REVIEW

acta orthopaedica belgica, 2024, 90, 769-776

doi.org/10.52628/90.4.13052

Fracture-Related Infection Diagnostic Tools in the Upper Extremity: A Scoping Review

Cristian A. DESIMONE[1], Alexander J. ADAMS[1], Nathaniel P. KERN[1], Amir R. KACHOOEI[2], Pedro BEREDJIKLIAN[1]

[1]Department of Orthopedic Surgery, Rothman Institute at Thomas Jefferson University, 925 Chestnut Street, Philadelphia, PA 19107, USA; [2]Department of Orthopedic Surgery, Rothman Orthopaedics Florida at AdventHealth, 265 East Rollins Street, Orlando, FL 32804, USA.

Correspondence at: Cristian A. DeSimone, BS, Rothman Institute at Thomas Jefferson University, 925 Chestnut Street 5th Floor, Philadelphia, PA 19107; USA. Email: cristiandesimone30@gmail.com - Tel.: 610-937-0292 (cell)

Fracture-related infection (FRI) is a serious orthopaedic complication and its diagnosis, particularly in the upper extremity, is difficult and poorly defined in current literature. An international consensus definition of FRI was published in 2018, and our scoping review aims to investigate FRI diagnostic tools reported in the primary literature and their biostatistical utility.

A review of articles generated from the PubMed/NCBI search term "fracture-related infection" was undertaken using PRISMA methodology. The included studies were published from January 2018 to June 2022 and referred to FRI diagnosis in the upper extremity.

Of 224 returned studies, 32 articles were selected for further review after fellowship-trained senior author assessment. Of these, 16 had quantitative and reportable data regarding the diagnosis of upper extremity FRI. The most common diagnostic methods reported were CRP (8 studies), WBC (7), and ESR (5), consistent with 1 of the six suggestive criteria from the consensus definition. Meta-analysis was performed.

Primary literature regarding the diagnosis of upper extremity fracture-related infections is sparse and variable despite FRI's diagnostic and therapeutic complexity. Recent literature does not reflect the proposed criteria of the 2018 consensus definition; further primary research is needed to validate these criteria and their accuracy and utility

Level of Evidence: 3b

Keywords: Diagnosis, Fracture-related infection, Scoping Review, Upper Extremity.

INTRODUCTION

Despite advancements and modern innovations in orthopaedic trauma surgery, fracture-related infection (FRI) remains one of the most challenging and dreaded complications[1]. FRI occurs when pathogenic bacteria contaminate a fracture site managed operatively or nonoperatively, diverting the body's bone healing response to an inflammatory and antibacterial response that delays and disrupts bone healing[1,2]. The detriment of FRI can be severe, leading to unplanned surgeries, non-union, and even loss of limb, all detrimental to patient quality of life[2-4]. Recent literature shows that the average costs per patient doubles when FRI occurs, and treatment success ranges from only 70-90%[3,4]. Furthermore, late infections in which periosteal new bone forms around the periphery of an infected area can create a walled off involucrum that requires repeated debridement and further long-term deficits for bone health and recovery[5]. Due to the complexity of the extrinsic and intrinsic factors underlying the pathogenesis of FRI, it continues to be a catastrophic event for both patients and clinicians[1,3,6].

Diagnosis of FRI, particularly in the upper extremity, is difficult and poorly defined in current literature[6,7]. This is a challenging issue for hand/upper extremity surgeons. To address the absence of a working definition of FRI both in clinical practice and published randomized control trials, an international convention was held in 2018, and a consensus definition was published by Metsemakers et al. This definition consisted of four confirmatory criteria (fistula/sinus/wound breakdown present, purulent drainage or pus during surgery, indistinguishable pathogens obtained from two separate deep tissue cultures, or histopathological confirmation of deep tissue microorganism), and suggestive criteria (clinical signs, radiological signs, new-onset joint effusion, elevated inflammatory markers, persistent/increasing/new wound drainage, or a pathogenic

organism from a single deep culture)[2]. This stepwise approach to the diagnosis of FRI required validation with prospective studies and primary literature, which was a major goal of the experts on the panel following the closure of the convention.

