Diagnosis and Management of Prosthetic Joint Infection: Clinical Practice Guidelines by the Infectious Diseases Society of America

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These guidelines are intended for use by infectious disease specialists, orthopedists, and other healthcare professionals who care for patients with prosthetic joint infection (PJI). They include evidence-based and opinion-based recommendations for the diagnosis and management of patients with PJI treated with debridement and retention of the prosthesis, resection arthroplasty with or without subsequent staged reimplantation, 1-stage reimplantation, and amputation.

Keywords. prostatic joint infection, PJI, surgical intervention, antimicrobial.

EXECUTIVE SUMMARY

Background

Joint replacement is a highly effective intervention that significantly improves patients’ quality of life, providing symptom relief, restoration of joint function, improved mobility, and independence. Prosthetic joint infection (PJI) remains one of the most serious complications of prosthetic joint implantation. The management of PJI almost always necessitates the need for surgical intervention and prolonged courses of intravenous or oral antimicrobial therapy [1–4]. Despite a significant amount of basic and clinical research in this field, many questions pertaining to the definition of infection as well as diagnosis and management of these infections remain unanswered. The focus of these guidelines is to provide a consensus statement that addresses the diagnosis and the medical and surgical treatment of infections involving a prosthetic joint. In many situations, the panel has made recommendations based on expert opinion, realizing that the amount of data to support a specific recommendation is limited and that there are diverse practice patterns which seem to be equally effective for a given clinical problem.

An essential component of the care of patients with PJI is strong collaboration between all involved medical and surgical specialists (eg, orthopedic surgeons, plastic surgeons, infectious disease specialists, internists). It is anticipated that consideration of these guidelines may help reduce morbidity, mortality, and the costs associated with PJI. The panel realizes that not all medical institutions will have the necessary resources to implement all the recommendations in...
Table 1. Strength of Recommendation and Quality of Evidence

<table>
<thead>
<tr>
<th>Category/Grade</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strength of recommendation</td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>Good evidence to support a recommendation for or against use.</td>
</tr>
<tr>
<td>B</td>
<td>Moderate evidence to support a recommendation for or against use.</td>
</tr>
<tr>
<td>C</td>
<td>Poor evidence to support a recommendation.</td>
</tr>
<tr>
<td>Quality of evidence</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>Evidence from &gt;1 properly randomized, controlled trial.</td>
</tr>
<tr>
<td>II</td>
<td>Evidence from &gt;1 well-designed clinical trial, without randomization; from cohort or case-controlled analytic studies (preferably from &gt;1 center); from multiple time-series; or from dramatic results from uncontrolled experiments.</td>
</tr>
<tr>
<td>III</td>
<td>Evidence from opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.</td>
</tr>
</tbody>
</table>

Source: [5]. Adapted and reproduced with the permission of the Minister of Public Works and Government Services Canada, 2009.

these guidelines. Proper referral to specialty centers may need to occur.

Each section of the guideline begins with a specific clinical question and is followed by numbered recommendations and a summary of the most relevant evidence in support of the recommendations. The panel followed a process used in the development of other Infectious Diseases Society of America (IDSA) guidelines, which included a systematic weighting of the quality of the evidence and the grade of recommendation [5] (Table 1). A detailed description of the methods, background, and evidence summaries that support each of the recommendations can be found in the full text of the guideline. Areas of controversy in which data are limited or conflicting and where additional research is needed are indicated throughout the document and are highlighted in the “Research Gaps” section in the full text of the guideline.

I. What preoperative evaluation and intraoperative testing should be performed to diagnose PJI and what is the definition of PJI?

