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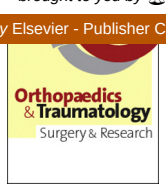

Original article

Potential changes to French recommendations about peri-prosthetic infections based on the international consensus meeting (ICMPJI)

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ABSTRACT

Background: Despite the large volume of studies on the prevention, diagnosis, and treatment of peri-prosthetic infections, surgical practice often rests on limited scientific evidence in this field. The vast International Consensus Meeting on Peri-prosthetic Joint Infection (ICMPJI) held in 2013 produced robust recommendations.
Hypothesis: French consensus conference recommendations show no major differences with ICMPJI recommendations.
Materials and methods: The 207 recommendations developed by 300 experts at the ICMPJI were translated, and the translation was then examined by four reviewers, including 2 having participated in the consensus conference. The reviewers looked for any differences with French practices and recommendations.
Results: Twenty-three major differences or innovations were identified compared to French recommendations and standard practice. Among them, pre-operative screening for nasal or urinary micro-organisms is performed routinely in France but should be reserved according to the ICMPJI for symptomatic patients and/or patients at high risk for infection. The ICMPJI emphasizes the role for the operating room environment as a vector for infection; more specifically, the operating lamp handle and suction cannula deserve close attention. A wound discharge persisting longer than 5–7 days requires irrigation and debridement. This procedure is effective only within the first 3 post-operative months and/or the first 3 weeks after symptom onset and must include exchange of all modular implants. The ICMPJI warns against both irrigation-debridement in fungal infections (suggesting two-stage prosthesis replacement) and one-stage replacement in patients with sinus tracts. The use of spacers (articulating at the knee) is recommended in the event of two-stage prosthesis replacement.
Discussion: The ICMPJI recommendations differed in many ways with French recommendations and standard practice. They can be expected to impact practices in France, although a point worth noting is that only 1 of the 207 recommendations received unanimous agreement by the conference experts (keeping operating room traffic to a minimum).

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1. Introduction

Several sources have developed recommendations about the diagnosis, prevention, and treatment of orthopaedic hardware infections [1–5]. Recommendations on prophylactic antibiotic therapy issued by the French Society for Anaesthesiology and Intensive Care (Société Française d'Anesthésie Réanimation, SFAR) are updated regularly (last update, 2010) [1], and the French Society for Orthopaedic and Trauma Surgery (Société Française de Chirurgie Orthopédique et de Traumatologie, SOFCOT) has developed rules for using antibiotic-impregnated cement [2]. In 2009, these two societies and the French-Speaking Society for Infectious Diseases (Société de Pathologie Infectieuse de Langue Française, SPILF) held a vast consensus conference about the prevention and treatment of orthopaedic hardware infections [3]. In 2013, two consensus conferences organized by US organizations (Infectious Diseases Society of America, IDSA [4] and International Consensus Meeting on Peri-prosthetic Joint Infection [ICMPJI] [5]) issued recommendations on peri-prosthetic joint infections (PJIs) that largely support previous recommendations but also introduce differences regarding many points. Thus, the ICMPJI [5] advises against one-stage surgery in the event of a sinus tract, whereas several French groups found no evidence that a sinus tract increased the risk of one-stage exchange failure [6,7]. Similarly, the ICMPJI [5] indicates that screening for methicillin-resistant *Staphylococcus aureus* (MRSA) decreases the risk ofPJI, a conclusion not supported by a meta-analysis by Lévy et al. [8]. Although experts from France and other European countries participated in the ICMPJI, which was directed by Parvizi and Gehrke [5], the ICMPJI recommendations show many differences with standard practice and recommendations in Europe. Here, we identify and discuss the main differences. Hypothesis: french consensus conference recommendations show no major differences with ICMPJI recommendations.

2. Materiel and methods

The ICMPJI was held in July 2013 and attended by 300 participants from 51 countries. The goal of the conference was to obtain expert opinions about 15 broad groups of questions in the field of PJIs. For each question, the percentages of experts who agreed, disagreed, or abstained from voting was used to establish the strength of the consensus based on the following scale:

- simple majority, no consensus (50.1%–59% agreement);
- majority, weak consensus (60%–65% agreement);
- super majority, strong consensus (66%–99% agreement);
- unanimous (100% agreement).