Outside of this preliminary work, literature is sparse on prevention, diagnosis, and treatment compared to other topics, such as prosthetic joint infection (PJI)[2,3]. The purpose of this scoping review was thus to investigate FRI diagnostic tools reported in the primary literature and their biostatistical utility since the consensus definition publication was published in 2018.

MATERIALS AND METHODS

Literature Search for Systematic Review

This systematic review follows the guidelines established by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). Using the PubMed database, we searched for diagnostic studies of Fracture Related Infection (FRI) of the upper extremity. We identified articles published from January 2018 – June 2022 using the "fracture-related infection" search term. We limited the search to studies published in the past four years to assess how the literature has adapted to the FRI consensus definition established by an international expert group in 2018. Articles from the initial search were included if the full text was available in English. All studies were subsequently reviewed manually to determine if they met inclusion criteria.

Study Selection and Data Collection

Each study was first screened by title and abstract. Afterwards, full texts of selected articles were assessed for a final decision on study inclusion. We included studies relevant to the diagnosis of confirmed cases of FRI with no restriction on methodology or specific measurement. Furthermore, we included studies in which the independent variable was a specific diagnostic test, and the dependent variable was the accuracy of the tests' ability to correctly identify an FRI based on the established consensus definition or a reference standard disclosed in the study. Articles about the epidemiology, etiology, treatment, and prevention of FRI were excluded. Review articles, case studies/series, and discussions were excluded. We also excluded articles in which FRI cases were discussed without the methodology used to determine diagnosis, as well as papers that solely evaluated FRI of the lower limb (Figure 1). The diagnostic methods and reported diagnostic accuracy of each method was extracted from each study. If available in each study, a short description of the FRI, the time from fracture/surgery to diagnosis, and the gold standard to which the test was compared was reported. Variables represented and reported in at least 3 of 32 studies were included in the meta-analysis, which included sensitivity, specificity, PPV, and NPV of CRP (8

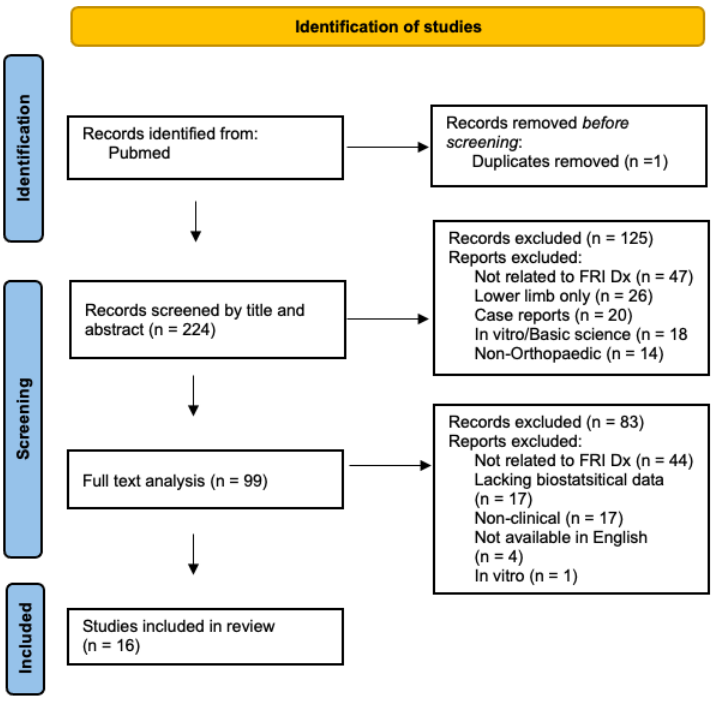

Fig. 1 — PRISMA Consort Diagram.

studies), WBC (7 studies), and ESR (5 studies).

Statistical Analysis

Meta-analysis was performed using weighted means due to differing numbers of samples per study, and data was presented as a weighted mean (95% confidence interval).

