Is Joint Aspiration to Rule Out Prosthetic Joint Infection Required Before every Revision Joint Arthroplasty? Validation of Institutional Criteria using the New European Bone and Joint Infection Society definition

É Necessária a Realização de Artrocentese para Exclusão de Infeção antes de cada Artroplastia de Revisão? Validação dos Critérios Institucionais Utilizando a Nova Definição da new European Bone and Joint Infection Society

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ABSTRACT

Introduction: Synovial fluid investigation is the best alternative to diagnose prosthetic joint infection (PJI) before adequate microbiological/histology sampling during revision surgery. Although accurate preoperative diagnosis is certainly recommended, puncturing every patient before revision arthroplasty raises concerns about safety and feasibility issues especially in difficult to access joint (e.g., hip). Currently, there is no clear guidelines regarding optimal indications to perform preoperative joint aspiration to diagnose PJI before revision surgery. We hypothesize that our institutional criteria are appropriate to identify potentially infected joints before surgery while saving an unnecessary number of procedures.

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The main goal of this study is to determine the accuracy of our institutional criteria in picking up potentially infected joints using the new New European Bone and Joint Infection Society (EBJIS) PJI definition as the standard.
Methods: We performed a retrospective review including all patients that underwent total hip or knee arthroplasty single or first-stage revision surgery (regardless of preoperative diagnosis) between January 2013 and December 2019. We applied the new EBJIS PJI definition criteria and we studied patients whose institutional criteria were applied to perform preoperative joint aspiration.
Results: After applying the EBJIS definition 38 (35.8%) were classified as confirmed infections, 10 (9.4%) as likely infected and 58 (54.7%) as infection unlikely. Of those, 37 confirmed infection cases, 9 likely infected cases and 32 infection unlikely cases did have indication for preoperative synovial fluid collection before surgery.
Conclusion: Our proposed institutional criteria identify the majority of infected or likely infected patients, while saving a significant number of unlikely infected cases from unnecessary and potentially risky procedures.

Keywords: Arthroplasty, Replacement, Hip; Prosthesis-Related Infections; Synovial Fluid

RESUMO

Introdução: A investigação do líquido sinovial é a melhor alternativa para diagnosticar a infeção da articulação protésica (IAP) antes da recolha de amostras microbiológicas/histológicas adequadas durante a cirurgia de revisão. Embora um diagnóstico pré-operatório preciso seja certamente recomendado, a punção de todos os doentes antes da artroplastia de revisão suscita preocupações quanto a questões de segurança e viabilidade, especialmente em articulações de difícil acesso (por exemplo, anca). Atualmente, não existem diretrizes claras relativamente às indicações ideais para realizar a aspiração articular pré-operatória para diagnosticar a IAP antes da cirurgia de revisão. A nossa hipótese é que os nossos critérios institucionais são adequados para identificar articulações potencialmente infetadas antes da cirurgia, poupando um número desnecessário de procedimentos. O principal objetivo deste estudo é determinar a precisão dos nossos critérios institucionais na identificação de articulações potencialmente infetadas, utilizando a nova definição de IAP da New European Bone and Joint Infection Society (EBJIS) como padrão.
Métodos: Realizámos uma revisão retrospetiva incluindo todos os doentes que foram submetidos a cirurgia de revisão de artroplastia total da anca ou do joelho simples ou de primeiro estágio (independentemente do diagnóstico pré-operatório) entre janeiro de 2013 e dezembro de 2019. Aplicámos os novos critérios de definição de IAP da EBJIS e estudámos os doentes cujos critérios institucionais foram aplicados para realizar aspiração articular pré-operatória.
Resultados: Após a aplicação da definição EBJIS, 38 (35,8%) foram classificados como infeções confirmadas, 10 (9,4%) como infeções prováveis e 58 (54,7%) como infeções improváveis. Destes, 37 casos de infeção confirmada, 9 casos de infeção provável e 32 casos de infeção improvável tinham indicação para recolha de líquido sinovial pré-operatório antes da cirurgia.
Conclusão: Os critérios institucionais propostos identificam a maioria dos doentes infetados ou provavelmente infetados, poupando um número significativo de casos de infeção improvável a procedimentos desnecessários e potencialmente arriscados.