The experts developed 207 recommendations, which were translated into French by a single translator. The translation was then corrected and amended by four reviewers (ES, HM, JNA, and MO), of whom two had participated in the conference (JNA and ES). These four reviewers then read the final French version and identified the 25 recommendations deemed most innovative or most different from French recommendations [3,4]. For editorial reasons, we have confined the present discussion to the 23 variations that met with strong agreement (66%–99%) during the conference. Of these 23 variations, 3 were identified by all four reviewers, 13 by three reviewers, and 6 by 2 reviewers, as constituting either innovations or differences compared to French recommendations. These 23 recommendations are described in detail in the results section.

3. Results

3.1. Variation 1 (workgroup 1 question 3A): what should the process be for methicillin-resistant S. aureus (MRSA) and methicillin-sensitive S. aureus (MSSA) screening?

Consensus: the workgroup does not recommend routine screening and decolonization of all patients undergoing elective total arthroplasty (ETA). It accepts that pre-operative screening for MSSA and MRSA and decolonisation decreases the rate of surgical site infection (SSI) and the incidence of both staphylococcal and non-staphylococcal infections.

3.2. Variation 2 (workgroup 1, question 5): what is the role of routine urine screening in patients undergoing elective arthroplasty?

Consensus: routine urine screening is not recommended before ETA. Urine screening before ETA should be reserved for patients with a present history or symptoms of urinary tract infection.

3.3. Variation 3 (workgroup 3, question 1): what is the optimal timing of the pre-operative dose of antibiotics?

Consensus: the pre-operative dose of antibiotics should be administered within 1 hour before the surgical incision; this can be extended to 2 hours for vancomycin and fluoroquinolones. Surveillance measures are critical in ensuring clinician compliance with this crucial recommendation.

3.4. Variation 4 (workgroup 3, question 5B): what antibiotic should be administered in a patient with a known non-anaphylactic penicillin allergy?

Consensus: in a patient with a reported non-anaphylactic reaction to penicillin, a second-generation cephalosporin can be used safely, as there is limited cross-reactivity. Penicillin skin testing may be helpful in certain situations to clarify whether the patient has a true penicillin allergy.

3.5. Variation 5 (workgroup 3, question 6): what are the indications for prophylactic vancomycin administration?

Consensus: Vancomycin should be considered in patients who are current MRSA carriers or who have a known history of anaphylactic allergy to penicillin.

Consideration should be given to screening high risk patients such as:

- patients in regions with a high prevalence of MRSA;
- institutionalised patients (nursing home residents, chronic haemodialysis patients, and patients with a history of intensive care unit admission);
- healthcare workers.

3.6. Variation 6 (workgroup 3, question 17B): should MRSA carriers or patients with a prior history of MRSA infection be re-screened? What peri-operative prophylactic antibiotics should be chosen in these patients?

Consensus: MRSA carriers and patients with a prior history of MRSA infection should be re-screened pre-operatively. If the tests are negative for MRSA, routine peri-operative antibiotic prophylaxis should be given.

3.7. Variation 7 (workgroup 4, question 6): should operating lights be controlled with a foot pedal as opposed to a device located above eye level?

Consensus: we recommend a general awareness that light handles can be a source of contamination and to minimize handling of lights as much as possible. Other strategies for light control need to be developed in the future.

3.8. Variation 8 (workgroup 4, question 24): should suction tips be regularly changed during surgery? If so, how frequently? Should suction tips enter the femoral canal?

Consensus: we recommend changing suction tips every 60 minutes based on studies showing higher rates of contamination. Suction tips can be introduced into the femoral canal for the time necessary to evacuate fluid but should not be left in the canal, where they circulate large amounts of ambient air carrying particles that may contaminate the surgery.