RESULTS

Of 224 returned studies, 32 articles were selected for further review after fellowship-trained senior author assessment. Of these, 16 had quantitative and reportable data regarding the diagnosis of upper extremity FRI (Table I). The most common diagnostic methods reported were CRP (8 studies), WBC (7), and ESR (5), consistent with 1 of the six suggestive criteria from the consensus definition. Meta-analysis was performed (Table III). Only one study reported on confirmatory criteria of pathogen culture (Table II). There were 21 diagnostic methods reported outside of the consensus definition diagnostic criteria (Table IV). No studies exclusively examined upper extremity patients. Of the consensus defined statistics analyzed through a meta-analysis, CRP was found to be the most sensitive when evaluating for FRI (.5839), WBC most specific (.9271), and ESR demonstrated the highest PPV and NPV (.7830/.6740). The most utilized criteria outside the consensus definition were WBC scintigraphy and circulating IL-6 levels. Of these, WBC scintigraphy showed a greater propensity for specificity ranging from .836 to .97, though IL-6 levels also had similar specificity data (.834-.846). Neither of these commonly tracked markers had consistent sensitivity data. The total platelet count to mean platelet volume ratio had a sensitivity of 100% in one study that utilized this ratio as a potential diagnostic tool.

DISCUSSION

Our investigation into the diagnostic utility of various testing parameters for FRI of the upper extremity showed sparse data in the literature on the utility of diagnostic tests. Most importantly, very few papers exist on this topic isolated to the upper extremity (Table I). Overall, the studies included did not utilize the 2018 consensus criteria for diagnosing FRI, making it extremely difficult to decide whether this criterion is accurate or effective in diagnosing FRI in the upper extremities and guiding patient care decisions. In addition, the low number of patients

Table I. — Summary of Included Articles.

Paper	Author (Year)	Country	Journal	Type	Upper/Lower Extremity	Patient Numbers	FRI Numbers
1	Bellova et al. (2021)	England	J Orthop Surg Res.	Clinical	Both	230	107
3	Bosch et al. (2021)	USA	Diagnostics	Clinical	Both	153	10
4	Bosch et al. (2018)	Germany	J Bone Jt Infect.	Clinical	Both	365	168
5	Brinker et al. (2021)	USA	J Orthop Trauma.	Clinical	Both	211	40
6	Cichos et al. (2022)	USA	Clin Orthop Relat Res.	Clinical	Both	310	93
10	Declercq et al. (2021)	Germany	Arch Orthop Trauma Surg.	Clinical	Both	530	502
11	Farooq et al. (2022)	USA	J Orthop Trauma.	Clinical	Both	13	13
13	Govaert et al. (2018)	USA	Injury	Clinical	Both	192	192
17	Lemans et al. (2019)	Germany	Eur J Nucl Med Mol Imaging.	Clinical	Both	135	135
19	Morgenstern et al. (2018)	England	Bone Joint. J	Clinical	Both	156	64
20	Onsea et al. (2022)	USA	Injury	Clinical	Both	637	480
25	Sigmund et al. (2020)	England	Bone Joint J.	Clinical	Both	106	46
28	Wang et al. (2021)	England	J Orthop Surg Res.	Clinical	Both	48,186	744
29	Wang et al. (2019)	New Zealand	Infect Drug Resist	Clinical	Both	66	32
31	Zhang et al. (2021)	Germany	Arch Orthop Trauma Surg	Meta-Analysis	Both	610	610
32	Zhao et al. (2022)	Switzerland	Front. Microbiol.	Clinical	Both	50	20

Table II. — Reported Biostatistics for Consensus Definition Criteria CRP, WBC, ESR, Culture.

Paper	Author (Year)	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value	Positive Likelihood Ratio	Negative Likelihood Ratio	Diagnostic Accuracy	Area Under ROC Curve	Area Under Curve	Odds Ratio
C-Reactive Protein (CRP)											
4	Bosch et al. (2018)	0.38	0.34	0.42	0.78			0.52	0.64		
5	Brinker et al. (2021)	0.35	0.78	0.27	0.84	1.57	0.84				1.87
11	Farooq et al. (2022)	0.462	0.923							0.692	
20	Onsea et al. (2022)	0.784	0.526							0.66	
25	Sigmund et al. (2020)	0.674	0.612	0.604	0.682	1.739	0.532	0.641		0.532	
28	Wang et al. (2021)	0.471	0.917	0.727	0.786	5.7	0.6	0.774		0.752	
29	Wang et al. (2019)	0.406	0.882	0.765	0.612						
32	Zhao et al. (2022)										1.42
White Blood Cell (WBC) Count											
4	Bosch et al. (2018)	0.39	0.74	0.46	0.67			0.61	0.6		
5	Brinker et al. (2021)	0.1	0.91	0.2	0.81	1.07	0.99				1.1
19	Morgenstern et al. (2018)	0.80	1.00	1.00	0.84			0.90			
20	Onsea et al. (2022)	0.396	0.891							0.64	
25	Sigmund et al. (2020)	0.174	0.95	0.727	0.60	3.478	0.87	0.613		0.562	
29	Wang et al. (2019)	0.125	0.941	0.667	0.533						
32	Zhao et al. (2022)										1.2
Erythrocyte Sedimentation Rate											
4	Bosch et al. (2018)	0.62	0.64	0.45	0.76			0.8	0.58		
5	Brinker et al. (2021)	0.5	0.61	0.23	0.84	1.27	0.83				1.54
20	Onsea et al. (2022)	0.622	0.875							0.75	
29	Wang et al. (2019)	0.563	0.853	0.783	0.674						
32	Zhao et al. (2022)										1.11
Peri-Implant Culture											
1	Bellova et al.	0.841	0.732								

