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EKA survey: diagnosis of prosthetic knee joint infection

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Abstract
Purpose Due to the juvenility of research in the field of periprosthetic joint infection (PJI), approaches employed for diagnosis of PJI vary amongst surgeons in different geographic regions. The aim of this study was to determine common diagnostic approaches utilized by European knee arthroplasty surgeons for the diagnosis of PJI.
Methods A task force was established for questionnaire development, consisting of surgeons and clinical researchers who each had a record of publishing in the field of PJI. A pool of items was initially generated from a Medline literature search. These were organized into a file and independently sent to each task force member for evaluation and additional supplementation. After reaching a consensus, a final online version was generated and administered to all 4865 members of the "European Society of Sports Traumatology Knee Surgery & Arthroscopy".
Results There were 262 respondents between August 2015 and March 2016. Most European surgeons (41.1 %) diagnose between 2 and 5 PJIs yearly, and only 5.8 % diagnose >30 PJIs per year. Serum tests to rule out infection were commonly CRP (97.7 %), leucocyte count (73.6 %) and microbiology cultures (45.3 %), while serum interleukins were least common (<5 %). Synovial fluid exams most commonly included microbiology (97.7 %), leucocyte count (74.8 %), percentage polymorphonuclear cells (65.8 %), synovial fluid CRP (26.4 %) and α-defensin (19.4 %). Conventional radiographs represent the most common radiographic exam (87.6 %) followed by SPECT-CT scans (41.7 %). The majority (93.6 %) take biopsies at the time of surgery, 62.0 % take 1–5 biopsies, and 34.9 % take >5. Most biopsies (98.8 %) are sent for culture exams and 72.5 % for histology, and 36.4 % of surgeons send the implants for sonication.
Conclusion Microbiology and cell count remain the most commonly applied synovial fluid tests in Europe, while α-defensin and leucocyte esterase are currently less common. Serum interleukins have not gained widespread use. Implant sonication, despite evidence of diagnostic effectiveness, was only applied by one-third of survey respondents, highlighting the problematic issues of cost and accessibility of some tools. The results highlight the current state of European diagnostic practice, emphasizing the areas of divergence from state of evidence and demonstrating the need for development of standard diagnostic algorithms.
Level of evidence Cross-sectional survey, Level IV.

Keywords Prosthetic joint infection · PJI · Knee infection · Diagnosis · Diagnostic · TKA · Knee replacement

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Introduction

The rising number of total joint arthroplasty (TJA) procedures performed annually is being accompanied by an increase in encountered complications [8]. Prosthetic joint

infection (PJI) is one of the major complications increasingly gaining attention from the orthopaedic community.

Accurate and timely diagnosis of PJI is of fundamental importance and has a great impact on the subsequent treatment regime [7]. While "diagnosing a PJI" sounds like a simple concept, the wide diversity of proposed diagnostic tools that are increasing in number indicates that diagnosis of PJI is complex [1]. There is no general agreement on the tools and pathways for the diagnosis and management of PJI.

Due to the difficulty of conducting research in the field of PJI, expert opinion and consensus still play an important role in assembling clinical recommendations. These furthermore initiate the basis for clinical research questions, which can subsequently be addressed by higher-level studies [12]. Surveys also ensure a concordance between the state of practice and the level of available evidence as a form of audit.

An international survey was performed in order to analyse the different modalities of diagnosing PJI. The aim of this study was to capture the current state of practice regarding diagnosis of knee PJI by surveying European knee surgeons.

Materials and methods

Survey development

With the support of the European Knee Associates (EKA), a questionnaire evaluating the diagnosis of PJI was developed to determine the common practices and preferences of European surgeons. A task force was established for item development, consisting of surgeons and clinical researchers who each had a record of publishing in the field of PJI.

A pool of items was initially generated from a literature search; these were organized into a file and independently sent to each task force member for evaluation and additional inputs. An independent investigator collected the responses from each member. A final version comprised 12 question categories on the diagnosis of PJI and was sent to all members for final discussion and consensus agreement ("Appendix" section).

Survey administration

The final items of the survey were incorporated into an online form using a web-based survey tool (Survey Monkey, surveymonkey.com, Portland, OR). The survey was launched in August 2015 by sending a web-based link to all 4865 members of the "*European Society of Sports Traumatology, Knee Surgery & Arthroscopy*" (ESSKA). The links were also published on the EKA website.

