



ELSEVIER

General Review

Perigraft Seroma after Extra-anatomic Bypass: Case Series and Review of the Literature

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Background: Extra-anatomic bypass (EAB) remains a viable alternative for lower limb revascularization if aorto-bifemoral bypass and endovascular therapy are contraindicated. Among EAB, periprosthetic seroma (PS) occurs in about 4% of cases. Diagnostic and therapeutic management, as well as standardized treatment paradigm, are still not well defined. The aim of this study is to report 5 PS cases in EAB and to review literature about similar cases.

Methods: We retrospectively reviewed EAB performed during the period 2002–2015. Among these, we described PS cases. A similar description for all cases found in the literature through research on the major international databases (PubMed, Scopus, EMBASE) was made.

Results: During the study period, 797 bypasses—528 (66.3%) anatomical and 269 (33.7%) extra-anatomical—were performed. Among the latter, 169 femoro-femoral (FF), 20 axillo-femoral (AXF), 22 axillo-bifemoral (AxBF), and 58 aortouni-iliac endoprosthesis (AUI) + FF bypasses were performed. Five cases (1.86%) of PS in EAB population were detected: 3 after AxBF and 2 after AUI + FF. Although we initially preferred percutaneous drainage, a surgical choice with graft explant and replacement were imposed by the high recurrence rate. Literature analysis identified 19 additional cases (11 after AxBF, 7 after AXF and after AUI + 1 FF).

Conclusions: Our case series and the literature confirm that the most widely used therapy is the surgical drainage with primary or secondary replacement of the graft of a different material. Percutaneous drainage has proved ineffective because not conclusive and potential to increase risk of graft infection. Careful follow-up, even years after surgery, remains necessary for diagnosis of this complication, to document the possible PS and prevent potential infection.

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INTRODUCTION

Extra-anatomic bypass (EAB) grafts, that is, axillo-femoral (AxF), axillo-bifemoral (AxBF), or femoro-femoral (FF), are excellent alternatives for

revascularization of aorto-iliac occlusive disease in high-risk patients (HRP).^{1–3} Moreover, the aortouni-iliac (AUI) repair with FF bypass is the ideal solution in case of endovascular aneurysm repair (EVAR) of an abdominal aortic aneurysm (AAA) with poor iliac axes, showing good long-term patency rates.⁴

However, they can be burdened with several complications that all bypass grafts have in common, such as thrombosis, infections, pseudoaneurysms, and so on. Among these, perigraft seroma (PS) is a peculiar complication of EAB grafts that consists in persistent sterile fluid that collects around the graft with pseudocapsules formation.

The real prevalence of PS is difficult to estimate, considering its sporadic nature and late onset. Its prevalence has been reported between 0.48% and 4.2%.^{5–8}

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Etiology and natural history of PS have not yet been clearly clarified, nor therapeutic indications. Several hypotheses have been advanced to explain the serum accumulation after vascular graft implants, including both graft- or patient-related factors, although the pathogenesis appears to be multifactorial.

Clinical presentation includes a nonpulsatile, nontender swelling along the course of the bypass. Usually, there is no discomfort at rest, but pain is sometimes caused by palpation or by coughing, particularly when PS occurs after FF bypass. Sometimes a slight erythema of the overlying skin can be observed.^{9,10} Because this collection is asymptomatic in most cases and the graft remains patent, the patient usually shows up when the PS has achieved relevant dimensions, feeling anxious and afraid about progressive growth of the mass along the graft in a subcutaneous location.

Diagnosis is primarily clinical: patient's history together with physical examination is mandatory to steer the surgeon in diagnostic and therapeutic choices. The time interval of PS development and the presence of fever or other systemic symptoms must be always investigated. Blood tests including complete blood count, coagulation, C-reactive protein, and erythrocyte sedimentation rate are required to exclude infection.

Doppler ultrasound (DUS) is the first choice instrumental investigation to evaluate graft patency and PS size. Computed tomographic angiography (CTA) should be considered only as a second-level test to assess PS extension and to exclude anastomotic pseudoaneurysms.