Recommendations

Preoperative Evaluation (Figure 1)

1. Suspect PJI in patients with any of the following (B-III):
   A sinus tract or persistent wound drainage over a joint prosthesis, acute onset of a painful prosthesis, or any chronic painful prosthesis at any time after prosthesis implantation, particularly in the absence of a pain-free interval, in the first few years following implantation or if there is a history of prior wound healing problems or superficial or deep infection.
   2. Evaluation of the patient with a possible PJI should include a thorough history and physical examination (C-III). Items that should be obtained in the history include the type of prosthesis, date of implantation, past surgeries on the joint, history of wound healing problems following prosthesis implantation, remote infections, current clinical symptoms, drug allergies and intolerances, comorbid conditions, prior and current microbiology results from aspirations and surgeries, and antimicrobial therapy for the PJI including local antimicrobial therapy (C-III).
   3. A test for sedimentation rate or C-reactive protein (CRP) should be performed in all patients with a suspected PJI when the diagnosis is not clinically evident. The combination of an abnormal sedimentation rate and CRP seems to provide the best combination of sensitivity and specificity (A-III).
   4. A plain radiograph should be performed in all patients with suspected PJI (A-III).
   5. A diagnostic arthrocentesis should be performed in all patients with suspected acute PJI unless the diagnosis is evident clinically and surgery is planned and antimicrobials can be safely withheld prior to surgery. Arthrocentesis is also advised in patients with a chronic painful prosthesis in whom there is an unexplained elevated sedimentation rate or CRP level (A-III) or in whom there is a clinical suspicion of PJI. It may not be necessary if in this situation surgery is planned and the result is not expected to alter management. Synovial fluid analysis should include a total cell count and differential leukocyte count, as well as culture for aerobic and anaerobic organisms (A-III). A crystal analysis can also be performed if clinically indicated.
   6. In PJI where the patient is medically stable, withholding antimicrobial therapy for at least 2 weeks prior to collection of synovial fluid for culture increases the likelihood of recovering an organism (B-III).
   7. Blood cultures for aerobic and anaerobic organisms should be obtained if fever is present, there is an acute onset of symptoms, or if the patient has a condition or suspected condition or concomitant infection or pathogen (eg Staphylococcus aureus) that would make the presence of a bloodstream infection more likely (B-III).
   8. Imaging studies such as bone scans, leukocyte scans, magnetic resonance imaging, computed tomography, and positron emission tomography scans should not be routinely used to diagnose PJI (B-III).

Intraoperative Diagnosis of PJI

9. Intraoperative histopathological examination of periprosthetic tissue samples is a highly reliable diagnostic test provided that a pathologist skilled in interpretation of periprosthetic
tissue is available. It should be performed at the time of revision prosthetic joint surgery, when available, if the presence of infection is in doubt based on the clinical suspicion of the surgeon and the results will affect management, for example, in deciding between revision arthroplasty and 2-stage exchange (B-III).

10. At least 3 and optimally 5 or 6 periprosthetic intraoperative tissue samples or the explanted prosthesis itself
should be submitted for aerobic and anaerobic culture at the time of surgical debridement or prosthesis removal to maximize the chance of obtaining a microbiologic diagnosis (B-II).

11. When possible (see above), withholding antimicrobial therapy for at least 2 weeks prior to collecting intraoperative culture specimens increases the yield of recovering an organism (A-II).

Definition of PJI

12. The presence of a sinus tract that communicates with the prosthesis is definitive evidence of PJI (B-III).

13. The presence of acute inflammation as seen on histopathologic examination of periprosthetic tissue at the time of surgical debridement or prosthesis removal as defined by the attending pathologist is highly suggestive evidence of PJI (B-II).

14. The presence of purulence without another known etiology surrounding the prosthesis is definitive evidence of PJI (B-III).

15. Two or more intraoperative cultures or combination of preoperative aspiration and intraoperative cultures that yield the same organism (indistinguishable based on common laboratory tests including genus and species identification or common antibiogram) may be considered definitive evidence of PJI. Growth of a virulent microorganism (eg, S. aureus) in a single specimen of a tissue biopsy or synovial fluid may also represent PJI. One of multiple tissue cultures or a single aspiration culture that yields an organism that is a common contaminant (eg, coagulase-negative staphylococci, Propionibacterium acnes) should not necessarily be considered
evidence of definite PJI and should be evaluated in the context of other available evidence (B-III).

16. The presence of PJI is possible even if the above criteria are not met; the clinician should use his/her clinical judgment to determine if this is the case after reviewing all the available preoperative and intraoperative information (B-III).

