Current situation and development of local antimicrobial agents in revision arthroplasty for periprosthetic joint infection (PJI)

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Abstract

Aim

To determine current situation and development of local antimicrobial agents in revision arthroplasty for periprosthetic joint infection (PJI).

Methods

A cross-sectional study was conducted at First Affiliated Hospital of Xinjiang Medical University, Urumqi, Xinjiang China, which was performed between March 2022 and January 2024, The total number of patients in our study were 110. The number of Male patients were 43 and females were 67. Hip patients were more as compared to knee joint. In 110 consecutive patients who underwent for blood tests and Procedures. We took a brief history from all patients. Data was tabulated and analyzed by SPSS version 25.

Results

The mean value of all enrolled 110 patients was 62.36±13.0 years. The mean ESR, CRP and recovery time were 37.15±5.45, 6.85±2.65 and 4.69±1.0 respectively. Out of total 43(39.1%) were male and 67(60.9%) were female. 82(74.5%) patients were suffering from joint pain. Site of Arthoplasty were Right knee 25(22.7%), Right hip 39(35.5%), Left knee 18(16.4%) and Right hip 28(25.5%). 103 (93.6%) patients were suffering from Erythema. Patients with joint swelling were Joint swelling 92(83.6%).
 102(92.7%) patients were suffering from fever. Gram-positive bacteria and gram-negative bacteria were found in 72 (65.5%) and 38(34.5) patients respectively. Complications were found in terms of Hematoma (60.9%) and Superficial

SSI (36.3%). Stratification of bacteria on the basis of different variables were given in table 3 with insignificant P-Value in all cases.
P-value for gender is 0.3 and P- value of complication 0.36

Conclusion

Local antimicrobial agents in revision arthroplasty for periprosthetic joint infection (PJI) is one of the best methods to recover patients quickly with a low complication rate. The recovery time of patients from Periprosthetic joint infection (PJI) was 3 to 6 weeks. Gram-positive bacteria were more in our study as compared to gram-negative bacteria. We can diagnose patients of Periprosthetic joint infection (PJI) on blood test C-reactive protein (CRP) and Erythrocyte sedimentation rate (ESR). In our study females were more as compared to males.

Keywords: *Periprosthetic joint infection (PJI), Revision arthroplasty, Arthroplasty.*

Introduction

Periprosthetic joint infection (PJI) occurs in 1% to 2% of primary and in 4% of revision arthroplasties.[1] With an incidence ranging from 0.3% to 2.9%, peri-prosthetic joint infection (PJI) is one of the most undesirable consequences of original total hip arthroplasty (THA) and the third most prevalent reason of revision surgery after.[2] One of the most severe side effects of total joint arthroplasty (TJA) in general and total knee arthroplasty (TKA) in particular is periprosthetic joint infection (PJI). Numerous institutes have reported that infection is the primary cause of TJA failure. Apart from the healthcare costs associated with PJI, which are four to five times greater than those of a typical primary TJA, there is a significant morbidity and mortality rate, comparable to that of oncologic patients.[3,4] One of the most feared side effects of joint replacement therapy is periprosthetic joint infection (PJI). Treatment for early and haematogenous PJI that is accepted is "debridement, antibiotics, and implant retention" (DAIR).[5,6] Gram-positive bacteria are the most frequent cause of pressure injuries, particularly staphylococci.[7,8]

Acute and chronic PJIs can be distinguished in order to establish a treatment plan. Type 1 refers to acute infections that happen within the first four to six weeks following surgery; Type 2 refers to chronic infections that develop beyond the first four to six weeks following surgery; Type 3 refers to acute haematogenous infections associated with a documented event of bacteraemia, occurring at a distance from the surgical procedure; Type 4 refers to the presence of a positive culture following aseptic revision surgery. Tsukayama et al. A prompt diagnosis is necessary in every situation to ensure the effectiveness of therapy.[9]