Table III. — Meta-Analysis Results of CRP, WBC, ESR with Weighted Means (95% CI).

Diagnostic Test	CRP	WBC	ESR
Sensitivity	0.5839 (0.4118 – 0.7560)	0.2318 (0.0683 – 0.3953)	0.5934 (0.5357 – 0.6512)
Specificity	0.7342 (0.5435 – 0.9249)	0.9271 (0.8908 – 0.9634)	0.8649 (0.8434 – 0.8864)
PPV	0.6841 (0.5263 – 0.8419)	0.6996 (0.6410 – 0.7582)	0.7830 (0.7609 – 0.8051)
NPV	0.6472 (0.5786 – 0.7158)	0.5669 (0.5012 – 0.6325)	0.6740 (0.6561 – 0.6919)

per study and the total number of patients involved in these investigations makes applying the findings to the larger population much more tedious. Overall, the results of our query demonstrated the poor biostatistical utility of consensus agreed upon tests in isolation and the poor diagnostic ability of most non-consensus tests with very limited data on both.

The biostatistical data on consensus agreed upon investigations is widely varied. This calls into question the ability of the selected test to help guide FRI-related diagnosis on their own. In analyzing C-reactive protein (CRP) as a means of diagnosing FRI, biostatistical analysis revealed a wide range of reported outcomes. Onsea et. Al (2022) reported a sensitivity of .784, while another recent study by Brinker et. Al (2021) found the sensitivity to be .34. Specificity of CRP varied similarly to 0.923 on the upper end, as seen by Farooq in 2022, and .34, as noted by Bosch in 2018. Fewer studies reported on the PPV and NPV of CRP, but the inconsistency in data remains. This wide variance in biostatistical data of incredibly poor and low utility outcomes to the robust ability to rule in infection leads

Table VI. — Reported Statistics for Non-Consensus Definition Diagnostic Tools.

Paper Nr.	Author (Year)	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value	Positive Likelihood Ratio	Negative Likelihood Ratio	Diagnostic Accuracy	Area Under ROC Curve	Area Under Curve	Odds Ratio
		Percent Neutrophils									
25	Sigmund et. Al (2020)	13(5.82-6.2)	87.7(75.5-93.9)	42.9 (16.9-68.8)	56.5 (46.9-66.7)	.978 (.365-2.633)	1.003 (.458-1.119)	54.7 (45.2-64.2)		.499(.432-.564)	
		Neutrophil to Lymphocyte Ratio									
25	Sigmund et. Al (2020)	28.3(17.3-42.7)	80(68-88.3)	52 (32.4-71.6)	59.3 (48.6-70)	1.413 (.713-2.801)	.541 (.458-.625)	57.5 (48.1-67)		.541 (.458-.625)	
		Sonicate Fluid Culture									
1	Bellova et. Al (2021)	90.7%(p=.065)	73.2%(p=.003)								
		WBC Scintigraphy									
3	Bosch et. Al (2021)	>0% increase: 30%; >10% increase: 18.2%; > 20% increase: 0%	>0% increase: 45%; >10% increase: 82.4%; > 20% increase: 88.9%					>0% increase: 40%; >10% increase: 66.3%; > 20% increase: 66.7%	0.37		
13	Govaert et. Al (2018)	0.79	0.97	0.91	0.93	26.3	0.22	0.92			126.7
20	Onsea et. Al (2022)	50 (29.1-70.9)	85(62.1-96.8)							0.68 (0.55-0.81)	
31	Zhang et. Al (2021)	.86(.53-.97)	.96(.92-.98)			21.4 (10.5-43.9)	.14 (.03-.063)	.97(.950.98)			149 (22-1023)
		Interleukin-6									
11	Farooq et. Al (2022)	0.539	0.846								
32	Zhao et. Al (2022)										1.2 (1,1.44)
33	Zhao et. Al (2021)	0.575	0.836							0.718	
		Platelet-Derived Growth Factor AB;BB									
11	Farooq et. Al (2022)	0.615	0.846							0.731	
		Vascular Endothelial Growth Factor A									
11	Farooq et. Al (2022)	0.385	0.923							0.654	
		Tumor Necrosis Factor-α									
33	Zhao et. Al (2022)										1.23 (.96,1.57)
32	Zhao et. Al (2021)	57.5	83.6								
		Serum Amyloid A									
33	Zhao et. Al (2022)										1.16 (1.01, 1.32)
		Uric Acid									
33	Zhao et. Al (2022)										1 (.99, 1.09)

