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ORIGINAL RESEARCH

The Role of Applying Metagenomic Next-Generation Sequencing (mNGS) in Periprosthetic Joint Infection with Sinus Tract: A Retrospective Study

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Background: Diagnosing periprosthetic joint infection (PJI), especially with sinus tracts, is challenging using traditional cultures. Metagenomic next-generation sequencing (mNGS) offers a culture-independent diagnostic approach. We evaluated mNGS's role in diagnosing and guiding treatment for PJI with sinus tracts.

Methods: This retrospective analysis included 52 PJI patients (2019–2024). An mNGS group (n=43; 18 sinus PJI, 25 non-sinus PJI) was compared to a non-mNGS control group (n=9; all sinus PJI, culture-diagnosed). We compared pathogen detection rates. For sinus PJI patients (two-stage revision), 2-year cure rates and antibiotic duration were compared between mNGS-guided and non-mNGS-guided therapy.

Results: In sinus PJI cases (n=18), mNGS achieved significantly higher pathogen detection (88.9%, 16/18) versus culture (50.0%, 9/18) (Relative Risk [RR] 1.78; P=0.027). mNGS also detected more polymicrobial infections (38.9%, 7/18) compared to culture (5.6%, 1/18) (RR 7.00; P=0.041). For sinus PJI treatment, mNGS-guided therapy yielded a significantly higher 2-year cure rate (94.4%, 17/18) than non-mNGS therapy (55.6%, 5/9) (Absolute Risk Increase 38.9%; RR 1.70; P=0.03). Mean antibiotic duration was significantly shorter with mNGS guidance (35.62 ± 5.42 vs 47.11 ± 6.53 days; difference 11.49 days; P<0.01), with a trend towards fewer antibiotic-related complications (11.1% vs 55.6%; P=0.23).

Conclusion: mNGS significantly improves pathogen detection, especially polymicrobial infections, in sinus tract PJI. mNGS-guided therapy for sinus PJI is associated with substantially improved cure rates and shorter antibiotic duration, highlighting its utility in guiding targeted anti-infection strategies for these complex cases.

Keywords: prosthetic joint infection, metagenomic next-generation sequencing, mNGS, sinus tract, bacteria, diagnosis

Introduction

Periprosthetic joint infection (PJI) is a devastating complication following primary total joint arthroplasty (TJA).[1] As up to 25% of knee arthroplasties and 15% of hip arthroplasties fail due to infection.[2] The five-year mortality associated with PJIs surpasses that of many common cancers.[3] Sinus tracts are considered one of the major diagnostic criterion for PJI and can be present in both acute and chronic cases.[4] These sinus tracts are often accompanied by necrotic tissue, biofilm formation, and polymicrobial infections, further complicating the diagnosis and treatment process. PJI requires further

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surgery and prolonged antibiotic therapy, and in rare instances may culminate in amputation, disarticulation, or even death.[5]

Sinus tract may serve as both a reservoir for pathogens and a conduit for virulence factors to enter the joint space, thereby increasing the likelihood of polymicrobial infections and complicating the identification of true pathogens in patients with sinus tract-associated PJI.[6] Compared to monomicrobial PJI, polymicrobial PJI is often associated with poorer clinical outcomes.[7,8] Conventional microbiological cultures have notable limitations, as they rely heavily on specific culture techniques, specialized media, and incubation methods.[9,10] Additionally, competitive inhibition between bacterial species in cultures further hampers diagnostic accuracy.[11,12] Consequently, culture positivity rates are low, the process is time-consuming (ranging from several days to weeks), and the detection of fastidious bacteria, anaerobes, or fungi is often insufficient. These limitations may result in missed diagnoses, inadequate antibiotic coverage, and ultimately reduced cure rates.