3.9. Variation 9 (workgroup 7, question 1A): what is the definition of peri-prosthetic joint infection (PJI)?

Consensus: PJI is defined as:

- two positive peri-prosthetic cultures with pathogens exhibiting identical antibiotic susceptibility/resistance phenotypes, or;
- a sinus tract communicating with the joint, or;
- presence of three of the following minor criteria:
  - elevated serum C-reactive protein (CRP) AND erythrocyte sedimentation rate (ESR),
  - elevated synovial fluid white blood cell (WBC) count OR++ positive result of urine leukocyte esterase dipstick testing of joint fluid,
  - elevated synovial fluid polymorphonuclear neutrophil percentage (PMN%),
  - positive histological analysis of peri-prosthetic tissue,
  - a single positive culture.

3.10. Variation 10 (workgroup 7, question 8): is there a role for routine sonication of the prosthesis? If so, in which group of patients should this be done?

Consensus: no. We do not recommend routine sonication of implants. Sonication should be limited to cases of suspected PJI (based on the clinical presentation and screening tests) in which pre-operative aspiration does not yield a positive culture and antibiotics have been administered within the previous 2 weeks.

3.11. Variation 11 (workgroup 8 question 3B): what are surgical strategies to address a draining wound after TJA? What are surgical strategies to address a draining wound after total arthroplasty?

Consensus: surgical management consisting of opening the fascia, performing a thorough irrigation and debridement (I & D) with exchange of modular components should be considered if wound drainage has persisted for 5 to 7 days after the index procedure. Deep specimens for microbiological studies should be obtained upon re-operation. Wound swab cultures are not recommended.

3.12. Variation 12 (workgroup 9, question 1): is there a functional difference in the use of non-articulating or articulating spacers for the treatment of peri-prosthetic joint infection (PJI) in the knee, between the two-stages of exchange arthroplasty?

Consensus: articulating spacers provide better function than non-articulating spacers. An articulating spacer is especially preferred for patients who are likely to have a spacer in place for longer than 3 months.

3.13. Variation 13 (workgroup 9, question 5): is there a difference in re-implantation (surgical ease) with the use of non-articulating or articulating spacers for the treatment of PJI in the knee and hip?

Consensus: yes. Re-implantation surgery is easier overall in patients receiving articulating spacers compared to non-articulating spacers.

3.14. Variation 14 (workgroup 10, question 1A): when can irrigation and debridement (I&D) be considered?

Consensus: I & D may be performed for early post-operative infections that occur within 3 months of index primary arthroplasty and within 3 weeks after symptom onset.

3.15. Variation 15 (workgroup 10, question 5): should the modular part always be exchanged during I&D?

Consensus: yes. All modular components should be removed and exchanged, if possible.

3.16. Variation 16 (workgroup 10, question 10): should culture samples be taken during I&D? If so how many and from where?

Consensus: between 3 and 6 tissue and fluid samples should be taken from the peri-prosthetic region or the most suspicious regions.

3.17. Variation 17 (workgroup 11, question 1): for antibiotic therapy, can the oral route be substituted for the intravenous route for the initial treatment of PJI after resection and while awaiting exchange prosthesis implantation?

Consensus: there is evidence to support pathogen-specific, highly bio-available oral antibiotic therapy for the treatment of PJI after resection and while awaiting exchange prosthesis implantation.

3.18. Variation 18 (workgroup 11, question 3): what is the ideal length of antibiotic treatment following removal of the infected implant?

Consensus: there is no conclusive evidence regarding the ideal duration of antibiotic therapy. However, we recommend a period of antibiotic therapy between 2 to 6 weeks.

3.19. Variation 19 (workgroup 11, question 6): does the use of rifampin in conjunction with IV antibiotic therapy following removal of the infected implant lead to a more rapid and definitive eradication of staphylococcal infection (particularly methicillin-resistant S. aureus [MRSA])?

Consensus: there is no evidence to support the use of rifampin in conjunction with IV antibiotic therapy as a more adequate treatment option than either agent used alone following implant removal.

3.20. Variation 20 (workgroup 11, question 8): how long should antibiotic treatment be given following a single-stage exchange arthroplasty performed for PJI?