II. What different surgical strategies should be considered for treatment of a patient with PJI?

Recommendations

17. The ultimate decision regarding surgical management should be made by the orthopedic surgeon with appropriate consultation (eg, infectious diseases, plastic surgery) as necessary (C-III).

18. Patients diagnosed with a PJI who have a well-fixed prosthesis without a sinus tract who are within approximately 30 days of prosthesis implantation or <3 weeks of onset of infectious symptoms should be considered for a debridement and retention of prosthesis strategy (Figure 2; A-II). Patients who do not meet these criteria but for whom alternative surgical strategies are unacceptable or high risk may also be considered for a debridement and retention strategy, but relapse of infection is more likely (B-III).

19. A 2-stage exchange strategy is commonly used in the United States and is indicated in patients who are not candidates for a 1-stage exchange who are medically able to undergo multiple surgeries and in whom the surgeon believes reimplantation arthroplasty is possible, based on the existing soft tissue and bone defects (Figure 3; B-III). Obtaining a pre-revision sedimentation rate and CRP is recommended by the panel to assess the success of treatment prior to reimplantation (C-III). The panel believes that in selected circumstances more than one 2-stage exchange if the first attempt fails can be successful (C-III).

20. A 1-stage or direct exchange strategy for the treatment of PJI is not commonly performed in the United States but may be considered in patients with a total hip arthroplasty (THA) infection who have a good soft tissue envelope provided that the identity of the pathogens is known preoperatively and they are susceptible to oral antimicrobials with excellent oral bioavailability. There may be a greater risk of failure if bone grafting is required and effective antibiotic impregnated bone cement cannot be utilized (Figure 3; C-III).

21. Permanent resection arthroplasty may be considered in nonambulatory patients; patients with limited bone stock, poor soft tissue coverage, or infections due to highly resistant organisms for which there is limited medical therapy; patients with a medical condition precluding multiple major surgeries; or patients who have failed a previous 2-stage exchange in which the risk of recurrent infection after another staged exchange is deemed unacceptable (Figure 4; B-III).

22. Amputation should be the last option considered but may be appropriate in selected cases. Except in emergent cases, referral to a center with specialist experience in the management of PJI is advised before amputation is carried out (Figure 4; B-III).

III. What is the medical treatment for a patient with PJI following debridement and retention of the prosthesis?

Recommendations

Staphylococcal PJI

23. Two to 6 weeks of a pathogen-specific intravenous antimicrobial therapy (Table 2) in combination with rifampin 300–450 mg orally twice daily followed by rifampin plus a
companion oral drug for a total of 3 months for a THA infection and 6 months for a total knee arthroplasty (TKA) infection (A-I). Total elbow, total shoulder, and total ankle infections may be managed with the same protocols as THA infections (C-III). Recommended oral companion drugs for rifampin include ciprofloxacin (A-I) or levofloxacin (A-II). Secondary companion drugs to be used if in vitro susceptibility, allergies, intolerances, or potential intolerances support the use of an agent other than a quinolone include but are not limited to co-trimoxazole (A-II), minocycline or doxycycline (C-III), or oral first-generation cephalosporins (eg, cephalixin) or antistaphylococcal penicillins (eg, dicloxacillin; C-III). If rifampin cannot be used because of allergy, toxicity, or intolerance, the panel recommends 4–6 weeks of pathogen-specific intravenous antimicrobial therapy (B-III).

24. Monitoring of outpatient intravenous antimicrobial therapy should follow published guidelines (A-II) [6].
25. Indefinite chronic oral antimicrobial suppression may follow the above regimen with cephalexin, dicloxacillin, co-trimoxazole, or minocycline based on in vitro susceptibility, allergies, or intolerances (Table 3; B-III). Rifampin alone is not recommended for chronic suppression, and rifampin combination therapy is not generally recommended. One member of the panel uses rifampin combination therapy for chronic suppression in selected situations (A. R. B.). The recommendation regarding using suppressive therapy after rifampin treatment was not unanimous (W. Z., D. L.). Clinical and laboratory monitoring for efficacy and toxicity is advisable. The decision to offer chronic suppressive therapy must take into account the individual circumstances of the patient including the ability to