In recent years, metagenomic next-generation sequencing (mNGS) has demonstrated significant advantages in diagnosing infectious diseases due to its high-throughput capabilities and unbiased pathogen detection. Its adoption in clinical settings for the diagnosis of complex infections has notably increased over the last decade, offering new possibilities beyond traditional methods. This technology enables the direct sequencing of all microbial nucleic acids present in clinical samples, facilitating the rapid identification of bacteria, fungi, viruses, and resistance genes. It is particularly well-suited for diagnosing complex infections involving negative cultures, polymicrobial infections, or rare pathogens.[13] Previous studies have confirmed that the pathogen detection rate of mNGS in bone and joint infections is significantly higher than that of traditional methods.[14,15] However, despite its promise, there remains a significant gap in the literature, as its clinical utility and impact on patient outcomes in the specific and challenging context of sinus tract-associated PJI have not yet been systematically evaluated. Notably, the unbiased nature of mNGS often results in the detection of multiple non-significant microbes, complicating result interpretation.[16,17] Although abundance thresholds have been proposed to distinguish pathogens from background microflora, robust validation of the clinical relevance of mNGS-detected microbes in PJI remains insufficient. Given that sinus tracts are a major risk factor for polymicrobial PJI and contribute to increased microbial complexity, there is an urgent need to assess the diagnostic value of mNGS in sinus tract-associated PJI. Furthermore, evidence-based guidelines for translating mNGS findings into personalized treatment strategies, including antibiotic selection and surgical timing optimization, are still lacking.

Based on the enhanced detection capabilities of mNGS for complex infections, we hypothesized that its application in patients with sinus tract-associated PJI would lead to improved pathogen identification, facilitate more targeted antimicrobial therapy, and ultimately result in better clinical outcomes compared to traditional diagnostic approaches. Therefore, this study aims to investigate the role of mNGS. This study aims to investigate the role of mNGS by retrospectively analyzing clinical data from patients with sinus tract-associated PJI, in order to assess its diagnostic efficacy and potential impact on clinical management.

Materials and Methods

Study Population

This retrospective study was conducted at the First Affiliated Hospital of Fujian Medical University, involving patients with periprosthetic joint infection (PJI) who underwent surgical intervention between January 2019 and January 2024. To evaluate the effect in guiding the treatment of metagenomic next-generation sequencing (mNGS) in sinus tract PJI patients, a control group consisting of sinus tract PJI patients who did not undergo mNGS testing (non-mNGS sinus tract PJI) during the same period was included. The inclusion criteria were: (i) PJI patients meeting the MSIS criteria;[18] (ii) patients undergoing the first stage of two-stage revision surgery; (iii) patients who underwent mNGS testing. The exclusion criteria were: (i) incomplete clinical and laboratory data; (ii) contaminated or suspected contaminated specimens; (iii) infections at other anatomic sites. Demographic characteristics, medical history, signs, presence of sinus tract, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), synovial fluid white blood cell count (SF-WBC), synovial fluid polymorphonuclear percentage (SF-PMN%), conventional culture results, and mNGS results were

collected. Based on the inclusion and exclusion criteria, this study was approved by the Institutional Review Board (IRB) of our institution in accordance with the Declaration of Helsinki (Approval No. 2018[026]).

Sample Collection and Transport Conditions

Synovial fluid (SF): Samples were collected from patients who had not received preoperative antimicrobial drugs. Obtained preoperatively via joint aspiration, with aspiration performed at the superolateral or inferolateral aspect of the knee and under ultrasound guidance for the hip, avoiding sinus tract drainage. Intraoperatively, SF was aspirated with a syringe prior to arthrotomy to avoid blood contamination. If inadequate synovial fluid was obtained, arthrotomy was performed followed by direct visualization and aspiration.

Tissue homogenate (TH): At least 5 prosthetic tissue specimens were collected intraoperatively from sites of greatest inflammation. The tissues were cut into 0.5 cm blocks on the back table under sterile conditions by a surgical assistant and placed in sterile containers for transport.

Sonication of prostheses (SP): The explanted prosthesis was immediately packed in a sterile sealed container and subjected to sonication as described in previous reports.[19,20] Specimens were delivered to the microbiology lab for culture within 30 minutes of collection.