Consensus: there is no conclusive evidence regarding the ideal duration of antibiotic therapy for a single-stage exchange arthroplasty. We recommend parenteral antibiotic therapy for 2 to 6 weeks after single-stage exchange arthroplasty, with consideration for longer-term oral antibiotic therapy.

3.21. Variation 21 (workgroup 12, question 1): what are the indications and contra-indications for one-stage exchange arthroplasty?

Consensus: one-stage exchange arthroplasty is a reasonable option for the treatment of peri-prosthetic joint infection (PJI) in circumstances where effective antibiotics are available (rifampin for Gram-positive cocci and fluoroquinolones for Gram-negative rods), except in patients with systemic manifestations of infection (sepsis) in whom resection arthroplasty and reduction of bioburden may be necessary. Relative contraindications to performing a one-stage exchange may include lack of identification of an organism pre-operatively, the presence of a sinus tract or severe soft tissue involvement that may lead to the need for flap coverage.

3.22. Variation 22 (workgroup 13, question 5): what is the best way to surgically manage fungal PJI: irrigation and debridement, one-stage exchange, two-stage exchange, or permanent resection arthroplasty?

Consensus: on the basis of the current literature, two-stage exchange arthroplasty is the recommended treatment option to manage fungal PJI. However, the success rate is lower than that of bacterial cases.

3.23. Variation 23 (workgroup 15, question 4): should prophylactic antibiotic therapy be given before dental procedures in patients with total arthroplasties?

Consensus: the decision to use dental antibiotic prophylaxis in patients with total arthroplasties should rest on the individual patient-related risk factors and the complexity of the dental procedure to be performed. Patients with total arthroplasty who are at high risk for infection should receive lifetime dental antibiotic prophylaxis. We recommend the administration of a single antibiotic dose prior to dental procedures.

4. Discussion

The usefulness of *S. aureus* screening and of decolonisation measures in the event of a positive result has been established in heart surgery but not in orthopaedic surgery (Variation 1 [workgroup 1, question 3-A]. Variation 6 (workgroup 3, question 17B) recommends re-screening of known MRSA carriers followed by standard prophylactic antibiotic therapy in the event of a negative result. For the pre-operative work-up, Variation 2 (workgroup 1, question 5) does not recommend screening for asymptomatic bacteriuria before arthroplasty and reserves urine microscopy and culture for patients with symptoms.

The interval recommended by the ICMPJI between prophylactic antibiotic administration and the incision is 1 hour (Variation 3 [workgroup 3, question 1]) compared to only 30 minutes in previous recommendations [1]. Use of a second-generation cephalosporin (C2G) is suggested for patients with penicillin allergy. The risk of cross-reactions between penicillin and C3G is usually recognised as very small, less than 5%, and although this risk seems higher with C2G the ICMPJI recommendations suggest the use of these drugs in patients with severe allergic manifestations and after allergen testing if appropriate (Variation 4 [workgroup 3, question 5B]). This recommendation constitutes a major departure from the strategy advised by the SFAR, which involves using a glycopeptide or clindamycinin patients with beta-lactam allergies [1]. Prophylactic vancomycin therapy should be reserved, according to the ICMPJI recommendation, for confirmed MRSA carriers (variation 5 [workgroup 3 question 6]), whereas the SFAR advises that vancomycin be given to all patients potentially colonised by nosocomial organisms [1]. In addition, the ICMPJI (Variation 6 [workgroup 3 question 17B]) recommends re-screening of patients with a history of carriage followed by the use of glycopeptides only in the event of a positive result. French recommendations [1–3] do not mention the risks related to operating light handles or suction cannulas (Variation 7 [workgroup 4, question 6] and Variation 8 [workgroup 4, question 24]).

