Specific pathogens indicate higher risk of polymicrobial periprosthetic joint infection: a single-center retrospective study

Hao Li
Chinese PLA general hospital
Qiao Jiang
Chinese PLA General Hospital
Jiying Chen (chenjiyingpla@sina.com)
The First Medical Center, Chinese PLA General Hospital https://orcid.org/0000-0002-1313-0651

Research article

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Abstract

Background

Polymicrobial periprosthetic joint infection is a subset of periprosthetic joint infection and indicates disastrous outcomes. However, the incidence of polymicrobial PJI can be underestimated so we perform a single-center retrospective study with an intention to predict the incidence of polymicrobial PJI based on culture results.

Materials and methods

Medical records about 153 patients with PJI between 2017/1/1 and 2018/12/31 in a joint center were selected retrospectively. Multivariable analysis was utilized to evaluate the association between various pathogens and polymicrobial PJI.

Result

Staphylococcus aureus (OR:3.83, 95%CI(1.30,11.27), p-value = 0.015), coagulase negative staphylococci (OR: 2.68 ,95%CI: (1.10, 6.25), p-value = 0.028), Enterococcus spp (OR:6.46;95%CI(1.35,30.87),P-value = 0.020)andStreptococcusspp(OR:19.38, 95%CI:(3.57,105.21), p-value = 0.001) indicate higher risk of polymicrobial pathogens compared with other pathogens

Conclusion

Streptococcus spp and Enterococcus spp are associated with higher risk of polymicrobial PJI and more pathogens are like to be found in additional culture when these pathogens are detected by a single culture.

Introduction:

Total joint arthroplasty (TJK) is one of the most successful operations during the last century by which millions of patients with advanced joints diseases achieve pain-relief and recover joints function greatly[1, 2]. Despite the advantages of TJA, some complications occur following TJK. Periprosthetic joint infection (PJI) which is defined as infection involving the prosthesis and adjacent tissues is of most disastrous outcomes after prosthesis implantation.

PJI can be classified into monomicrobial PJI and polymicrobial PJI according to pathogens causing this dismal disease[1, 3, 4]. Polymicrobial PJI account for 10% of all PJI cases. Many studies report that polymicrobial PJI occur more frequently in the early period after prosthesis implantation. And traditionally, polymicrobial PJI have been considered to be consistently related to worse outcomes but have been

investigated in a relatively low number of studies[3]. The literatures about PJI mainly focus on monomicrobial infection.

Additionally, only very few risk factors of polymicrobial PJI have been identified until now. Marculescu and Cantey identified soft tissue defect, wound drainage and age>65 years as independent risk factors[5].

The interaction between pathogens and the association between causative agents and hosts become complex in polymicrobial infection compared to monomicrobial infection. Some bacteria suppress the growth of other pathogens when incubated in a same medium. Besides, a number of Researchers point out that some bacteria synergize with other pathogens in a bid to get through the burden of host immune response[6]. Biofilm, consisted of fibrinogen and protein deriving from hosts and pathogen respectively, is one way by which pathogens can perform immune evasion, resistance and pathogenicity[7]. coagulase negative staphylococci (CNS) play an important part in biofilm formation by facilitating the attachment of bacteria. And various pathogens are of different roles in forming biofilm[3].

Particular pathogen can interact with others in the process of polymicrobial PJI and may be the only detectable pathogen in one cultivation. We hypothesis that we can find particular pathogen that hint the existence of polymicrobial PJI in an effort to guide the diagnosis and treatment of this polymicrobial infection. As a result, we perform a retrospective single-center study with an intention to predict the risk of polymicrobial PJI based on causative agents revealed by culture results.

