Title

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Journal

Journal of Vascular and Interventional Radiology, 31(3)

ISSN

1051-0443

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Publication Date

2020-03-01

DOI

10.1016/j.jvir.2019.08.013

Peer reviewed

HHS Public Access

Author manuscript

J Vasc Interv Radiol. Author manuscript; available in PMC 2021 March 01.

Published in final edited form as:

J Vasc Interv Radiol. 2020 March ; 31(3): 464–472. doi:10.1016/j.jvir.2019.08.013.

Diagnostic Performance of CT-guided Bone Biopsies in Patients with Suspected Osteomyelitis of the Appendicular and Axial skeleton with a Focus on Clinical and Technical Factors Associated with Positive Microbiology Culture Results

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Abstract

Purpose—The aims of this study were (i) to assess the diagnostic performance of computed-tomography (CT)-guided percutaneous needle bone biopsy (CTNBB) in patients with suspected osteomyelitis and (ii) to analyze if certain clinical or technical factors were associated with positive microbiology results.

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Conflict of interest: none

Materials-Methods—All CTNBB performed in a single center for suspected osteomyelitis of the appendicular and axial skeleton between 2003–2018 were retrospectively reviewed. Specific inclusion criteria included clinical and radiological suspicion for osteomyelitis. The standard of reference was defined using the outcome of surgical histopathology and microbiology culture, as well as clinical and imaging follow-up. Information about technical and clinical data (needle size, comorbidities, clinical factors, laboratory values, blood cultures) was collected. Logistic regression was performed to assess associations between technical/clinical data and microbiology biopsy outcome.

Results—A total of 142 CTNBB were included (46.5% female; age [±SD] 46.10 [±22.8years]), 72 (50.7%) from the appendicular and 70 (49.3%) from the axial skeleton. CTNBB showed a sensitivity of 42.5% [95% CI 32.0%−53.6%], in isolating the causative pathogen. A higher rate of positive microbiology results was found in patients with intravenous drug use (odds ratio (OR)=5.15; 95% CI 1.2–21.0 p=0.022) and elevated WBC value ≥10×109/L (OR=3.9; 95% CI 1.62–9.53; p=0.002). Furthermore, fever (≥38C°) was another clinical factor associated with positive microbiology results: OR=3.6;95%CI 1.3–9.6; p=0.011.

Conclusion—CTNBB was found to have a low sensitivity of 42.5% for isolating the causative pathogen. The rate of positive microbiology samples was significantly higher in subjects with intravenous drug use, elevated WBC values and fever.

INTRODUCTION

The incidence of osteomyelitis in the United States has increased over the last decades, reaching a peak of 24.4 cases per 100.000 person-years between 2000 to 2009. The increased incidence seems to be related to both increase in life expectancy in elderly people and predisposing factors such as diabetes, HIV-infection, intravenous drug use and immunosuppression (1, 2). A delay in diagnosis or improper patient management can lead to dramatic complications including osteonecrosis, amputation and poor functional outcome (3). Imaging can provide information about the location, extension, and the differential diagnosis. Plain radiographs are usually the first examination yet not very sensitive (0.60; 95% CI [0.28–0.86]) (4). The lesions are usually detected in an advanced phase, as regional osteopenia, focal bony lysis and loss of bony trabecular architecture. MRI is the most sensitive and specific imaging technique (5). Computed tomography (CT)-guided percutaneous biopsy of bone lesions is a minimally invasive procedure that can establish the ultimate diagnosis of osteomyelitis by showing that the causative pathogen is growing in the culture medium (6, 7) which allows tailored antimicrobial therapy.

Despite, the potential usefulness of deep bone biopsies in confirming clinical and imaging findings in suspected osteomyelitis, the diagnostic success rate of this procedure is low. Prior studies have shown that the rate of positive microbiology cultures ranged from 20.7% (8) to 34% in cases with histopathological proven osteomyelitis (7, 9, 10). In pyogenic vertebral osteomyelitis the rate of positive microbiology samples from percutaneous biopsies varied between 14–76% (2, 11–14).

Given the previously published limitations of CT-guided percutaneous needle bone biopsy (CTNBB) with variable success rates and unclear predictors of microbiology culture positive

outcome, the aims of the study were (i) to assess the diagnostic performance of CTNBB in patients with suspected osteomyelitis and discitis and (ii) to analyze whether certain technical or clinical factors were associated with positive microbiology culture results.

MATERIAL and METHODS

Subject selection

After approval of the local Institutional Review Board, all CTNBB performed for suspected osteomyelitis and discitis between January 2003 and July 2018 using research report database tool, were retrospectively reviewed. This observational time frame was chosen in order to get a large sample size while using standardized biopsy techniques. The key words “CT” and “bone biopsy” were used to identify subjects for this study. The inclusion criteria were clinical or imaging findings suspicious for osteomyelitis within the appendicular (AS) or axial skeleton (AXS). This included either acute or chronic osteomyelitis. Moreover, at least one specimen had to undergo microbiology or histopathology analysis. Subjects were only included if they had post-biopsy follow-up indicating management including clinical notes and cross-sectional imaging. Follow-up information was obtained from the hospital’s electronic health records. Patients with biopsies performed for suspected malignancy were excluded. Detailed information about subject selection is illustrated in Figure 1.