Table VI. — Reported Statistics for Non-Consensus Definition Diagnostic Tools - part 2.

Paper Nr.	Author (Year)	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value	Positive Likelihood Ratio	Negative Likelihood Ratio	Diagnostic Accuracy	Area Under ROC Curve	Area Under Curve	Odds Ratio
		Vitamin D									
33	Zhao et. Al (2022)										.99 (.9, 1.09)
		Glucose									
33	Zhao et. Al (2022)										1.28 (.51, 3.21)
		Fluorodeoxyglucose (FDG)-Positron Emission Tomography (PET) or PET-CT									
17	Lemans et. Al (2019)	0.89	0.8	0.74	0.91	4.39	0.14	0.83		0.89	
31	Zhang et. Al (2021)	.91 (.85,.94)	.78(.69,.85)			4.2(2.8, 6.1)	.12 (.07,.2)			.93(.9,.95)	34(15-78)
		F-FDG PET Only									
20	Onsea et. Al (2022)	65.2 (42.7-83.6)	100(63.1-100)							.83(.73-.93)	
31	Zhang et. Al (2021)	.93(.83,.97)	.79(.61-.9)			4.4(2.2-8.7)	.09 (.03-.024)			.95 (.92-.96)	47 (10-215)
		F-FDG PET + CT									
31	Zhang et. Al (2021)	.89(.81-.94)	.78(.72-.84)			4.1(3.1-5.4)	.14(.08-.25)			.83 (.79-.86)	29(14-61)
		Agranulocyte Scintigraphy									
31	Zhang et. Al (2021)	.78(.4-.97)	.89(.52-1)								
		Bone Scintigraphy + WBC									
31	Zhang et. Al (2021)	.82 (.68-.9)	.83(.66-.93)								
		Isothermal Microcalorimetry									
6	Cichos et. Al (2022)	87	100	100	74			0.9			
		Perioperative Antibiotic Prophylaxis									
10	Declercq et. Al (2021)										3.61
		D-Dimer									
29	Wang et. Al (2019)	75(56.25-87.87)	91.2 (75.19-97.69)	88.9 (69.7-97.09)	79.5 (63.06-90.13)						
		Platelet Count to Mean Platelet Volume Ratio									
27	Strony et. Al (2020)	100(80.5-100)	55.6(38.1-72.1)	51.5	100	2.3	0			0.814	0.698
		ESR + CRP + Platelet Volume Ratio Cluster									
27	Strony et. Al (2020)	64.7 (38.8-85.8)	97.2(85.5-99.9)	91.7	85.4	23.3	0.4	0.868		0.879	

to the conclusion that CRP should be used cautiously on its own to guide FRI diagnosis in the upper extremity.

White Blood Cell Count (WBC) shows similar variance and low degree of diagnostic utility in our analysis. Multiple studies reported sensitivity data of less than 20% for WBC8-11, with Morgenstern and colleagues as an outlier of 80%. Most patients with confirmed FRI had elevated WBC, as evidenced by the reported specificity data, with all studies analyzed demonstrating 76% plus specificity for this value, with most reported specificities over 90%[8-10]. Even with these more promising values in specificity, NPV

and PPV still showed low utility for WBC as a solo tool for diagnostics.

