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Original article

Analysis of Specimens Collected form Highest and Lowest Uptake Areas According to 18F-FDG PET/CT in Chronic Osteomyelitis

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Abstract:

Background: The purpose of study was to evaluate the microbiological and histopathological findings of samples taken from the highest uptake areas (HUA) and the lowest uptake areas (LUA) of 18F-fluorodeoxyglucose positron emission tomography/computed tomography (18F-FDG PET/CT) in cases of fracture-related chronic osteomyelitis (COM). **Patients and Methods:** This prospective study included 14 males with a mean age of 44.2 years having fracture-related COM. The maximum standardised uptake value (SUVmax) was recorded in the axial cuts of PET/CT. Separate deep surgical samples were taken from HUA and LUA areas. Samples were subjected for microbiological (three to four samples) and histopathological (one additional sample) examination. **Results:** The affected bones had sinuses draining pus and included eight tibiae, four femora, one fibula, and one ulna. The mean injury-to-infection duration was 6.1 months. The mean infection duration was 15.9 months. The mean number of previous surgeries was 3.4 procedures. Eleven fractures were non-united. SUVmax in HUA (mean 9.9) was significantly higher than SUVmax in LUA (mean 3.9). All histopathological samples revealed active COM. Microbiological findings revealed Gram-positive (42.9%), Gram-negative (28.6%), and both Gram-positive and negative (28.6%) organisms. Bacterial cultures were different between HUA and LUA in seven patients including six cases with no growth in LUA. Three cases had same pathogen with one added organism in one area. **Conclusion:** The variability of isolated bacteria highlights the critical value of collecting samples from both HUA and LUA because one area may have different and/or additional pathogens necessitating changes in the antibiotic plan for better COM treatment.

Key words: 18F-FDG PET/CT; fracture-related infections; open fractures; chronic osteomyelitis; postoperative infection

Introduction

Bone infection is considered a major nemesis facing the orthopaedic surgeons with poor effects on the patient's quality of life [1]. Chronic osteomyelitis (COM) is difficult to be eradicated completely and one or more septic bone foci may persist [2]. Surgical debridement is the cornerstone in the management of COM. The procedure should include sample collection from the infection site [3]. There is agreement upon the standards of sampling, including antibiotic cessation before surgery, multiple (three to five) deep bone and soft tissue samples collection, using different instruments, and one sample collection for histopathology [4,5]. However, there is no specific guidance on where to collect samples. It is understood that surgeons may collect samples from different areas without precise mapping.

Identifying the causative organism is mandatory to prescribe the targeted antibiotic therapy toward the isolated bacteria, which helps eradicate infectious agents, decrease recurrence, and secure union in cases of infected non-union [6]. Even with all precautions, there is still a proportion of negative cultures ranging between 10 to 35 % [7,8]. No growth was attributed to nonculturable organisms, anaerobic organisms, or other pathogens.

^{18}F-fluorodeoxyglucose positron emission tomography (^{18}F-FDG PET) is a hybrid imaging technique that depends on the Warberg effect of increasing Glucose uptake in actively dividing cells (infection, inflammation, tumours). Combining ^{18}F-FDG PET images with low-dose computed tomography (CT) images creates a three-dimensional map that localizes the infection precisely in different planes. It has been proved in many reports that ^{18}F-FDG PET/CT have the highest sensitivity and specificity compared to other modalities in diagnosis of post-traumatic COM [9].

The ^{18}F-FDG uptake is measured by the standardised uptake value (SUV) in the regions of interest (ROIs). Up to the authors' best knowledge, there is no available published studies comparing between the samples from the highest uptake areas (HUA) and the lowest uptake areas (LUA) in COM. We hypothesised that there could be a difference in the microbiology or the histopathology between samples taken from HUA and LUA in cases of post-traumatic COM. We question the value of reading the SUV uptake and the consequent planning of surgical sampling and debridement.

Patients and methods

This prospective study was conducted in Benha University Hospitals between January 2021 and March 2022 following the approval of the institutional Research Ethics Committee (RECFOMBU) {M.S.19.8.2019}. The inclusion criteria were skeletally mature patients with fracture-related COM. Infection was diagnosed by the presence of purulent discharge from sinus communicating with the bone or the implant. This is confirmatory criterion for diagnosis of fracture-related infection according to [10].

A primary inclusion condition was to have distinct red (HUA) and green (LUA) zones on PET/CT images that can be sampled separately in patients without surgical interventions in the last 4 months. Acute osteomyelitis, paediatric patients, diabetic foot osteomyelitis and spine osteomyelitis were excluded. Patients gave informed consent to participate in the study.

A detailed history was obtained including the type of open fractures according to Gustilo and Anderson classification [11], associated injuries, previous surgeries, used implants, comorbidities, and smoking habit. Besides general examination, clinical evaluation included local soft tissue condition, presence of sinuses, and neurovascular assessment. Cierny-Mader classification was used to classify osteomyelitis [12].

