Infectious olecranon and patellar bursitis: short-course adjuvant antibiotic therapy is not a risk factor for recurrence in adult hospitalized patients

Cédric Perez1†, Angela Huttner2**, Mathieu Assal1, Louis Bernard1,3,4, Daniel Lew2, Pierre Hoffmeyer1 and Ilker Uçkay1,2

1Orthopaedic Surgery Service, Geneva University Hospital and Faculty of Medicine, University of Geneva, Geneva, Switzerland; 2Service of Infectious Diseases, Geneva University Hospital and Faculty of Medicine, University of Geneva, Geneva, Switzerland; 3Service of Infectious Diseases, Raymond Poincaré University Hospital, Garches, France; 4Assistance Publique–Hôpitaux de Paris, University of Versailles St Quentin en Yvelines, Garches, France

*Corresponding author. Tel: +41-22-372-3311; Fax: +41-22-372-9599; E-mail: angela.huttner@hcuge.ch
†These authors made equal contributions as first authors.

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Objectives: No evidence-based recommendations exist for the management of infectious bursitis. We examined epidemiology and risk factors for recurrence of septic bursitis. Specifically, we compared outcome in patients receiving bursectomy plus short-course adjuvant antibiotic therapy (≤7 days) with that of patients receiving bursectomy plus longer-course antibiotic therapy (>7 days).

Patients and methods: Retrospective study of adult patients with infectious olecranon and patellar bursitis requiring hospitalization at Geneva University Hospital from January 1996 to March 2009.

Results: We identified 343 episodes of infectious bursitis (237 olecranon and 106 patellar). Staphylococcus aureus predominated among the 256 cases with an identifiable pathogen (85%). Three hundred and twelve cases (91%) were treated surgically; 142 (41%) with one-stage bursectomy and closure and 146 with two-stage bursectomy. All received antibiotics for a median duration of 13 days with a median intravenous component of 3 days. Cure was achieved in 293 (85%) episodes. Total duration of antibiotic therapy [odds ratio (OR) 0.9; 95% confidence interval (95% CI) 0.8–1.1] showed no association with cure. In multivariate analysis, only immunosuppression was linked to recurrence (OR 5.6; 95% CI 1.9–18.4). Compared with ≤7 days, 8–14 days of antibiotic treatment (OR 0.6; 95% CI 0.1–2.9) or >14 days of antibiotic treatment (OR 0.9; 95% CI 0.1–10.7) was equivalent, as was the intravenous component (OR 1.1; 95% CI 1.0–1.3).

Conclusions: In severe infectious bursitis requiring hospitalization, adjuvant antibiotic therapy might be limited to 7 days in non-immunosuppressed patients.

Keywords: bursectomy, parenteral, septic bursitis

Introduction

Although primary infectious olecranon and patellar (pre- and infrapatellar) bursitis occur frequently, there are few data concerning their optimal surgical and antibiotic management. Case reports and epidemiological studies date from the 1970s and 1980s and involve from a few dozen cases to at most 118 cases. Often there is no demarcation between infectious and non-infectious bursitis. Recommendations remain contradictory. While some advocate outpatient treatment with percutaneous needle aspiration, antibiotics and immobilization, others recommend hospitalization with surgical drainage or suction-irrigation. Some advocate intravenous (iv) therapy for up to 4 weeks in non-operative cases, others, for 2–3 days followed by oral therapy for 10 days in operative cases. Some experts distinguish between protracted and early presentation, advocating a longer antibiotic course for the former, while others specifically recommend a longer course of parenteral therapy for the immunocompromised.

Given today’s dual predicament of rising antimicrobial resistance and antibiotic cost, a review of prescription practices is warranted for all common infections. In this study, we examine the epidemiology of infectious bursitis requiring hospitalization and risk factors for recurrence. With an eye to reducing catheter-related complications, patient and nurse...
Patients and methods