Palavras-chave: Artroplastia da Anca; Infecções Relacionadas com a Prótese; Líquido Sinovial

INTRODUCTION

Total joint arthroplasty (TJA) is considered one of the most successful surgical procedures in modern times. It can restore joint mobility, provide pain relief, and improve quality of life.[1] Prosthetic joint infection (PJI) represents the second most frequent complication, after aseptic loosening, but also the major threat.[1] It is a severe healthcare and socio-economic issue even now, occurring worldwide in 1.4%–2.5% of patients with total arthroplasty.[2] PJI presents with a wide variety and severity of signs and symptoms, from full blown sepsis to a paucisymptomatic joint mimicking aseptic complications.[3] This group of so-called "low-grade" PJI is difficult to diagnose but, if not treated properly, leads to infection persistence, multiple revisions surgeries and severe impairment of quality of life.[4,5] Recently, the European Bone and Joint Infection Society (EBJIS) proposed a new PJI definition[6] that captures more of these patients. It has been shown to have increased sensitivity compared to previously proposed

definitions, i.e., classifies as infected cases that would otherwise be called not infected.[6,7]

Synovial fluid investigation is the best alternative to diagnose PJI preoperatively before adequate microbiological/histology sampling during surgery. Nonetheless, there are no clear guidelines regarding optimal indications to perform preoperative joint aspiration before revision surgery. Some feel that if serum inflammatory parameters such as c-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) are normal the likelihood of infection is low and there is no need to do it. Considering seronegative PJI do exist,[8-10] others advocate for preoperative aspiration in every case where revision surgery is being considered. Still, puncturing every patient before revision arthroplasty raises concerns about safety and feasibility issues especially in difficult to access joint that require imaging guided procedures.

For the past few years, we have developed our own institutional recommendations on when to perform joint aspiration before revision arthroplasty. We hypothesize that our institutional criteria are appropriate to identify potentially infected joints before surgery while saving an unnecessary number of procedures. The main goal of this study is to determine the accuracy of our institutional criteria in picking up potentially infected joints using the new EBJIS PJI definition as the standard.

MATERIAL AND METHODS

We performed a retrospective review of our institution's prospective database. We included all patients that underwent total hip or knee arthroplasty single or first-stage revision surgery (regardless of preoperative diagnosis) at our institution between January 2013 and December 2019. We received IRB approval prior to the initiation of the present study.

Data concerning patient demographics and original joint replacement surgery were collected. Detailed clinical information before revision surgery was collected with a special emphasis on variables relevant for the diagnosis of PJI (e.g., presence of sinus tract, history of recent fever or bacteremia, antibiotic therapy at the time of surgery and blood inflammatory parameters). Synovial fluid investigation results as well as intraoperative findings (e.g., purulence) and definitive microbiologic and histological results were also recorded.

Cases without minimum required diagnostics to classify them as aseptic: less than four intraoperative microbiology samples (synovial fluid, tissue samples, implant sonication) (n=183) and no preoperative/intraoperative synovial fluid differential leukocyte count (n=64) were excluded. To reduce bias, we also excluded cases with conditions that influence synovial fluid testing accuracy (i.e., inflammatory arthritis, metal-on-metal bearing, periprosthetic fracture, antibiotic within two weeks prior to revision surgery, revision surgery less than 6 weeks after index procedure and also acute hematogenous infections with less than 4 weeks symptoms) (n=11).

After applying the new EBJIS PJI definition criteria, we were able to categorize our patient population into three distinct groups: (1) unlikely infection, (2) likely infection or (3) confirmed infection.