Radiological assessment

Standard plain radiographs were done to evaluate the bone quality, sequestrated bone, sclerosis, the union of fractures, and implant loosening. ^{18}F-FDG PET/CT scan was done to provide a three-dimensional analysis of the infected area, helping the pre-operative planning, and determining the extent of resection during surgical debridement. Original images imported from radiologists were reconstructed into the golden gradient, which makes differentiating between the uptake intensity difficult. *RadiAnt DICOM Viewer* (Medixant company, Poznan, Poland) was used to reproduce images with a rainbow gradient (Red, yellow, and green), where red represents the HUA, and green represents the LUA.

^{18}F-FDG uptake was analysed qualitatively and quantitatively. The qualitative analysis included reviewing the reconstructed images (axial, coronal, and sagittal) and the three-dimensional CT reconstruction. This helps to precisely locate the areas candidate for sampling i.e., HUA and LUA. The quantitative analysis measured the maximum standardised uptake value (SUV_{max}) in the regions of interest (ROIs). SUV_{max} was recorded in the axial cuts. SUV_{max} at the same level on the other healthy side was also recorded as a reference to calculate SUV_{ratio}.

Surgical debridement and samples collection

Based on the SUV_{max} and PET/CT images, the site of sampling and extent of surgical debridement were carefully planned preoperatively. Samples were collected from HUA and LUA with great care using different instruments to decrease cross-contamination. Three to four deep tissue samples were collected from each area for bacterial culture and sensitivity testing. An additional sample was also collected from each area for a histopathological examination.

Standard precautions of tissue sampling were applied [4]. All patients had no prior antibiotic for 14 days. The intraoperative empirical antibiotic was given after obtaining the samples. Different instruments were used to collect the samples. Sterile containers were used and immediately transferred to the laboratory.

Statistical analysis

SUV uptake results, the microbiology results, and the histopathology results were plotted together to compare the findings of HUA and LUA. Data management and statistical analysis were done using SPSS version 28 (IBM, Armonk, New York, United States). Quantitative data were assessed for normality using the Shapiro-Wilk test and direct data visualisation methods. According to normality testing, numerical data were summarised as means and standard deviations or medians and ranges. Categorical data were summarised as numbers and percentages. SUV_{max} was compared between different zones using Friedman's test. Post-hoc comparisons were adjusted using Bonferroni's method. Correlations were done using Spearman's correlation. All statistical tests were two-sided. P values less than 0.05 were considered significant.

Results

^{18}F-FDG PET/CT was performed for 40 cases with clinically evident COM. However, the qualitative analysis of imaging showed only 14 patients with distinct areas of high and low uptake. These were the finally included cases. The remaining 26 cases had intermingled uptake distribution that cannot be considered for separate sampling during the surgery, and consequently these cases were excluded from the study.

Table (1): Show the included 14 patients were males, with a mean age of 44.2 (range 22-73; SD 15.14) years, and ten patients (71.4%) were smokers. Two cases were diabetic. All patients had fractures. The most frequent cause of fractures was road traffic accidents (12 patients; 85.7%), and two cases (14.3%) were due to fall from a height. The fractures affected the tibia (eight patients; 57.1%), the femur

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(four patients; 28.6%), the fibula (one patient; 7.1%), and the ulna (one patient; 7.1%). The mean injury-to-infection duration was 6.1 (range 0.23-41.2; SD 10.7) months, while the mean infection duration was 15.9 (range 4.6-43.2; SD 11) months.

The cause of infection was post-operative infection after the fixation of closed fractures in eight patients (57.1%) and complicating open fractures in six cases (42.9%). Gustilo and Anderson classification types of open fractures were grade I (one ulna), grade II (three tibiae), and grade IIIA (one tibia and one femur). The mean number of previous surgical procedures was 3.4 (range 1-8; SD 2.02) including internal fixation (plate and screws, and nails), external fixation (monolateral and circular), implant removal, and repeated debridement. At presentation, the fractures were fixed by intramedullary nail (five cases; 35.7%) (fig. 1b, 2b), plate and screws (three cases; 21.4%), and external fixator (one patient; 7.1%). The other five cases (35.7%) were tibial fractures presented after previous removal of their implants (fig 3b) and external fixators. Two of them were united fractures, and the remaining three nonunions presented in cast or splint.

Patient had one or more sinuses draining pus at the presentation time without skin defects (fig 1a, 2a, 3a). Cierny-Mader class was diffuse osteomyelitis in ten cases (71.4%), followed by intramedullary and localised COM in three cases (21.4%) and one case (7.1%), respectively. Eleven patients (78.6%) had non-united fractures. The remaining three fractures were united.

Table 1: Demographics of patients.