As for the previous issues, ideal treatment has not yet been defined and indications range from *watchful waiting* approach to complete removal of EAB graft and its substitution with a graft of different material. We present a case series of PS after AxBF bypass and AUI endograft + FF crossover bypasses, together with a literature review of similar cases, to define clinical presentation, therapeutic decision making, and outcomes of this unusual but potentially serious complication.

CASE SERIES

Case 1

A 75-year-old woman with a history of chronic obstructive pulmonary disease, hypertension, and myocardial infarction underwent polytetrafluoroethylene (PTFE) AxBF bypass graft due to an aorto-bifemoral bypass graft thrombosis, 15 months after surgery for an AAA. Duplex ultrasonography

scan (DUS), performed 8 months after EAB surgery, showed graft's patency and a 40 × 250 mm diameter capsulated PS along the EAB graft left branch. Seroma was initially drained by percutaneous puncture. Because of its rapid recurrence, 3 months later the patient underwent a left branch excision and replacement with a Dacron graft. After 17 months from replacement, no periprosthetic collections are detected by DUS. The patient has always remained asymptomatic.

Case 2

A 70-year-old woman showed an asymptomatic swelling in correspondence to Dacron AxBF bypass graft, performed 2 years before for aorto-enteric fistula (AEF) and aorto-bifemoral bypass graft infection. Blood tests showed no abnormalities. CT-scan with contrast media (CTA) revealed periprosthetic collection along the whole bypass course, more visible in the suprapubic tract, with a maximum diameter of 128 mm. At first, the patient underwent PS surgical drainage and muscular wrapping of the graft in the axillary and suprapubic region. A second surgical drainage with total PS capsule removal till the breast region was performed 15 months later because of recurrence. Capsule microscopic examination revealed mature connective tissue with congested and swollen vessels, focal extravasation bleeding, and acute inflammation. A new relapse complicated by *Staphylococcus aureus* spp. graft infection required a complete EAB graft replacement with a new PTFE graft. Twenty-two months later, no PS recurrence was observed by CDUS examination.

Case 3

Our recent publication⁵ described a 75-year-old man with a tender and pulseless suprapubic mass, painful when coughing. The patient had a history of Leriche's syndrome treated by right Dacron AxBF bypass performed 2 years earlier. A CT-scan showed the presence of a 121-mm diameter giant PS, extending from the bifurcation to the anastomosis of the receiving limb. The bypass was patent and no visible signs of periprosthetic infection were demonstrated. The patient subsequently underwent surgical drainage of the mass content, removing the capsule and the affected graft portion, with reconstruction of the contralateral bypass branch in expanded polytetrafluoroethylene (ePTFE 8 mm) graft. PS contained serous and sterile fluids. Fibrous and adipose tissue with vascular ectasia, extravasations, and chronic inflammation were found in the pseudocapsule specimen. Six months later, a DUS revealed a modest, periprosthetic,

221 asymptomatic PS recurrence. The patient has not
222 yet undergone reoperation due to comorbidities.
223

224 Case 4

225 A 70-year-old man suffering from a 6.7-cm AAA
226 underwent EVAR with left AUI stent graft (Zenith
227 Flex; Cook Medical, Bloomington, IN) and left to
228 right Dacron knitted FF crossover bypass graft.
229 Twelve months after surgery, DUS revealed a
230 57 × 31 mm right FF anastomosis PS. First, the pa-
231 tient underwent surgical drainage and muscle flap
232 coverage of the graft. A second surgical drainage
233 was performed 4 months later because of recur-
234 rences. Eight months later, an *Staphylococcus aureus*
235 spp. prosthetic infection occurred and the FF cross-
236 over bypass graft was replaced with an 8-mm
237 silver-coated Dacron graft. Intraoperative findings
238 showed a well healed left anastomoses, whereas
239 the right one appeared unstuck from surrounding
240 tissues. The DUS performed 1 year after surgery
241 showed extra-anatomic graft patency with no new
242 signs of periprosthetic collections.
243

245 Case 5

246 An 84-year old man with a clinical history of hyper-
247 tension, chronic lymphocytic leukemia, and chronic
248 occlusion of the right common iliac artery under-
249 went EVAR for an 8.25 cm AAA. A left AUI stent
250 graft (Endurant II; Medtronic, Santa Rosa, CA)
251 together with a left to right FF PTFE bypass graft
252 were performed.
253