The collected samples were immediately transferred to the microbiology department for further processing. The samples were packaged in sterile containers that were sealed, dry, sterile, and free of nucleic acid. The samples were stored at 4 °C during transportation.

Microbiological Culture

For culture, 0.1 mL aliquots of SF, TH, and SP were inoculated onto sheep blood agar (Thermo Fisher Scientific, Waltham, MA, USA) for anaerobic and aerobic incubation at 35–37°C with 5–7% CO2 for 14 and 7 days, respectively. The remaining sample was inoculated into Bactec Peds Plus/F bottles and incubated anaerobically and aerobically in the Bactec 9050 instrument (Becton Dickinson GmbH, Germany) for 14 and 5 days, respectively.[15] Positive Bactec bottles were then subcultured onto sheep blood agar. Isolated bacteria and antimicrobial susceptibilities were identified using the Vitek 2 line (bioMérieux Vitek, Inc., Cambridge, MA, USA). Culture positivity was defined as isolation of identical microorganisms from any two separate patient samples.

mNGS mNGS Process and Interpretation of mNGS Results

The mNGS procedure was performed as previously described.[9] The major steps included nucleic acid extraction from specimens, library construction and sequencing, and bioinformatic analysis. Quantified libraries were subjected to 500 bp single-end sequencing on the BGISEQ-2000 platform (BGI, Wuhan, China). Finally, raw sequencing data were analyzed using a bioinformatic pipeline developed by BGI. Interpretation of mNGS results was performed by a multidisciplinary team comprised of infectious disease physicians, microbiologists, orthopedic PJI specialists, and laboratory engineers according to the method described by Huang et al.[21]

Definition of Successful Treatment of PJI

Treatment success was assessed according to the 2013 international consensus[22] and included three aspects: (i) infection eradication evidenced by a well-healed wound, absence of drainage, sinus tract, or wound pain; (ii) no surgery related to infection after reimplantation; and (iii) no infection-associated mortality (eg, sepsis, necrotizing fasciitis).

Definition of Antibiotic Complications

Antibiotic-related complications were defined according to Xu et al[23] as follows: (i) bone marrow suppression - preoperative routine white blood cell (WBC) count > 4 × 10^9/L, maximal WBC value during intravenous or oral antibiotics < 3 × 10^9/L; (ii) hepatic injury - preoperative alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels within the normal range, with peak ALT and AST values increased by > 1.5-fold during intravenous or oral antibiotics; (iii) renal dysfunction - preoperative renal function within the normal range, with creatinine levels increased by > 1.5-fold over initial values during intravenous or oral antibiotics.

Data Analyses

Statistical analysis was performed using SPSS 26.0 (IBM, Armonk, New York, USA). Variables conforming to a normal distribution were described as mean ± standard deviation, while non-normally distributed variables were depicted as median and interquartile range. Statistical significance was analyzed using the *t*-test, chi-square test, Fisher's exact test, or Mann–Whitney *U*-test, as appropriate based on variable characteristics. $P < 0.05$ were considered statistically significant.

Results

Demographic Characteristics

The demographic characteristics and clinical presentation of the patients are shown in Table 1. 52 cases were included in this study, categorized into those with sinus tract involvement (Sinus PJI) and those without (No Sinus PJI), as well as a control group of non-mNGS patients with Sinus PJI. There were no significant differences in gender, age, BMI, joint involvement, comorbidities, Antibiotics within 2 weeks prior to surgery, or inflammatory markers between the Sinus PJI and No Sinus PJI subgroups within the mNGS group ($P > 0.05$ for all comparisons) or between the mNGS and non-mNGS sinus PJI groups ($P > 0.05$ for all comparisons). These findings suggest that the presence of sinus tract involvement does not significantly influence the clinical presentation or diagnostic outcomes of patients with PJI, particularly when utilizing advanced mNGS diagnostic tools.