	Age (yrs)	**Infected bone**	**Open fracture**	**Injury to infection duration months**	**Infection duration months**	**Number of previous surgeries**	**SUV_{max} Red**	**SUV_{max} Green**
1	34	Tibia	Grade II	4.37	11.4	2	3.25	1.08
2	54	Femur	Grade IIIA	0.23	11.6	4	5.63	4.43
3	29	Femur	Closed	0.99	9.87	1	12.14	6.01
4	32	Tibia	Closed	0.99	5.07	2	9.09	2.73
5	53	Ulna	Grade I	3.12	4.63	5	2.57	1.34
6	22	Femur	Closed	1.97	27.13	4	8.78	4.89
7	50	Tibia	Grade II	41.16	28.83	4	12.86	4.09
8	35	Tibia	Closed	1.35	15.23	4	23.92	5.81
9	73	Tibia	Grade IIIA	7.89	18.57	2	8.44	2.95
10	67	Tibia	Closed	2.86	7.37	2	12.49	7.85
11	48	Fibula	Closed	0.69	7.9	1	2.89	1.18
12	55	Femur	Closed	4.41	43.17	8	14.75	6.69
13	34	Tibia	Closed	13.61	21.97	6	5.58	2.71
14	33	Tibia	Grade II	1.74	9.87	2	16.52	3.73

Table (2): SUV_{max} in HUA (mean 9.9; range 2.6-23.9; SD 6.04) (fig 1c, 2c, 3c) was significantly higher ($p < .001$) than the SUV_{max} in LUA (mean 3.9; range 1.2-7.8; SD 2.1) (fig 1d, 2d, 3d), and both were significantly higher ($p < .001$) than the contralateral normal side (mean 1.1; range 0.3-2.8; SD 0.61). There were no significant correlations between SUV_{max} (in each of LUA and HUA) and age, injury-infection duration, infection duration, and number of operations.

Histopathological examination revealed chronic active osteomyelitis in all LUA and HUA samples. Microbiologically, the mean number of cultured samples was 6.4 (range 5-8; SD 0.93). Gram-positive organisms grew in 42.9% of samples, and Gram-negative organisms in 28.6%. Four patients (28.6%) had both Gram-positive and negative cultures.

Table (3): Four patients (28.6%) had the same pathogen in both HUA and LUA (cases No. 3, 4, 8, and 9). Seven patients (50%) had different results in HUA compared to LUA including six cases (No. 2,5,7,11,13, and 14) with no growth in LUA, and one (case No. 1) with completely different organisms in the two areas. Three cases (No. 6,10, and 12) (21.4%) had same pathogen with one added organism in one area. The most frequent organism in HUA cultures was methicillin-resistant *Staphylococcus aureus* MRSA (57.1%), followed by klebsiella (21.4%) and Gram-negative bacilli (14.3%). The most frequent organism in LUA cultures was MRSA (28.6%), followed by klebsiella and pseudomonas (14.3%).

Table 2 Correlation between SUV max in the green and red zones and other parameters.

	SUV max (green)		SUV max (red)	
	r	*p*	*r*	*p*
Age	0.145	0.62	-0.053	0.858
Injury-infection duration (months)	-0.088	0.765	0.031	0.917
Infection (duration months)	0.299	0.299	0.328	0.253
Number of operations	0.134	0.647	0.057	0.847

r: Spearman's rho correlation coefficient. *p*: *p* value

Table 3: Culture results of the studied patients.

	Red zone HUA		Green zone LUA	
	Number of samples	**Isolated bacteria**	**Number of samples**	**Isolated bacteria**
1	3	MRSA	3	Pseudomonas
2	3	Gram -ve bacilli	3	No growth
3	3	Klebsiella + Enterococcus fecalis	3	Klebsiella + Enterococcus fecalis
4	3	MRSA	3	MRSA
5	4	MRSA	4	No growth
6	4 3	MRSA Acinetobacter baumannii	3	MRSA
7	3	MRSA	2	No growth
8	3	MRSA	3	MRSA
9	3	MRSA	3	MRSA
10	3	pseudomonas	3	pseudomonas + Stenotrophomonas
11	2	Gram -ve bacilli	3	No growth
12	3	Klebsiella + Proteus	3	Klebsiella
13	5	Klebsiella + staph	3	No growth
14	3	MRSA	3	No growth

