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**Pubic osteomyelitis: epidemiology and factors associated with treatment failure**  
**Ostéomyélites pubiennes : épidémiologie et facteurs associés au risque d'échec de traitement**

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**Mots clés :** infections ostéoarticulaires, pubis, échec des antibiotiques

## **Abstract**

**Objective.** To describe the epidemiology of pubic osteomyelitis (PO) and to look for factors associated with treatment failure.

**Method.** Retrospective study describing PO according to outcome: success or failure of initial management. Factors associated with failure determined by univariate Cox analysis. Kaplan-Meier curve compared between groups by log-rank test.

**Results.** 25 patients were included over a 13-year period; 24% of PO had blood-borne infection. Failure (44%) was always observed in chronic postoperative presentations (76%). Fistula (32%) was only observed in postoperative presentations and was significantly associated with failure (HR 5.1;  $p=0.011$ ). Other risk factors were pelvic malignant tumor history, abscess, infection due to extended-spectrum beta-lactamase-producing Enterobacteriaceae, and polymicrobial infection.

**Conclusion.** PO is most often a chronic postoperative polymicrobial infection in patients with comorbidities at high risk of relapse. Studies in larger cohorts could assess the efficacy of more aggressive surgical strategies in patients at high risk of failure.

## Résumé

**Objectif.** Décrire l'épidémiologie des ostéomyélites pubiennes (PO) et rechercher les facteurs de risque d'échec de prise en charge.

**Matériel et méthode.** Étude rétrospective décrivant les PO et facteurs d'échec de traitement, déterminés par analyse de Cox univariée. Courbes de Kaplan-Meier comparées entre les groupes par test du log-rank.

**Résultats.** Parmi les 25 PO décrites (sur 13 ans), 24 % étaient d'origine hématogène. Tous les échecs (44 %) étaient des formes chroniques post-opératoires (76 %). La présence d'une fistule clinique (32 %), observée uniquement dans les formes post-opératoires, était significativement associée à l'échec (HR 5,1;  $p=0,011$ ). Les autres facteurs de risque potentiellement associés à l'échec étaient néoplasie pelvienne, abcès, infection à entérobactérie productrice de bêta-lactamases à spectre étendu et infection polymicrobienne.

**Conclusion.** Les PO sont majoritairement chroniques, post-opératoires, polymicrobiennes, survenant chez des patients comorbides, à risque de rechute. Des études sur de plus larges cohortes permettraient d'évaluer l'efficacité de stratégies chirurgicales d'emblée plus agressives chez les patients à haut risque d'échec.

## **INTRODUCTION**

Pubic osteomyelitis is a poorly reported bone and joint infection (BJI) compared with other localizations such as the knee, hip, or tibia. It is a rare infection and the outcome varies depending on the etiological mechanism [1]. Little data is available in the literature on pubic osteomyelitis, with a predominance of case reports [1,3,4]. Intensive management is required, especially for postoperative presentations in patients who may present with comorbidities and frailty. The risk of treatment failure is therefore significant [2,3]. We aimed to describe the various clinical presentations of pubic osteomyelitis and their medico-surgical management, and to identify risk factors potentially associated with treatment failure to target at-risk patients who could benefit from the most aggressive management strategies.

## **MATERIAL AND METHODS**

We report the results of a series of 25 cases of pubic osteomyelitis managed at the interregional reference centers for complex BJIs (French acronym CRIOAc). We performed a retrospective cohort study between 2003 and 2016 in the CRIOAc of Lyon and Lille-Tourcoing, and included patients managed for pubic osteomyelitis. Patients were either identified retrospectively using the French hospital discharge database (French acronym PMSI), or prospectively when discussing their files at multidisciplinary meetings. Clinical, microbiological, and radiological data was retrospectively collected from the patients' files. Patients aged below 16 years and patients presenting with ischiopubic osteomyelitis on ischial bedsores were excluded. Pubic osteomyelitis was defined by:

- the presence of a clinical or radiological fistula communicating with the pubis, and/or;
- symptoms associated with compatible radiological signs (pus near the pubis, bone erosions, osteolysis, parasymphysis fracture), and/or;
- inflammatory signs at histopathological examination of samples collected during the procedure, and/or;
- a positive culture result of a reliable microbiological sample (microbiological documentation was considered reliable when blood cultures, abscess or synovial fluid aspiration, or radiologically or surgically guided bone biopsy were performed).

Patients were divided into two groups depending on their results: initial treatment success or failure. Treatment failure was defined by:

- the persistence of clinical signs despite treatment,
- clinical relapse with persistence of the same microorganisms despite treatment,
- infection recurrence with one or various microorganisms,
- new signs of infection (abscess, fistula) with the same localization, and with no microbiological documentation possible.