Most patient-generated infections (PJIs) result from intra-operative contamination and can be either early or delayed.[10]Patients have total joint replacement surgery for a variety of reasons. The most common reason for the procedure is symptomatic osteoarthritis, which is usually followed by inflammatory arthrites, like rheumatoid arthritis, or joint damage from trauma, tumors, or osteoporosis; these conditions, irrespective of the underlying disease, cause pain, limited joint mobility, and/or a general decline in quality of life.[11,12] Joint replacement surgery typically results in significant pain relief and the restoration of joint function; nevertheless, 1 to 3% of patients need revision surgery as a result of problems including non-infectious arthroplasty failure (NIAF) or periprosthetic joint infection (PJI).[13, 14]

PJI is linked to a number of risk factors, such as smoking, obesity, immune-disrupting conditions, and the medications used to treat them, such as rheumatoid arthritis and diabetes mellitus. It has been noted that men are more likely than women to become infected, yet it is unclear what biological basis there is for this finding.[15,16,17] About 10–20% of patient-related infections (PJIs) are caused by streptococci, with total knee and hip arthroplasties (TKA and THA) being the most common sources of isolation.[18]

It is crucial to diagnose PJI early on in order to preserve joint function and the prosthetic implant.[19] Clinical indicators are one of the elements that need to be taken into account while making a diagnosis. Both local (pain, erythema, edema, and reduced joint function) and systemic (fever) clinical symptoms can indicate an acute infection. The existence of a sinus tract or purulent around the prosthesis, however, is one of the most obvious indicators indicating the infection if other possible reasons, such as an allergic reaction to the metal or reactive arthritis, are ruled out.[20]

When it comes to imaging diagnostics, conventional radiography is most frequently used to make the initial diagnosis of PJIs. Traditional radiograph analysis may be useful in the early detection of asepticity loss. It is difficult to distinguish between infection and loss of asepticity in prosthetic joints because X-ray radiography has a low sensitivity and specificity for diagnosing infections, even though certain PJI features, such as osteolysis, subperiosteal elevation, and transcortical fistulas, can be identified by this method.[21] Computed tomography (CT) can be employed in the pre-operative examination of bone abnormalities since it provides a reasonable resolution of the surrounding soft tissue and bone.[22] Patients without ferrimagnetic implants can benefit from magnetic resonance imaging (MRI). MRI is quite sensitive (92%) and specific (99%) for PJI diagnosis in knee arthroplasty cases. Furthermore, MRI does not require ionizing radiation or contrast chemicals and provides superior resolution of bone and soft tissue compared to CT and conventional radiography. The primary drawback of CT and MRI methods is picture interference in the vicinity of metal implants.[23] Serum biomarkers, including leukocyte counts, procalcitonin, interleukins, CRP (crisis-reactive protein), and ESR (erythrocyte sedimentation rate), are typically used in conjunction with other diagnostic procedures to diagnose prosthetic infections.[24] Although precise data on the number of DAIR procedures performed is still unknown, it is likely the most commonly used initial therapeutic option for acute PJI. Debridement should be carried out as soon as acute pressure injury (PJI) is suspected (or verified) based on the previously stated criteria, while simultaneously maintaining patient health optimization.[25, 26]

Methods

A cross-sectional study was conducted at First Affiliated Hospital of Xinjiang Medical University, Urumqi, Xinjiang China, which was performed between March 2022 and January 2024, The total number of patients in our study were 110. The number of Male patients were 43 and females were 67. Hip patients were more as compared to knee joint. In 110 consecutive patients who underwent for blood tests and Procedures. We took a brief history from all patients. Data was tabulated and analyzed by SPSS version 25.

Results

Table 1: Mean value of different characteristics of all the enrolled patients (*n=110*)

Variables	Minimum	Maximum	Mean±SD
Age (Years)	28	89	62.36±13.0
ESR	30	46	37.15±5.45
CRP	4	12	6.85±2.65
Recovery Time	3	6	4.69±1.0