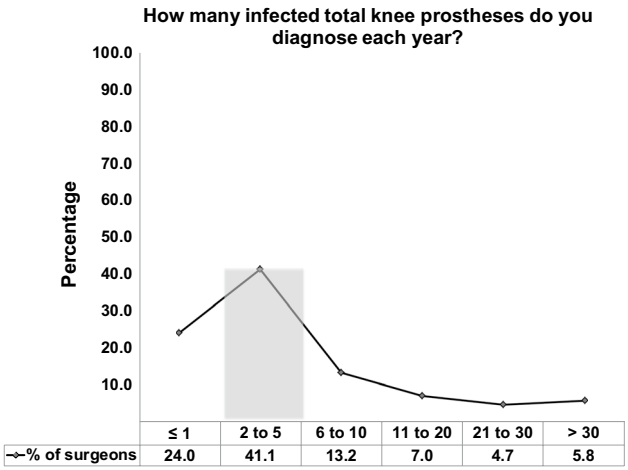

Fig. 1 Graph showing the number of PJI diagnosed per respondent

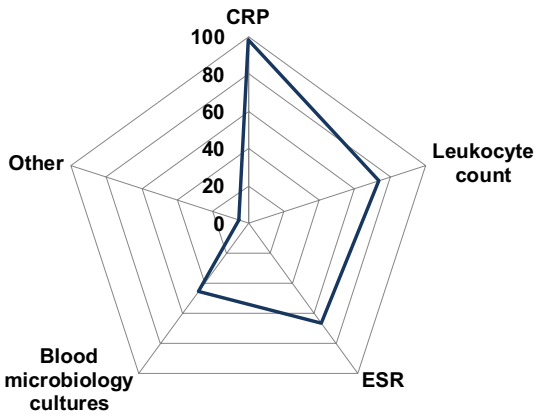

Fig. 2 Web graph demonstrating the most frequently tested serum parameters for the diagnosis of PJI. Other: procalcitonin, interleukin-6, septifast, glucose, fibrinogen, alpha-defensin. *CRP* C-reactive protein, *ESR* erythrocyte sedimentation rate

Statistical analysis

Based on the population size of 4865 society members to which the survey was sent and assuming a normal distribution with a 6 % margin of error, the minimum required survey respondents were calculated to be 253 using the following formula:

$$\frac{\frac{Z^2 p(1-p)}{e^2}}{1+\frac{Z^2 p(1-p)}{e^2 N}}$$

Z is the number of standard deviations; a given proportion is away from the mean, p percentage in decimal form, N population size, e margin of error.

All survey results were tabulated and frequencies calculated. Results were presented as means and percentages.

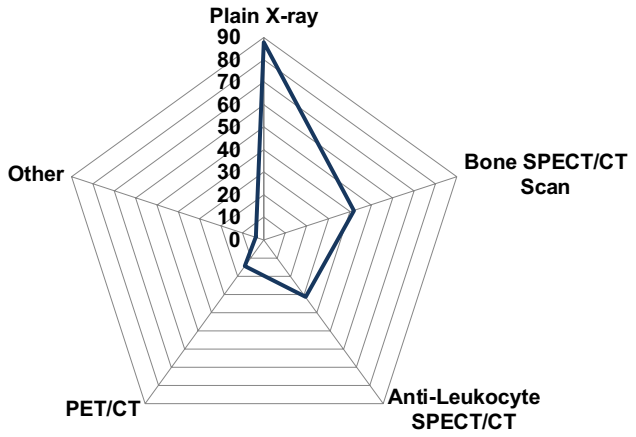

Fig. 3 Web graph illustrating the most commonly used radiographic exams. *CT* Computed tomography, *PET* positron emission tomography, *SPECT* single-photon emission computed tomography