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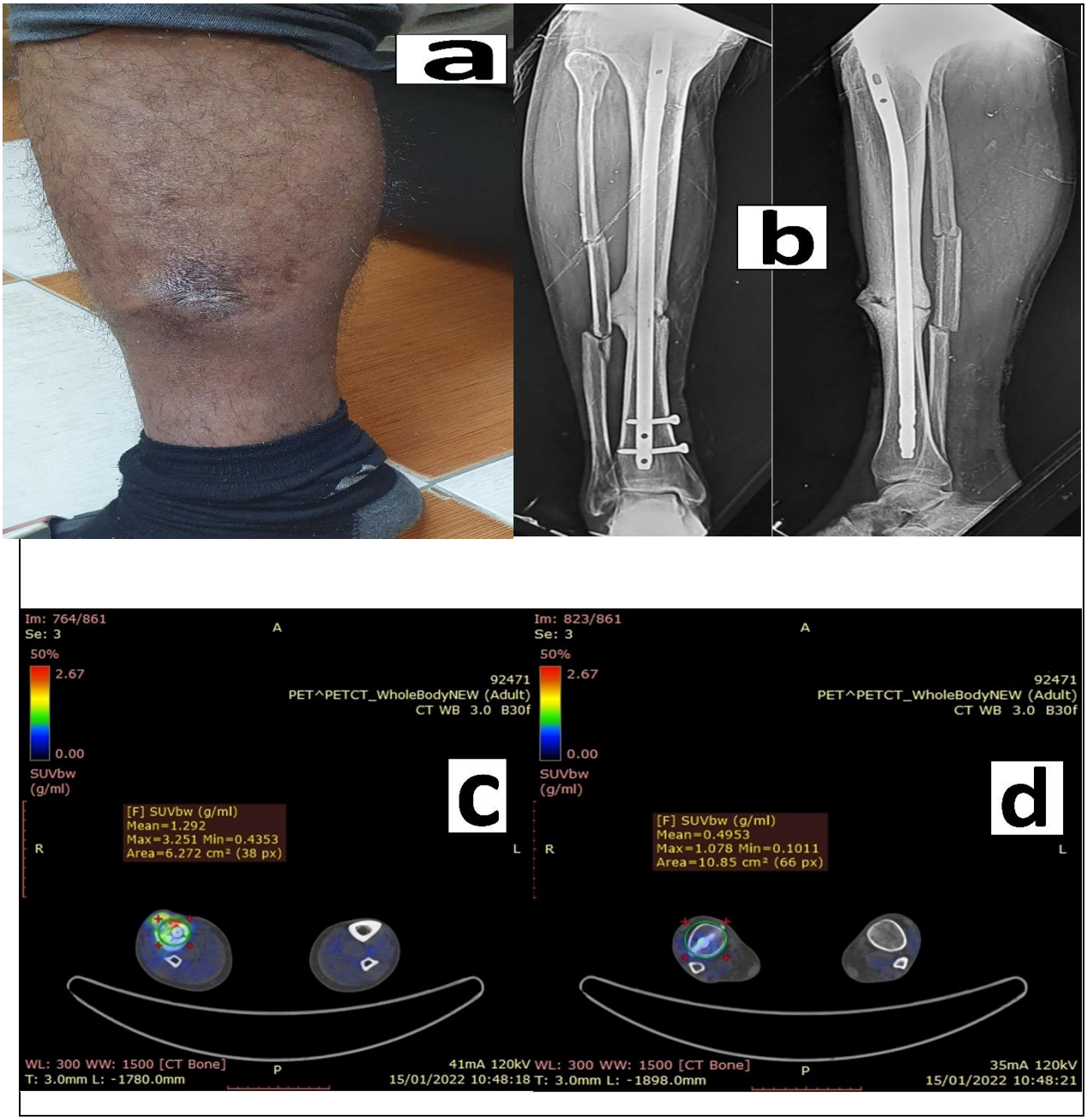

Fig. 1: A 34-year-old smoker male (No. 1) had open grade II right tibial fracture treated by closed intramedullary nailing. Infection developed after 4.37 months of injury (a) The patient presented with infection duration of 11.4 months with a draining sinus (b) The radiographs at presentation (c) PET/CT SUV_{max} at the red zone (HUA) was 3.25. Three samples from HUA (fracture site) grew MRSA (d) At the green zone (LUA), SUV_{max} was 1.08. Three samples from the green zone (distal locking screws) grew Pseudomonas (i.e., different organism).