Setting and management of infectious bursitis

The Geneva University Hospital is a 2200 bed tertiary hospital. In 2007 there were 5374 surgical procedures performed at an orthopaedic service with 119 acute care beds and a dedicated infectious diseases consultant. One day of hospitalization at standard insurance costs ~1300 CHF (where CHF stands for Confoederatio Helvetica franc (Swiss currency); US $1130 or €725). Typically, bursectomy is performed at admission, with immediate closure when the wound is grossly clean or secondarily after 2–4 days of antibiotic treatment; these interventions are followed by daily dressing changes by specialized nurses. The decision for open or closed bursectomy is made by the treating surgeon and is based upon local findings. Open bursectomy is usually chosen when the involved bursa reveals extensive purulence or frank necrosis. Empirical antibiotics are administered iv until closure or availability of a microbial resistance panel, when a switch to oral medication is made. The overall duration of antibiotic therapy and its iv component depend on the treating physicians. No intrabursal antibiotics are administered. All patients wear splints for a period of 2–3 weeks; no padding is recommended thereafter. Patients are monitored in our outpatient clinic until removal of sutures and complete clinical cure.

Data collection

Databases from the Laboratory of Bacteriology and the Administrative Coding Centre were retrospectively searched for olecranon and patellar bursitis in adult hospitalized patients from January 1996 to March 2009. Forty-eight variables for each episode were assessed with information pertaining to demographic characteristics, Charlson co-morbidity index, immunosuppression, microbiology, surgical and antibiotic treatment modalities and outcomes. Patients were monitored until 7 April 2009. Data sampling was approved by the hospital’s Ethics Committee (no. 08-017R); informed consent was not required.

Inclusion criteria and definitions

The definition of infectious bursitis required the following: clinical suspicion of infectious bursitis in the absence of other documented pathology; surgical and antibiotic treatment targeting infection; and the presence of pus upon bursectomy when performed. Immunosuppression was defined as the presence of the following co-morbidities: diabetes mellitus; HIV infection with CD4 count <350/mm³; status post-transplantation requiring prolonged immunosuppressive therapy; alcoholism; renal failure requiring dialysis; Child–Pugh class B or C liver cirrhosis; and active malignancy without remission (chemotherapy either ongoing or discontinued for palliative purposes). Advanced age and polytrauma were not counted as factors defining immunosuppression. Bacteraemia was defined as positive blood cultures yielding a known pathogenic bacterium, where blood cultures were drawn before initiation of antibiotic therapy. C-reactive protein (CRP) levels were recorded only when drawn before surgical intervention and initiation of antibiotics. Cure was defined as complete clinical and microbiological resolution of bursitis at final follow-up. Recurrence was demonstrated by clinical signs of infection at least 2 weeks after termination of treatment for the first episode and isolation of the same pathogen in bursal specimens.

Exclusion criteria

Ambulatory and paediatric patients (age <17 years) were excluded, as were those with the following conditions: non-olecranon, non-patellar bursitis; non-primary (recurrent) infectious bursitis; non-infectious bursitis, such as crystal-induced bursitis (even if co-infection); and the presence of an orthopaedic implant adjacent to the infected bursa. Finally, bursitis patients with concomitant infections requiring antibiotic treatment were excluded, such as underlying osteomyelitis diagnosed clinically, by imaging or by bone biopsy.

Statistical analyses

Group comparisons of categorical variables were performed using the Pearson χ² test. For group comparisons of non-parametrically distributed continuous variables we used the Wilcoxon rank sum test (comparison of two groups) or the Kruskal–Wallis test (comparison of three groups). Logistic regression analysis determined associations with recurrence. Only first episodes of bursitis were included in the regression analysis. Independent variables with a P value ≤0.05 in the univariate analysis were introduced stepwise in the multivariate analysis. In line with new statistical research data,18 we included ~7–10 outcome events per predictor variable. Age, CRP and the duration of total or iv antibiotic treatment were analysed as continuous and categorical variables. All variables were checked for confounding, co-linearity and interaction, the latter by Mantel–Haenszel estimates. According to these criteria, the variables included in the stepwise procedure were the following: age; CRP; Charlson score; immunosuppression; one-stage bursectomy; duration of iv antibiotic therapy; and duration of total antibiotic therapy. All remained in the final model.

We assessed a possible linearity of the duration of antibiotic administration and recurrence of infection by linear regression analysis and standard logistic regression. This procedure was performed first with continuous and categorical variables, then repeated with quadratic and logarithmic (ln) transformations of these variables. Further, we investigated the potential presence of a threshold beneath which the duration of anti-biotic administration could be associated with enhanced recurrence risk by graphical plotting of all recurrent cases in relation to their antibiotic duration.

