Can the presence of an infection be predicted before a revision total hip arthroplasty? Preliminary study to establish an infection score

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A R T I C L E   I N F O

Article history:
Received 17 July 2015
Accepted 9 December 2015

Keywords:
Infection
Revision
Total hip arthroplasty
Preoperative diagnosis

A B S T R A C T

Introduction: The diagnosis of periprosthetic joint infection can be challenging, in part because there is no universal diagnostic test. Current recommendations include several diagnostic criteria, and are mainly based on the results of deep microbiological samples; however, these only provide a diagnosis after surgery. A predictive infection score would improve the management of revision arthroplasty cases. The purpose of this study was to define a composite infection score using standard clinical, radiological and laboratory data that can be used to predict whether an infection is present before a total hip arthroplasty (THA) revision procedure.

Hypothesis: The infection score will make it possible to differentiate correctly between infected and non-infected patients in 75% of cases.

Material and methods: One hundred and four records from patients who underwent THA revision for any reason were analysed retrospectively: 43 with infection and 61 without infection. There were 54 men and 50 women with an average age of 70 ± 12 years (range 30–90). A univariate analysis was performed to look for individual discriminating factors between the data in the medical records of infected and non-infected patients. A multivariate analysis subsequently integrated these factors together. A composite score was defined and its diagnostic effectiveness was evaluated as the percentage of correctly classified records, along with its sensitivity and specificity.

Results: The score consisted of the following individually weighed factors: body mass index, presence of diabetes, mechanical complication, wound healing disturbance and fever. This composite infection score was able to distinguish correctly between the infected patients (positive score) and non-infected patients (negative score) in 78% of cases; the sensitivity was 57% and the specificity 93%.

Discussion: Once this score is evaluated prospectively, it could be an important tool for defining the medical – surgical strategy during THA revision, no matter the reason for revision.

Level of evidence: Level IV – retrospective study.

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1. Introduction

Infection after total hip arthroplasty (THA) occurs in about 1% of primary implantation cases [1]. The diagnosis of periprosthetic joint infection (PJI) can be difficult to make [2,3], in part because there is no universal diagnostic test – the diagnosis is made based on a body of evidence, with no individual element having a perfect predictive value [4]. Recommendations have recently been made to guide the diagnosis of PJI that are accepted as the international reference [5]. Among these diagnostic criteria, the results of intraoperative microbiological cultures are an essential element. However, these criteria only provide a diagnosis after surgery, which can lead to treatments being used that can be costly and potentially harmful to the microbial flora, or that are inadequate and increase the risk of failure.

A predictive infection score could improve the care of patients during THA revision. Knowledge, or at least a well-argued presumption, before the procedure of the presence or absence of an infection would make it possible to adapt the surgical strategy, discuss the validity of antimicrobial prophylaxis and guide the collection of intraoperative microbiological samples [6]. This led us to carry out a retrospective study to define a composite infection score using...
standard clinical, radiological and laboratory data that can be used to predict whether an infection is present or not before a THA revision procedure. We hypothesised that the infection score will make it possible to differentiate accurately between infected and non-infected patients in 75% of cases.

2. Material and methods

2.1. Patients

One hundred and four records from patients undergoing THA revision for any reason were collected from members of the French Hip and Knee Society (SFHG) and analysed retrospectively. The records were selected randomly from each participating centre, with the sole criteria being at least 1 year of follow-up. There were 54 men and 50 women with an average age of 70 ± 12 years (range 30–90). Forty-three records were for patients with a confirmed infection (positive deep microbiological culture) and 61 records were for patients for whom an infection had been ruled out after 1 year of follow-up. The distribution and source of the records are given in Table 1.