Patients and study characteristics

In total 132 subjects and 142 biopsies were included in this study (46% female; mean age [±SD] 45.7 [±23.3 years]). Twenty-eight subjects had type 2 diabetes mellitus, 6 had HIV infection, 9 were active intravenous drug users, 19 were smokers on a daily basis and 33 had a malignancy. Fever was documented in 21/110 subjects. Elevated WBC values were found in 29/132 subjects, elevated CRP and/or ESR were found in 98/120 subjects. Blood cultures were performed in 88 subjects, of these 12 had a positive result. In 128 biopsies information was available concerning previous antimicrobial therapy. Forty patients were treated with antimicrobial medications within the last 48 hours prior to the biopsy. Of these, 18/45 were administered antimicrobials within 24 hours prior the procedure. In 116/142 biopsies information was available concerning the needle size. Patients and procedural characteristics are summarized in Table 1.

CT-guided percutaneous biopsy procedure

All 142 CT-guided percutaneous biopsies were performed by trained musculoskeletal or neuroradiologists. Five musculoskeletal and 10 neuroradiologists with 6 to 25 years of experience performed all studies; the former performed procedures of the appendicular skeleton, the latter performed procedures of the axial skeleton. During the observational period CT scanners were exchanged and new physicians performed the procedures but using the same methods and equipment. Written informed consent was obtained before the procedure. All the CTNBB were performed using a Discovery 750HD CT scanner (General Electric, Milwaukee, USA).

Procedures were performed under local anesthesia with 1% lidocaine applied to the superficial soft tissues and the periosteum. In 19 of 142 procedures general anesthesia was

administered. The sampling techniques depended on the anatomic site: long bone with intact cortex were generally biopsied using Bonopty® needles while pelvis, flat bones and destroyed cortex were biopsied with Jamshidi® needles to avoid crush artifacts. Core biopsy systems were used in a co-axial configuration with Bonopty penetration sets, to access destructed and softened tissue within the osteomyelitis region. Spine procedures were performed with co-axial needle systems used to access bone, endplate, disc and paraspinal soft tissue. The AVAmax ® bone coaxial biopsy needle kit and On-control ® biopsy kit were usually used. Routinely FNAs were performed along with core biopsies.

In 110/142 information was available concerning type of biopsy needles used and included Bonopty (AprioMed AB, Uppsala, SE) n=29, Chiba (CookMedical, Bloomington, USA) n=20, AVAmax (CareFusion, San Diego, USA) n=18, Temno (Meritmedical, South Jordan, USA) n=10, Bard (Bard Biopsy, Tempe, USA) n=2, Vidacare (Teleflex Inc., Wayne, USA) n=1, Avaflex (Stryker, Kalamazoo, USA) n=1, Arrow OnControl (Teleflex Inc., Wayne, USA) n=1, Jamshidi needle (CareFusion, San Diego, USA) n=26. At least one core sample or FNA was obtained in all cases. All samples were placed in saline solution (2 ml NaCl 0.9%) in a sterile jar and sent to microbiology, in addition a formalin fixed specimen was sent to pathology. All microbiology samples were sent for routine aerobic, anaerobic, mycobacteria and fungal cultures using solid and liquid cultures (15). Gram stain was performed on all specimens. For all cultured microorganisms, identification and antimicrobial susceptibility pattern were obtained. The specimens were processed concurrently for mycobacteria using liquid and solid culture.

Data related to the biopsy technique were obtained including number of biopsy attempts, number of core biopsies, number of fine needle aspirations, size of needle used and presence of complications. The number of attempts in performing biopsies in non- or weight- bearing bones, was not different. However, the number of biopsies was restricted if there was significant bony destruction with concern for pathological fracture. Also, in long bones smaller size needles (≥ 15 G) needles were used. Complications were defined according the ACR–SIR–SPR practice parameter for the performance of image-guided percutaneous needle biopsy (PNB): in minor and major complications.

Clinical and laboratory data

Information on the following comorbidities was recorded: diabetes mellitus, HIV infection, intravenous drug use (IVDU), smoking status, and malignancies. The following clinical and laboratory data were collected: presence/absence of fever, white blood cell count, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and results of blood culture. Fever was defined as a temperature ≥38C° within seven days prior to the biopsy and blood cultures were performed within one week before the procedure during a period of active fever. Abnormal laboratory values were defined as a WBC $\geq 10\times10^9$/L, an ESR ≥10 mm/h and a CRP ≥6mg/L at the initial presentation before the biopsy (7). Detailed information was collected on antimicrobial therapy to assess the effect of antibiotic treatment on microbiology results. Patient history, clinical, and laboratory data were obtained from the hospital’s electronic health records. According to Infectious Diseases Society of America

Guidelines (16) a subject was defined to be on antimicrobial therapy during the biopsy if pharmacotherapy was administered within 48 hours prior to the biopsy.