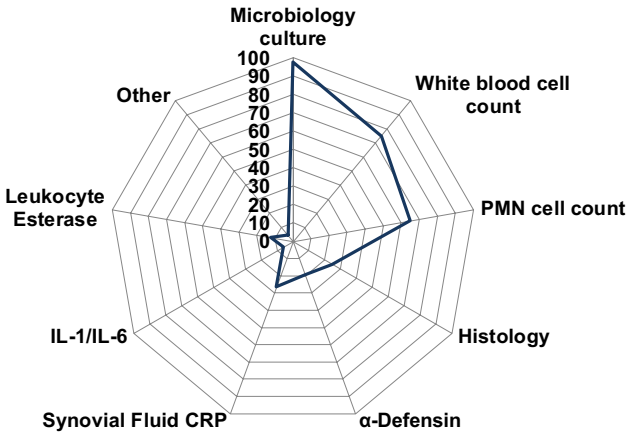

Fig. 4 Web graph illustrating the most commonly applied synovial fluid tests. *CRP* C-reactive protein, *IL* interleukin, *PMN* polymorphonucleocyte

Results

By March 2016, 262 respondents completed the survey. They performed an estimated 31,575 knee replacement procedures annually and diagnosed 1907 knee PJIs per year. Although most respondents 107 (41.1 %) diagnosed between 2 and 5 PJIs per year, the majority of cases 1050 (55 %) were diagnosed in high volume centres (at least 20 knee PJI per year) (Fig. 1). Over 50 % of respondents agreed on the following definitions for infection:

1. Acute infection: <4 weeks of symptoms
2. Delayed onset: 3–12 months duration of symptoms
3. Late onset: Symptoms begin >12 months from index procedure

The most commonly examined serum parameter for the diagnosis of PJI was C-reactive protein (CRP), commonly used by 258/262 (97.7 %) of surgeons; the least common were serum interleukin-6 and pro-calcitonin which were used by <5 % of surgeons (Fig. 2). Conventional radiography was the most frequently used radiographic tools for the initial diagnosis of PJI (229/262, 87.6 %, Fig. 3).

Most respondents (256/262, 97.7 %) would request microbiology cultures of synovial fluid aspirate, followed by synovial fluid white cell count (193/262, 74.8 %) and synovial cell polymorphonucleocyte percentage (172/262, 65.8 %) (Fig. 4).

Most would take tissue (239/262, 91.5 %) and synovial fluid (235/262, 89.9 %) cultures, while 70 (26.7 %) of those surveyed still take swab cultures. The majority of surgeons take tissue biopsies during the revision procedure (245/262, 93.6 %); however, 109 (41.5 %) would perform separate arthroscopic biopsies, and 55/262 (21.2 %) would perform separate open biopsies. The preferred number of biopsies ranged between 1 and 5 (162/252, 62 %); 92/262 (35 %) would take >5 biopsies. Biopsy samples are most frequently sent for microbial culture exams (259/262, 98.8 %) for a mean of 11 ± 7 days, 189/262 (72.4 %) would request histological evaluation, and 44/262 (16.3 %) would request polymerase chain reaction (PCR) of the samples. Most respondents rely on an internal laboratory within the same premises (186/262, 71.2 %), while the remaining depend on an external laboratory. The majority of respondents (168/262, 64 %) do not sonicate the explanted prosthesis.

Discussion

The most important finding of the present study was that there was a very high agreement amongst respondents on the use of serum CRP, tissue biopsies and conventional radiographs as aids for diagnosing PJI. Most surgeons do not sonicate the implants highlighting difficulties associated with the accessibility and costs of the diagnostic tool. Furthermore, it is apparent that the majority of PJIs are diagnosed in high volume centres. This trend can be encouraging, given that literature data demonstrate that the outcome of disease entities such as PJI requiring multidisciplinary management is improved when treated in high volume centres [2].

The fact that nearly all respondents routinely test for serum CRP is concordant with the evidence of its high effectiveness for ruling out PJI [3]. Serum leucocyte count,

representing the second most commonly examined serum parameter by respondents, has been shown in literature to neither be reliable for ruling out nor confirming PJI [1]. Thus, it is less useful as a diagnostic tool, but does play a role as a septic criterion [3]. The most effective laboratory serum marker for ruling out PJI is interleukin-6 (IL-6) [3], but its utility amongst European surgeons is however limited to a minority of respondents comprising <5 %. Serum IL-6 testing may be prohibitive secondary to cost, accessibility and practicality issues that may need to be addressed in the future. Further markers such as procalcitonin levels in serum and erythrocyte sedimentation rate (ESR) have shown either low sensitivity or specificity, respectively [4, 5].