254 Approximately 1 month after EVAR, he came
255 back to our department because of a small, painless
256 mass along the FF bypass, particularly close to the
257 left section. Conservative therapy was useless and
258 3 weeks later percutaneous aspiration was per-
259 formed, with complete recovery. DUS performed 6
260 months later revealed graft patency and mild
261 asymptomatic recurrence.
262

264 METHODS

265 We retrospectively investigated all EAB grafts per-
266 formed at our division between January 1, 2002
267 and December 31, 2015 and detected, among these,
268 all cases of PS, referring to the definition offered by
269 Blumenberg: “a collection of clear, sterile fluid,
270 confined within at nonsecretory fibrous pseudo-
271 membrane surrounding a vascular graft.”¹⁰
272

273 A review of the current literature on main inter-
274 national scientific medical databases (PubMed,
275 EMBASE, Scopus) was simultaneously conducted,
276 using as keywords the terms “perigraft seroma,”

276 “perigraft hygroma,” “extra-anatomical bypass
277 graft,” and “vascular surgery complication,” with
278 no language or time filters. We took into account
279 exclusively cases of PS following EABs (AxBF,
280 AxF, or FF). Articles describing patient and bypass
281 characteristics, first surgical procedure, diagnostic
282 process, therapeutic methods, and clinical outcomes
283 were included in the analysis.
284

286 RESULTS

287 During the study period, 797 lower limb bypasses
288 have been performed in our division. Among these,
289 528 (66.3%) anatomic and 269 (33.7%) extra-
290 anatomic (among these 169 FF, 20 AxF, 22 AxBF,
291 and 58 AUI + FF) were realized. Five PS (1.86%)
292 among EAB population (3 after AxBF and 2 after
293 AUI + FF) occurred. One case occurred after a
294 femoro-popliteal bypass was excluded from the
295 analysis. [Table 1](#) shows own case series characteris-
296 tics and outcomes.
297

298 Patients involved were 3 men and 2 women with
299 an average age of 75 ± 5 years. PS diameters at diag-
300 nosis were between 57 and 250 mm. Graft material
301 implicated was Dacron knitted in 3 cases and PTFE
302 in those remaining. The graft was patent in all
303 patients at the time of PS diagnosis.
304

305 Conservative approach with percutaneous
306 drainage was initially performed in 2 cases, while
307 surgical drainage without graft removal was chosen
308 for 3 patients. In 4 cases, because of the high recur-
309 rence rate, patients had been subjected to a subse-
310 quent invasive approach with surgical drainage
311 and affected graft substitution. The replacement
312 was performed in all cases with grafts of different
313 materials. The liquid collected was always clear
314 and sterile. Two pseudocapsules were analyzed
315 with no interesting results. Graft’s muscular
316 coverage was performed in just one case although
317 being ineffective for recurrence of PS.
318

319 Literature review showed 20 additional cases of
320 PS after extra-anatomical bypass ([Table II](#)): 15
321 men, 1 woman, and 4 cases not specified.^{9–20} Pa-
322 tients’ average age reported was 68 ± 11 years (16
323 cases analyzed). Indications for primary surgery
324 were aortic or aorto-iliac occlusion (7 cases),
325 aorto-bifemoral ABF bypass (2 cases) or AAA infec-
326 tion (1 case), and lower limb revascularization or
327 AAA correction in HRP (4 cases). In one case, the
328 procedure was performed for AEF, in another one
329 for noncomplicated AAA, and in a third case for
330 contralateral AxBF thrombosis. Seven AxFs (3 right
331 AxFs, 3 left AxFs, 1 not specified), 11 AxBFs, and 1
332 AUI endograft + FF bypass graft were described.

