



# Management strategies for prosthetic joint infection: long-term infection control rates, overall survival rates, functional and quality of life outcomes

Theofilos Karachalios<sup>1,2</sup>

George A. Komnos<sup>1</sup>

- DAIR (debridement, antibiotics, and implant retention), one-stage and two-stage revision surgery are the most common management strategies for prosthetic joint infection (PJI) management. Our knowledge concerning their efficacy is based on short to medium-term low-quality studies.
- Most studies report infection recurrence rates or infection-free time intervals. However, long-term survival rates of the infection-free joints, functional and quality of life outcome data are of paramount importance.
- DAIR, one-stage and two-stage revision strategies are not unique surgical techniques, presenting several variables. Infection control rates for the above strategies vary from 75% to 90%, but comparisons are difficult because different indications and patient selection criteria are used in each strategy.
- Recent outcome data show that DAIR and one-stage revision in selected patients (based on host, bacteriological, soft tissue and type of infection criteria) may present improved functional and quality of life outcomes and reduced costs for health systems as compared to those of two-stage revision.
- It is expected that health system administrators and providers will apply pressure on surgeons and departments towards the wider use of DAIR and one-stage revision strategies. It is the orthopaedic surgeon's responsibility to conduct quality studies in order to fully clarify the indications and outcomes of the different revision strategies.

**Keywords:** functional recovery; PJI clinical outcomes; quality of life

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## Introduction

Prosthetic joint infection (PJI) represents one of the most devastating complications in joint arthroplasty, with a prevalence of 1–2% after primary joint replacement

and 4% after revision.<sup>1,2</sup> It is also the most common reason for early revision (Fig. 1).<sup>3</sup> PJI has a severe impact on morbidity and mortality rates, and quality of life is severely affected in these patients.<sup>4</sup> Diagnosis of PJI is sometimes difficult and any delays can lead to multiple surgeries, lower survival rates and impairment of function and quality of life.<sup>5</sup> Optimal treatment of PJI remains controversial. The most widely used management strategies are one-stage and two-stage revisions.<sup>6</sup> DAIR (debridement, antibiotics, and implant retention) is also indicated for early or acute infections. Other strategies, with specific indications, which are less popular and produce poorer results, include antibiotic suppression, arthrodesis, and even amputation.<sup>6</sup> The cost of management of PJI patients is quite high when compared to primary arthroplasties.<sup>7,8</sup> As a result, economic health providers and health administrators have recently focused on the PJI problem, asking for detailed comparative clinical outcome data and the introduction of multi-disciplinary management approaches.<sup>8–10</sup> In order to throw light on this topic, a detailed review of medium and long-term outcomes of the various PJI management strategies is presented. We also focus on the few studies which report on survival rates of infection-free joints and on functional and quality of life outcomes.



**Fig. 1** Intra-operative picture of early steps of one-stage revision surgery for infected total hip arthroplasty (THA).

**Table 1.** Outcomes of prosthetic joint infection (PJI) management strategies. Medium to long-term outcome studies presenting survival rates of the infection-free joints are shown