Figure 4. Management of prosthetic joint infection when patients are not a candidate for new prosthesis. Abbreviations: TEA, total elbow arthroplasty; TKA, total knee arthroplasty.
<table>
<thead>
<tr>
<th>Microorganism</th>
<th>Preferred Treatment</th>
<th>Alternative Treatment</th>
<th>Comments</th>
</tr>
</thead>
</table>
| Staphylococci, oxacillin-susceptible  | Nafcillin sodium 1.5–2 g IV q4-6 h  
Cefazolin 1–2 g IV q8 h  
Ceftriaxone 1–2 g IV q24 h | Vancomycin IV 15 mg/kg q12 h  
Daptomycin 6 mg/kg IV q24 h  
Linezolid 600 mg PO/IV every 12 h | See recommended use of rifampin as a companion drug for rifampin-susceptible PJI treated with debridement and retention or 1-stage exchange in text |
| Staphylococci, oxacillin-resistant    | Vancomycin 9 IV 15 mg/kg q12 h | Daptomycin 6 mg/kg IV q24 h  
Linezolid 600 mg PO/IV q12 h | See recommended use of rifampin as a companion drug for rifampin-susceptible PJI treated with debridement and retention or 1-stage exchange in text |
| Enterococcus spp, penicillin-susceptible | Penicillin G 20–24 million units IV q24 h continuously or in 6 divided doses  
Ampicillin sodium 12 g IV q24 h continuously or in 6 divided doses | Vancomycin 15 mg/kg IV q12 h  
Daptomycin 6 mg/kg IV q24 h  
Linezolid 600 mg PO or IV q12 h | 4–6 wk. Aminoglycoside optional  
Vancomycin should be used only in case of penicillin allergy |
| Enterococcus spp, penicillin-resistant | Vancomycin 15 mg/kg IV q12 h | Linezolid 600 mg PO or IV q12 h | 4–6 wk. Addition of aminoglycoside optional |
| Pseudomonas aeruginosa                | Cefepime 2 g IV q12 h  
Meropenem 1 g IV q8 h | Ciprofloxacin 750 mg PO bid  
400 mg IV q12 h  
Ceftazidime 2 g IV q8 h | 4–6 wk  
Addition of aminoglycoside optional  
Use of 2 active drugs could be considered based on clinical circumstance of patient. If aminoglycoside in spacer, and organism aminoglycoside susceptible than double coverage being provided with recommended IV or oral monotherapy |
| Enterobacter spp                      | Cefepime 2 g IV q12 h  
Ertapenem 1 g IV q24 h | Ciprofloxacin 750 mg PO or 400 mg IV q12 h | 4–6 wk |
| Enterobacteriaceae                    | IV β-lactam based on in vitro susceptibilities  
Ciprofloxacin 750 mg PO bid | | 4–6 wk |
| β-hemolytic streptococci             | Penicillin G 20–24 million units IV q24 h continuously or in 6 divided doses  
Ceftriaxone 2 g IV q24 h | Vancomycin 15 mg/kg IV q12 h | 4–6 wk  
Vancomycin only in case of allergy |
### Table 2 continued.

<table>
<thead>
<tr>
<th>Microorganism</th>
<th>Preferred Treatmenta</th>
<th>Alternative Treatmentb</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Propionibacterium acnes</strong></td>
<td>Penicillin G 20 million units IV q24 h continuously or in 6 divided doses or Ceftriaxone 2 g IV q24 h</td>
<td>Clindamycin 600–900 mg IV q8 h or clindamycin 300–450 mg PO qid or Vancomycin 15 mg/kg IV q12 h</td>
<td>4–6 wk Vancomycin only in case of allergy</td>
</tr>
</tbody>
</table>

Abbreviations: bid, twice daily; IV, intravenous; PJI, prosthetic joint infection; q, every; PO, per oral; qid, 4 times daily.