PJI Pathogen Detection: MNGS Vs Conventional Cultures

Among the 43 PJI cases in the mNGS group, the pathogen detection rate by mNGS was significantly higher than that by conventional culture ($P<0.01$), with details shown in Supplementary Table 1. Similarly, in the sinus tract PJI subgroup of

Table 1 Clinical Data of the Patients Included

Parameters	Patients (mNGS)				Control (Non mNGS of sinus PJI, n=9)	P value*
	Total (n=43)	Sinus PJI (n= 18)	No sinus PJI (n=25)	P value[#]		
Age, years, X ± SD	67.81±7.70	69.06±8.65	66.92±6.98	0.25[a]	64.54±14.33	0.28[a]
Female, n	26	12	14	0.48[b]	8	0.16[c]
BMI (kg/m2), X ± SD	25.85±2.78	25.87±2.88	25.84±2.76	0.98[a]	24.41±2.71	0.17[a]
Joint involved (n)						
Hip	25	10	15	0.77[b]	9	0.48[c]
Knee	18	8	10		4	
Comorbidities (n)						
Diabetes	11	4	7	0.43[b]	5	0.43[c]
Hypertension	17	9	8	0.23[b]	4	0.46[c]
Smoking	14	6	8	0.93[b]	6	0.71[c]
Drinking	8	3	5	0.50[b]	4	0.41[c]
Antibiotics within 2 weeks prior to surgery, n	21	7	14	0.27[b]	8	0.29[c]
SF-WBC ($\times 10^6$/L), median, IQR	19693.6 (3419.0,20,617.0)	19,900.2 (6208.5,21,344.8)	19,544.8 (2569.5, 24,985.0)	0.34[d]	75208.6 (2486.0, 75,469.5)	0.83[d]
SF-PMN%, median, IQR	84.3(77.9,92.1)	85.18(77.3,93.4)	83.7(77.6,91.5)	0.21[d]	82.2(74.7,89.8)	0.11[d]
ESR (mm/h), median, IQR	61.1(40.0,81.0)	61.8(46.0,78.0)	60.6(33.0,83.0)	0.73[d]	68.4(48.5,88.5)	0.57[d]
CRP (mg/L), median, IQR	37.1(10.5,65)	34.6(6.3,67.5)	38.9(17.2,55.5)	0.38[d]	36.8(16.7,56.6)	0.44[d]
Culture positive, (n)	22	9	13	>0.05[b]	5	>0.05[c]
mNGS positive, (n)	38	16	22	0.69[b]	N/A	N/A

Notes: [a]Independent samples *t*-test; [b]Chi-squared test; [c]Fisher's Exact Test; [d]Mann–Whitney *U*-test; [#]Sinus PJI vs no sinus PJI; * mNGS of Sinus PJI vs no mNGS of sinus PJI.
Abbreviations: PJI, Periprosthetic joint infection; SF-WBC, Synovial fluid white blood cell; SF-PMN, Synovial fluid polymorphonuclear; BMI, Body mass index; mNGS, metagenomic next-generation sequencing; N/A, not applicable.

the mNGS group, the pathogen detection rate by mNGS was also significantly higher than that by culture (P=0.027), with details shown in Supplementary Table 2.

Comparison of mNGS Detection Results Between PJI with and without Sinus Tract

The mNGS detection results for the sinus tract PJI and non-sinus tract PJI groups are shown in Table 2. The sinus tract PJI group had a higher number of bacterial species detected by mNGS (45 species) compared to the non-sinus tract PJI group (29 species) (P=0.047), suggesting potentially more complex bacterial communities involving more bacterial species in sinus tract PJI cases. The pathogen detection results of mNGS in Sinus PJI are presented in Supplementary Figure 1. Furthermore, we observed that mNGS exhibited a higher capability of detecting polymicrobial PJI than conventional culture in the sinus tract PJI patients (P=0.041). Details are shown in Supplementary Table 3.