Methods And Materials:

Study design:

This single-center retrospective cohort study major in patients undergoing periprosthetic joint infection (PJI) which was diagnosed according to Musculoskeletal Infection Society criteria (MSIS) for periprosthetic joint infection. We obtained the clinical records of patients who suffered from PJI between 2017/1/1 and 2018/12/31 to predict the risk of polymicrobial PJI based on culture results of pathogens. After selection, a total of 153 patients were included and the process was shown in figure 1.[8]

Polymicrobial PJI was defined according to the criteria proposed by Steckelberg and Osmon[4]. It was summarized in three different parts:

1). Two or more identical infectious organisms detected by joint aspiration and at least one intraoperative tissue sample

2). Two or more identical infectious organisms detected by at least two intraoperative tissue samples

3). Two or more identical infectious organisms detected by at least one intraoperative tissue sample and a clinically evident PJI (i.e. sinus tract communication with the joint space, purulence in the joint, acute inflammation)

Patients were included according to following criteria:

1. PJI patients were diagnosed according to MSIS
2. PJI patients undergoing one-stage revision and two-staged revision because of PJI
3. Their culture results were accessible to researchers.

Patients were excluded according to the following criteria.

1. Their medical records were not accessible
2. Patients undergoing revisions because of dislocation, aseptic loosening and periprosthetic fracture.

Specimen used for culture were synovial fluids and tissue. Synovial fluids were obtained by arthrocentesis before revisions and Saline solution lavage was used if we were not accessible to enough synovial fluid(dry type)[9]. Specimen used in tissue culture were obtained intraoperatively. The duration of culture lasted for 2 weeks.

Statistical analysis:

The baseline characterizes of this study population are described as frequencies and percentages. T test is adapted if normal distribution is achieved for continuous variables. Otherwise rand sum test is utilized. Dichotomous data are described by chi-squared test when the value is greater than 5. And when the values are fewer than 5, Fisher exact test is used to finish comparation. The association between polymicrobial PJI and different pathogens is analyzed by logistic regression. variables in this logistic regression model includes BMI, ASA score and different pathogens and these pathogens entered regression model one by one. Statistics results were considered as significant if corresponding OR>1 and p value<0.05. SPSS21.0 was used to perform statistical analyses.

Results:

Demographic data and results of univariate analysis

Of the 153 total patients who underwent surgery, 29 cases were noted to be polymicrobial infection. The average age of monomicrobial PJI patients and polymicrobial PJI is 61.4 and 57.9, respectively. Univariate analysis results didn't indicate significant statistic difference(P=0.233). Females accounted for 54% of monomicrobial PJI patients and 44.8% of patients with polymicrobial PJI comparatively. Similarly, there is no significant difference between the two groups in BMI, percentage of hips, height, weight, ASA score, diabetes, kidney diseases, inflammatory joint diseases and other conditions. These details had been summarized in figure 2.

Variables	Monomicrobial PJI	Polymicrobial PJI	P-value
Age（mean）	61.4	57.9	0.233
Sex, F/M(%female)	54	44.8	0.372
Height(m)	1.64	1.65	0.340
Weight(kg)	69.1	78.5	0.141
BMI (kg/m*2)	25.5	28.6	0.355
Hips, n (%)	49.2	65.5	0.113
Knees, n (%)	50.8	34.5	0.113
ASA	2.06	2.07	0.811
Diabetes n (%)	15.7	17.2	0.798
Kidney disease n (%)	0.8	0	1
Liver disease n (%)	2.4	3.4	0.755
Lung disease n (%)	1.6	0	1.0
Heart disease n (%)	1.6	3.4	0.47
Inflammatory joint disease n (%)	6.5	13.8	0.347

Pathogens Hinting the Existence of Polymicrobial Infection:

In a bid to maintain enough samples size, pathogens detected in this research were classified into CNS(42 cases), Staphylococcus aureus(8 cases), streptococcus spp(17 cases), fungi(3 cases), Enterococcus spp(7 cases), Gram-negative bacteria(6 cases), and other pathogens(11 cases). Then logistic regression was performed and the result was shown in figure3. Staphylococcus aureus (OR:3.83 , 95%CI(1.30,11.27), p-value=0.015) , CNS(OR: 2.68 ,95%CI: (1.10, 6.25), p-value=0.028), Enterococcus spp (OR:6.46; 95%CI(1.35,30.87,P-value=0.020)and Streptococcus spp(OR:19.38, 95%CI:(3.57,105.21), p-value=0.001) indicate higher risk of polymicrobial pathogens compared with other pathogens. While similar results hadn’t be found in other pathogens such as Gram-negative bacteria and fungi.