Erythrocyte sedimentation rate (ESR) - the third and final consensus criteria evaluated, showed low sensitivity throughout the studies (.5-.727) and wide variation of specificity data (.61-.917). This variation and low utility translate to poor predictive outcomes for this test in isolation.

As an additional measure, we conducted a meta-analysis on these tests (Table III), confirming the overall poor utility of these tests in isolation. Of note, WBC did demonstrate a specificity of over 90%. Still, due to its poor predictive ability and low sensitivity, this data should not be taken in isolation and requires further investigation due to WBC-wide application inside the field of infectious disease.

There were 21 diagnostic tools analyzed by studies outside the purview of the 2018 consensus statement on FRI diagnosis. Most of these variables were researched in single publications, and few had multiple data sets to report on. This limited insight makes interpretation difficult and should be considered in the very early phases of the investigation. A few of these parameters show promise and warrant further investigation, most notably the ESR, CRP, and Platelet Volume Ratio Cluster reported by Stroney et al. in 2020. Before discussing the biostatistics of this test, it should be important to note that this cluster considers 2 of the three consensus criteria for circulating factors in the diagnostic algorithm. With a sensitivity of 64.7%, specificity of 97.2%, PPV of 91.7%, and NPV of 85.4%, this cluster may be useful in the workup of patients with suspected FRI. The benefit of a high PPV in the diagnostic workup should not be overlooked, though in only a single study, more work is needed to confirm these findings and help guide clinical decision-making. One other test work noting is WBC scintigraphy. Though only one study[12] analyzed PPV and NPV, 91% and 93% of findings in these variables make scintigraphy of WBCs an interesting proposition. The three studies analyzing this test[12-14] all found specificities greater than 85% and as high as 97% in one[12], though sensitivity data was varied and poor.

The major limitation of this study was the lack of reported data on the 2018 consensus criteria definition of FRI diagnosis. Of the 19 confirmatory and suggestive diagnostic criteria reported in this definition, only three were investigated in the literature, while 21 other factors outside these suggested methods were utilized. More work needs to be done utilizing these criteria to better assess the ability of these tests and methods to identify FRI in the upper extremity and note the ability of these criteria to guide patient-care decisions. Most studies included in our investigation reported biostatistical data on individual markers. Future insights should be sought to utilize these criteria in conjunction with each other to see if the consensus criteria as a whole can be more effective in diagnosis than its individual components. In addition to the low total study number, reported data on factors outside the consensus criteria is severely lacking. If our field is to consider some of these other variables to guide treatment courses, these investigations must be scrutinized to a higher degree in future works. Our search was limited to papers published in English. Though a select few were excluded due to these criteria, it should be noted that information from other countries may prove useful in fully understanding the impact of the 2018 consensus statement. Overall, more institutions should shift to consensus diagnostic tests to gain a deeper understanding of the efficacy of the developed recommendations and their impact on upper extremity fracture-related infections.