The mean value of all enrolled 110 patients were 62.36±13.0 years. The mean ESR, CRP and recovery time were 37.15±5.45, 6.85±2.65 and 4.69±1.0 respectively. The maximum age were 89 while the minimum ages were 28. The maximum ESR were 46 while the minimum were 30. The maximum CPR were 12 and the minimum were 4. The Maximum recovery time for patients were 6 days while the minimum were 3 days. (Table 1)
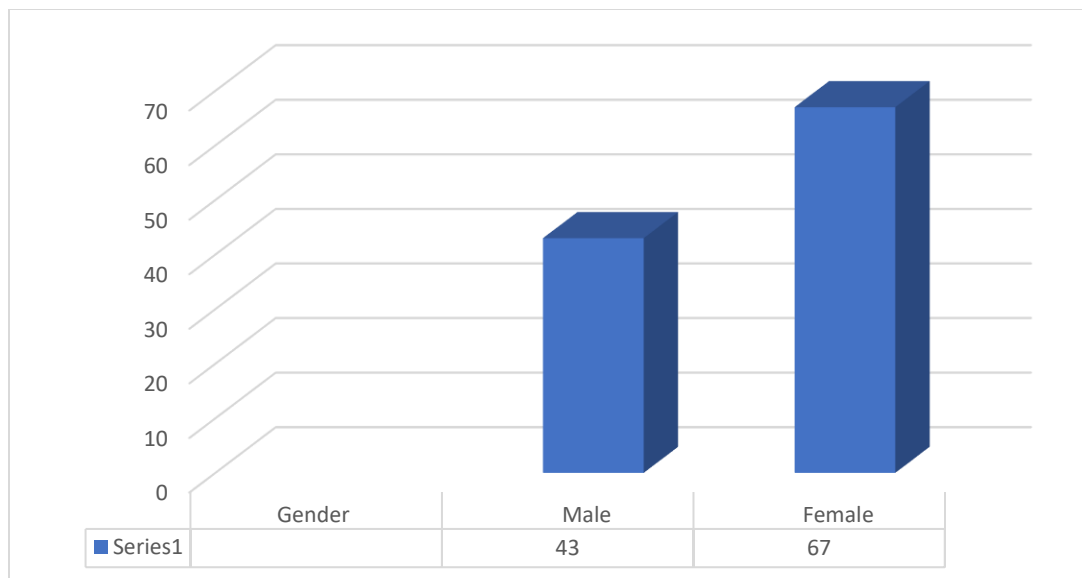
Fig 1: Bar graph showing gender distribution

The above bar graph shows gender distribution in which 43 patients were males and 67 were females.

Table 2: *Patient characteristics of enrolled patients (n=110)*

Variables		
Gender	Frequency	Percentage
Male	43	39.1
Female	67	60.9
Joint Pain	82	74.5
Site of Arthoplasty		
Right knee	25	22.7
Right hip	39	35.5
Left knee	18	16.4
Left hip	28	25.5
Erythema	103	93.6
Joint swelling	92	83.6
Fever	102	92.7
Antimicrobial therapy (DAIR)	106	96.4
Bacteria		
Gram positive bacteria	72	65.5
Gram negative bacteria	38	34.5
Types Of Prostheses		
Knee	42	38.2
Hip	68	61.8
Complication		

Hematoma	70	60.9
Superficial SSI	40	36.4

Patient characteristics of enrolled patients in table 2 were (n=110). The frequency of male patients were 43 and its percentage were 39.1. The frequency of female patients were 67 and its percentage were 60.9. The frequency of joint pain were 82 while its percentage were 74.5. The frequency of right knee were 25 and its percentage were 22.7. The frequency of Right hip were 39 and its percentage were 35.5. The frequency of left knee were 18 and its percentage were 16.4 while the the frequency of left hip were 28 and its percentage were 25.

The frequency of erythema were 103 and its percentage were 93.6. The joint swelling frequency were 92 and its percentage were 83.6. The frequency of fever were 102 and its percentage were 92.7. The frequency of antimicrobial theraphy (DAIR) were 106 and its percentage were 96.4

The frequency of Gram positive bacteria were 72 and is percentage were 65.5. The frequency of gram negative bacteria were 38 and its percentage were 34.5.

The frequency of the type of prosthesis of knee were 42 and its percentage were 38.2. The frequency of the type of prosthesis of hip were 68 and its percentage were 61.8. The complication frequency of hematoma were 70 and its percentage were 60.9 while the frequency of superficial SSI were 40 and its percentage were 36.4.