Pathogens	number	Polymicrobial PJI, n	OR	95%CI for OR	P-value
Staphylococcus aureus	17	7	3.83	(1.30,11.27)	0.015
CNS	42	13	2.63	(1.10,6.25)	0.028
Enterococcus spp	7	4	6.46	(1.35,30.87)	0.020
Streptococcus spp	8	6	19.38	(3.57,105.21)	0.001
Gram-negative bacteria	6	2	2.279	(0.39,13.28)	0.362
Fungi	3	0	0.00	(0, ∞)	0.999
Other pathogens	11	5	3.67	(0.96,14.09)	0.58

Discussion:

Polymicrobial infection, accounting for up to 10% of PJI, indicates disastrous outcomes in total joint arthroplasty compared with monomicrobial infection[10, 11]. Polymicrobial PJI is caused by more than one pathogen and the interaction between pathogens and hosts is more complex. These different pathogens collaborate with each other in a community to form biofilms, establish drug resistance and propagate infections[11, 12]. This synergistic interaction between pathogens makes difficult the pathogenicity and treatment of infection. As a result, polymicrobial PJI often point to worse outcomes and heavier burden.

This study is the first to estimate the association between different pathogens detected in a single culture and the risk of polymicrobial PJI. Data provided by out study can server as a guide in predicting the existence of polymicrobial PJI. Our results revealed that streptococcus spp, CNS Staphylococcus aureus and Enterococcus spp indicated higher risk of polymicrobial infection. However, CNS and Staphylococcus aureus are the most common pathogens in PJI. This hints that CNS and staphylococcus can interact with others to establish PJI and evade their hosts. It is a terrible news because the pathogenicity of traditional monomicrobial PJI can be more intricate than we think.

Our results also suggested that streptococcus spp and enterococcus spp detected by culture indicate higher risk of polymicrobial PJI compared to other pathogens. This means that other pathogens are more likely to be found in additional specimen culture when either of the two pathogens is revealed by a single culture. It hints that surgeons can send more specimens for culture during operation to guide the application of postoperative antibiotics if streptococcus spp or enterococcus spp was grown in preoperative culture medium because these two pathogens indicated higher risk of polymicrobial PJI and additional culture are likely to show “new” bacteria. The following antimicrobial susceptibility testing (AST) results of these pathogens could help doctors eradicate remaining causative agents more

effectively. Besides, mNGS(metagenomic next generation sequencing) can be utilized in these specimen to detect more species because of higher sensitivity compared to culturation.

Our multivariable analysis indicated that enterococcus spp had a high correlation with polymicrobial periprosthetic PJI (OR=7). A European study focused on PJI caused by enterococcus spp identified 107 polymicrobial PJI cases out of 203 patients[13]. An American study focused on PJI pathogens had comparable results[14, 15]. Despite relatively small sample size, our results are in accordance with their observations. Here are several explanations of this phenomenon. Enterococcus spp is an important part of Intestinal tract normal flora and enterococcus infection may indicate the impairment in gut barrier by which most of intestinal flora are trapped in gut. So periprosthetic infection caused by enterococcus spp which is shown in culture is likely to be triggered by polymicrobial infection, not just enterococcus spp alone.

There are also some limitations in this research: the first limitation of this study is reflected by the retrospective design. Secondly, our institution is a tertiary medical center that provided therapy for PJI patients who had received treatments from a different institution and this can lead to selection bias. Thirdly, the infected joints included in this study were hips and knees and there were no elbows, ankles and other joints. Finally, this research was performed in a single center and the sample size of this study is relatively small, especially PJI cases caused by fungi.