Concerning follow-up: all clinical and imaging data were reviewed for a period of at least 6 months providing detailed information on the course of the osteomyelitis or continued absence of disease.

Combined standard of reference

A combined standard of reference was used to assess the diagnostic performance of the CTNBB for (i) microbiology only, and (ii) microbiology and histopathology (at least one positive). A positive case of osteomyelitis or discitis was defined as the presence of at least one of the following criteria as a standard of reference: (1) positive microbiology cultures in specimens acquired by biopsy or surgery, (2) histopathology indicating acute or chronic osteomyelitis in specimens acquired by biopsy or surgery, or (3) improvement after empiric and/or tailored antimicrobial treatment at clinical and/or imaging follow-up (17, 18). A negative osteomyelitis case was defined by (1) negative microbiology culture specimens provided by open biopsy or surgical excision, (2) histopathological results of either the biopsy, open biopsy or surgical excision showing other pathologies such as malignancy and no infection and finally (3) clinical follow-up with improvement after immunosuppressants and/or anti-inflammatory drugs.

Statistical analysis

Statistical analysis was performed using STATA version 13 software (StataCorp LP, College Station, TX). The biopsy performance was determined based on the standard of reference, and the specificity, the sensitivity and area under the ROC curve were calculated. A positive biopsy was defined based on positive results from microbiology and/or histopathology exams and as described in detail above. Analyses were subdivided by skeletal site (AS and AXS) and whether subjects were on antimicrobial therapy. Pearson's X squared test was used to assess whether biopsy results varied by site or antimicrobial therapy. Logistic regression was performed to assess associations between needle size, comorbidities, clinical factors, laboratory values, blood cultures and positive microbiology biopsy outcome. A p-value < 0.050 was considered statistically significant.

RESULTS

Microbiology and Histopathology Results

In 135/142 biopsies at least one sample was sent to microbiology. Forty-five (33.5%) biopsies had positive microbiology results, but in 7 cases positive microbiology was considered to be due to contamination. Of these 38, 22 were from the axial skeleton (vertebral disc aspiration n=9; vertebral body n=4; vertebral disc-endplate n=6; vertebral transverse process n=1; vertebral facet n=1;mandibula=1), and 16 were from the appendicular skeleton (upper extremities n=2; pelvis n=7;lower extremities n=7). Staphylococcus aureus and epidermidis were the most common pathogens isolated in the AS and AXS cultures (Figure 2). The isolated pathogens and biopsy locations are shown in Table 2. No statistically significant differences were found in positive microbiology results

between the AS (16/38) and AXS (22/38) groups (p=0.63). Moreover, no statistically significant differences were found for microbiology positive results of subjects with (15/45) and without (27/90) antimicrobial therapy at the time of the biopsy (p=0.79).

In 111/142 biopsies at least one sample was sent to histopathology. Positive histopathology results were found in 32/111 (28.8%) biopsies. Of these 32 cases 13 were diagnosed as having acute osteomyelitis, while 12 cases had chronic osteomyelitis. Four cases showed signs of acute and chronic osteomyelitis and three cases demonstrated granulomatous inflammation.

In 23/104 (22.1%) cases histopathology and microbiology culture results were positive for infection. In 56/142 (39.4%) at least one (microbiology or histopathology) was positive.

Complications

There were two minor complications in all performed biopsies; both were small superficial hematomas.

Diagnostic performance of CT-guided biopsies—Using the combined standard of reference (including microbiology, histopathology and clinical/imaging follow-up findings) to assess the diagnostic performance of the CTNBB for (i) microbiology only 87/135 cases were defined as positive for infection, while for (ii) microbiology and histopathology (at least one positive) 89/142 cases were defined as positive for infection. The remaining 53/142 cases were defined as negative for infection. Of these 53 cases, other pathologies were found in 16 cases: metastasis (n=3), neoplasms (n=7), osteoid osteomas (n=2), and miscellaneous benign pathologies (n=4). Six of these 53 cases were eventually diagnosed as Chronic Recurrent Multifocal Osteomyelitis (CRMO).

Using the combined standard of reference, for microbiology only CTNBB showed a sensitivity of 42.5% [95% CI 32.0%−53.6%], a specificity of 83.0% [95% CI 69.2% −92.3%], an accuracy of 56.7% [95% CI 47.9%−65.2%], and an area under the ROC curve of 0.62 [OR=3.60; 95% CI 1.50–8.62] in isolating the causative pathogen. For a combination of microbiology and histology CTNBB had a sensitivity of 53.9% [95% CI 43.0%−64.6%], a specificity of 84.6% [95% CI 71.9%−93.1%], an accuracy of 65.2% [95% CI 56.8%−73.0%], and an area under the ROC curve of 0.69 [OR=6.43; 95% CI 2.72–15.23].