2.2. Methods

The following parameters were extracted from the records retrospectively:

- general criteria– age, weight, height, body mass index (BMI), ASA classification, history with emphasis on infection risk factors (diabetes, cancer, immunosuppression);
- status of the operated joint before the primary THA procedure with emphasis on wound healing disturbances and any sign of potential infection;
- postoperative course of the primary THA procedure with emphasis on wound healing disturbances, mechanical complications and bleeding-related complications;
- clinical signs at the time of the revision such as pain, fever and wound healing disturbances;
- CRP levels at the time of the revision;
- imaging data at the time of the revision – any type of abnormal prosthetic or periprosthetic findings with emphasis on periosteal apposition, ossification, presence of radiolucent lines or cysts, and implant migration.

2.3. Statistical methods

The statistical analysis was performed with the R software (version 3.0.1, R Foundation for Statistical Computing, Vienna, Austria). Significance threshold was set at 0.05. Comparison of the variables between the infected and non-infected cases was performed with Wilcoxon signed-rank test (quantitative variables) or Fisher’s exact test (qualitative variables). A univariate analysis was performed to look for individual discriminating factors between the records of infected and non-infected patients. The construction of a composite infection score (CIS) that is able to predict the presence of an infection was performed using a logistic regression model that incorporated the collected data. The explanatory variables in the model were extracted using a step-by-step approach based on a calculation of the Akaike Information Criterion by including only variables that have a significant relationship with the infection variable ($P < 0.05$) in the various univariate models. The odds ratio of the retained variables and area under the curve were calculated with 95% confidence intervals. The agreement between the predicted and observed outcome was analysed using a Hosmer–Lemeshow test in the ResourceSelection package included in the R software. The percentage variance explained by the model was estimated by calculating McFadden’s pseudo-R$^2$. The score’s sensitivity and specificity were determined to evaluate the model’s predictive ability.

3. Results

3.1. Univariate analysis

The univariate analysis isolated the following significant factors (Tables 2 and 3): BMI, diabetes, presence of mechanical complication at the time of the re-operation, fever, presence of a wound-healing defect. All of these factors were significantly associated with increased frequency of an infection diagnosis. The results are shown in Table 4.

3.2. Multivariate analysis

The CIS was defined with the following elements:

- BMI (kg/m$^2$ in absolute value) with a weight of 0.09;
- presence of diabetes: $D = 1$ if present, and 0 if not present, with a weight of 0.94;
- presence of a mechanical complication after the primary THA: $C = 1$ if present, and 0 if not present, with a weight of $–1.34$;
- presence of a wound healing disturbance after the primary THA: $IC = 1$ if present, and 0 if not present, with a weight of 17.55;
- presence of fever: $F = 1$ if present, and 0 if not present, with a weight of 1.22;
- a constant = $–3.63$.

The CRP levels were not included in the multivariate analysis because there were too many missing values (14/61 infected cases and 30/43 non-infected cases).

The full CIS model was:

$$(0.09 \times BMI) + (0.94 \times D) -(1.34 \times CM) + (17.55 \times IC) + (1.22 \times F) - 3.63$$
Table 2
Comparative analysis – quantitative variables (mean ± standard deviation, minimum, maximum).

<table>
<thead>
<tr>
<th>Factor</th>
<th>Infection (n = 43)</th>
<th>No infection (n = 61)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>69 ± 11 (30–87)</td>
<td>71 ± 12 (47–90)</td>
<td>0.65</td>
</tr>
<tr>
<td>Mass (kg)</td>
<td>86 ± 18 (45–150)</td>
<td>73 ± 20 (45–135)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>169 ± 10 (150–190)</td>
<td>166 ± 9 (148–186)</td>
<td>0.30</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>30.2 ± 6.7 (16.2–58.0)</td>
<td>26.1 ± 6.9 (16.0–56.0)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>ASA score</td>
<td>2.3 ± 0.5 (1–3)</td>
<td>2.1 ± 0.5 (1–3)</td>
<td>0.20</td>
</tr>
<tr>
<td>Number of previous procedures</td>
<td>1.9 ± 0.2 (1–4)</td>
<td>2.2 ± 0.3 (1–4)</td>
<td>0.34</td>
</tr>
<tr>
<td>CRP (mg/L)</td>
<td>12.8 ± 8.6 (0–25)</td>
<td>8.4 ± 5.5 (0–24)</td>
<td>0.03*</td>
</tr>
</tbody>
</table>

BMI: body mass index; ASA: American Society of Anesthesiology.
* Significant difference at 5%.