Conclusions:

In summary, our results have revealed that streptococcus spp and enterococcus spp are associated with higher risk of polymicrobial PJI which indicates worse outcomes. Surgeons can send more specimen for additional culture and antimicrobial susceptibility testing (AST) when these pathogens are detected by preoperative culture in a bid to guide precise utility of postoperative antibiotics.

Abbreviations:

TJA: Total joint arthroplasty

PJI: periprosthetic joint infection

MSIS: Musculoskeletal Infection Society criteria

CNS: coagulase negative staphylococci

AST: antimicrobial susceptibility testing

Declarations:

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Availability of data and materials:

All data and materials were in full compliance with the journal's policy.

Ethics approval and consent to participate

This study was approved by the institutional review board of our hospital (Chinese People's Liberation Army General Hospital).

Consent for publication

We have obtained consent to publish from the participants.

Competing interests

All authors declare that they have no competing interests.

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Figures

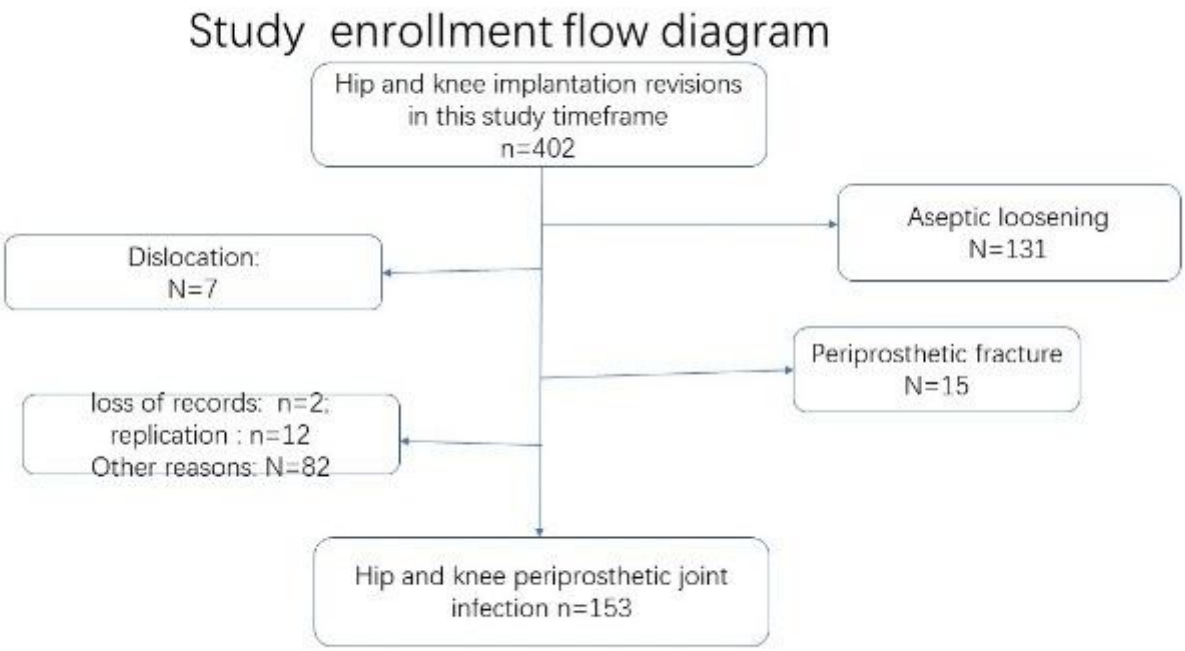

Figure 1

Study enrolment flow diagram

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Figure 2

the demographic characteristics of PJI patients

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Figure 3

Pathogens Indicating the Existence of Polymicrobial PJI