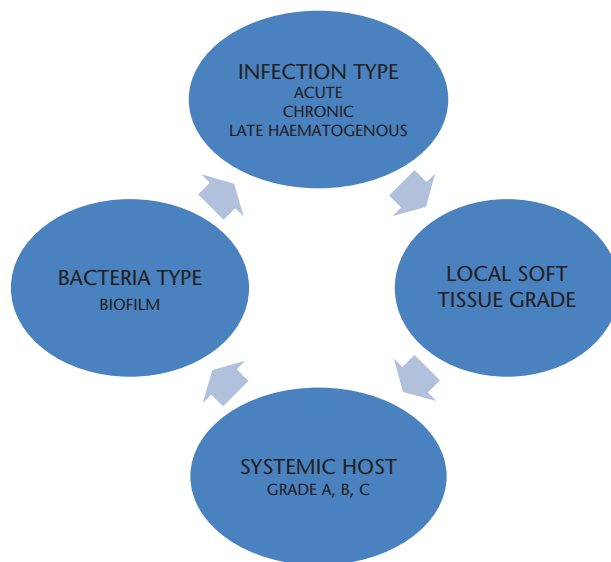
Author	Year	Strategy	THAs	TKAs	Type of study	Survival rates with infection as an end point	Survival rates with aseptic loosening as an end point	Follow-up
Grammatopoulos et al <sup>27</sup>	2017	DAIR	122		Retrospective consecutive case series	85%	77% for aseptic loosening	18 yrs
Sendi et al <sup>26</sup>	2017	DAIR	46		Retrospective case series	90%	100% for aseptic loosening	2–10 yrs
Claus et al <sup>28</sup>	2020	DAIR	57		Retrospective double cohort	93%	76% for any reason	6 yrs
Zahar et al <sup>32</sup>	2019	One-stage cemented fixation	85		Retrospective cohort study	94%	75.9% for any reason	10 yrs
Wolff et al <sup>33</sup>	2021	One-stage cemented fixation	26		Retrospective cohort study	96.2%	76.9% for any reason	10–24 yrs
Born et al <sup>34</sup>	2016	One-stage cementless fixation	28		Retrospective cohort study	96%	97% for aseptic loosening	7 yrs
Petis et al <sup>36</sup>	2019	Two-stage mixed cemented/less fixation	164		Retrospective cohort study	85%	96.7% for aseptic loosening	10–15 yrs
Born et al <sup>34</sup>	2016	Two-stage cementless fixation	53		Retrospective cohort study	94%	97% for aseptic loosening	7 yrs
Hoberg et al <sup>43</sup>	2016	Two-stage revision	45		Retrospective double cohort	4.4% reinfection rate	82.7% for any reason	10 yrs
Bongers et al <sup>37</sup>	2020	Two-stage revision		113	Retrospective cohort study	85.7%	92% for aseptic loosening	8 yrs
Petis et al <sup>38</sup>	2019	Two-stage revision		245	Retrospective cohort study	83%	93% for aseptic loosening	15 yrs

Note. DAIR, debridement, antibiotics, and implant retention; THA, total hip arthroplasty; TKA, total knee arthroplasty.

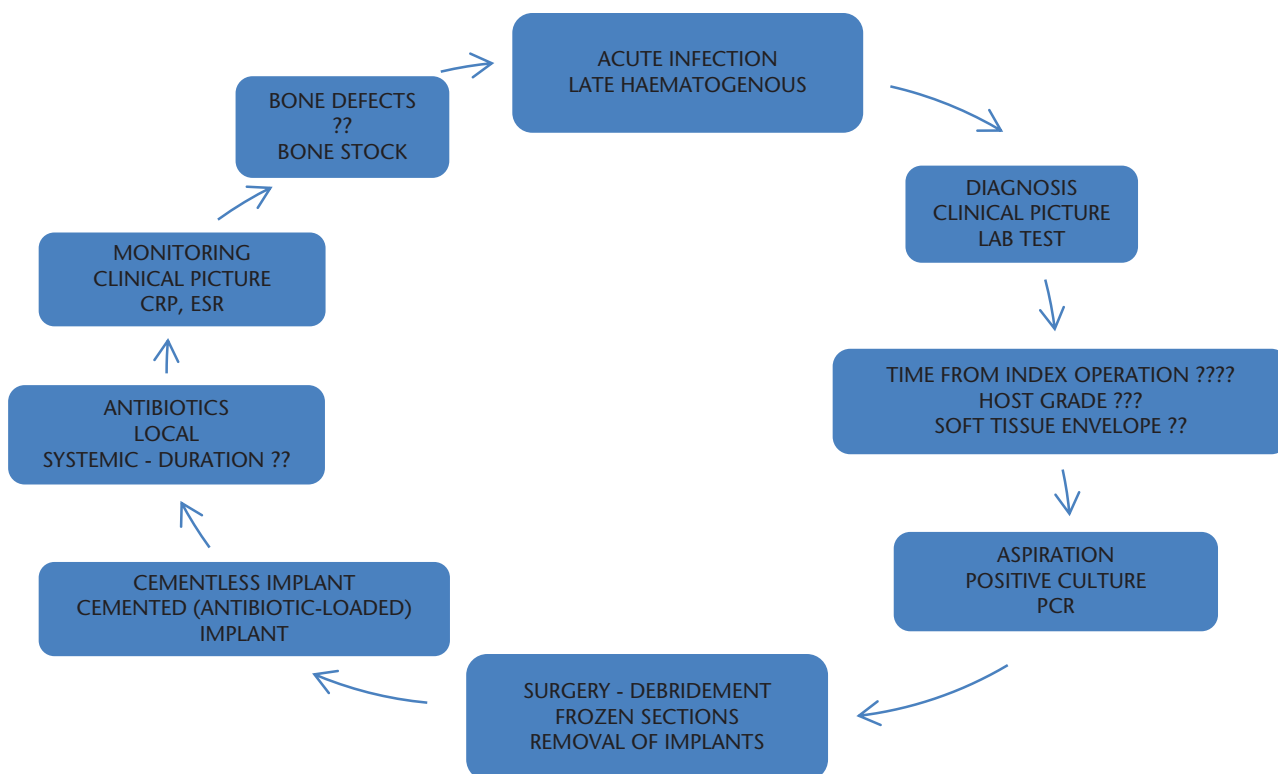
### Observations and arguments based on literature search