Table 3
Comparative analysis – qualitative variables (number and percentage).

<table>
<thead>
<tr>
<th>Presence of factor</th>
<th>Infection (n = 43)</th>
<th>No infection (n = 61)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>18 women (42%)</td>
<td>32 men (52%)</td>
<td>0.32</td>
</tr>
<tr>
<td>General history</td>
<td>35 (81%)</td>
<td>40 (66%)</td>
<td>0.12</td>
</tr>
<tr>
<td>Diabetes</td>
<td>13 (30%)</td>
<td>7 (11%)</td>
<td>0.03*</td>
</tr>
<tr>
<td>Cancer</td>
<td>3 (7%)</td>
<td>9 (15%)</td>
<td>0.35</td>
</tr>
<tr>
<td>Immunosuppression</td>
<td>2 (5%)</td>
<td>4 (7%)</td>
<td>1</td>
</tr>
<tr>
<td>Surgical history before primary THA</td>
<td>25 (58%)</td>
<td>31 (51%)</td>
<td>0.84</td>
</tr>
<tr>
<td>Complications due to any cause before primary THA</td>
<td>8 (19%)</td>
<td>2 (3%)</td>
<td>0.01*</td>
</tr>
<tr>
<td>Wound healing disturbance before primary THA</td>
<td>7 (16%)</td>
<td>2 (3%)</td>
<td>0.07</td>
</tr>
<tr>
<td>Confirmed infection before primary THA</td>
<td>7 (16%)</td>
<td>1 (2%)</td>
<td>0.02</td>
</tr>
<tr>
<td>Complication due to any cause after primary THA</td>
<td>11 (26%)</td>
<td>2 (3%)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Wound healing disturbance after primary THA</td>
<td>19 (44%)</td>
<td>0</td>
<td>0.001*</td>
</tr>
<tr>
<td>Mechanical complication after primary THA</td>
<td>16 (37%)</td>
<td>43 (70%)</td>
<td>0.001*</td>
</tr>
<tr>
<td>Bleeding complication after primary THA</td>
<td>3 (7%)</td>
<td>2 (3%)</td>
<td>0.40</td>
</tr>
<tr>
<td>On-going pain</td>
<td>25 (58%)</td>
<td>32 (52%)</td>
<td>0.29</td>
</tr>
<tr>
<td>On-going fever</td>
<td>7 (16%)</td>
<td>2 (3%)</td>
<td>0.03*</td>
</tr>
<tr>
<td>On-going wound healing disturbance</td>
<td>6 (14%)</td>
<td>0</td>
<td>0.002*</td>
</tr>
<tr>
<td>Abnormal imaging findings</td>
<td>10 (23%)</td>
<td>24 (39%)</td>
<td>0.17</td>
</tr>
</tbody>
</table>

* Significant difference at 5%.

The odds ratio and the associated confidence intervals are shown in Table 5. The area under the curve was 0.7974 (95% CI = 0.72–0.89). The Hosmer–Lemeshow test was not significant (P = 0.78) suggesting that the model was consistent with the data. McFadden’s pseudo-R² was 0.226.

The CIS distinguished correctly between the infected patients (positive score) and the non-infected patients (negative score) in 78% of cases, with a sensitivity of 57% (95% CI = [0.42–0.73]), specificity of 93% (95% CI = [0.79–0.95]), positive predictive value of 0.78 (95% CI = [0.60–0.91]) and a negative predictive value of 0.75 (95% CI = [0.63–0.84]).

4. Discussion
The CIS defined here was able to predict whether a THA revision was infected or not; four of out every five cases were correctly classified retrospectively. This score could be an important tool for defining the medical–surgical strategy during THA revision, no matter the reason for revision.