Impact of clinical and technical factors on positive biopsy microbiology results—Table 3 summarizes the impact of clinical and technical factors on microbiology results. There were no statistically significant differences between positive and negative microbiology culture results for age, sex, HIV infection, diabetes mellitus, smoking status and malignancies. However, we found a higher rate of positive microbiology cultures in patients with intravenous drug use; 7/10 had a positive microbiology result (odds ratio (OR)=5.15; 95% confidence interval (CI): 1.2–21.0; p=0.022) (Figure 3). Likewise, elevated WBC values ($\geq 10\times10^9$/L) were found in 16/45 (38%) microbiology positive cases and were significantly associated with positive results [OR=3.9; 95% CI 1.6–9.5; p=0.002] (Figure 4). Elevated CRP/ESR values were found in 35/45 (85%) microbiology positive cases but were

not significantly associated with positive microbiology culture results, [OR=1.36; 95% CI 0.5–3.9; p=0.562]. Fever was present in 12/45 (34%) positive microbiology cases and was significantly associated with a higher rate of positive results [OR=3.6; 95% CI 1.3–9.6; p=0.011]. The rate of positive microbiology results was not significantly different in patients with antimicrobial therapy 15/45 (36%) compared to patients without antimicrobial therapy at the time of the biopsy 27/90 (33%) [OR=1.11; 95% CI 0.502.42; p=0.792]. There was a difference in the blood culture results, with positive blood cultures showing a statistical trend in both AS and AXS [OR=3.16; 95% CI 0.90–11.01; p=0.070]. In biopsies performed within the AXS a significant association between positive blood cultures and biopsies was demonstrated [OR=6.92; 95% CI 1.2–38.9; p=0.028].

No statistically significant association was found between positive microbiology results and the average number of specimens collected for core bone biopsies [OR=0.77, 95% CI 0.55–1.08; p=0.143], and fine needle aspirations [OR=1.34, 95% CI 0.97–1.87; p=0.072], respectively. Also, no significant difference in microbiology results was found between 10–19G needles (27/89) and 20–22 G needles (11/27) [p=0.520], in 7 cases with positive microbiology the needle size was not known. In the 38 cases with known needle size and positive microbiology the sample was a bone core in 27 cases (10–19G needle) and a fine needle aspiration in 11 cases (20–22G needle).

Clinical outcome

In the 37 patients with positive microbiology results (out of the 87 with infection when compared to the standard of reference 42.5%) a tailored antimicrobial treatment was administered, and in addition 10 (27%) of these patients underwent a complementary surgical debridement. In the remaining 50/87 (57.5%) patients either one additional open surgical biopsy (n=6) or repeated open surgical biopsies (n=29) were performed. The final 15 patients received empirical antimicrobial treatment. Surgical open biopsies revealed positive findings in 26/35 (74%) patients and antimicrobial therapy was tailored accordingly. In the 9 remaining patients with negative open biopsy empirical antimicrobial treatment was performed.

Of the 55 subjects without osteomyelitis in 48/55 with negative microbiology and 7/55 in which only histopathology but not microbiology was available, antimicrobial treatment was terminated in 8 patients and in the remainder of the patients clinical and imaging follow-up confirmed absence of osteomyelitis and no antimicrobial therapy was administered.

DISCUSSION

The diagnostic performance of CTNBB performed in patients with suspected osteomyelitis and the association between positive microbiology outcome and clinical and technical factors, were analyzed. CTNBB showed positive microbiology results in 33.5% cases and a sensitivity of 42.5% in demonstrating a causative microorganism. Intravenous drug use, fever and elevated WBC values were all associated with a higher rate of positive microbiology results.

Given the low diagnostic yield in depicting the causative pathogen and the consequentially limited clinical utility in starting a tailored antimicrobial therapy 27% (37/135), the present study is aligned with Kasalak et.al and Kim et. al works (13, 19).

Intravenous drug use was associated with a higher rate of positive microbiology results. The lack of aseptic technique during drug application is typically associated with a higher load of microorganisms, in return leading to a higher diagnostic yield (20). Consistent with the findings of Okay et al (21), an association between elevated WBC values and a higher rate of positive microbiology results was found. As WBC values are typically elevated in more severe stages of infection (22), the load of microorganisms is likely higher, therefore increasing the likelihood of a positive microbiology sample. An association between fever (≥38C°) and a higher rate of positive microbiology results was also demonstrated (23). These findings may have clinical implications in timing biopsies and could potentially improve the microbiology yield.