We analysed antibiotic duration variables within three strata (rather than dichotomous variables) in order to yield more detailed results. The cut-off values for these strata were established as follows. The middle stratum was positioned around the median value of that variable. The inferior and superior limits were chosen according to threshold values of a potentially increased recurrence risk. If these values were not present, the choice was made relying on the 33% and 66% percentiles of the distribution of values of that variable. Finally, the limits were rounded up to clinically practical durations. According to this approach, the total duration of antibiotic treatment was analysed as a continuous variable and as a categorical variable with the following three strata: 0–7 days; 8–14 days; and ≥14 days. This approach was similar for the duration of parenteral antibiotic therapy, with the following strata: 0–2 days; 3 days; and ≥3 days. P values ≤0.05 (all two-tailed) were considered significant. STATA software (v. 9.0; Stata, College Station, TX, USA) was used.

Results

Patients and bursitis

A total of 343 primary patellar (n=106) and olecranon (n=237) bursitis episodes in 339 patients were identified for analysis [median age 51 years; 281 males (82%), Table 1]. The median length of hospital stay was 8 days [interquartile range (IQR), 6–13 days]. In 88 episodes (26%), patients were substantially immunocompromised as defined by the presence of diabetes
mellitus (n=39; 25 insulin dependent), active progressive metastatic malignancy without remission (n=12; five undergoing chemotherapy, seven without treatment for palliative reasons), active alcoholism (n=10), autoimmune disease requiring steroids (n=18), HIV infection (n=7; median CD4 count of 180 cells/mm³), solid organ transplantation (n=1) and splenectomy (n=1).

Seventeen patients demonstrated multifactorial immunosuppression with combinations of the above conditions plus haemodialysis (n=1) or liver cirrhosis (n=1). In autoimmune patients, the median dose of steroid therapy was equivalent to 13.75 mg of prednisolone daily (range 7.5–70 mg). Non-penetrating trauma was the most frequent cause of bursitis (166/343; 48%), followed by unrecalled/unknown source in 130 cases (38%), furunculosis (n=18), a history of pressure on the bursa (n=13), scratching (n=8), insect bite (n=5), drug injection (n=2) and thorn prick (n=1). Olecranon bursitis was linked to physical, occupation-related activity (58% versus 42%, χ² test, P=0.023).

**Microbiology**

In 87 cases, no pathogen could be isolated. Among culture-positive infections, *Staphylococcus aureus* was the most frequent pathogen (217/256; 85%), of which three were methicillin resistant, followed by *Streptococcus pyogenes* (n=16), other streptococci (n=15), *Enterococcus faecalis* (n=4) and coagulase-negative staphylococci (n=2). With the exception of one infection with *Klebsiella oxytoca* alone, four other Gram-negative organisms were co-pathogens with *S. aureus*. Among the 71 episodes with blood culture sampling before the introduction of antibiotics, only three (3/71, 4%) yielded the same organism as found in bursal specimens.

**Antibiotic treatment**

All patients received systemic antibiotics for a median total duration of 13 days; the median duration of i.v. antibiotic administration was 3 days. Among parenteral antibiotics, amoxicillin/clavulanic acid was most frequently employed (n=146), followed by flucloxacillin (n=60) and clindamycin (n=20). Of the oral antibiotics, clindamycin was preferred (n=119), followed by amoxicillin/clavulanic acid (n=100) and flucloxacillin (n=37). Of note, 34 episodes (34/343, 10%) were not treated at all with iv antimicrobials, while in 31 cases, antibiotic therapy was strictly iv. Table 2 displays patient characteristics according to the length of antibiotic therapy.
Surgical treatment

All but 31 patients (9%) underwent bursectomy a median of 3 days after onset of infection. The median number of surgical interventions was 1 and the median interval between bursectomy and final closure was 3 days. In 142 episodes (41%), patients underwent one-stage bursectomy with immediate closure. In 170 episodes, there were multiple surgical interventions; in 146 cases, lavage and closure followed the first bursectomy after a median interval of 2 days, while 24 episodes required more than two debridements. Patients undergoing one-stage bursectomy had a significantly shorter length of hospital stay than patients with two-stage bursectomy (6 versus 10 days, \( P < 0.005 \)).