a Antimicrobial dosage needs to be adjusted based on patients’ renal and hepatic function. Antimicrobials should be chosen based on in vitro susceptibility as well as patient drug allergies, intolerances, and potential drug interactions or contraindications to a specific antimicrobial. Clinical and laboratory monitoring for efficacy and safety should occur based on prior IDSA guidelines [6]. The possibility of prolonged QTc interval and tendinopathy should be discussed and monitored when using fluoroquinolones. The possibility of Clostridium difficile colitis should also be discussed when using any antimicrobial.

b Flucloxacillin may be used in Europe. Oxacillin can also be substituted.

c There was not a consensus on the use of ceftriaxone for methicillin-resistant Staphylococcus aureus (MRSA) infections have been published. These guidelines suggest that dosing of vancomycin be considered to achieve a vancomycin trough at steady state of 15 to 20. Although this may be appropriate for MRSA PJI treated without rifampin or without the use of local vancomycin impregnated spacers, it is unknown if these higher trough concentrations are necessary when rifampin or vancomycin impregnated spacers are utilized. Trough concentrations of at least 10 mg/L may be appropriate in this situation. It is also unknown if treatment of oxacillin-resistant, coagulase-negative staphylococci require vancomycin dosing to achieve these higher vancomycin levels.

d Other antipseudomonal carbapenems can be utilized as well.

e Other antipseudomonal carbapenems can be utilized as well.

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**V. What is the medical treatment for a patient with PJI following 1-stage exchange?**

29. Four to 6 weeks of pathogen-specific intravenous antimicrobial therapy should follow published guidelines (A-II) [6].

30. Monitoring of outpatient intravenous antimicrobial therapy should follow published guidelines (A) [6].

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**VI. What is the medical treatment for a patient with PJI following reimplantation?**

26. Four to 6 weeks of pathogen-specific intravenous antimicrobial therapy should follow published guidelines (A-II) [6].

27. Monitoring of outpatient intravenous antimicrobial therapy should follow published guidelines (A-II) [6].

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**VII. What is the medical treatment for a patient with PJIs due to Other Organisms?**

28. Indefinite chronic oral antimicrobial suppression therapy should follow published guidelines (B-III) [6].

29. Four to 6 weeks of pathogen-specific intravenous or highly bioavailable oral antimicrobial therapy follow the above regimen (Table 3) based on in vitro sensitivity.

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**IX. What is the medical treatment for a patient with PJIs due to Other Organisms following exchange revision and arthroplasty?**

30. Monitoring of outpatient intravenous antimicrobial therapy should follow published guidelines (A-II) [6].

31. Two to 6 months of chronic suppression therapy should follow the above regimen (Table 3) based on in vitro sensitivity. If rifampin cannot be used because of allergy, toxicity, or intolerance, other than the panel recommends 4–6 weeks of pathogen-specific intravenous antimicrobial therapy.
32. Monitoring of outpatient intravenous antimicrobial therapy should follow published guidelines (A-II) [6].

33. Indefinite chronic oral antimicrobial suppression may follow the above regimen with either cephalexin, dicloxacillin, co-trimoxazole, or minocycline or doxycycline based on in vitro susceptibility, allergies, or intolerances (Table 3; B-III).

Rifampin alone is not recommended for chronic suppression, and rifampin combination therapy is also not generally recommended. One member of the panel uses rifampin combination therapy for chronic suppression in selected situations (A. R. B.). The recommendation regarding using suppressive therapy after rifampin treatment was not unanimous (D. L., W. Z.). Clinical and laboratory monitoring for efficacy and toxicity is advisable. The decision to offer chronic suppressive therapy must take into account the individual circumstances of the patient including the ability to use rifampin in the initial phase of treatment, the potential for progressive implant loosening and loss of bone stock, and the hazards of prolonged antibiotic therapy; it is therefore generally reserved for patients who are unsuitable for, or refuse, further exchange revision, excision arthroplasty, or amputation.