A positive blood culture was significantly associated with a higher rate of positive microbiology samples for biopsies performed within the axial skeleton 85.7% (6/7) but not the appendicular skeleton 14.3% (1/7). The high concordance of positive blood and biopsies culture within the axial skeleton, can be associated with its pathogenic mechanism which is usually hematogenous seeding (24).

Similar to this work, several previous studies showed that antimicrobial therapy applied before the bone biopsies did not affect the microbiology yield (7, 8, 13, 17, 25–28). In accordance to the Infectious Disease Society of America (IDSA) guidelines (16) subjects were defined to be on antibiotic/antimicrobial therapy if they received a dose of antimicrobials within 48 hours before the biopsy. However, different temporal ranges were used by other studies raging from 24 hours before the biopsy to three-week, nevertheless a significant influence of antimicrobial therapy on the biopsy result was not found. These findings suggest that a biopsy should not be avoided or deferred if antimicrobial treatment is administered.

The rate of positive microbiology results did not differ per size of needle used: 27/38 core biopsies (10–19G) and 11/38 FNA (20–22 G) obtained using a co-axial technique. The average of samples collected either for core biopsies (1.8±0.9) or FNAs (1.9 ±1.3) did not influenced the biopsy outcome.

This study has several limitations: Firstly, the standard of reference was based on specimen analysis which included CTNBB and surgical debridement as well as clinical and imaging follow-up, this may have influenced the assessment of the sensitivity and accuracy of CTNBB in this study. Unfortunately, to date there is no established gold standard for the diagnosis of osteomyelitis associated with CTNBB. Secondly, the heterogeneity of the study population and the methods may also be considered as a potential limitation of this study, but analyzing the subgroups in a sensitivity analysis no significant differences for different anatomic locations and some of the methods were found, which in fact may strengthen the generalizability of this study.

In conclusion, CTNBB when positive is a useful minimally invasive technique for the definitive diagnosis of osteomyelitis and discitis. Nevertheless, this procedure was found to have a low sensitivity of only 42.5% for isolating the causative pathogen. The rate of positive microbiology samples was significantly higher in subjects with intravenous drug use, elevated WBC values and fever. These findings could potentially improve the microbiology yield by optimizing the timing of the CTNBB.

Acknowledgments

This study was funded by NIH/NIAMS R01-AR064771 and a scholarship grant to Silvia Schiro, MD by the University of Parma, Italy 43106.

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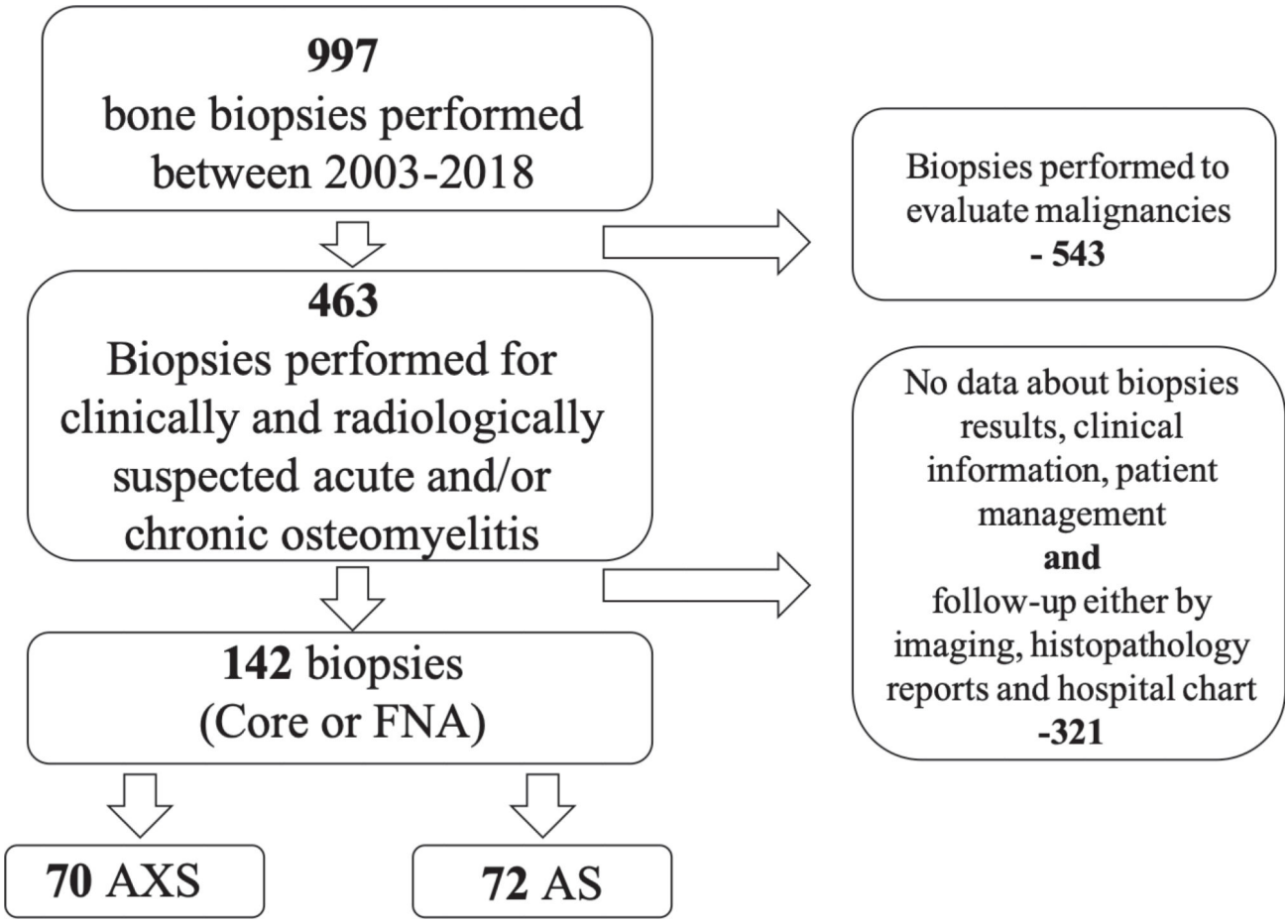