Initially, four quality (systematic reviews) studies were identified which have compared one-stage to two-stage revision for both total hip and total knee arthroplasties.<sup>11–14</sup> A common observation in these reviews has been that the quality of the studies included was poor and the strength of the conclusions weak. Subsequently, a thorough literature review (PubMed) of PJI management related outcome studies was performed. Selection criteria for the published articles to be evaluated were studies reporting on survival rates with re-infection as an end point, on survival rates of infection-free joints and on functional and quality of life outcomes. Exclusion criteria included follow-up of less than six years, case reports or reviews, studies not referring to aseptic loosening and non-English language. A total of 53 studies were identified and evaluated and, of those, 11 which fulfilled the above criteria were reviewed (Table 1). Due to several methodological problems MOOSE and PRISMA guidelines and Cochrane methodology were not applied and thus data presentation from these papers is not considered as a systematic review. Most of the rest studies were retrospective, with a small number of patients and a short to medium-term (2–8 years) follow-up evaluation period. Prospective randomized studies were not found. Additionally, the following confounding factors of outcome evaluation were identified: (1) Indications for DAIR and one and two-stage

revision strategies are different, and the few comparative studies found are restricted by patient selection bias. (2) PJI treatment outcomes depend on various factors,<sup>3,15</sup> and for technical reasons no studies are able to stratify patients (in reasonable numbers) according to these factors (Fig. 2, Fig. 3). Management strategies (especially one-stage and two-stage revisions) are not uniform and



**Fig. 2** Factors affecting the outcome of different prosthetic joint infection (PJI) treatment strategies are shown.



**Fig. 3** Different steps and variables of one-stage revision strategy are shown. Question marks indicate technical steps for which there is a lack of agreement in the literature.

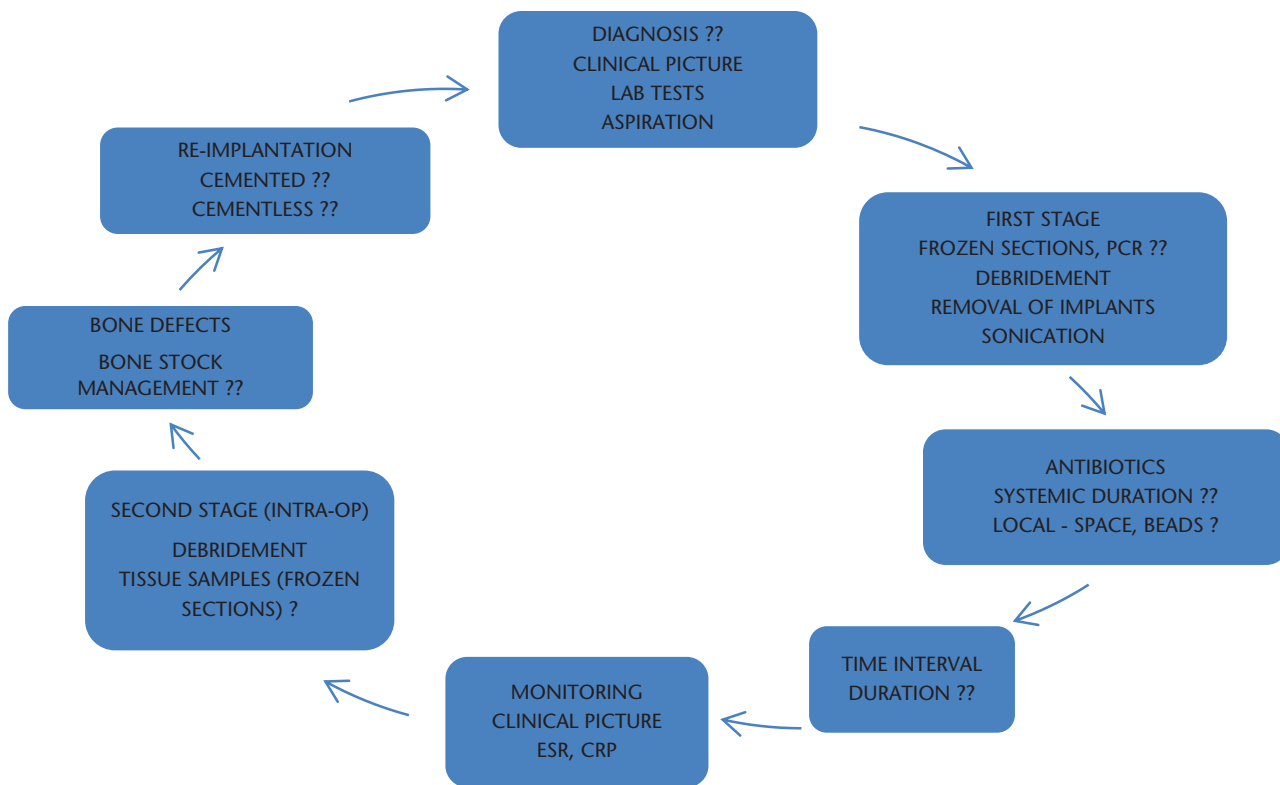
Note. PCR; CRP; ESR.