Comparison of Treatment Outcomes in PJIs with Sinus Tract Between Using and Non-Using mNGS

Sinus tract PJI patients were followed up for 2 years after the first stage of two-stage revision surgery. The 2-year cure rate was significantly higher in the 18 mNGS cases compared to the 9 non-mNGS cases (94.4% vs 55.6%, P=0.03), as shown in Table 3. The survival curves for the two groups are depicted in Figure 1. Additionally, the mNGS group tended to have fewer antibiotic complications and a shorter antibiotic duration than the non-mNGS group, although the difference in complication rates was not statistically significant (P =0.23). However, the antibiotic duration was significantly shorter in the mNGS group (P <0.01).

Discussion Our Study

Our study explores the application value of mNGS in the diagnosis and treatment of periprosthetic Joint Infection with Sinus Tract, The research results indicate that mNGS exhibits significant advantages in pathogen detection rate, complex infection identification, and treatment outcome optimization, especially in cases of multiple microbial infections and

Table 2 Microbiology Finding of mNGS in PJI

	PJI (mNGS)		P value
	Sinus PJI (n=18)	No sinus PJI (n=25)	
Staphylococcus aureus	8	6	
CoNS[a]	6	5	
Streptococcus[b]	5	3	
Gram-negative bacilli[c]	5	5	
Pseudomonas[d]	3	2	
Candida[e]	3	4	
Enterococcus faecalis	2	1	
Salmonella	3	1	
Mycoplasma hominis	4	1	
Other organisms[f]	6	1	
Total	45	29	0.047[g]

Note: [a]Coagulase negative staphylococcus; [b]Including Streptococcus agalactiae, Streptococcus dysgalactiae, Streptococcus gallolyticus, Streptococcus anginosus, Streptococcus spp; [c]Including Escherichia coli, Stenotrophomonas maltophilia, Enterobacter hormaechei, Afipia broomeae; [d]Including Pseudomonas alcaligenes, Pseudomonas aeruginosa, Pseudomonas monteilii, Pseudomonas spp; [e]Including Candida albicans, Candida parapsilosis; [f]Including Corynebacterium striatum, Cutibacterium acnes, Finegoldia magna, Enterococcus casseliflavus, Neisseria spp. Kinds of antibiotics use: The total number of types of antibiotics used during PJI treatment, [g]Chi-squared test.

Abbreviations: PJI, Periprosthetic joint infection; mNGS, metagenomic next-generation sequencing.

Table 3 The Two years Follow-up Clinical Outcomes of Use or No Use mNGS in Sinus PJI

	Sinus PJI		P value
	mNGS (n=18)	Non mNGS (n=9)	
Recurrence rate of PJI	1	4	0.03[a]
Antibiotic complication(all)	2	5	0.23[a]
Myelosuppression	0	2	
Hepatic dysfunction	2	1	
Kidney dysfunction	0	2	
Antibiotic duration(days), $X \pm S$	35.62±5.42	47.11±6.53	<0.01[b]

Note: [a]Fisher's Exact Test. [b]Independent samples *t*-test. Kinds of antibiotics use: The total number of types of antibiotics used during PJI treatment.
Abbreviations: mNGS, metagenomic next-generation sequencing; PJI, Periprosthetic joint infection.

culture negative cases. The results demonstrate the advantages of mNGS technology, consistent with previous research.[24–26]

Conventional microbiological culture is limited by factors including pre-sampling antibiotic use,[27] bacterial biofilm formation,[28] and competitive inhibition during culture,[11] often resulting in insufficient diagnosis of polymicrobial PJIs and low culture positivity rates, impacting treatment efficacy. In contrast, mNGS can directly and broadly detect all types of organisms from patient samples in an unbiased manner, providing quantitative results to identify polymicrobial infections and contaminants.[29] In the present study, the pathogen detection rate using mNGS was significantly higher in both overall PJI cases and cases with sinus-associated PJI, compared to conventional culture methods ($P < 0.01$ and $P = 0.027$, respectively). Notably, in cases with sinus tract involvement, mNGS detected a broader diversity of bacterial species ($P = 0.047$), suggesting that the sinus tract may present a more complex ecological niche conducive to polymicrobial infections. Furthermore, mNGS demonstrated superior sensitivity in identifying multiple microbial infections ($P = 0.041$), which is crucial for informing clinical treatment strategies. Given the association between polymicrobial infections and poor clinical outcomes, the application of mNGS can offer a more comprehensive pathogen profile, thereby supporting the development of precise and effective anti-infective treatment regimens.