Table 3: stratification of bacteria on the basis of different varaiables (*n=110*)

	Bacteria		Total	P-value
	Gram positive bacteria	Gram Negative bacteria		
Erythema	68	35	103	0.63
Joint swelling	60	33	93	0.62
Complication				
Hematoma	48	22	70	0.36
Superficial SSI	24	16	40	
Types Of Prostheses				
Knee	28	14	42	0.83
Hip	44	24	68	
Gender				
Male	30	13	43	0.44
Female	42	25	68	

In table 3 erythema patients with gram-positive bacteria were 68 and gram-negative bacteria were 35. The total number of patients with erythema were 103 and its P- value were 0.63. Joint swelling patients with gram-positive bacteria were 60 and gram-negative bacteria were 33. The total number of patients with Joint swelling were 93 and its P- value were 0.62. Hematoma patients with gram-positive bacteria were 48 and gram-negative bacteria were 22. The total number of patients with Joint swelling were 70 and its P- value were 0.36. Superficial SSI patients with gram-positive bacteria were 24 and gram-negative bacteria were 16. The total number of patients with Superficial joint swelling

were 40 and its P- value were 0.36. Knee patients with gram-positive bacteria were 28 and gram-negative bacteria were 14. The total number of patients with knee were 42 and its P- value were 0.83. Hip patients with gram-positive bacteria were 44 and gram-negative bacteria were 24. The total number of patients with hip were 68 and its P- value were 0.83.Male patients with gram-positive bacteria were 30 and gram-negative bacteria were 13. The total number of male patients were 43 and its P- value were 0.44.Female patients with gram-positive bacteria were 42 and gram-negative bacteria were 25. The total number of female patients were 68 and its P- value were 0.44.

Discussion

Following total joint replacement surgery, periprosthetic joint infection (PJI) continues to be a fatal consequence. The bacteria that cause these diseases are well known for their ability to form a biofilm matrix and stick to foreign surfaces. Eradication is challenging because these biofilms shield the bacteria from immune system attacks and antibiotic therapy. The current therapeutic approaches, which include one- and two-stage revisions, debridement, antibiotics, and implant retention, still have a comparatively high overall failure rate. The absence of a reliable method for treating bacterial biofilm is one of the primary issues linked to this high failure rate. In order to battle PJI, we will discuss novel approaches in this review that aim to disrupt biofilm integrity, allowing the immune system and antibiotics to penetrate the internal network.[27] Several classifications, definitions, and diagnostic instruments for diagnosing PJI were gathered and examined, together with the use of DAIR, to produce a strong set of therapy suggestions.

The first challenge facing scientists and medical professionals is how to accurately make the diagnosis. Pre-operative joint aspiration, intraoperative samples, blood analysis, physical examinations, and patient interviews are all equally important and need to be used. All of these definitions and criteria are helpful in general, even though different authors employ different ones. However, the precise definition and cut-off point for an acute illness are still up for debate. While some writers define it as shorter than 4 weeks, others use 6 weeks or even less than 3 months. Is there literature that indicates that a 3-month term yields inferior results than a 4-week period.

The majority of the risk variables linked to DAIR treatment failure also increase the likelihood of developing PJI.[28] A significant risk associated with joint replacement surgery is arthroplasty failure. It is commonly treated with surgery and, in certain cases, resection and reimplantation of implanted devices. It can be brought on by non-infectious etiologies or periprosthetic joint infections (PJI). The distinction between non-infectious arthroplasty failure (NIAF) and pressure injury (PJI) must be made quickly and accurately in order to guide surgical and medicinal interventions; in many instances, this distinction may not be evident. The two entities can be distinguished from one another using conventional culture, RNA amplification tests, metagenomic, and metatranscriptomic methods for microbial detection; nevertheless, microbiologically negative apparent PJI is still difficult to distinguish.[29] Considering that the clinical picture may be confused by heterogeneity in the host factors (such as age and comorbidities), variability in the infection duration, variance in the anatomical position of the affected joint, and variations in the pathogenicity/virulence of the causative organisms, PJI diagnosis could not be made solely based on clinical manifestations. Moreover, the primary cause of early or delayed infection is thought to be intra-operative contamination, with hematogenous dissemination being the most common method. To put it another way, chronic late infections are caused by less deadly bacteria and typically present in a more quiescent manner, whereas early and hematogenous infections frequently begin abruptly. Not to mention, fungi and viruses have a part in the pathophysiology of PJI.[30]

Conclusion

Local antimicrobial agents in revision arthroplasty for periprosthetic joint infection (PJI) is one of the best methods to recover patients quickly with a low complication rate. The recovery time of patients from Periprosthetic joint infection (PJI) was 3 to 6 weeks. Gram-positive bacteria were more in our study as compared to gram-negative bacteria. We can diagnose patients of Periprosthetic joint infection (PJI) on blood test C-reactive protein (CRP) and Erythrocyte sedimentation rate (ESR). In our study females were more as compared to males.