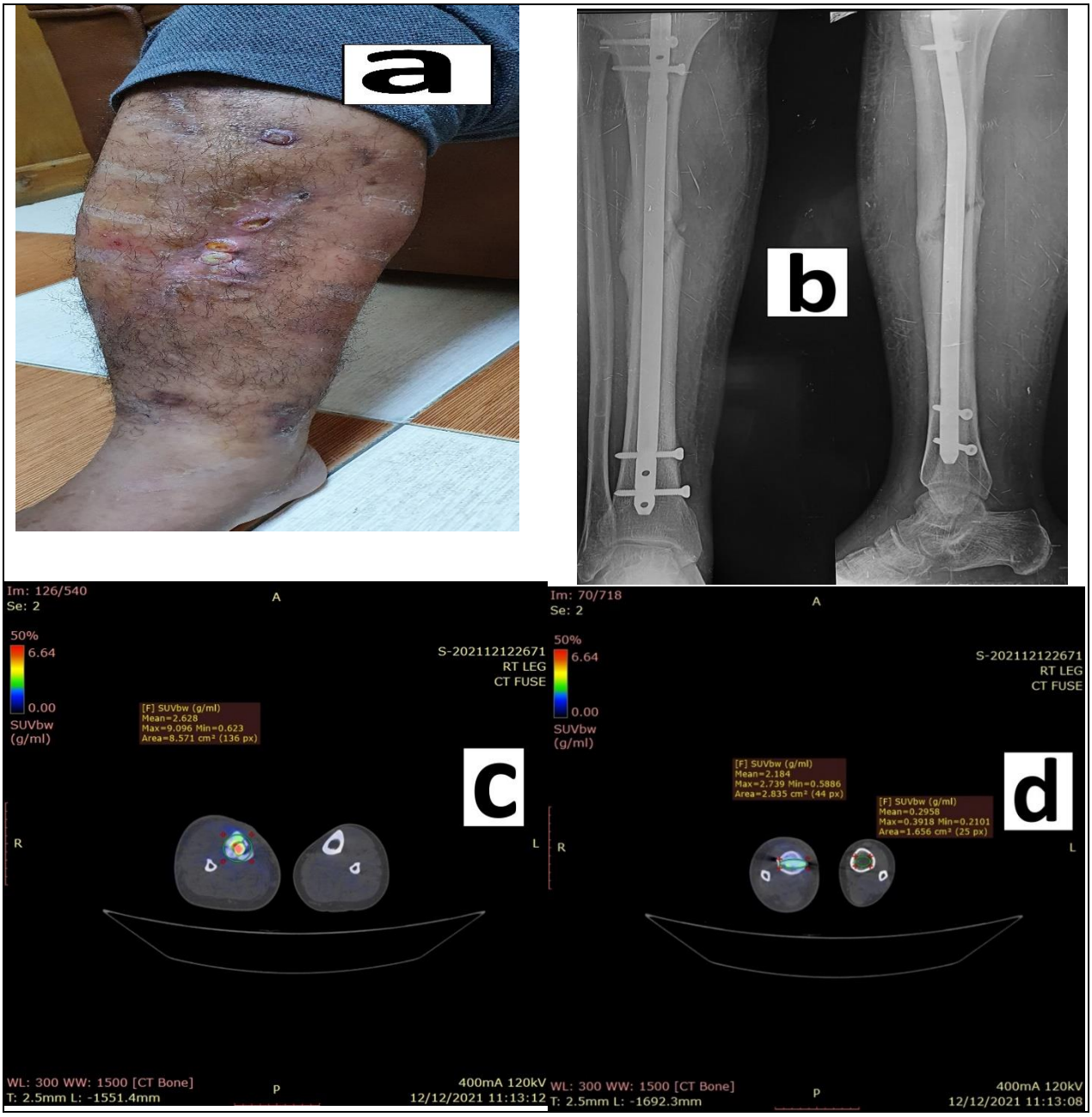

Fig. 2: A 32-year-old smoker male (No. 4) had closed fracture mid-shaft right tibia treated by closed intramedullary nailing. Infection occurred one month later (a) The patient at presentation with infection duration of five months (b) The radiographs at presentation (c) PET/CT SUV_{max} at the red zone (HUA) was 9.09 (d) At the green zone (LUA), SUV_{max} was 2.73. The six samples from the red (fracture site) and green (distal locking screws) zone grew MRSA (i.e., the same organism).

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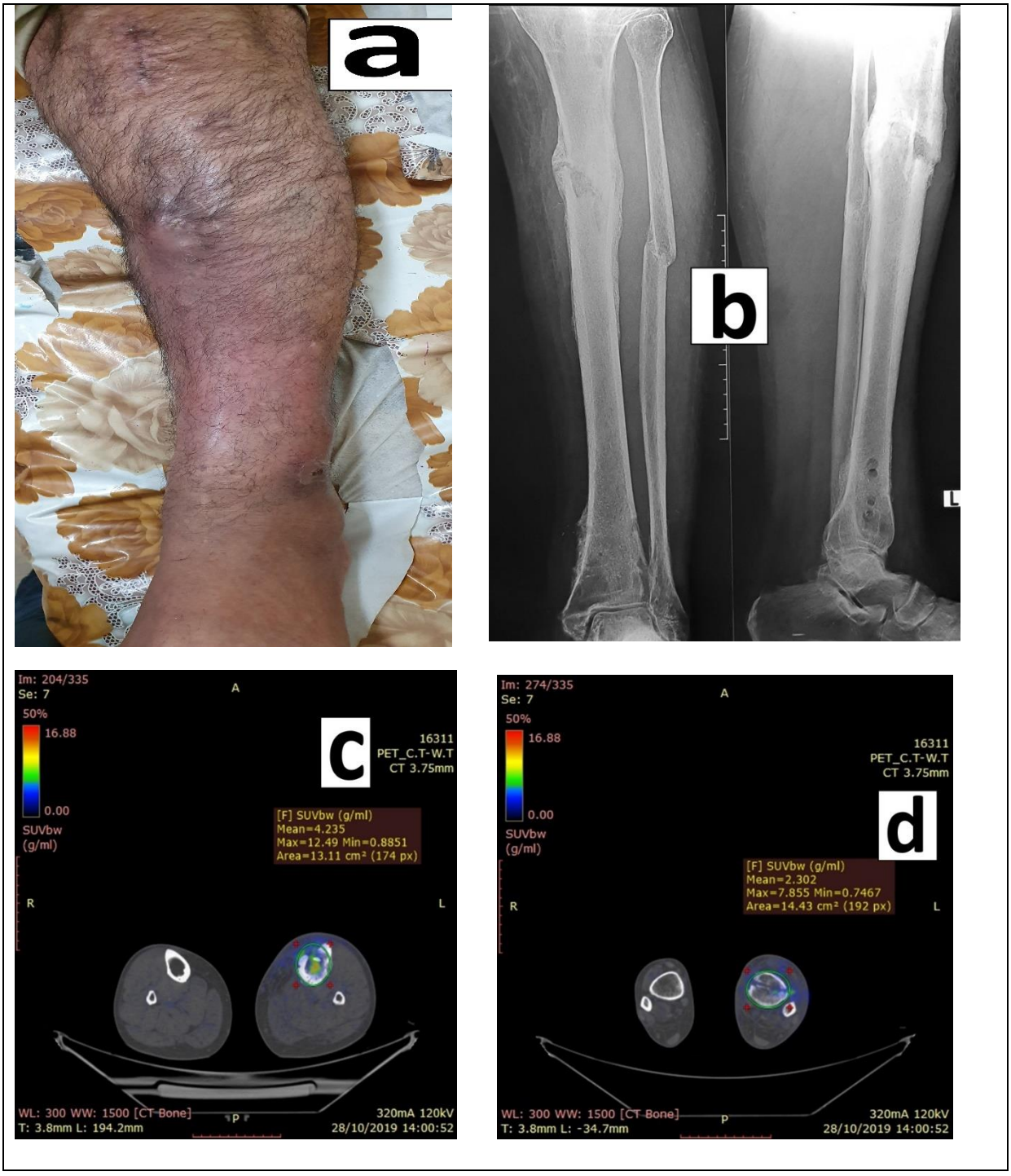