present several controlled and uncontrolled variables (Fig. 3, Fig. 4). Furthermore, the majority of studies report on either infection recurrence rates or infection-free time intervals, and present survival curves with revision for reinfection as an end point, and when reporting functional outcomes the conventional Harris Hip Score (HHS) and Knee Society Score (KSS) scales are mostly used.<sup>11–14,16,17</sup> It has to be stressed that Jafari et al have shown that 25 (22%) of their 112 septic total hip arthroplasty (THA) revisions failed due to reinfection and 21 (19%) failed due to other reasons.<sup>18</sup> Therefore, medium to long-term outcome data related to infection-free reconstructed joints are also needed (Table 1) and appropriate functional and quality of life outcome data are also of major importance.

### Outcomes of the DAIR procedure

The DAIR procedure, with or without exchange of modular parts, is technically less demanding, and can therefore be considered as an option for the treatment of early infections.<sup>19,20</sup> DAIR is indicated in early post-operative infections (less than four weeks from index operation), late haematogenous PJI with short duration of symptoms

(less than four weeks), good soft tissue envelope, known gram-positive pathogen with good antibiotic sensitivity and minimally inhibitory bacterial concentrations, stable implant and when host grade is not compromised.<sup>21,22</sup> Higher success rates (above 80%) are expected when strict patient selection criteria are introduced.<sup>21,22</sup> In a systematic review and meta-analysis, Kunutsor et al reported an overall 61.4% pooled estimate for rate of infection control for DAIR.<sup>23</sup> Tözün et al also reported that DAIR infection control rates for infected total knee arthroplasty (TKA) vary across different studies, ranging from 16% to 82%.<sup>24</sup> Exchange of mobile components also improves outcomes.<sup>25</sup> Sendi et al reported a 90% survival rate for aseptic loosening in 46 THAs treated with DAIR at 8–10 year follow-up.<sup>26</sup> Grammatopoulos et al reported an 85% infection irradiation rate and 77% survival rate for aseptic loosening at 18-year follow-up in 122 THAs treated with DAIR (Oxford database).<sup>27</sup> Finally, Clauss et al analysed implant survival rates after successful treatment of infection in 57 THAs treated with DAIR.<sup>28</sup> A 16% revision rate for any reason and 9% for aseptic loosening of any component were reported at six-year follow-up, with both figures being comparable to those of the control group.<sup>28</sup>



**Fig. 4** Different steps and variables of two-stage revision strategy are shown. Question marks indicate technical steps for which there is a lack of agreement in the literature.

Note. PCR; CRP; ESR.