Sinus tracts connect the joint space to the exterior, potentially allowing microbes to enter along the tract and cause polymicrobial PJIs.[6] However, some retrograde pathogens entering the joint may be low in quantity and obscured by dominant microbes, evading culture detection. This study analyzed two-year follow-up data post-two-stage revision surgery and found significantly higher cure rates in patients with sinus PJIs who underwent metagenomic next-generation sequencing (mNGS) testing compared to those who did not (94.4% vs 55.6%, P=0.03). These results indicate that mNGS improves pathogen identification, supporting better antimicrobial strategies. Additionally, mNGS-treated patients had shorter antibiotic use (P<0.01) and fewer complications, highlighting its role in optimizing therapy and reducing adverse effects. While the generally enhanced diagnostic yield of mNGS in PJI aligns with reports by Mei et al.[15] Our study

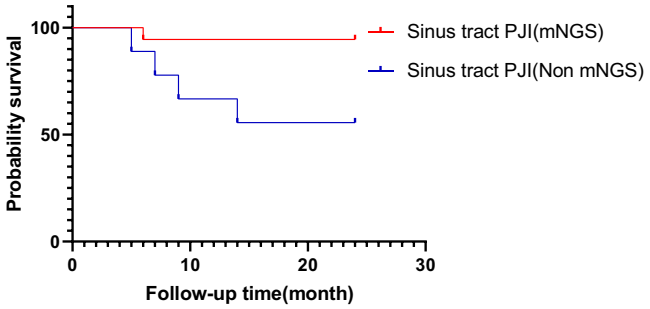

Figure 1 Kaplan-Meier survival analysis demonstrated that, at the two-year postoperative follow-up, the survival rate in sinus tract PJI patients who underwent mNGS testing was higher than that in the non-mNGS group ($P < 0.05$).

provides specific insights into the context of sinus tract PJI. The pronounced microbial diversity and the high rate of polymicrobial infections (eg, 38.9% detected by mNGS in our sinus tract cohort) that we observed underscore the unique microbiological challenges of this PJI subtype, which may be less prominent in broader PJI cohorts not stratified by sinus tract presence. Furthermore, the significant improvement in 2-year cure rates (94.4%) with mNGS-guided therapy in these complex cases extends the findings by demonstrating a substantial clinical outcome benefit in a particularly difficult-to-treat PJI population, beyond improved pathogen detection alone".

While the upfront cost of mNGS is higher than conventional microbiological cultures, its potential for cost-effectiveness in managing complex PJI, such as those with sinus tracts, warrants consideration. The significantly improved cure rates (94.4% vs 55.6%) and markedly shorter antibiotic duration ($P < 0.01$) observed in our mNGS-guided sinus PJI cohort suggest potential for substantial downstream cost savings. However, formal pharmacoeconomic studies are needed to definitively establish the cost-effectiveness of mNGS in this specific patient population.

Although mNGS offers significant advantages in pathogen detection,[14] the interpretation of its results remains challenging. Due to the unbiased nature of mNGS, a substantial number of non-pathogenic microorganisms may be detected in clinical samples, making the interpretation of mNGS findings critically important. Although studies have proposed using abundance thresholds for assessment, their clinical relevance still requires further validation. In this study, a multidisciplinary team comprising infectious disease specialists, microbiologists, orthopedic PJI experts, and laboratory engineers collaborated to comprehensively interpret mNGS results, integrating them with conventional culture findings to formulate personalized treatment plans. For instance, in our practice, when interpreting mNGS results from sinus tract PJI, our MDT meticulously considered microbial relative abundance, known pathogenicity in joint infections, the presence of common skin or environmental flora (being particularly cautious with potential contamination via the sinus tract), correlation with inflammatory markers and clinical signs, and concordance with conventional culture findings. This multi-faceted assessment was crucial for distinguishing probable pathogens from background microbiota, especially in samples from this open environment. Despite these measures, the potential for mNGS to detect non-viable organisms or incidental colonizers remains a challenge that necessitates ongoing refinement of interpretive criteria.