References:

[1] Corvec, S., Portillo, M. E., Pasticci, B. M., Borens, O., & Trampuz, A. (2012). Epidemiology and new developments in the diagnosis of prosthetic joint infection. *The International journal of artificial organs*, *35*(10), 923-934.

[2] Kurtz, S., Ong, K., Lau, E., Mowat, F., & Halpern, M. (2007). Projections of primary and revision hip and knee arthroplasty in the United States from 2005 to 2030. *Jbjs*, *89*(4), 780-785.

[3] Bozic, K. J., Kurtz, S. M., Lau, E., Ong, K., Chiu, V., Vail, T. P., ... & Berry, D. J. (2010). The epidemiology of revision total knee arthroplasty in the United States. *Clinical Orthopaedics and Related Research®*, *468*, 45-51.

[4] Shahi, A., Tan, T. L., Chen, A. F., Maltenfort, M. G., & Parvizi, J. (2017). In-hospital mortality in patients with periprosthetic joint infection. *The Journal of Arthroplasty*, *32*(3), 948-952.

[5] Chotanaphuti, T., Courtney, P. M., Fram, B., den Kleef, N. I., Kim, T. K., Kuo, F. C., ... & Veltman, E. S. (2019). Hip and knee section, treatment, algorithm: proceedings of international consensus on orthopedic infections. *The Journal of Arthroplasty*, *34*(2), S393-S397.

[6] Argenson, J. N., Arndt, M., Babis, G., Battenberg, A., Budhiparama, N., Catani, F., ... & Zmistowski, B. (2019). Hip and knee section, treatment, debridement and retention of implant: proceedings of international consensus on orthopedic infections. *The Journal of arthroplasty*, *34*(2), S399-S419.

[7] Benito, N., Franco, M., Ribera, A., Soriano, A., Rodriguez-Pardo, D., Sorlí, L., ... & Puente, A. (2016). Time trends in the aetiology of prosthetic joint infections: a multicentre cohort study. *Clinical Microbiology and Infection*, *22*(8), 732-e1.

[8] Tai, D. B. G., Patel, R., Abdel, M. P., Berbari, E. F., & Tande, A. J. (2022). Microbiology of hip and knee periprosthetic joint infections: a database study. *Clinical Microbiology and Infection*, *28*(2), 255-259.

[9] T TSUKAYAMA, D. E. A. N., Estrada, R., & Gustilo, R. B. (1996). Infection after total hip arthroplasty. A study of the treatment of one hundred and six infections. *JBJS*, *78*(4), 512-23.

[10] Zimmerli, W., Trampuz, A., & Ochsner, P. E. (2004). Prosthetic-joint infections. *New England Journal of Medicine*, *351*(16), 1645-1654.

[11] Pivec, R., Johnson, A. J., Mears, S. C., & Mont, M. A. (2012). Hip arthroplasty. *The Lancet*, *380*(9855), 1768-1777.

[12] Tande, A. J., & Patel, R. (2014). Prosthetic joint infection. *Clinical microbiology reviews*, *27*(2), 302-345.

[13] Ledford, C. K., Perry, K. I., Hanssen, A. D., & Abdel, M. P. (2019). What are the contemporary etiologies for revision surgery and revision after primary, noncemented total hip arthroplasty?. *JAAOS-Journal of the American Academy of Orthopaedic Surgeons*, *27*(24), 933-938.

[14] Mathis, D. T., Lohrer, L., Amsler, F., & Hirschmann, M. T. (2021). Reasons for failure in primary total knee arthroplasty-An analysis of prospectively collected registry data. *Journal of Orthopaedics*, *23*, 60-66.

[15] Pulido, L., Ghanem, E., Joshi, A., Purtill, J. J., & Parvizi, J. (2008). Periprosthetic joint infection: the incidence, timing, and predisposing factors. *Clinical orthopaedics and related research*, *466*, 1710-1715.