### Outcomes of one-stage revision

One-stage revision can be a viable and efficient strategy when appropriate indications are fulfilled. It is indicated in acute (less than four weeks from index operation), rather in chronic post-operative infections, good soft tissue envelope, known gram-positive pathogen with good antibiotic sensitivity and minimally inhibitory bacterial concentrations, and when host grade is not compromised.<sup>29,30</sup> Extensive debridement with removal of all devitalized tissue material during the operation is one of the most important factors affecting the final outcome. Local and systemic antibiotic delivery tailored to the known pathologic organism is an integral part of the technique, but the duration of systematic antibiotic administration is still being discussed.<sup>29–31</sup> Early to medium-term infection control, for properly indicated single-stage revision, varies from 77–100% across a variety of studies.<sup>29–31</sup> The Hamburg Group reported a minimum 10-year infection-free survival of 94% and surgery-free survival of 75.9% in 85 hips undergoing one-stage revision with cemented implants.<sup>32</sup> The same group reported 10–24 year infection-free survival of 96.2% and surgery-free survival of 76.9% in 26 hips in patients younger than 45 years.<sup>33</sup> Born et al reported a

seven-year infection-free survival of 96% and an aseptic-loosening-free survival of 97% in 28 hips undergoing one-stage revision with cementless implants.<sup>34</sup>

### Outcomes of two-stage revision

Two-stage revision is still considered the gold standard of treatment. It is indicated more in chronic infections (more than four weeks from index operation), late haematogenous PJI with long duration of symptoms (more than four weeks), when the host grade and local tissue are compromised, in gram-negative, methicillin-resistant staphylococcus and fungal infections and when the organism is unknown.<sup>35</sup> It involves resection of the prosthesis with or without placement of an antibiotic spacer, antibiotic treatment, following the patient’s response to treatment and re-implantation of a new prosthesis.<sup>35</sup> Numerous studies have reported that two-stage revision with the use of antibiotic spacers can result in infection eradication rates at the level of 80–95%, and the use of articulating spacers improves functional outcomes.<sup>35</sup> Petis et al reported an infection recurrence of 15%, an incidence of aseptic revisions of 3.3% and an incidence of all revisions of 16%, at 10 to 15 years, in 164 patients with infected THAs treated with two-stage revision using mixed cemented

and cementless implants (Mayo Clinic Group).<sup>36</sup> Born et al reported a seven-year infection-free survival of 94% and an aseptic-loosening-free survival of 97% in 53 infected THAs undergoing two-stage revision with cementless implants.<sup>34</sup> There is no evidence to suggest that the type of fixation at the time of re-implantation affects infection recurrence rates, but it may affect long-term implant survival. Bongers et al reported, at eight-year follow-up, 17% re-revision surgery, 11% due to infection and 6% due to aseptic loosening, in 113 infected TKAs treated with two-stage revision.<sup>37</sup> Petis et al reported 17% infection recurrence, 7% incidence of aseptic revisions and 8.4% incidence of all revisions at 15 years in 245 patients with infected TKAs treated with two-stage revision (Mayo Clinic Group).<sup>38</sup>

### Comparative studies

In an early systematic review and meta-analysis evaluating 36 infected THA studies, Lange et al reported a 13.1% re-infection rate in one-stage and 10.4% in the two-stage cohorts.<sup>11</sup> Kunutsor evaluated 44 cohorts across four continents on behalf of the Global Infection Orthopaedic Management Collaboration, and reported re-infection rates per 1000 person-years of follow-up (mean four years) as 16.8% for a one-stage and 32.3% for a two-stage revision strategy.<sup>39</sup> Engesæter et al evaluated patients from the Norwegian Arthroplasty Registry and found a 1.4 times increased risk of re-revision for any reason and two times increased risk of re-revision for infection in a one-stage as compared to a two-stage infected THA revision strategy.<sup>40</sup> Svensson et al evaluated patients from the Swedish arthroplasty registry and found a similar risk for re-revision for infection (0.7) and aseptic loosening (1.2) when they compared patients who had undergone one-stage and two-stage revision for infected THA.<sup>41</sup> Pangaud et al, in a systematic review, analysed 14 articles with one-stage (687 patients) and 18 articles with two-stage (1086 patients) revision for infected TKA, and reported an average eradication rate of 87.1% in the one-stage and 84.8% in the two-stage procedure.<sup>42</sup> Although one-stage revision can provide better results than the two-stage revision procedure, one should keep in mind that one-stage revision is indicated in selected patients (based on host, bacteriological, soft tissue and type of infection criteria).