This approach may provide a referential framework for the clinical application of mNGS. Based on our findings of improved pathogen identification and enhanced cure rates in sinus tract PJI, we propose that mNGS could be prioritized in clinical practice for PJI cases presenting with a sinus tract. This would be particularly relevant when conventional cultures are negative, polymicrobial etiology is suspected, or if patients have a history of extensive prior antibiotic exposure. A potential diagnostic algorithm could involve early utilization of mNGS for all suspected sinus tract PJIs, or its application as an advanced second-line diagnostic tool when initial microbiological investigations are inconclusive. Effective clinical integration would greatly benefit from the establishment of local MDTs, mirroring our approach, to comprehensively interpret complex mNGS reports and translate findings into actionable, personalized treatment strategies. However, how to standardize the interpretation process of mNGS results and integrate them with existing PJI diagnostic and therapeutic guidelines remains an area requiring further research and practical experience.

This study has some limitations: (i) This was a single-center retrospective study with a small sample size, and bias may exist in case enrollment and data collection; (ii) We focused on short- to medium-term clinical outcomes of sinus tract PJIs with and without mNGS testing in our center, and longer follow-up is needed to compare long-term clinical outcomes; (iii) The study did not conduct an in-depth analysis of the specific efficacy of different antibiotic regimens. Future prospective or randomized controlled trials are needed to further validate the value of mNGS in PJI treatment; (iv) The potential of mNGS in detecting antibiotic resistance genes was not fully explored in this study. Future research could integrate mNGS-based resistance gene analysis to further optimize antibiotic selection, particularly in cases of multi-drug -resistant infections. (v) The study did not perform a detailed analysis of specific sinus tract characteristics, such as length, duration of formation, or discharge type, and their potential impact on mNGS diagnostic yield or treatment outcomes. These factors could influence the microbial biofilm complexity and host response, and their investigation warrants future prospective research. (i) This was a single-center retrospective study with a small sample size, and bias may exist in case enrollment and data collection.

Conclusions

This retrospective study found that mNGS significantly enhances pathogen detection in PJI with sinus tracts, particularly for polymicrobial infections (38.9% via mNGS vs 5.6% via culture) and culture-negative cases. Critically, mNGS-guided antibiotic regimens for these patients were associated with substantially improved 2-year cure rates (94.4% vs 55.6%) and shorter antibiotic durations (mean difference 11.49 days). These findings highlight mNGS as a valuable tool for optimizing targeted therapy in this complex PJI subtype. While these retrospective cohort results are promising, cautious interpretation is warranted. Further prospective, larger-scale studies are needed to validate these benefits and establish standardized protocols for mNGS in PJI management.

Data Sharing Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Ethics Approval and Consent to Participate

The study was conducted in accordance with the Declaration of Helsinki, and the protocol was reviewed and approved by the Ethics Committee of the First Affiliated Hospital of Fujian Medical University (approval number: 2018 [026]). Given the retrospective nature of this study and the use of anonymized patient data, the Ethics Committee of the First Affiliated Hospital of Fujian Medical University waived the requirement for written informed consent from individual patients. Patient data confidentiality was maintained in compliance with the Declaration of Helsinki.

Consent for Publication

All authors reviewed and edited the manuscript and approved the final version of the manuscript.

Acknowledgments

The study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki and was approved by the Ethics Committee of First Affiliated Hospital of Fujian Medical University.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest in this work.

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