Table 1. Own case series

| Author, year | No. | Sex | Age | Procedure | Graft type | Maximum diameter (mm) | Time for diagnosis | Symptoms | Therapy | Outcome |
|---------------------|-----|--------|-----|--------------------------------------|------------|-----------------------|--------------------|------------|---------------------------------------------------------------------------------------|-----------------------------|
| Present cases, 2016 | 1 | Female | 75 | AxBF for ABF bypass graft thrombosis | PTFE | 40 × 250 | 8 months | Asx | Multiple drainage, then replacement with PTFE graft | No recurrence at 17 months |
| | 2 | Female | 70 | AxBF for secondary AEF | Dacron | 128 | 2 years | Asx | Surgical drainage → graft infection, then replacement with PTFE graft | No recurrence at 22 months |
| | 3 | Male | 75 | AxBF for Leriche syndrome | Dacron | 121 | 2 years | Discomfort | Surgical drainage, then replacement with ePTFE graft | Mild recurrence at 6 months |
| | 4 | Male | 70 | EVAR + FF | ePTFE | 57 × 31 | 1 year | NS | Multiple surgical drainage + subfascial packaging, then replacement with Dacron graft | No recurrence at 12 months |
| | 5 | Male | 84 | EVAR + FF | PTFE | NS | 28 days | Asx | Percutaneous drainage | Mild recurrence at 6 months |

Asx, asymptomatic; NS, not specified.

The prosthetic material used was Dacron (10 cases) or PTFE (9 cases). In one case, no information regarding graft material was specified. The time interval between graft insertion and manifestation of seroma was quite variable (median 3 months; interquartile range 2–16 months).

All studies published reported patency of the EAB at the time of PS diagnosis. The maximum diameters of PS were declared only in 3 cases. In half of the reported cases symptoms were described and most patients were asymptomatic.

Therapy was conservative in 4 cases; local compression (1 case), fibrin sealing technique (1 case), percutaneous drainage (2 cases), surgical drainage (2 cases), multiple drainages followed by graft replacement and seroma removal (7 cases), and primary surgical graft removal (2 cases). In one case, microfibrillar collagen (MFC) was injected into the seroma after multiple surgical drainage and graft replacement. The drained clear serous fluid was sterile in all cases. When the surgical option was preferred to treat PS, all patients were submitted to graft removal and replacement, with a different prosthetic material (7 cases from Dacron to ePTFE, 3 cases from ePTFE to Dacron).

The follow-up period of the analyzed studies was rather variable (from a few days up to 4 years) and there were no enlargements or recurrence, with the exception of one case where continuous percutaneous drainage was necessary to control rapid recurrence.

DISCUSSION

The real prevalence of PS is difficult to estimate and data collected from literature refer to monocentric case series or surveys and date at least 25 years ago.^{6–8} Current literature does not offer review regarding PS development after AUI and FF bypass.

In our experience, the incidence of PS after EABs was lower compared with the one reported in the literature although it remains still uncertain, for the reasons previously described.

The etiology of PS remains still unidentified. Several hypotheses have been advanced to explain the serum accumulation after vascular graft implants, including both graft- or patient-related factors, although the pathogenesis appears to be multifactorial. The most likely theories include *host versus graft* reaction,⁹ *pseudoinfection*,²¹ immunoallergic reaction,^{6,22} ultrafiltration,^{8,10} anomalous graft incorporation,^{23–26} failure of wound repair process,²⁶ fibroblast transformation⁷ with fluid exudation by *neobursa*, and intraoperative lymphatic damage.²⁷