Hoberg et al evaluated 37 hips which underwent revision surgery for aseptic loosening, and 45 hips which underwent revision for septic loosening, using cementless implants, and found a similar survival rate of 85.6% and 82.7%, respectively, at 10 years with revision for aseptic loosening as an end point.<sup>43</sup> Konrads et al compared patients who underwent two-stage revision for septic TKA (52 patients) and one-stage aseptic total knee revision arthroplasty (83 patients).<sup>44</sup> Early outcomes

were similar in both groups in terms of KSS, Oxford Knee and SF-36 scores.

To the best of our knowledge, no studies comparing DAIR to either one-stage or to two-stage revision have been ever published.

### Functional and quality of life outcomes

In 2010, Oussedik et al were the first to show significant improvements in mean HHS and visual analogue scores for satisfaction at five years, in one-stage septic THA revisions as compared to two-stage revisions.<sup>45</sup> In a systematic review comparing one-stage to two-stage revision for infected THA, a trend towards better functional outcomes was shown in the one-stage group.<sup>12</sup> One-stage revision strategy for infected THA showed improved functional outcome, reduced cost and improved survival rates in the most recent studies in a systematic review and meta-analysis.<sup>46</sup> Two-stage revision for infected TKA using articulating spacers in comparison to static ones resulted in better infection eradication rates as well as better functional outcomes and improved quality of life.<sup>47</sup> Grammatopoulos et al showed that DAIR for infected THA is better than a two-stage revision regarding functional outcome.<sup>48</sup> Barros et al also showed that DAIR for infected THA and TKA is safe, effective and has satisfactory functional results when compared to two-stage revision.<sup>49</sup> Aboltins et al showed that infected THA and TKA treated with DAIR had a similar improvement in quality of life (according to the SF-12 survey) from pre to 12 months post arthroplasty as compared to arthroplasty patients without infection.<sup>50</sup> Poulsen et al suggested that patients who undergo two-stage revision after infected THA have lower scores on health-related quality of life than the general population.<sup>51</sup> Palmer et al showed that, at 18 months, patients undergoing two-stage revision with an excised THA or a cement spacer described severe mobility restrictions which affected all aspects of their lives, while those undergoing one-stage revision, or two-stage revision with an articulating spacer were more mobile and independent, with some limitations.<sup>52</sup> Participants in all treatment groups also expressed considerable emotional resilience during recovery from revision.<sup>52</sup> Rietbergen et al, in a systematic review of 12 papers describing two-stage revision for infected THA, assessed health-related quality of life (HRQoL).<sup>53</sup> Patients presented substantially lower physical component HRQoL scores, but mental scores were comparable to the general population.<sup>53</sup> Kildow et al, in a review paper, observed the increasing popularity of one-stage revision for infected total joint arthroplasty (TJA) as compared to two-stage revision based on recent literature demonstrating comparable success rates, lower morbidity rates, potential functional benefits to the patients, and a decreased economic burden on the healthcare system.<sup>54</sup>

## Conclusions

Despite current advances in orthopaedic adult reconstruction practices, PJI still represents one of the most devastating complications in implant surgery. Concerning management outcomes, our knowledge is based on poor-quality studies. DAIR, one-stage and two-stage revision surgery strategies have different indications and are not uniform techniques, with the relevant importance of their various parameters and steps remaining to be evaluated. Recent studies show that all three strategies show variable satisfactory infection control rates; however, a considerable number of infection-free joints fail for other reasons. This has also been confirmed in the Swedish Joint Registry, in which lower survival rates in revision THA for infection were observed.<sup>55</sup> Orthopaedic surgeons should pay attention to performing high-quality infected joint revision surgery as in revision cases for aseptic loosening. Recent data show that DAIR and one-stage revision result in superior functional and quality of life outcomes and reduced costs for health systems. However, one should keep in mind that the outcomes of the DAIR procedure vary and that both DAIR and one-stage procedures are indicated for selected patients only.

### AUTHOR INFORMATION

<sup>1</sup>Department of Orthopaedics and Musculoskeletal Trauma, University General Hospital of Larissa, Greece.

<sup>2</sup>School of Health Sciences, Faculty of Medicine, University of Thessalia, Larissa, Greece.

Correspondence should be sent to: Theofilos Karachalios, Department of Orthopaedics and Musculoskeletal Trauma, University General Hospital of Larissa, School of Health Sciences, Faculty of Medicine, University of Thessalia, Biopolis, Mezourlo Region, 41110 Larissa, Greece.  
Email: kar@med.uth.gr

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