Cure and recurrence of bursitis

A total of 293 episodes (85%) achieved clinical cure, with a median follow-up of 23 months (IQR, 2.7–67 months). Recurrence occurred in 50 episodes (50/343, 14.6%) (Table 1) after a median period of 25.5 days after discontinuing antibiotic therapy. There was an increased risk of further recurrences after the initial recurrence; while 40 patients witnessed only one recurrence, 10 patients with a first recurrence (20%) witnessed further episodes (7 patients experienced two recurrences, 2 patients experienced three recurrences and 1 patient experienced four recurrences despite extensive debridement and weeks-long antibiotic therapy). Of the 30 patients treated only pharmacologically, 24 (80%) experienced recurrence.

Lack of threshold and linearity between duration of antibiotic treatment and recurrence risk

There was no threshold in the duration of total antibiotic treatment beneath which the recurrence risk was increased (Figure 1). Recurrence occurred within a range of 2–60 days for total antibiotic therapy, and 1–21 days for iv antibiotic administration. Likewise, the association of antibiotic duration with recurrence was not linear according to simple linear regression, or according to regression using quadratic or logarithmic transformation of antibiotic-duration variables.

Logistic regression analyses of risk factors for recurrent bursitis

Due to differences in the crude group comparisons (Tables 1 and 2) as well as statistically significant associations with recurrence...
in univariate analysis (Table 3), a multivariate analysis was performed in order to adjust for case mix. ‘No surgical intervention’ was strongly related to recurrence in univariate analysis [odds ratio (OR) 50; 95% confidence interval (95% CI) 19–135]. Because this factor was present in only a small minority of patients, it was excluded from the multivariate model. The final model goodness-of-fit test was 0.994, with an area under the ROC curve of 0.835 (where ROC stands for receiver operating characteristic).

In multivariate analysis, only the presence of immunosuppression could be linked to recurrence (OR 5.6; 95% CI 1.9–18.4). Neither the total duration of antibiotic treatment (OR 0.9; 95% CI 0.8–1.1) nor its parenteral component (OR 1.1; 95% CI 1.0–1.3) was significantly associated with recurrence. Compared with ≤7 days, 8–14 days of treatment (OR 0.6; 95% CI 0.1–2.9) or >14 days of treatment (OR 0.9; 95% CI 0.1–10.7) was equivalent. While the one-stage approach yielded a trend toward a higher recurrence rate (OR 3.5; 95% CI 0.6–21.0), this was not statistically significant.

Because immunosuppression was revealed to be significant, we stratified the regression analysis accordingly. In both strata (immunosuppressed and immunocompetent), no single surgical or antibiotic-related variable was statistically associated with recurrence. In immunosuppressed episodes, the CIs were wide, representing possible under-powering for this stratum: age (OR 1.0; 95% CI 0.9–1.0); time interval between bursectomy and closure (OR 1.0, 95% CI 0.8–1.1); one-stage bursectomy (OR 1.4, 95% CI 0.2–12.1); total duration of antibiotic treatment (OR 0.9, 95% CI 0.8–1.1); or iv treatment for >3 days (OR 0.8, 95% CI 0.2–3.5).