We were also able to identify patients that should have undergone joint investigation to rule out infection, according to our own institutional criteria. Preoperative joint aspiration is recommended if any of the following criteria are met: 1) elevated CRP and/or ESR; 2) early failure (in the first 2 years) or repeat failure (after previous revision arthroplasty either septic or aseptic); 3) high clinical suspicion/risk factors are present, such as previous wound healing issues after index procedure, joint pain arising after documented or presumed bacteremia, history of previous PJI (either in the same or a different joint) or immunosuppressed patients.

Statistical analysis

An analysis of the institutional criteria performance was made between the three groups, to calculate values of sensitivity and negative predictive values (NPV), and specificity and positive predictive values (PPV) with 95% of CI. Accuracy values are expressed in percentage.

RESULTS

A total of 364 revision THAs or TKAs were performed during the study period. After excluding criteria, a total of 106 patients were included. After applying the EBJIS definition 38 (35.8%) were classified as confirmed infections, 10 (9.4%) as likely infected and 58 (54.7%) as infection unlikely. Of those, 37 confirmed infection cases, 9 likely infected cases and 32 infection unlikely cases did have indication for preoperative synovial fluid collection before surgery (Table 1).

Table 2 summarizes performance of described institutional criteria. As we are mostly interested in not missing potentially infected joints, we calculated the criteria's sensitivity by grouping infected likely and confirmed cases together. Both sensitivity and negative predictive value are over 90%.

Table 1. Cross tabulation between definitive PJI status and indication to perform preoperative joint puncture.

	EBJIS Classification	Patients selected to preoperative arthrocentesis
Confirmed infection	38	37
Likely infection	10	9
Unlikely infection	58	32

Table 2. Diagnostic accuracy of selected criteria.

Statistic	%	95% CI
Sensitivity	95.8% (46/48)	85.8-99.5
Specificity	44.8% (26/58)	31.7-58.5
Positive Predictive Value	59.0%	47.2-70.0
Negative Predictive Value	92.9%	76.5-99.1
Accuracy	67.9%	58.2-76.7

DISCUSSION

PJI diagnosis remains challenging due to the lack of a gold-standard test. Nevertheless, it is indisputable that accurate diagnosis is the starting point for correct PJI management. It greatly influences the planned medical and/or surgical treatment. Preoperative diagnosis is even more difficult as you do not have complete information that adequate intraoperative microbiological and histological examination can offer and it is therefore often not possible to be sure especially in low grade infections [1]

There is nowadays a greater understanding of the so-called low-grade infections and how unrecognized infections may negatively influence outcome after revision arthroplasty.[11,12] With these concerns in mind, the European Bone and Joint Infection Society (EBJIS) recently proposed a three-level diagnostic approach for PJI definition.[6] Not only has it been shown to increase diagnostic sensitivity,[7,13,14,15] but also that diagnosis made with preoperatively available information correlates better with definitive diagnosis after revision surgery.[7,15]

At the preoperative stage, synovial fluid investigation is the best alternative to diagnose PJI.[16] It not only allows assessment for microbiological analysis but also looks at the host's inflammatory response within the affected joint. There are nonetheless no clear guidelines on which patients require joint aspiration before revision arthroplasty. It is not clear if all revision arthroplasty candidates should be systematically investigated or whether some set of criteria is adequate for patient selection.

It has previously been suggested that patients with normal serum inflammatory markers have a very low probability of infection and it is therefore not necessary to investigate further.[17] However, it is now clear that PJI may be present without elevated serum inflammatory markers especially in the presence of less virulent microorganisms.[8-10] Consequently, there are those advocating for joint aspiration before every revision joint arthroplasty. Puncturing every patient before revision arthroplasty raises concerns about safety and feasibility issues especially in difficult to access joint (e.g., hip), that often require operative room time, fluoroscopy/ultrasound guidance thus increasing resource consumption and costs.

To help identify patients who should not undergo revision surgery without having the joint investigated for infection, our multidisciplinary infection team, developed its own institutional criteria.