Table II. Current literature results

| Author, year | No. | Sex | Age | Procedure | Graft type | Maximum diameter (mm) | Time for diagnosis | Symptoms | Therapy | Outcome |
|--------------------------------|-----|------|-----|--------------------------------------------------------------|------------|-----------------------|--------------------|---------------|--------------------------------------------------------------------------------------|------------------------------------------------------------------------|
| Kaupp, 1979 ⁹ | 1 | NS | NS | AxBF for AEF | Dacron | NS | 8 weeks | NS | Antibiotics irrigation and drainage, then replacement with PTFE graft | No complications at 26 months |
| | 2 | NS | NS | AxBF | Dacron | NS | 10 weeks | Mild erythema | Replacement with PTFE graft | No complications at 26 months |
| | 3 | NS | NS | AxBF | Dacron | NS | 24 weeks | Mild erythema | Replacement with PTFE graft | No complications at 26 months |
| Blumenberg, 1985 ¹⁰ | 4 | Male | 65 | AxF(R) for iliac occlusion in HRP | PTFE | NS | 8 weeks | NS | Multiple drainage, then replacement with Dacron graft | No recurrence at 38 months |
| | 5 | Male | 86 | AxF(L) for iliac and femoral occlusion | PTFE | NS | 1 month | NS | Multiple drainage | Progressive diminution at 9 months |
| | 6 | Male | 63 | AxBF for infected AAA | Dacron | NS | 3 years | Asx | None | Progressive diminution at 2 years |
| Buche, 1986 ¹¹ | 7 | Male | 65 | AxF(L) for aortic barrage after contralateral amputation | ePTFE | NS | 6 months | NS | Punctured percutaneously, then drained surgically | Rapid recurrence if not drained periodically. Graft patency at 2 years |
| | 8 | Male | 39 | AxF(L) for ABF bypass failure after contralateral amputation | ePTFE | NS | 7 months | NS | None | No seroma enlargement and graft patency at 14 months |
| | 9 | Male | 63 | AxBF for aortic occlusion | PTFE | NS | 3 months | NS | None | No seroma enlargement and graft patency at 5 months |
| Rhodes, 1986 ¹² | 10 | Male | 63 | AxBF for AAA in HRP | Dacron | NS | NS | NS | Multiple drainage, then replacement with PTFE graft. After recurrence, MFC injection | No fluid accumulation at 3 months |
| Iizima, 1991 ¹³ | 11 | Male | 70 | AxF(R) for PAD after contralateral amputation | ePTFE | NS | NS | Asx | Multiple drainage, then replacement with Dacron graft | No postoperative complication |

(Continued)

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Table II. Continued

| Author, year | No. | Sex | Age | Procedure | Graft type | Maximum diameter (mm) | Time for diagnosis | Symptoms | Therapy | Outcome |
|----------------------------------|-----|--------|-----|--------------------------------------------------------------|------------|-----------------------|--------------------|---------------|-------------------------------------------------------|---------------------------------------------|
| Inari, 2005 ¹⁴ | 12 | Male | 77 | AxBF for aortic occlusion | Dacron | NS | 2 months | NS | Multiple drainage, then replacement with ePTFE graft | No postoperative recurrence |
| | 13 | Male | 60 | AxF(R) for iliac occlusion in a patient with hostile abdomen | Dacron | NS | 9 days | Asx | None | No postoperative recurrence |
| Zanow, 2010 ¹⁵ | 14 | Male | 77 | AxBF in HRP | Dacron | NS | 26 days | NS | Local compression | NS |
| | 15 | NS | NS | AxF | ePTFE | NS | 32 months | NS | FST | No recurrence. Patient died 28 months later |
| Fukunaga, 2013 ¹⁶ | 16 | Male | 81 | AxBF for ABF graft infection | ePTFE | NS | NS | Asx | Surgical drainage | No recurrence at discharge |
| Ho, 2013 ¹⁷ | 17 | Male | 79 | AxBF for infected ABF Dacron graft | Dacron | 90 | 2 years | Discomfort | Multiple drainage, then replacement with PTFE graft | No recurrence. Patient died 4 years later |
| Romera Barba, 2015 ¹⁸ | 18 | Female | 76 | EVAR + FF | NS | 98 | 3 years | Inguinal pain | Percutaneous drainage | No recurrence at 3 years |
| Gazi, 2015 ¹⁹ | 19 | Male | 54 | AxBF for aortic thrombosis in HRP | ePTFE | NS | 7 weeks | Discomfort | AxBF explantation, then ABF Dacron bypass replacement | No recurrence at 12 months |
| Kunimoto, 2015 ²⁰ | 20 | Male | 75 | AxBF(L) for AxBF(R) thrombosis after mycotic AAA | Dacron | 90 × 130 | 8 months | NS | Multiple drainage, then replacement with PTFE graft | No recurrence at 13 months |

Asx, asymptomatic; FST, fibrin sealing technique; NS, not specified.