### Table 3. Predictors for recurrence of bursitis (logistic regression)

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Univariate analysis</th>
<th>Multivariate analysis (only variables included in the final model)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR (95% CI)</td>
<td>P value(^a)</td>
</tr>
<tr>
<td>Female gender</td>
<td>1.3 (0.6–2.8)</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>1.03 (1.01–1.05)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Charlson score(^17)</td>
<td>1.5 (1.3–1.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Immunosuppression(^b)</td>
<td>3.3 (1.8–6.1)</td>
<td></td>
</tr>
<tr>
<td>steroid medication</td>
<td>1.1 (1.0–1.2)</td>
<td></td>
</tr>
<tr>
<td>Occupation requiring physical activity</td>
<td>0.4 (0.2–1.0)</td>
<td></td>
</tr>
<tr>
<td>Psychiatric co-morbidities</td>
<td>1.3 (0.6–2.8)</td>
<td></td>
</tr>
<tr>
<td>Olecranon bursitis</td>
<td>1.3 (0.7–2.6)</td>
<td></td>
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<tr>
<td>Left side involvement</td>
<td>1.7 (0.9–3.1)</td>
<td></td>
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<tr>
<td>CRP before surgery</td>
<td>1.0 (1.0–1.0)</td>
<td></td>
</tr>
<tr>
<td>Bursitis due to <em>Staphylococcus aureus</em></td>
<td>0.8 (0.4–1.4)</td>
<td></td>
</tr>
<tr>
<td>Traumatic origin</td>
<td>1.0 (0.5–1.8)</td>
<td></td>
</tr>
<tr>
<td>Number of surgical interventions</td>
<td>0.1 (0.1–0.2)</td>
<td>0.000</td>
</tr>
<tr>
<td>one-stage bursectomy with closure</td>
<td>3.6 (1.5–8.8)</td>
<td>0.005</td>
</tr>
<tr>
<td>Interval between onset of symptoms and surgery</td>
<td>1.0 (1.0–1.0)</td>
<td></td>
</tr>
<tr>
<td>Interval between first and second surgery</td>
<td>0.9 (0.8–1.0)</td>
<td></td>
</tr>
<tr>
<td>Interval between bursectomy and closure</td>
<td>0.9 (0.8–1.0)</td>
<td></td>
</tr>
<tr>
<td>Total duration of total antibiotic therapy</td>
<td>1.0 (1.0–1.0)</td>
<td></td>
</tr>
<tr>
<td>8–14 days compared with ≤7 days</td>
<td>0.4 (0.1–1.0)</td>
<td></td>
</tr>
<tr>
<td>&gt;14 days compared with ≤7 days</td>
<td>0.7 (0.3–1.5)</td>
<td></td>
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<tr>
<td>Total duration of intravenous therapy</td>
<td>0.9 (0.8–1.1)</td>
<td></td>
</tr>
<tr>
<td>3 days compared with ≤2 days</td>
<td>0.4 (0.1–1.4)</td>
<td></td>
</tr>
<tr>
<td>&gt;3 days compared with ≤2 days</td>
<td>0.7 (0.4–1.4)</td>
<td></td>
</tr>
</tbody>
</table>

Variables not included in the final model do not appear in the multivariate analysis column.

\(^a\) Only significant P values ≤0.05 (two-tailed) are displayed.

\(^b\)Immunosuppression = diabetes mellitus, steroids, transplantation, HIV infection, alcoholism, dialysis, cirrhosis (class Child–Pugh B or C), malignancy.
Discussion

Recurrence of septic olecranon and patellar infectious bursitis is common among severe illnesses requiring hospitalization. While univariate analyses yielded several risk factors among 343 episodes, adjustment in multivariate analysis revealed only immunosuppression as a risk factor for recurrence. The number of surgical interventions, the timing of bursectomy and the interval between first surgery and closure did not influence recurrence risk. This was equally true for antibiotic-related parameters. The overall duration of antibiotic therapy and the duration of parenteral therapy or the lack thereof bore no influence on recurrence risk. Compared with ≤7 days, 8–14 or >14 days of treatment was equivalent as was the iv component. However, the total median duration of antibiotic therapy in patients with and without recurrence was 12 and 14 days, respectively, while a small minority of patients were treated for ≤7 days. Thus, under-powering for this particular stratum could have been an issue. On the other hand, the relatively small CIs for all strata argue against substantial under-powering. Moreover, the goodness-of-fit test as well as the area under the ROC curve were excellent, yielding a more than acceptable predictive value for our multivariate model.

Of note, all our patients received antibiotics. Hence we were unable to estimate recurrence rates by surgical procedures alone.

Since immunosuppression was an independent, major risk factor, we examined whether surgical- and antibiotic-related variables might differ when controlled and stratified based on immune status. They did not, suggesting that immunosuppression is an independent risk factor whose mitigation is difficult to achieve with therapy modifications. A parallel finding was that prior recurrence itself was a strong predictor for further recurrent episodes, suggesting a central role for endogenous host factors. These as-yet poorly defined elements may be only weakly influenced by medical or surgical intervention and thus are difficult to characterize in the setting of a retrospective study based on clinical parameters. We therefore excluded subsequent recurrent episodes to avoid a massive clustering effect.