REFERENCES

1. Moriarty TF, Metsemakers WJ, Morgenstern M, Hofstee MI, Vallejo Diaz A, Cassat JE, Wildemann B, Depypere M, Schwarz EM, Richards RG. Fracture-related infection. Nat Rev Dis Primers. 2022 Oct 20;8(1):67. doi: 10.1038/s41572-022-00396-0. PMID: 36266296.
2. Depypere M, Morgenstern M, Kuehl R, Senneville E, Moriarty TF, Obremskey WT, Zimmerli W, Trampuz A, Lagrou K, Metsemakers WJ. Pathogenesis and management of fracture-related infection. Clin Microbiol Infect. 2020 May;26(5):572-578. doi: 10.1016/j.cmi.2019.08.006. Epub 2019 Aug 22. PMID: 31446152.
3. Berkes M, Obremskey WT, Scannell B, Ellington JK, Hymes RA, Bosse M; Southeast Fracture Consortium. Maintenance of hardware after early postoperative infection following fracture internal fixation. J Bone Joint Surg Am. 2010 Apr;92(4):823-8. doi: 10.2106/JBJS.I.00470. PMID: 20360504.
4. Tschudin-Sutter S, Frei R, Dangel M, Jakob M, Balmelli C, Schaefer DJ, Weisser M, Elzi L, Battegay M, Widmer AF. Validation of a treatment algorithm for orthopaedic implant-related infections with device-retention-results from a prospective observational cohort study. Clin Microbiol Infect. 2016 May;22(5):457.e1-9. doi: 10.1016/j.cmi.2016.01.004. Epub 2016 Jan 20. PMID: 26806134.
5. Metsemakers WJ, Kuehl R, Moriarty TF, Richards RG, Verhofstad MHJ, Borens O, Kates S, Morgenstern M. Infection after fracture fixation: Current surgical and microbiological concepts. Injury. 2018 Mar;49(3):511-522. doi: 10.1016/j.injury.2016.09.019. Epub 2016 Sep 11. PMID: 27639601.
6. He SY, Yu B, Jiang N. Current Concepts of Fracture-Related Infection. Int J Clin Pract. 2023 Apr 25;2023:4839701. doi: 10.1155/2023/4839701. PMID: 37153693; PMCID: PMC10154639.
7. Metsemakers WJ, Morgenstern M, McNally MA, Moriarty TF, McFadyen I, Scarborough M, Athanasou NA, Ochsner PE, Kuehl R, Raschke M, Borens O, Xie Z, Velkes S, Hungerer S, Kates SL, Zalavras C, Giannoudis PV, Richards RG, Verhofstad