All analyses were performed using the SPSS software. Results are expressed as numbers (percentages) for dichotomous variables and as median (interquartile range [IQR]) for continuous variables. The number of missing data was excluded from the denominator when calculating each percentage. Factors associated with initial surgical treatment failure were determined by univariate Cox analysis (hazard ratio [HR] and 95% confidence interval). A *p* value <0.05 was considered statistically significant. Kaplan-Meier curves were compared between groups using the log-rank test.

## RESULTS

A total of 25 patients were included over 13 years (2003-2016). The mean age was 58.8 years (median age: 67 years). Nineteen patients were males (76%). The mean ASA score was 2.36 (median ASA score: 3). Fifteen patients had a history of pelvic neoplasia (60%), 12 had received radiotherapy at the infection site (48%), and 19 (76%) had already underwent surgery at a contact localization with the pubis within the months or years preceding pubic osteomyelitis onset (1 month to 11 years). A minority of patients (16%, *n*=4) presented with orthopedic material-related infection. Other frequent comorbidities included undernourishment for 14 patients (56%), obesity for 13 patients (52%), history of cardiac disease for 12 patients (48%), diabetes for eight patients (32%), severe immunosuppression for six patients (24%), chronic renal failure for four patients (16%), or history of intravenous drug use for one patient (4%). Three patients (12%) were engaged in an intensive sporting activity. The main characteristics of patients are detailed in Table I.

Fever was reported in 11 patients (44%). Fever was not more frequently reported in blood-borne acute presentations (4/11 cases, 36%). The main clinical signs and symptoms were pain and functional impairment (23 patients, i.e. 92% of cases), altered general status (14 patients, i.e. 56% of cases), and gait disorders (14 patients, i.e. 56% of cases). Cutaneous fistulas (Figure 1) were observed in eight patients (32% of cases), but only in postoperative presentations

(Table II). Biological inflammatory syndromes were observed in most cases (21 patients, 84% of cases), but hyperleukocytosis was not always observed (eight patients, 32% of cases). The main clinical and biological signs observed at diagnosis are detailed in Figure 2.

All patients underwent standard radiography. CT scan findings contributed to confirming the diagnosis in 100% of cases, with the presence of radiological fistula in 16 cases (64%) and pus in 21 cases (84%). The CT scan contributed to the radioguided aspiration of pus in 6/21 cases (29%). One patient underwent bone scintigraphy with results confirmed by MRI. MRIs were performed to monitor the outcome of 17 patients (68%). The microbiological diagnosis was considered reliable in 88% of cases, confirmed by blood cultures in six cases (24%) – all positive for *Staphylococcus aureus* – or by abscess aspiration in four cases (16%). Surgical bone biopsies were required for microbiological documentation in 12 cases (48%). Documentation was based on data from the cytobacteriological examination of urine (two patients, i.e. 8% of cases) or from fistula sample data (one patient, i.e. 4% of cases). Documentation was monomicrobial in eight cases (32%), including 100% of the blood-borne acute presentations (six cases) and 8% of the chronic presentations. Documentation was polymicrobial in 68% of cases, including 32% with bacteria associated with several types of antibiotic resistance. Six of the 25 patients included (24%) presented with a blood-borne acute presentation of pubic osteomyelitis, 19 (76%) with a postoperative chronic presentation including four (16%) detected after an acutization episode. The initial treatment of 13 patients (52%) included surgery. Six of the patients who did not undergo surgery had a blood-borne presentation and six other had a postoperative chronic presentation. Fourteen treatment successes (56%) were reported after initial management. All patients experiencing treatment failure were presenting with a postoperative chronic presentation. Among the 11 patients experiencing treatment failure (44% of cases), two patients (18%) had been treated with antibiotic therapy alone and nine patients (82%) with a medico-surgical strategy. The minimum antibiotic treatment duration was six weeks. Sixteen patients experienced an adverse event (no severe adverse event) due to the antibiotic therapy, including six requiring antibiotic change. Five patients (20%) received a suppressive antibiotic therapy, without duration limitation.

Among the 11 patients experiencing treatment failure, results of the univariate Cox analysis identified factors potentially associated with a risk of treatment failure (Table II): pelvic

neoplasia (HR 3.791;  $p=0.089$ ), clinical fistula (HR 5.066;  $p=0.011$ ), and polymicrobial infection (HR 70.503;  $p=0.090$ ).