Figure 1.
Flow-chart illustrating detailed information about subject selection process.

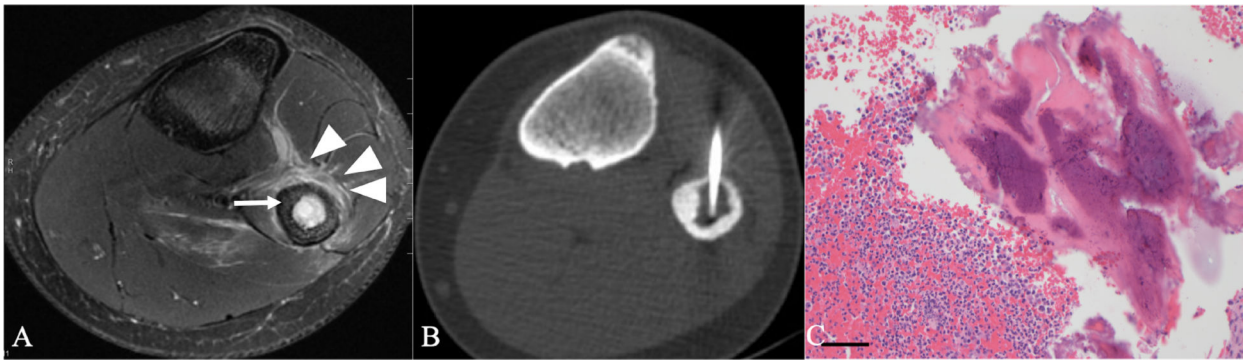

Figure 2.

15-year-old boy, presenting with knee pain without history of trauma. (A) Axial fluid-sensitive sequence with fat suppression demonstrates well-circumscribed focus of intermediate and high signal (arrows) of the proximal fibula metaphysis representing intraosseous abscess. In addition, edema of surrounding soft tissues is shown (arrowheads). (B) Axial Computed Tomography image shows a satisfactory needle position within the ill-defined lytic lesion. The biopsy yielded a positive culture for Staphylococcus aureus. (C) Hematoxylin and Eosin stained 5 μ thick sections, captured at 200X, scale bars are 100 μm. The image shows osteonecrosis with a mixed acute and chronic inflammatory infiltrate.

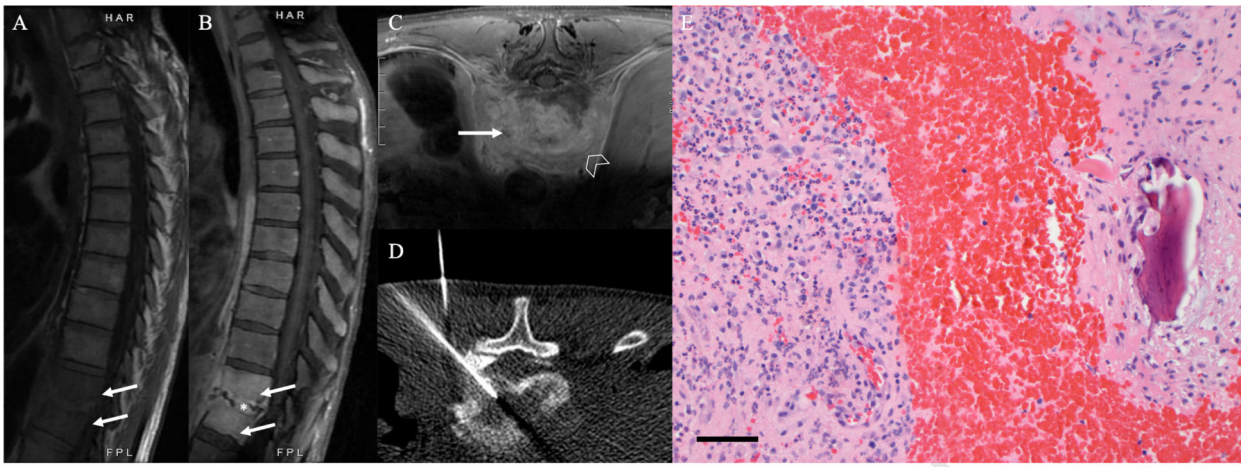

Figure 3.