Fig. 3: A 67-year-old male (No. 10) had closed left tibial fracture treated by closed intramedullary nailing. Infection developed about three months later (a) The patient at presentation with infection duration of 7.4 months despite previous nail removal (b) The radiographs at presentation (c) PET/CT SUV_{max} at the red zone (HUA) was 12.49. Three samples from the red zone (fracture site) grew Pseudomonas (d) At the green zone (LUA), SUV_{max} was 7.85. Three samples from the green zone (distal locking screws) grew Pseudomonas and stenotrophomonas (different added organisms).

Discussion

Besides being the most common complication following fracture fixation, chronicity of fracture-related infections and their challenging treatment represent a hot topic for orthopaedic surgeons. The primary factor in their high recurrence rate is difficult accurate determination of the infection extent [13]. Furthermore, many systemic and local host factors contribute to recurrence such as diabetes, and peripheral vascular disease [14, 15].

It was found that osteomyelitis patients treated by orthopaedics specialty alone had 4.6 times higher risk of recurrence compared to cases treated by team of orthopaedics and infectious disease specialties. Many factors related to the causative organisms, sensitivities, duration of treatment and route of administration were discussed. [16]

It was emphasized two critical aspects before operating on COM (existence and extent of infection) [17].

It was stated that "the quality of surgical debridement remains absolutely the most critical factor in the successful management of chronic orthopaedic infections". However, determining the margins of the infected segment remains challenging. [18]

Pre-operative planning is complex in patients with COM. The margins of resection, pockets of infection, and bone viability are identified only through intraoperative exploration [14]. As a result, the need for a non-invasive technique with high accuracy and three-dimensional spatial properties in diagnosis and pre-operative planning has become critical [19].

It was pointed out that despite the paramount importance of adequate debridement of COM, there was no description of how to identify the margin. They found wide debridement secured no recurrence. Marginal debridement had some success in type A hosts. Intralesional debridement had 100% recurrence. They reported that the determination of this margin depended on clinical judgment intraoperatively, and MRI was not helpful in cases with previous metal implants. [14]

Accurate localisation of COM, complete debridement, and sampling of all foci provide better chances of organism identification and proper antimicrobial therapy, which significantly impacts patient outcomes [14]. The available radiological methods provided different amounts of help in pre-operative planning [20]. Radionuclide scans, especially hybrid scans were heavily studied in terms of sensitivity, specificity, and accuracy [21]. ^{18}F-FDG PET is an excellent diagnostic tool for detecting and localising acute and chronic musculoskeletal infections showing a sensitivity of up to 100% and a specificity of 88-93% in patients with or without metallic implants. FDG PET combined with CT creates high-quality pictures in different planes. The utilisation of PET-CT in fracture-related infection and osteomyelitis has been studied in different ways [9, 22]. However, there were no details or recommendations on the site for obtaining samples and their relation to the SUV analysis.