## **DISCUSSION**

No recommendation is available for the management of pubic osteomyelitis because this type of osteomyelitis is rare. Literature data is currently limited. The incidence of pubic osteomyelitis is hard to measure, especially as the various nosological definitions are rather vague in the literature. One of the difficulties we faced with this literature review was to differentiate infectious pubic disorders from inflammatory disorders wrongly termed “osteitis pubis” in some of the articles where the distinction was unclear. The distinction relies on the microbiological and histopathological analysis of samples. Clinical signs and symptoms are similar to those of pubic osteomyelitis although with negative infectious results; cautious documentation is therefore required [4]. Our study reveals that the management of these infections is often complex, and that outcome is often influenced by the causative etiological mechanism. The two main etiologies observed in our study highlight (i) a blood-borne mechanism, responsible for secondary septic localization during bacteremia, or (ii) the direct inoculation of bone at the time of surgery. The diagnosis of pubic osteomyelitis is also hard to establish and is often delayed because most symptoms are non-specific. Fever was only observed in 44% of cases in our study (11 patients) and is not a discriminatory symptom. It was not more frequent in patients presenting with blood-borne acute presentations. Clinical signs and symptoms were pain, functional impairment (92% of cases, 23 patients), and gait disorders (14 patients, 56%) as described in the literature [5]. The physical examination often reveals pain at symphysis pressure and at hip mobilization. The presence of a skin fistula, which is almost pathognomonic of osteomyelitis, indicates the infectious origin. Skin fistulas were observed in 32% of our patients ( $n=8$ ), only in postoperative presentations, and significantly associated with treatment failure (HR 5.066;  $p=0.011$ ). A biological inflammatory syndrome is observed in most patients as reported in our study, but hyperleukocytosis is not always observed (eight patients in our study, i.e. 32% of cases). Hyperleukocytosis was reported in 35% of cases in the study by Ross et Hu [5]. The diagnosis is suspected based on clinical and biological signs and symptoms, but it is confirmed by morphological examinations. Conventional radiography remains important although modifications occur with a delay of

two to four weeks after onset of clinical symptoms. Standard imaging techniques look for irregular joint surfaces, widening of the articular joint space, and osteolytic findings. Technetium-99m bone scintigraphy contributes to early diagnosis, but this examination is being replaced by MRI. The MRI indeed tends to be the reference examination as it contributes to a comprehensive and early lesion assessment. CT scans may be easier to access and contribute to lesion assessment, to identifying sequestrum or abscesses, and to guiding sample collection (Figure 3F). As for all osteomyelitis cases, the origin of the infection must be precisely determined to achieve treatment success. The portal of entry must therefore be determined, and reliable microbiological documentation should be obtained. Reliable documentation of bone infection can only be obtained with the following procedures: blood cultures, analysis of synovial fluid by aspiration, or culture of bone biopsies collected in aseptic conditions. The causative agent is mainly isolated from blood cultures for blood-borne presentations, from radioguided bone needle biopsy, or from surgery for postoperative pubic osteomyelitis. Superficial sample collection must be avoided as much as possible. Ulcer swabs or fistula samples should no longer be collected as they are not correlated with deep bone and joint sample results in more than 50% of cases. This question was debated following a study published in 2010 reporting that the positivity of two successive fistula samples positive for the same bacterium had 94% susceptibility versus surgical biopsy in 77 patients presenting with monomicrobial chronic osteomyelitis. However, this figure decreased to 79% for polymicrobial osteomyelitis [6]. This procedure therefore seems difficult to use in patients presenting with pubic osteomyelitis as 64% of the infections observed in our study were polymicrobial. Ross et Hu [5] reported a higher frequency of *S. aureus* infection among athletes (17/19 cases, i.e. 89%) and of polymicrobial infections among patients presenting with pelvic cancer (10/17 cases, i.e. 59%), similarly to our findings. Our study is interesting as it focuses on analyzing the determinants of treatment failure. One should note that some bacteriological documentations were considered as potential risk factors for treatment failure: methicillin-resistant coagulase-negative staphylococci infections (HR 8.553;  $p=0.014$ ), non-fermenting Gram-negative bacilli infections (HR 13.885;  $p=0.005$ ), ESBL-producing Enterobacteriaceae infections (HR 2.789;  $p=0.116$ ), and polymicrobial infection (HR 70.503;  $p=0.090$ ). Such findings probably reflect the consequences of a limited antibiotic choice for the treatment of these infections.