The ICMPJI definition of prosthetic joint infection (Variation 9 [workgroup, 7 question 1A]) rests on the presence in two reliable samples (joint aspiration or intra-operative samples) containing the same micro-organism (that is, exhibiting identical antibiotic susceptibilities). This definition differs noticeably from that suggested in the IDSA consensus [4] (in which one or two cultures positive for a bacterial skin saprophyte are not sufficient to establish a diagnosis of PJI) and in the SPLIF consensus [2] (which requires a sample positive for a non-saprophyte or three cultures positive for a saprophyte). The group of ICMPJI experts reserved implant sonication to situations in which pre-operative documentation of the infection is in doubt and/or antibiotic therapy was given within 2 weeks before surgery, as this treatment might presumably result in negative intra-operative cultures (Variation 10 [workgroup 7, question 8]). Implant sonication is not performed routinely in most centres and its modalities are not fully standardised. In addition, implant sonication has not been proven to modify patient outcomes.

The management of wound drainage for longer than 5 days requires opening the incision (Variation 11 [workgroup 8, question 3B]). A crucial point is that no antibiotics should be started before this procedure. Emphasis should be put on the unfortunately widespread practice of obtaining samples from the incision and using the results to determine the need for antibiotic therapy. Inappropriate antibiotic therapy is unlikely to be effective in the absence of irrigation-debridement surgery and diminishes the likelihood of documenting the surgical site infection and therefore of selecting the optimal antibiotics. The French consensus conferences [2,3] did not underline the role for spacers in two-stage exchange arthroplasty and the importance of using articulating spacers at the knee (Variation 12 [workgroup 9, question 1] and Variation 13 [workgroup 9, question 5]), due both to a paucity of data and to a growing preference in France for one-stage exchange [6,7]. During re-operation for irrigation-debridement, the ICMPJI recommendations include taking several samples for microbiological cultures (Variation 16 [workgroup 10, question 10]) and changing modular implant components (Variation 15 [workgroup 10 question 5]), which constitute an adherence surface for the biofilm and therefore a major source of antibiotic treatment failure. The maximum times of 3 months after implantation and 3 weeks after symptom onset for performing irrigation-debridement (Variation 14 [workgroup 10, question 1A]) are somewhat longer than those suggested by the IDSA and by French recommendations (4 weeks after implantation and 3 weeks of clinical evidence of active infection) [3,4].

The antibiotics believed to be effective in PJI (rifampin for Gram-positive cocci and fluoroquinolones for Gram-negative rods) (Variation 17 [workgroup 11, question 1]) are those characterised by the best oral bioavailability (> 90% for rifampin and levofloxacin). Consequently, a rapid switch to the oral route seems reasonable

when these antibiotics are started parenterally (Variation 19 [workgroup 11, question 6]). Oral treatment from the outset has not been validated in PIJ and may be limited by the gastric tolerance problems that are common immediately after surgery. After one-stage exchange, parenteral antibiotic therapy is recommended for 4-6 weeks (Variation 20 [workgroup 11, question 8]), compared to 1 week in French recommendations [2,6].

The ICMPJI recommendations given preference to one-stage exchange arthroplasty except in patients with sepsis with systemic manifestations, sinus tracts, fungal infections, or extensive soft tissue lesions that may require flap coverage (Variation 21 [workgroup 12, question 1] and Variation 22 [workgroup 13, question 5]).

In the event of two-stage exchange arthroplasty, the ICMPJI experts recommend 4–6 weeks as the optimal antibiotic therapy duration after implant removal (Variation 18 [workgroup 11, question 3]). The SPILF, in contrast, suggests two options, either a brief interval of 4–6 weeks or a long interval of 3–6 months [2].

Finally, the ICMPJI adopted the recommendations issued by the various professional societies (NICE, American and French Dental Societies, and European Society of Cardiology) regarding the absence of benefits from prophylactic antibiotic therapy during dental procedures, except those known to carry a high risk of bacteraemia (Variation 23 [workgroup 15, question 4]) [9].

Disclosure of interest

Henri Migaud is an educational and research consultant for Tornier and Zimmer and has received royalties from Tornier. Eric Senneville is a consultant for Novartis and Pfizer; a speaker for Sanofi-Aventis, Astra-Zeneca, and Gilead; and a recipient of support for conventions by MSD. Jean-Noël Argenson is an educational and research consultant for Zimmer and perceives royalties from Zimmer.

Michel Drancourt and Matthieu Ollivier declare that they have no conflicts of interest concerning this article.

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