The current study evaluates both the microbiological findings and the histopathological examination of separate samples taken from HUA and LUA of ^{18}F-FDG PET/CT in cases of post-traumatic COM. Histopathological analysis of specimens collected from HUA and LUA revealed active chronic osteomyelitis in all samples. Nevertheless, the microbiological analysis was interesting. The LUA grew the exact organism profile as HUA in only four patients (29%). Three patients grew one more different organism (21%). One patient grew a different organism (7%). No growth from LUA was found in six patients (43%). These findings highlight the critical value of collecting samples from low- and high-uptake areas to avoid missing any organisms with consequent higher risk of treatment failure and recurrence of infection.

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Only few studies emphasized the three-dimensional and graphical role of ^{18}F-FDG PET/CT in providing a clear margin and precise location of COM infection [19,23]. It was used ^{18}F-FDG-PET and ^{18}F-sodium-fluoride PET-CT (NaF-PET) to localise and contrast dead bone from the viable bone in eight patients with COM [19]. They emphasised the value of these scans in presurgical planning of complicated post-traumatic chronic osteomyelitis. Compared resection margins based on plain X-rays of ten patients between ten surgeons; they found poor agreement between the surgeons in determining the length of the resection segment. [23] Compared to a plan based on ^{18}F-FDG PET/CT of the same patients, all parameters of the planned resection segment were in favour of PET-CT

Compared ^{18}F-FDG-PET/CT with histopathological findings of 16 cases of suspected osteomyelitis in tibiae, femora, metatarsals, a fibula, and a radius, it was found that the SUV cut-off values with a lower level of 2.00 and an upper level of 8.00 were accurate in visualizing the infection focus. However, their study lacks the intraoperative deep samples for bacterial identification. They used cultures from the fluid leaching from fistulae. Moreover, they included three cases with preoperative negative FDG-PET/CT findings [13].

One study analysed the SUV uptake in relation to the culture results reported heterogeneous 40 cases with positive FDG PET including patients with vertebral infections, tumours, and various bony affections. COM was present in 16 patients of this study. However, they did not combine FDG PET with CT imaging. The biopsy was obtained with variable techniques (open, CT-guided, MR-guided, percutaneous, and open through laminectomy). Half of COM cases had positive cultures, and the other half had negative cultures. They found no difference in SUV uptake between the two groups. The culture-negative samples represented a false negative culture. They attributed this to viable yet non-culturable biofilm organisms.[24]

In the current study, despite the proven histopathological diagnosis of COM in all samples, there was a statistically significant difference in the SUV_{max} uptake between the HUA and LUA, and microbiological culture was not positive in all cases. Even with very low SUV_{max}, we highlight that there might be on-going infection by the same organisms or by different organisms. There was no correlation between the level of SUV_{max} and the presence of positive or negative bacterial cultures. Causes of no growth were linked to the nature of the organism (low grade, anaerobic fungi), the analysis techniques (short period culture, absence of chemical or physical biofilm pre-treatment of samples), the lack of proper sampling technique, or the concurrent antibiotic therapy [4].

This study has some limitations due to the relatively small number of patients. This could be explained by the strict inclusion criteria to have a more homogenous group of patients with evident fracture-related COM of long bones. Moreover, PET/CT is an expensive modality which is not available in many cities. Another limitation was the inability to obtain eight to ten samples in each case for cost considerations. Despite these limitations, the results of the study may open the way for further future large sample studies.

Conclusions

The variability of results of bacterial cultures in the current study highlights the critical value of collecting samples from both HUA and LUA because one area may have a different and/or an additional pathogen which necessitates changes in the antibiotic plan for better infection control and avoiding recurrence of infection. FDG PET/CT would be a reliable tool to localise all infection spots in COM including hidden foci, plan debridement

and guide for proper sampling from all areas.

Conflict of interest

None of the contributors declared any conflict of interest.