It is widely recognized that elevated serum inflammatory parameters in the presence of a painful joint should raise the suspicion for PJI.[18,19] In these cases, it is indisputable that joint aspiration should be performed.[20-23] Timing of failure is also very important as it has been shown that early failures are more often associated with PJI than late failures.[24] The importance of careful clinical history should never be undervalued though. Previous wound healing issues after index procedure such as prolonged wound healing or superficial dehiscence have long been recognized as significant risk factors for PJI.[25,26] Painful joints in the context of bacteremia are also a significant risk factor for PJI[27,28] as is an history of PJI in the afflicted joint naturally but also in a different joint.[29]

Preoperative joint aspiration in our institution is therefore recommended if any of the following criteria are met: 1) elevated CRP and/or ESR; 2) early failure (in the first 2 years) or repeat failure (after previous revision arthroplasty either septic or aseptic); 3) high clinical suspicion/risk factors are present, such as previous wound healing issues after index procedure, joint pain arising after documented or presumed bacteremia, history of previous PJI (either in the same or a different joint) or immunosuppressed patients. If any of these criteria are met, preoperative joint aspiration and/or percutaneous biopsies should be performed. However, surgeons are still encouraged to investigate if there are any other concerns about the possibility of infection.

This paper shows the proposed criteria have very high sensitivity and negative predictive value even using the EBJIS PJI definition, who is at the high end of the sensitivity spectrum, as the reference standard. This means they are able to correctly identify those patients at risk of having PJI while avoiding a significant number of unnecessary procedures in patients with low risk of PJI.

In the present cohort, almost all patients who were ultimately diagnosed with infection confirmed or likely had a preoperative joint aspiration indicated. Still, this paper does not address is the accuracy and limitations associated with synovial fluid investigation for the PJI diagnosis. Microbiology has of course limited sensitivity, especially in cases of chronic low-grade infections,[30] and differential leukocyte count is also limited, especially in the context of active inflammatory disease (crystal arthropathy, active inflammatory disease, periprosthetic fracture or in the first few weeks after the index procedure) or previous antibiotic therapy.[6,31,32] This might be improved by the use of alternative biomarkers such as synovial c-reactive protein or others.[33,34]

On the other side, around half of the cases whose final diagnosis was infection unlikely, we avoided performing an unnecessary diagnostic procedure with associated risks and costs.

CONCLUSION

A successful screening test should have high sensitivity, be widely available and cost-effective. Our proposed institutional criteria identify the majority of infected or likely infected patients, while saving a significant number of unlikely infected cases from unnecessary and potentially risky procedures. They seem to be a valid rationale for selecting patients that should be punctured before revision arthroplasty.

Presentations/Apresentações:

Part of the work was presented as an oral presentation at the 39th Annual Meeting of the European Bone and Joint Infection Society - Ljubljana, 7-9 october 2021 and at the 23rd EFORT Annual Congress - Lisboa 22- 24 June 2022

Responsabilidades Éticas

Conflitos de Interesse: Os autores declaram a inexistência de conflitos de interesse na realização do presente trabalho.
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Confidencialidade dos Dados: Os autores declaram ter seguido os protocolos da sua instituição acerca da publicação dos dados de doentes.
Proteção de Pessoas e Animais: Os autores declaram que os procedimentos seguidos estavam de acordo com os regulamentos estabelecidos pelos responsáveis da Comissão de Investigação Clínica e Ética e de acordo com a Declaração de Helsínquia revista em 2013 e da Associação Médica Mundial.
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Declaração de Contribuição

RS: Preparação do material, recolha e análise de dados.
SED, AV e AR: Escreveram o primeiro rascunho e prepararam o material, recolheram dados e analisaram
Todos os autores contribuíram para a conceção e desenho do estudo e aprovaram o manuscrito final.

Contributorship Statement

RS: Prepared material preparation, collected data and analysis.
SED, AV and AR: Wrote the first draft and prepared material, collected data and analysis
All authors contributed to the study conception, design and approved the final manuscript.

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