51-year-old man with AIDS, IV drug use and fever presenting with back pain after six weeks of treatment with antibiotics. (A) Sagittal T1-weighted MR image shows hypointensity of T11 and T12 vertebral bodies (arrows). (B-C) Contrast-enhanced sagittal and axial T1-weighted IDEAL MR images show extensive enhancement of the T11 and T12 vertebral bodies (arrows), the T11–12 disc space (asterisk) and paraspinal soft tissues (arrowhead). (D) Bone biopsy procedure under CT guidance displaying the needle trajectory confirming a proper approach. The biopsy yielded a positive culture for Staphylococcus aureus. (E) Hematoxylin and Eosin stained 5 μ thick sections, captured at 200X, scale bars are 100μm. The image shows osteonecrosis with a mixed acute and chronic inflammatory infiltrate. Furthermore, the image shows scalloping of the bone surface suggesting increased resorption.

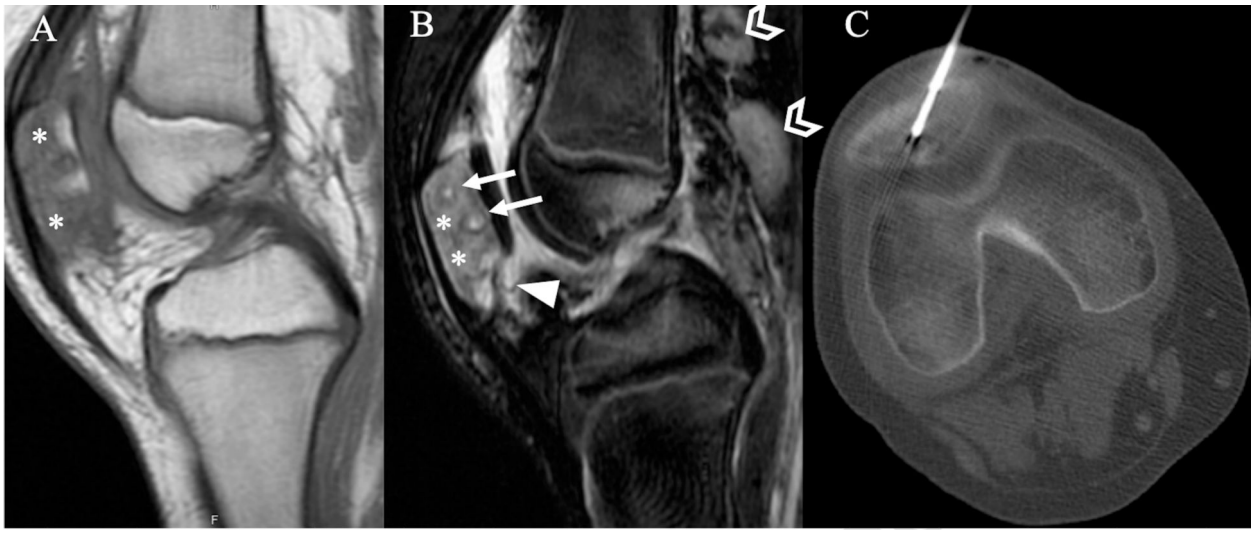

Figure 4.

8-year-old girl with fever and elevated WBC value, presenting with knee redness and swelling. (A) Sagittal T1-weighted MR image of right knee shows diffusely abnormal marrow signal (asterisks) in the patella. (B) Sagittal T2-weighted fat suppressed MR image shows extensive hyperintensity (asterisk) with more marked focal areas of increased T2 signal (arrows) with full thickness defect of patellar articular cartilage (arrowhead) associated. Moreover, enlarged popliteal lymph nodes are identified (chevrons). These findings are typical of osteomyelitis. (C) Axial Computed Tomography image shows a satisfactory needle trajectory. The biopsy yielded a positive culture for staphylococcus epidermidis.

Table 1.

Patient demographics and procedural characteristics.