**Table 3. Common Antimicrobials Used for Chronic Oral Antimicrobial Suppression (B-III Unless Otherwise Stated in Text)a,b**

<table>
<thead>
<tr>
<th>Microorganism</th>
<th>Preferred Treatment</th>
<th>Alternative Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Staphylococci, oxacillin-susceptible</td>
<td>Cephalexin 500 mg PO tid or qid</td>
<td>Minocycline 500 mg PO tid or qid</td>
</tr>
<tr>
<td></td>
<td>Cefadroxil 500 mg PO bid</td>
<td>Clindamycin 300 mg PO qid</td>
</tr>
<tr>
<td>Staphylococci, oxacillin-resistant</td>
<td>Cotrimoxazole 1 DS tab PO bid</td>
<td>Amoxicillin-clavulanate 500 mg PO tid</td>
</tr>
<tr>
<td>β-hemolytic streptococci</td>
<td>Penicillin V 500 mg PO bid to qid</td>
<td>Cephalexin 500 mg PO tid or qid</td>
</tr>
<tr>
<td></td>
<td>Amoxicillin 500 mg PO tid</td>
<td></td>
</tr>
<tr>
<td>Enterococcus spp, penicillin susceptible</td>
<td>Penicillin V 500 mg PO bid to qid</td>
<td>β-lactam oral therapy based on in vitro susceptibility</td>
</tr>
<tr>
<td></td>
<td>Amoxicillin 500 mg PO tid</td>
<td></td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>Ciprofloxacin 250–500 mg PO bid</td>
<td></td>
</tr>
<tr>
<td>Enterobacteriaceae</td>
<td>Cotrimoxazole 1 DS tab PO bid</td>
<td></td>
</tr>
<tr>
<td>Propionibacterium spp</td>
<td>Penicillin V 500 mg PO bid to qid</td>
<td>Minocycline or doxycycline 100 mg PO bid</td>
</tr>
<tr>
<td></td>
<td>Amoxicillin 500 mg PO tid</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: bid, twice daily; DS, double strength; PO, per oral; qid, 4 times daily; tid, 3 times daily.

a Antimicrobial dosage needs to be adjusted based on patients’ renal and hepatic function. Antimicrobials should be chosen based on in vitro susceptibility as well as patient drug allergies, intolerances, and potential drug interactions or contraindications to a specific antimicrobial.

b Clinical and laboratory monitoring for efficacy and safety should occur based on the clinical judgment of the clinician caring for the patient. The possibility of prolonged QTc interval and tendinopathy should be discussed and monitored when using fluoroquinolones. The possibility of Clostridium difficile colitis should also be discussed when using any antimicrobial.

34. Four to 6 weeks of pathogen-specific intravenous or highly bioavailable oral antimicrobial therapy is recommended (Table 2; A-II).

35. Monitoring of outpatient intravenous antimicrobial therapy should follow published guidelines (A-II) [6].

36. Indefinite chronic oral antimicrobial suppression should follow regimens in Table 3 and be based on in vitro sensitivities, allergies, and intolerances (B-III). Chronic suppression after fluoroquinolone treatment of gram-negative bacilli was not unanimously recommended (D. L., W. Z.). Clinical and laboratory monitoring for efficacy and toxicity is advisable. Similar considerations regarding hazards and effectiveness apply to those above.

**VI. What is the medical treatment for a patient with PJI following amputation?**

37. Pathogen-specific antimicrobial therapy should be given until 24–48 hours after amputation assuming all infected bone and soft tissue has been surgically removed and there is no concomitant sepsis syndrome or bacteremia. If sepsis syndrome or bacteremia are present, treatment duration is to be according to recommendations for these syndromes (C-III).

38. Four to 6 weeks of pathogen-specific intravenous or highly bioavailable oral antimicrobial therapy is recommended if, despite surgery, there is residual infected bone and soft tissue (ie, hip disarticulation for THA infection, long-stem TKA prosthesis where the prosthesis extended above the level of amputation; Table 2; C-III).
39. Monitoring of outpatient intravenous antimicrobial therapy should follow published guidelines (A-II) [6].

Notes

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Potential conflicts of interest. The following list is a reflection of what has been reported to IDSA. In order to provide thorough transparency, IDSA requires full disclosure of all relationships, regardless of relevancy to the guideline topic. The reader of these guidelines should be mindful of this when the list of disclosures is reviewed.

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All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

References