inhibitor^{33,34,38}, being successful in all cases in which that was used, as reported in the literature^{33,34,38}.

Taylor et al.¹⁸, comparing the results of the two techniques (compression versus thrombin injection), found the following results (Table 1):

Contraindications to this treatment would be the same as the compression treatment, except the first two, and added with APs with very wide neck and short or absent, originating from dehiscence of graft sutures and history of anaphylaxis using preparations containing thrombin.

The complications of this method are rare but must be mentioned:

- Thromboembolism^{33,34}
- Ipsilateral neurovascular compression¹⁸

- Ipsilateral venous thrombosis¹⁸
- Allergic reactions^{31,32}

Although rare, these complications were observed most frequently, especially in the initial phase of this treatment, when using large amounts of thrombin (sometimes up to 1500 IU), when it was not possible to adequately visualize the position of the needle tip, or even when risking treating PAs with very short necks.

With respect to treatment of possible thromboembolic complications, we must proceed in the same way as those resulting from compression treatment, assessing the possibility of thrombolysis or anticoagulation before referring the patient to surgery.

Ipsilateral venous thrombosis occurs when the PA is compressing the vein and the thrombosis of the PA determines a compression maintained on that vessel, determining venous stasis followed by thrombosis.



Figure 23 - Long-neck PA; view of the needle tip in the PA cavity; Long-neck pseudoaneurysm (A) already thrombosed (arrow B) and an artery below with normal flow in color (C).

Anaphylactic reactions occurred when using bovine thrombin, due to its high immunogenic power, there are reports of cases in the literature describing immunogenic complications, including the development of asthma and even laryngeal edema; another consequence of exposure to bovine thrombin is the potential development of antibodies to human coagulation proteins and thrombin, in particular factor V, which might result in excessive bleeding and coagulation disorder; these complications are no longer seen with the novel human thrombin products³⁹.

The thrombin injection guided by ultrasonography is an effective treatment, which requires little time, has a high

success rate, low morbidity, low cost, does not extend the hospitalization, which makes it a great treatment option for this type of vascular complication.

Moreover, according to several authors, it is the treatment of choice for femoral artery pseudoaneurysm⁴⁰.

Acknowledgements

"I, Antonio Carlos dos Santos Nogueira, particularly thank my wife Cristina, for her necessary understanding and collaboration. I also thank Doctor NicosLabropoulos, Master of Studies and Vascular Procedures, from whom I learned a lot."



Figure 24 - Brachial artery thrombosed after injection of thrombin in pseudoaneurysm (A); Brachial artery reassessed (B).

Table 1

	Compression	Thrombin injection
Success rate	63%	93%
Time to thrombosis	37 minutes	2 seconds
Time spent in the vascular laboratory	59 minutes	16 minutes
Severe pain during treatment	3	None
Complications	None	None
Average cost / patient	\$ 636	\$ 142

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