	N (%) or mean ± SD
Patient demographics	
Total	132
Patient age (years)	45.7 (±23.3)
Females (%) / Males (%)	63 (48) / 69 (52)
CTNBB Procedure	
Total	142
Average of attempts	
Core biopsies	1.20±0.61
Fine needle aspiration	1.22 ±0.75
Average of specimens collected	
Core biopsies	1.80 ±0.9
Fine needle aspiration	1.9 ±1.3
Site of Biopsies	
Appendicular skeleton	72 (51)
Upper extremities	11 (15)
Pelvis	26 (36)
Lower extremities	35 (49)
Positive microbiology results	16 (42)
Axial skeleton	70 (49)
Skull	2 (3)
Cervical spine	4 (6)
Thoracic spine	21 (30)
Lumbar spine	34 (49)
Sacrum	9 (13)
Positive microbiology results	22 (58)
Biopsied structure	
Disc space	20 (29)
Vertebral Body	28 (40)
End-plate and Disc	18 (26)
Facet joint or Transverse process or Pedicles	4 (6)
Biopsy Needles	
Total	116
Diameter	15.8 (±3.9)
Distribution	
10G	3 (2.6)
11G	22 (19)
13G	19 (16.4)

	N (%) or mean ± SD
14G	6 (5.2)
15G	17 (14.6)
15.5 G	2 (1.7)
16G	8 (7.0)
17G	1 (0.9)
18G	5 (4.3)
19G	6 (5.2)
20G	5 (4.3)
21G	1 (0.9)
22G	21 (18.3)

The table summarizes the participant demographics and procedural characteristics. Continuous data are expressed as mean ±SD. Categorical data are presented in numbers of participants with percentage in parentheses. Procedures at Th12-L1 and L5-S1 were listed as lumbar spine and sacrum, respectively.

Table 2.

Summary of isolated pathogens.

Pathogen	N (%)	Location
Staphylococcus aureus	8 (21.5)	vertebral disc (n=5); vertebral disc-endplate; fibula; femur
Staphylococcus epidermidis	4 (10.5)	patella; vertebral disc-endplate; iliac bone(n=2)
Cutibacterium acnes	4 (10.5)	pubic bone; iliac bone (n=2); vertebral disc; vertebral facet
Mycobacterium tuberculosis	2 (5.3)	vertebral disc-endplate; vertebral body
Streptococcus anginosus	2 (5.3)	femur; mandibula
Scedosporium apiospermum	2 (5.3)	sternum; vertebral disc
Enterococcus species	1 (2.6)	iliac bone
Propionibacterium species	1 (2.6)	vertebral disc-endplate
Mycobacterium chelonae	1 (2.6)	calcaneus
Viridans streptococci	1 (2.6)	vertebral body
Mycobacterium avium complex	1 (2.6)	femur
Bacillus fragilis group	1 (2.6)	pubic bone
Proteus vulgaris	1 (2.6)	vertebral disc
Enterococcus faecium	1 (2.6)	calcaneus
Corynebacterium species	1 (2.6)	pubic bone
Pseudomonas aeruginosa	1 (2.6)	vertebral body
Coccidioides immitis	1 (2.6)	vertebral body
Escherichia coli	1 (2.6)	vertebral disc-endplate
Clostridium perfringens	1 (2.6)	vertebral disc-endplate
Staphylococcus epidermidis + Coccidioides immitis	1 (2.6)	clavicula
Mycobacterium tuberculosis + Corynebacterium matruchotii	1 (2.6)	vertebral body
Salmonella B + Propionibacterium species	1 (2.6)	vertebral disc

The table depicts the isolated pathogen and location of the CTNBB.

Table 3.

Summary of clinical and technical factors associated with positive microbiology results.

Factors	Odds ratio	95% C.I.	P value
Comorbidities			
Diabetes mellitus	0.55	0.2,1.3	0.177
HIV infection	2.73	0.5,12	0.202
Intravenous drug use	5.15	1.2,21	**0.022**
Smoker	1.79	0.7,4.7	0.241
Malignancies	1.51	0.6,3.4	0.318
Clinical symptoms			
Fever (≥38 C°)	3.59	1.3,9.6	**0.011**
Laboratory values			
WBC (≥ 10×10^{9}\L)	3.93	16,9.5	**0.002**
CRP (≥6mg/L) + ESR (≥10mm/h)	1.36	0.4,3.8	0.562
WBC+CRP+ESR elevated	3.59	1.3,9.2	**0.008**
Blood culture AS+AXS	3.16	0.9,11.0	0.070
Blood culture AS	0.73	0.0,7.95	0.79
Blood culture AXS	6.92	1.2,38.9	**0.028**
Treatment			
Antimicrobial therapy	0.91	0.3,2.1	0.826
Procedure specification			
Needle Size: 11–19 Gauge	0.63	0.2,1.4	0.264
Needle Size: 20–22 Gauge	1.27	0.5,2.9	0.568
Average of core biopsy samples	0.82	0.5,1.3	0.426
Average of fine needle aspiration samples	1.46	10,2.5	0.191

The table shows the odds ratio values along with 95% confidence intervals. The significant statistical results ($p< 0.050$) are highlighted in bold.