This work highlights the importance of a multidisciplinary approach for the treatment of pubic osteomyelitis. Patients frequently undergo surgery (52% of cases in our study, n=13) and also receive prolonged antibiotic treatment that may be complex. Surgical indications are still poorly defined, and the type of procedures when surgery is indicated is not well defined. Literature data reveals that surgical bone curettage is indicated in patients presenting with abscesses or bone sequestrum, or experiencing antibiotic resistance [2,5]. Results from our univariate Cox analysis revealed that initial bone curettage was significantly associated with treatment failure (HR 4.192;  $p=0.04$ ), while exclusive medical treatment was a protective factor. This may be explained by most patients initially managed with curettage being frail and presenting with many comorbidities, unlike the non-surgical group of patients who presented with fewer comorbidities: 91% of surgical patients had a history of pelvic surgery including 82% for progressive neoplasia, 64% had a history of radiotherapy at the infection site, and 73% were considered undernourished, with a mean ASA score of 2.6 in this population. Results of the statistical analysis indicated that the following criteria were associated with treatment failure: presence of pelvic neoplasia (HR 3.791;  $p=0.089$ ) and a history of pelvic radiotherapy (HR 2.861;  $p=0.122$ ). Conversely, patients only receiving antibiotic therapy without surgery did not have any comorbidities and had blood-borne acute presentation of the infection for half of them, or presented with postoperative presentations but had fewer comorbidities: history of pelvic surgery in only 50% of cases, 30% of pelvic neoplasia, history of radiotherapy at the infection site in 25% of cases, and less than 50% of malnourished patients. The mean ASA score in this group was also lower (2.1).

Some factors described in the literature as risk factors for osteomyelitis (mainly material-related infection) could not be taken into account in the present study: duration of surgical procedures, recent history of bacteremia, current skin disorders, recent colonization or infection with ESBL-producing Enterobacteriaceae. This pitfall is due to the retrospective data collection, which cannot be exhaustive by nature.

We nevertheless focused on describing the various clinical presentations of pubic osteomyelitis as well as their medico-surgical management, and on identifying factors potentially associated with treatment failure. Literature data mainly focuses on risk factors for pubic osteomyelitis; our study is therefore original.

## **CONCLUSION**

Little recent data is available on the description of the various presentations of pubic osteomyelitis, their treatment, and patient outcome. Our study highlighted that among pubic osteomyelitis, there was: (i) a minority of *S. aureus* monomicrobial blood-borne acute presentations, which are mainly observed in patients without comorbidities and especially in young athletes. Those presentations do not require surgery in the absence of abscess or bone sequestrum; (ii) a majority of complex chronic postoperative presentations, which are often polymicrobial with a limited choice of antibiotics. Those presentations mainly occur in patients with comorbidities especially in those with pelvic neoplasia. Intensive antibiotic therapy is required, and patients are at high risk of relapse and must most often receive aggressive surgical management, especially those with a history of pelvic radiotherapy. When surgery can be performed, it can lead to extensive bone resections. When radical surgery cannot be performed, prolonged suppressive antibiotic therapy can be discussed. The long-term outcome of these patients is a real issue, which should be assessed in larger cohort studies evaluating the effectiveness of an initially more aggressive surgical strategy in patients at high risk of treatment failure.

## **Acknowledgment**

AB performed the data collection and literature analysis, and wrote the first draft of the article. All other authors contributed to improving the article. TF also designed the study. All authors approved the final version of the article.

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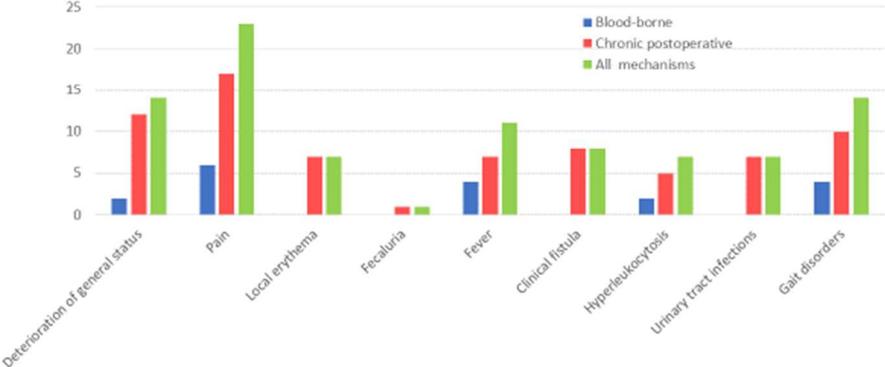
**Figure 1.** Fistule sus-pubienne peu productive chez un patient présentant une ostéomyélite polymicrobienne dans les suites d'une chirurgie urologique pour cancer de vessie.