The fact that plain X-ray represents the imaging modality of choice is likely resultant to its role during the primary diagnostic work-up of a painful prosthetic joint. Nuclear imaging, which follows as a preferred imaging modality in Europe based on the responses, has not been shown to be more effective than other more feasible diagnostic tools for ruling out PJI and is evidently poor for ruling in or confirming PJI [9–11].

It should be emphasized, taking into account the predominance of bacteriological testing in the results of the survey, that bacteriology of synovial fluid is highly effective for confirming an infection in case of positive microbial growth but has poor potency for ruling out PJI. However, the purpose of bacteriology is also to establish calculated antibiotic treatment [13]. This in turn underlines the importance of moving the spotlight towards other synovial parameters for which there is sufficient evidence supporting high potency and for ruling out PJI, including synovial fluid white cell count and synovial fluid polymorphonucleocyte differentiation (sensitivity 0.90 (95 % CI, 0.84–0.93), specificity 0.88 (95 % CI, 0.83–0.92)) [15]. Both synovial white cell count and polymorphonucleocyte differentiation were shown to be used by <75 % of surgeons, highlighting the need for more attention to this issue to increase the rate of application. On the other hand, swab cultures, despite being performed by a third of the respondents, have high false-positive and false-negative rates and were shown to not corroborate with intraoperative cultures (70 and 89 % sensitivity and specificity compared to 93 and 98 % tissue culture sensitivity) [6, 14].

With regard to diagnosing PJI using sonication, the majority of respondents did not sonicate implants. However, there is sufficient evidence to support that implant sonication is very effective for confirming PJI with the highest positive likelihood ratio amongst diagnostic tools [1, 10]. However, the lack of sonication highlights possible difficulties associated with accessibility and cost of the test.

Despite the interesting reflection of this study on the diagnostic practices for PJI in Europe, there are several limitations including the fact that the survey was sent out to members of ESSKA, which may not be representative of all surgeons in Europe. Furthermore, this is a surgeon-based survey, meaning that each respondent was given equal weight, independent of surgical volume; therefore, the survey provides a reflection of overall surgical opinion and may not be the actual way patients are treated in every case.

Conclusion

The results of this survey highlight a discrepancy between the current state of evidence and approaches commonly used by European surgeons for the diagnosis of PJI. There is a need for the development of diagnostic algorithms based on best available evidence. It is also important to improve the feasibility and accessibility of available tools to allow for standardized effective diagnostic protocols.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Funding No funding was received for the conduction of this study.

Ethical approval For this type of study, formal consent is not required.

Informed consent None.

Appendix

How many primary knee prostheses do you implant each year?

< 50	□	100 - 200	□
50 - 100	□	> 200	□

How many infected total knee prostheses do you diagnose each year?

Do you agree on the following classification of onset of infection?

Early onset: < 3 months	□	Delayed onset: 3-12 months	□
Late onset: > 12 months	□	From Symptom begin	□
From the first procedure	□	Other suggestions _____	

How do you diagnose periprosthetic knee joint infection? (Multiple answers are possible)

Joint aspiration:

- Microbiology culture □
- Cell count: □
  - White cell count (WCC) □
  - % PMN □
- Histology □
- Alpha-Defensin □
- C-reactive protein (CRP) □
- IL-1/IL-6 □
- Leukocytesterase □

Swab culture □

- Yes □
- No

Sonication □

Laboratory Investigation:

- C-reactive protein (CRP) □
- Leukocyte count □
- Erythrocyte sedimentation rate (ESR) □
- Blood microbiology cultures □

Biopsie:

- Only 1 □
- 1-5 Biopsies □
- > 5 Biopsies □
- Histology □
- PCR

Arthroscopic biopsy □

How many biopsoies du you take?

1	□	1-5	□
>5	□		

When are culture biopsies taken?

Seperate arthroscopic biopsies	□	Seperate open biopsies procedure	□
Biopsies at time of revision	□		

Which imaging investigations do you rely on?

Plain X-ray	□	Bone SPECT/CT Scan	□
Anti-Leukocyte SPECT/CT	□	PET/CT	□

Do you rely on an internal or external lab?

Internal	□	External	□

Which imaging investigations do you rely on?

Plain X-ray	□	Bone SPECT/CT Scan	□
Anti-Leukocyte SPECT/CT	□	PET/CT	□

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