661 There is no consensus regarding the preferential use
662 of Dacron or PTFE to prevent PS formation.

663 Advances in prosthetic materials manufacture
664 could have contributed to reducing the occurrence
665 of PS during the years. On account of the fact that
666 PS also occurred after subfascial graft coverage, we
667 assume that graft material should be involved in
668 the process of fluid collection more than the peri-
669 prosthetic environment. Moreover, partial incorpo-
670 ration of the graft at the anastomotic site was also
671 observed in our series (cases 4 and 5).

672 Therapeutic indications are not yet well defined.
673 The treatment can be conservative, mini-invasive,
674 or surgical, although when necessary, graft replace-
675 ment is often needed.

676 Watchful waiting with DUS follow-up and
677 compressive therapy is preferred in mild and asymp-
678 tomatic PS. Zanow recommends conservative
679 approach for seromas < 2 cm in diameter, without
680 anastomotic region involvement.¹⁵

681 If invasive treatment is needed, the therapy aims
682 to remove the swollen mass, to decrease symptoms
683 associated, to minimize PS recurrence rate, and to
684 avoid bypass occlusion and/or infection. Although
685 some authors support a primary mini-invasive
686 approach with percutaneous drainage,^{9,13,14,17,18}
687 this is not recommended considering its high recur-
688 rence rates and risks of seroma and, therefore, graft
689 infection. In our series, in fact, we have performed
690 PS drainage (with DUS control) mainly to delay sur-
691 gery in HRP with larger PS.

692 When needed, graft replacement with one of
693 different material appears to be the most definitive
694 treatment and can involve a decrease in graft
695 permeability and periprosthetic reaction to foreign
696 body. There is no difference in Dacron to ePTFE
697 replacement or vice versa. Pseudocapsule's removal
698 and surgical drainage alone should be avoided, since
699 not curative and causing a high rate of infection.¹⁰
700 Replacement with homograft²⁸ or native vein,²⁹
701 saphenous vein wrapping,³⁰ interposition of covered
702 stents,³¹ and MFC injection into the periprosthetic
703 space¹² are alternative therapies tested in a very
704 limited number of cases. Plasmapheresis²⁴ and intra-
705 venous fibrinogen administration³² were performed
706 to wash out hypothetical serum factors regarded as
707 likely to modify the normal graft permeability.

708 A fundamental issue in PS management is patient
709 counseling. It is extremely important to reassure
710 these patients on the kindness of such complication.
711 Even so, these patients often appear very apprehen-
712 sive and continuously requesting explanations on
713 the nature of the growing mass, particularly when
714 a complicated past medical history exists.

Treatment decision-making process should always
take into account important issues such as PS dimen-
sion and growth rate, symptomatology, and patient's
condition. Due to the lack of dimensions' data in the
literature, absolute treatment recommendations
remain aleatory and thereby therapy is often
patient-tailored. Our cases have larger diameters if
compared with those reported in the literature. There-
fore, we assume that the greater the size of PS, the
greater is the indication for surgical replacement ther-
apy, although there are no specific cutoff values. A
complete removal of the pseudocapsule together
with graft material replacement of the affected portion
is mandatory. Histopathological analysis of perigraft
fluid, pseudocapsule, and explanted graft specimen
may be avoided if no signs of infection are detected.

CONCLUSION

PS is a rare complication that can occur even after
several years from graft placement. Triggering factors
are not yet clarified, although graft-related and
patient-related elements may play a role in peripro-
sthetic fluid's accumulation. Several therapeutic op-
tions have been proposed, but none have reached
satisfactory results in a sufficient number of cases.
In our experience, both conservative treatment and
percutaneous/surgical drainage proved to be futile,
due to a higher risk of prosthesis infection and PS
recurrence. Graft removal and replacement with
another material had the best results, although not
yet optimal. Anyways, very few and selected patients
beneficiate from surgery which, on the basis of our
experience, is worthy only in case of greater swelling
and/or growing masses with reported inability to
walk, discomfort, or pain. Regarding EABs, we
recommend a long-term follow-up after surgery, to
assess graft patency and any periprosthetic fluid
collection worthy of further investigation.

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