[16] Namba, R. S., Inacio, M. C., & Paxton, E. W. (2013). Risk factors associated with deep surgical site infections after primary total knee arthroplasty: an analysis of 56,216 knees. *JBJS*, *95*(9), 775-782.

[17] Malinzak, R. A., Ritter, M. A., Berend, M. E., Meding, J. B., Olberding, E. M., & Davis, K. E. (2009). Morbidly obese, diabetic, younger, and unilateral joint arthroplasty patients have elevated total joint arthroplasty infection rates. *The Journal of arthroplasty*, *24*(6), 84-88.

[18] Frade, J. V., Sousa, I., Marques, T., & Filipe, P. (2023). Acute paronychia: an atypical presentation of Monkeypox infection. *Enfermedades infecciosas y microbiologia clinica (English ed.)*, *41*(5), 317.

[19] Vrancianu, C. O., Serban, B., Gheorghe-Barbu, I., Czobor Barbu, I., Cristian, R. E., Chifiriuc, M. C., & Cirstoiu, C. (2023). The Challenge of Periprosthetic Joint Infection Diagnosis: From Current Methods to Emerging Biomarkers. *International Journal of Molecular Sciences*, *24*(5), 4320.

[20] Kalbian, I., Park, J. W., Goswami, K., Lee, Y. K., Parvizi, J., & Koo, K. H. (2020). Culture-negative periprosthetic joint infection: prevalence, aetiology, evaluation, recommendations, and treatment. *International Orthopaedics*, *44*, 1255-1261.

[21] Romanò, C. L., Petrosillo, N., Argento, G., Sconfienza, L. M., Treglia, G., Alavi, A., ... & Signore, A. (2020). The role of imaging techniques to define a peri-prosthetic hip and knee joint infection: multidisciplinary consensus statements.

[22] Li, A. E., Sneag, D. B., Greditzer IV, H. G., Johnson, C. C., Miller, T. T., & Potter, H. G. (2016). Total knee arthroplasty: diagnostic accuracy of patterns of synovitis at MR imaging. *Radiology*, *281*(2), 499-506.

[23] Kwee, R. M., & Kwee, T. C. (2020). 18F-FDG PET for diagnosing infections in prosthetic joints. *PET clinics*, *15*(2), 197-205.

[24] Sigmund, I. K., Puchner, S. E., & Windhager, R. (2021). Serum inflammatory biomarkers in the diagnosis of periprosthetic joint infections. *Biomedicines*, *9*(9), 1128.

[25] Jaberi, F. M., Parvizi, J., Haytmanek, C. T., Joshi, A., & Purtill, J. (2008). Procrastination of wound drainage and malnutrition affect the outcome of joint arthroplasty. *Clinical orthopaedics and related research*, *466*, 1368-1371.

[26] Marchant Jr, M. H., Viens, N. A., Cook, C., Vail, T. P., & Bolognesi, M. P. (2009). The impact of glycemic control and diabetes mellitus on perioperative outcomes after total joint arthroplasty. *JBJS*, *91*(7), 1621-1629.

[27] Visperas, A., Santana, D., Klika, A. K., Higuera-Rueda, C. A., & Piuzzi, N. S. (2022). Current treatments for biofilm-associated periprosthetic joint infection and new potential strategies. *Journal of Orthopaedic Research®*, *40*(7), 1477-1491.

[28] Kuiper, J. W., Willink, R. T., Moojen, D. J. F., van den Bekerom, M. P., & Colen, S. (2014). Treatment of acute periprosthetic infections with prosthesis retention: review of current concepts. *World journal of orthopedics*, *5*(5), 667.

[29] Fisher, C. R. (2023). *Immune Response to Periprosthetic Joint Infection and Non-Infectious Arthroplasty Failure* (Doctoral dissertation, College of Medicine-Mayo Clinic).

[30] Tsikopoulos, K., Drago, L., Meroni, G., Kitridis, D., Chalidis, B., Papageorgiou, F., & Papaioannidou, P. (2023). In vitro laboratory infection research in orthopaedics: Why, when, and how. *World Journal of Orthopedics*, *14*(8), 598.