**Figure 1.** Suprapubic fistula in a patient with polymicrobial osteomyelitis after urological surgery for bladder cancer.



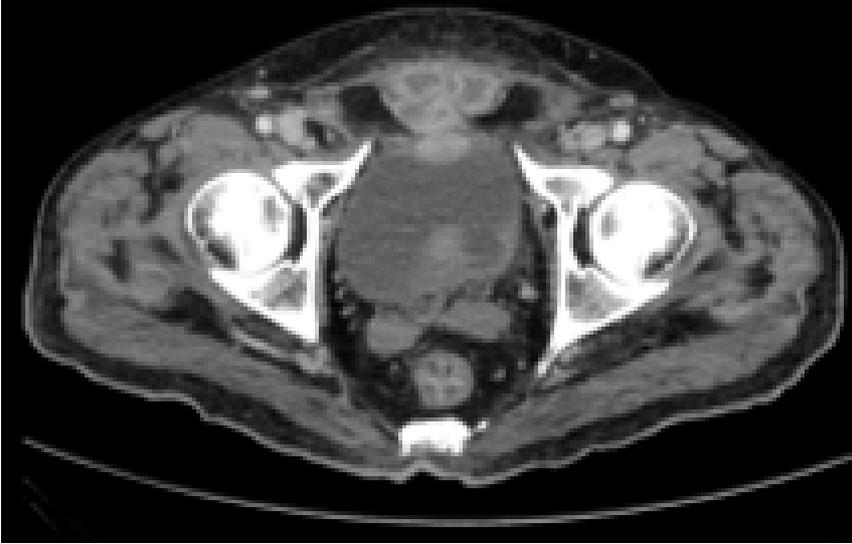
Figure 2. Signes clinico-biologiques au diagnostic selon le mécanisme étiologique

Figure 2. Clinical and biological signs at diagnosis according to the etiological mechanism



**Figure 3.** Ostéomyélite post-opératoire d'une chirurgie urologique chez un patient présentant un cancer de la vessie. Images scanner de collections multiples polylobées avec présence de gaz développées sur la face antérieure de la vessie, extension fistuleuse trans-symphysaire de l'abcès prévésical et aspect d'ostéoarthrite symphysaire étendue au périnée (Hospices Civils de Lyon)

**Figure 3.** Postoperative osteomyelitis of urological surgery in a patient presenting with bladder cancer. CT images of multi-lobed abscesses with presence of gas developed on the anterior surface of the bladder, trans-symphyseal fistulous extension of the pre-vesical abscess and appearance of perineal symphysis osteoarthritis (Hospices Civils de Lyon)



**Tableau I.** Caractéristiques des patients inclus**Table II.** Characteristics of patients

		TOTAL (n=25)
Age		67 [54-71]
ASA		3 [2-3]
Male sex		19 (76%)
<hr/>		
	Blood-borne	6 (24%)
	Postoperative	19 (76%)
<hr/>		
History		
	Cardiac disease	12 (48%)
	Undernourishment	14 (56%)
	Diabetes	8 (32%)
	Immunodeficiency	6 (24%)
	Chronic kidney disease	4 (16%)
	Obesity	13 (52%)
<hr/>		
History of pelvic disorders		
	Pelvic cancer	15 (60%)
	Pelvic surgery	19 (76%)

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Radiotherapy	12 (48%)
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ASA, American Society of Anesthesiologists

**Tableau II.** Facteurs potentiellement associés au risque d'échec thérapeutique en analyse de Cox univariée

**Table III.** Factors potentially associated with treatment failure in univariate Cox analysis

	Success (n=14)	Failure (n=11)	Total (n=25)	<i>p</i>
Pelvic neoplasia	6 (40%)	9 (60%)	15 (60%)	0.089
Clinical fistula	1 (12%)	7 (88%)	8 (32%)	0.011
Abscess	9 (45%)	11 (55%)	20 (80%)	0.343
Non-fermentative GNB ( <i>P. aeruginosa</i> , <i>S. maltophilia</i> )	0 (0%)	3 (100%)	3 (12%)	0.005
ESBL-producing Enterobacteriaceae	1 (12%)	7 (88%)	8 (32%)	0.116
Methicillin-susceptible <i>S. aureus</i>	6 (86%)	1 (14%)	7 (28%)	0.169
Methicillin-resistant CoNS	2 (33%)	4 (67%)	6 (24%)	0.014
Plurimicrobial	5 (31%)	11 (69%)	16 (64%)	0.090

ESBL, extended-spectrum beta-lactamase; CoNS, coagulase-negative staphylococci; GNB, Gram-negative bacilli.