References

1. Hosny, G. A., Ahmed, A. S. A. A., and Hussein, M. A. E. Clinical outcomes with the corticotomy-first technique associated with the Ilizarov method for the management of the septic long bones non-union. International orthopaedics 2018, 42, 2933-2939.
2. Mascioli, A. A., Shaw, M. L., Boykin, S., Mahadevan, P., Wilder, J. H., Bell, J. W., et al. Total knee arthroplasty in freestanding ambulatory surgery centers: 5-year retrospective chart review of 90-day postsurgical outcomes and health care resource utilization. Journal of the American Academy of Orthopaedic Surgeons 2021, 29(23), e1184-e1192.
3. Waldvogel, F. A., Medoff, G., and Swartz, M. N. Osteomyelitis: a review of clinical features, therapeutic considerations and unusual aspects. New England Journal of Medicine 1970, 282(5), 260-266.
4. Sousa, R., Carvalho, A., Santos, A. C., and Abreu, M. A. Optimal microbiological sampling for the diagnosis of osteoarticular infection. EFORT Open Reviews 2021, 6(6), 390.
5. Drago, L., Clerici, P., Morelli, I., Ashok, J., Benzakour, T., Bozhkova, S.,et al .The world association against infection in orthopaedics and trauma (WAIOT) procedures for microbiological sampling and processing for periprosthetic joint infections (PJIs) and other implant-related infections. Journal of Clinical Medicine 2019, 8(7), 933.
6. Li, H. K., Rombach, I., Zambellas, R., Walker, A. S., McNally, M. A., Atkins, B. L., et al. Oral versus intravenous antibiotics for bone and joint infection. New England Journal of Medicine 2019, 380(5), 425-436.
7. Sheehy, S. H., Atkins, B. A., Bejon, P., Byren, I., Wyllie, D., Athanasou, N. A.,et al The microbiology of chronic osteomyelitis: prevalence of resistance to common empirical anti-microbial regimens. Journal of Infection 2010, 60(5), 338-343.
8. Elsheikh, A., Hashish, A., Kamal, M., El-Mohammadi, S., and Ismael, Y. Aetiology of long bone chronic osteomyelitis: an analysis of the current situation in one region in Egypt. European Journal of Orthopaedic Surgery & Traumatology 2023, 33(3), 507-513.
9. Govaert, G. A., IJpma, F. F., McNally, M., McNally, E., Reininga, I. H., and Glaudemans, A. W. Accuracy of diagnostic imaging modalities for peripheral post-traumatic osteomyelitis–a systematic review of the recent literature. European journal of nuclear medicine and molecular imaging 2017, 44, 1393-1407.
10. Metsemakers, W. J., Morgenstern, M., McNally, M. A., Moriarty, T. F., McFadyen, I., Scarborough, M., et al. Fracture-related infection: a consensus on definition from an international expert group. Injury 2018, 49(3), 505-510.
11. Padegimas, E. M., and Ilyas, A. M. Distal radius fractures: emergency department evaluation and management. Orthopedic Clinics 2015, 46(2), 259-270.
12. Cierny Iii, G., Mader, J. T., and Penninck, J. J. The classic: a clinical staging system for adult osteomyelitis. Clinical Orthopaedics and Related Research (1976-2007) 2003, 414, 7-24.
13. Schoeneberg, C., Schilling, M., Burggraf, M., Fochtmann, U., and Lendemans, S. Reduction in mortality in severely injured patients following the introduction of the “Treatment of patients with severe and multiple injuries” guideline of the German society of trauma surgery–a retrospective analysis of a level 1 trauma center (2010–2012). Injury 2014, 45(3), 635-638.
14. Simpson, A. H. R. W., Deakin, M., and Latham, J. M. Chronic osteomyelitis: the effect of the extent of surgical resection on infection-free survival. The Journal of bone and joint surgery. British volume 2001, 83(3), 403-407.
15. Tice, A. D., Hoaglund, P. A., and Shoultz, D. A. Outcomes of osteomyelitis among patients treated with outpatient parenteral antimicrobial therapy. The American journal of medicine 2003, 114(9), 723-728.
16. Garcia Del Pozo, E., Collazos, J., Carton, J. A., Camporro, D., and Asensi, V. Factors predictive of relapse in adult bacterial osteomyelitis of long bones. BMC Infectious Diseases 2018, 18, 1-11.
17. Walenkamp, G. H. How I do it: Chronic osteomyelitis. Acta Orthopaedica Scandinavica 1997, 68(5), 497-506.
18. Tetsworth, K., and Cierny III, G. Osteomyelitis debridement techniques. Clinical Orthopaedics and Related Research 1999 (1976-2007), 360, 87-96.
19. Christersson, A., Larsson, S., and Sörensen, J. Presurgical localization of infected avascular bone segments in chronic complicated posttraumatic osteomyelitis in the lower extremity using dual-tracer PET/CT. EJNMMI research 2018, 8(1), 1-6.
20. Pineda, C., Espinosa, R., and Pena, A. Radiographic imaging in osteomyelitis: the role

DOI: 10.21608/bmfj.2023.212490.1821

of plain radiography, computed tomography, ultrasonography, magnetic resonance imaging, and scintigraphy. In Seminars in plastic surgery 2009 (Vol. 23, No. 02, pp. 080-089). © Thieme Medical Publishers.
21. Gemmel, F., Van den Broeck, B., Vanelstraete, S., Van Innis, B., and Huysse, W. Hybrid imaging of complicating osteomyelitis in the peripheral skeleton. Nuclear Medicine Communications 2021, 42(9), 941-950.
22. Casali, M., Lauri, C., Altini, C., Bertagna, F., Cassarino, G., Cistaro, A., et al State of the art of 18F-FDG PET/CT application in inflammation and infection: a guide for image acquisition and interpretation. Clinical and Translational Imaging 2021, 9(4), 299-339.
23. Elsheikh, A., Elazazy, M., and Elkaramany, M. Role of 18F-FDG PET-CT in Pre-Operative Planning of Surgical Debridement in Chronic Osteomyelitis. Indian Journal of Orthopaedics 2022, 56(12), 2237-2244.
24. Lankinen, P., Seppänen, M., Mattila, K., Kallajoki, M., Knuuti, J., and Aro, H. T. Intensity of 18F-FDG PET uptake in culture-negative and culture-positive cases of chronic osteomyelitis. Contrast media & molecular imaging, 2017.

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