MHJ. Fracture-related infection: A consensus on definition from an international expert group. Injury. 2018 Mar;49(3):505-510. doi: 10.1016/j.injury.2017.08.040. Epub 2017 Aug 24. PMID: 28867644.
8. Brinker MR, Macek J, Laughlin M, Dunn WR. Utility of Common Biomarkers for Diagnosing Infection in Nonunion. J Orthop Trauma. 2021 Mar 1;35(3):121-127. doi: 10.1097/BOT.0000000000001925. PMID: 33105452.
9. Sigmund IK, Dudareva M, Watts D, Morgenstern M, Athanasou NA, McNally MA. Limited diagnostic value of serum inflammatory biomarkers in the diagnosis of fracture-related infections. Bone Joint J. 2020 Jul;102-B(7):904-911. doi: 10.1302/0301-620X.102B7.BJJ-2019-1739.R1. PMID: 32600147.
10. Wang Z, Zheng C, Wen S, Wang J, Zhang Z, Qiu X, Chen Y. Usefulness of serum D-dimer for preoperative diagnosis of infected nonunion after open reduction and internal fixation. Infect Drug Resist. 2019 Jul 1;12:1827-1831. doi: 10.2147/IDR.S213099. PMID: 31308705; PMCID: PMC6612948.
11. Zhao X, Tang W, Wan H, Lan Z, Qin H, Lin Q, Hu Y, Yu G, Jiang N, Yu B. Altered Gut Microbiota as an Auxiliary Diagnostic Indicator for Patients With Fracture-Related Infection. Front Microbiol. 2022 Apr 14;13:723791. doi: 10.3389/fmicb.2022.723791. PMID: 35495685; PMCID: PMC9048737.
12. Govaert GAM, Bosch P, IJpma FFA, Glauche J, Jutte PC, Lemans JVC, Wendt KW, Reininga IHF, Glaudemans AWJM. High diagnostic accuracy of white blood cell scintigraphy for fracture related infections: Results of a large retrospective single-center study. Injury. 2018 Jun;49(6):1085-1090. doi: 10.1016/j.injury.2018.03.018. Epub 2018 Mar 15. PMID: 29625743.
13. Onsea J, Van Lieshout EMM, Zalavras C, Sliepen J, Depypere M, Noppe N, Ferguson J, Verhofstad MHJ, Govaert GAM, IJpma FFA, McNally MA, Metsemakers WJ. Validation of the diagnostic criteria of the consensus definition of fracture-related infection. Injury. 2022 Jun;53(6):1867-1879. doi: 10.1016/j.injury.2022.03.024. Epub 2022 Mar 12. Erratum in: Injury. 2023 Mar 21;: PMID: 35331479.
14. Zhang Q, Dong J, Shen Y, Yun C, Zhou D, Liu F. Comparative diagnostic accuracy of respective nuclear imaging for suspected fracture-related infection: a systematic review and Bayesian network meta-analysis. Arch Orthop Trauma Surg. 2021 Jul;141(7):1115-1130. doi: 10.1007/s00402-020-03506-3. Epub 2020 Jun 8. PMID: 32514833.
15. Bellova P, Knop-Hammad V, Königshausen M, Schildhauer TA, Gessmann J, Baecker H. Sonication in the diagnosis of fracture-related infections (FRI)-a retrospective study on 230 retrieved implants. J Orthop Surg Res. 2021 May 13;16(1):310. doi: 10.1186/s13018-021-02460-z. PMID: 33985549; PMCID: PMC8117644.
16. Bosch P, IJpma FFA, Govaert GAM, Reininga IHF, de Vries JPM, Glaudemans AWJM. White Blood Cell Scintigraphy for Fracture-Related Infection: Is Semiquantitative Analysis of Equivocal Scans Accurate? Diagnostics (Basel). 2021 Nov 29;11(12):2227. doi: 10.3390/diagnostics11122227. PMID: 34943464; PMCID: PMC8700476.
17. Bosch P, van den Kieboom J, Plate JDJ, IJpma FFA, Houwert RM, Huisman A, Hietbrink F, Leenen LPH, Govaert GAM. Limited Predictive Value of Serum Inflammatory Markers for Diagnosing Fracture-Related Infections: results of a large retrospective multicenter cohort study. J Bone Jt Infect. 2018 Jul 6;3(3):130-137. doi: 10.7150/jbji.26492. PMID: 30013894; PMCID: PMC6043470.
18. Cichos KH, Spitler CA, Quade JH, Johnson JP, Johnson MD, Ghanem ES. Isothermal Microcalorimetry Improves the Time to Diagnosis of Fracture-related Infection Compared With Conventional Tissue Cultures. Clin Orthop Relat Res. 2022 Aug 1;480(8):1463-1473. doi: 10.1097/CORR.0000000000002186. Epub 2022 Apr 5. PMID: 35383603; PMCID: PMC9278947.
19. Declercq P, Zalavras C, Nijssen A, Mertens B, Mesure J, Quintens J, De Ridder T, Belmans A, Nijs S, Spriet I, Metsemakers WJ. Impact of duration of perioperative antibiotic prophylaxis on development of fracture-related infection in open fractures. Arch Orthop Trauma Surg. 2021 Feb;141(2):235-243. doi: 10.1007/s00402-020-03474-8. Epub 2020 May 14. PMID: 32409906.
20. Farooq H, Wessel RP 3rd, Brown KM, Slaven JE, Marini F, Malek S, Natoli RM. Utility of Plasma Protein Biomarkers and Mid-infrared Spectroscopy for Diagnosing Fracture-related Infections: A Pilot Study. J Orthop Trauma. 2022 Oct 1;36(10):e380-e387. doi: 10.1097/BOT.0000000000002379. PMID: 35452050.
21. Lemans JVC, Hobbelink MGG, IJpma FFA, Plate JDJ, van den Kieboom J, Bosch P, Leenen LPH, Kruyt MC, Glaudemans AWJM, Govaert GAM. The diagnostic accuracy of 18F-FDG PET/CT in diagnosing fracture-related infections. Eur J Nucl Med Mol Imaging. 2019 Apr;46(4):999-1008. doi: 10.1007/s00259-018-4218-6. Epub 2018 Dec 7. PMID: 30523391; PMCID: PMC6450834.
22. Morgenstern M, Athanasou NA, Ferguson JY, Metsemakers WJ, Atkins BL, McNally MA. The value of quantitative histology in the diagnosis of fracture-related infection. Bone Joint J. 2018 Jul;100-B(7):966-972. doi: 10.1302/0301-620X.100B7.BJJ-2018-0052.R1. PMID: 29954215.
23. Wang B, Xiao X, Zhang J, Han W, Hersi SA, Tang X. Epidemiology and microbiology of fracture-related infection: a multicenter study in Northeast China. J Orthop Surg Res. 2021 Aug 12;16(1):490. doi: 10.1186/s13018-021-02629-6. PMID: 34384457; PMCID: PMC8357967.