If confirmed in prospective trials, our findings could have practical implications for hospitalized patients. First, bursectomy and closure could potentially be performed on a single-stage basis; delayed, two-stage closure might be reserved for patients with particularly infected or necrotic lesions and immunosuppressed patients. We note with caution, however, that this assumption needs confirmation by a randomized trial, as univariate analysis and crude group comparison identified closed bursectomy as a significant risk factor for recurrence. Statistical significance was lost, however, once analyses were adjusted for immunosuppression and other factors.

In our setting, one-stage bursectomy led to a hospital stay shortened by 4 days. At conservative estimates, considering ~1300 CHF ($1130) per day of hospitalization and 2000 CHF ($1740) per surgical intervention, savings of at least 7000 CHF ($6100) would be achieved in each case where one-stage bursectomy was performed. Secondly, in the absence of concomitant infections, iv medication could be limited to 1–2 days or avoided altogether (given an absence of clinical signs indicating compromised intestinal absorption), thus reducing the risk of catheter-related complications and costs. Third, limiting overall antibiotic therapy to 7 days would further decrease antibiotic consumption, cost, adverse effects and selection pressure leading to antimicrobial resistance. This approach would be restricted to patients undergoing surgical resection. Fourth, bursitis-related bacteraemia is extremely rare, thus routine sampling would not be recommended in patients without risk of secondary endovascular disease.

Our study confirms many aspects of previous reports about septic bursitis, i.e. predominance of S. aureus followed by S. pyogenes,1,3,6,7,11 young or middle-aged male patients,1,3 – 5,11 pre-notification of olecranon versus patellar involvement,1,19 and trauma as the most common origin.2,5 In contrast, we report a much lower incidence of positive blood cultures compared with other reports citing rates of 19%3 and 30%.9 These higher percentages remain somewhat debatable, as other authors showed no episodes of bacteraemia among their 16 cases of bursitis.6 We were not able to confirm any association between bursitis and occupations involving pressure on the bursa.1,2,20 An infection due to S. pyogenes, the most feared pathogen of necrotizing fasciitis,21 triggered a more aggressive initial inflammatory response (data not shown), yet no patient with a S. pyogenes infection witnessed recurrence.

Our study has its limitations. (i) It is retrospective and stems from a single institution, aspects that limit extrapolation of its findings. (ii) Of the 150 bursae in the human body, only olecranon and patellar bursitides were examined. These two are, however, the most relevant bursae in infectious bursitis.1,10 (iii) Recurrences may have been missed in patients who were treated elsewhere after their initial bacteraemia. Given, however, that Geneva University Hospital is the largest and sole public hospital with the largest orthopaedic unit in the area, and the thorough post-discharge follow-up of our patients, we consider this selection bias to be minimal. (iv) By definition, our study population is narrow, as we did not include milder cases of bursitis requiring outpatient management with antibiotic therapy or needle aspiration alone. Indeed, several authors contend that a substantial proportion of patients can be managed on a purely outpatient basis with oral antibiotics.5,10 This conservative approach, however, harbours a treatment failure rate varying from 9% to 32%,48% or 51%,5,11,20 and results in the prolongation of antibiotic therapy to a duration of up to 3 or 4 weeks,2 further complicating efforts to reduce antibiotic consumption and antimicrobial resistance. (v) Lack of any surgical intervention was the most important risk factor for recurrence of infectious bursitis. The OR in the univariate analysis was 50 times higher in non-operated patients than in patients with at least one surgery. Since we examined only hospitalized patients and did not include ambulatory controls receiving conservative treatment, we excluded lack of surgical intervention in our multivariate analysis in order to avoid a substantial selection bias. (vi) It is possible that certain patients with more minor infections both received a shorter course of antibiotics and had a more favourable outcome simply because their bursitides were less severe from the outset. This potential bias reinforces the need for randomized studies.

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**Transparency declarations**
None to declare.

Ilker Uçkay, MD, had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

**References**