Knowing whether an infection is present is an important factor in the treatment strategy when performing THA revision. Pre-operative microbiological sampling, particularly joint aspiration before the re-operation is not sufficient for a definitive decision to be made [7]. It is currently accepted that systematic collection of

| Table 4
Univariate analysis.

<table>
<thead>
<tr>
<th>Factor</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Positive predictive value</th>
<th>Negative predictive value</th>
<th>Correctness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight</td>
<td>0.65 [0.51–0.79]</td>
<td>0.79 [0.69–0.89]</td>
<td>0.68</td>
<td>0.76</td>
<td>0.73</td>
</tr>
<tr>
<td>BMI</td>
<td>0.49 [0.35–0.63]</td>
<td>0.90 [0.82–0.97]</td>
<td>0.78</td>
<td>0.71</td>
<td>0.73</td>
</tr>
<tr>
<td>CRP</td>
<td>0.55 [0.38–0.72]</td>
<td>0.94 [0.84–1.00]</td>
<td>0.89</td>
<td>0.69</td>
<td>0.75</td>
</tr>
<tr>
<td>Diabetes</td>
<td>0.36 [0.17–0.46]</td>
<td>0.88 [0.77–0.95]</td>
<td>0.65</td>
<td>0.63</td>
<td>0.64</td>
</tr>
<tr>
<td>Complications due to any cause before primary THA</td>
<td>0.25 [0.11–0.45]</td>
<td>0.97 [0.83–1.00]</td>
<td>0.88</td>
<td>0.58</td>
<td>0.62</td>
</tr>
<tr>
<td>Confirmed infection before primary THA</td>
<td>0.45 [0.30–0.61]</td>
<td>1.00 [0.91–1.00]</td>
<td>1.00</td>
<td>0.72</td>
<td>0.77</td>
</tr>
<tr>
<td>Mechanical complication after primary THA</td>
<td>0.37 [0.23–0.53]</td>
<td>0.30 [0.19–0.43]</td>
<td>0.27</td>
<td>0.40</td>
<td>0.33</td>
</tr>
<tr>
<td>On-going fever</td>
<td>0.16 [0.07–0.31]</td>
<td>0.97 [0.88–1.00]</td>
<td>0.78</td>
<td>0.62</td>
<td>0.63</td>
</tr>
<tr>
<td>On-going wound healing disturbance</td>
<td>0.16 [0.06–0.32]</td>
<td>1.00 [0.91–1.00]</td>
<td>1.00</td>
<td>0.66</td>
<td>0.68</td>
</tr>
</tbody>
</table>

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microbiological samples during a revision arthroplasty is desirable, even when no infection is suspected [8]. However, the findings can be difficult to interpret [9], particularly if single sample is positive for a cutaneous saprophyte such as Staphylococcus epidermidis, because it is impossible to rule out contamination during sample collection. In addition, the cost cannot be ignored, especially since multiple samples must be collected and analysed [5,6]. Thus it is important to know if these microbiological samples are appropriate and potentially useful before collecting them.

Moreover, intraoperative microbiological samples must generally be collected before any antimicrobial prophylaxis [10], even if this strategy has recently been debated [11]. Prophylactic antimicrobial agents significantly reduce the risk of postoperative infection only if they are administered before the incision is made [12]. Delaying the antimicrobial prophylaxis until after the deep samples are collected theoretically increases the risk of acquiring an infection during the revision. Some authors have even suggested that this scenario is a major reason why the treatment of PJIs fails [13,14]. The increased risk of postoperative infection is only acceptable if it is accompanied by a benefit elsewhere, which in this case, would be a better microbiological diagnosis of the infection. However, this is obviously only applicable in cases of infection. Thus it seems relevant to have a reliable method to determine whether an infection is present before starting the surgical procedure.

This study has significant limitations as it is only preliminary. The first limitation is the recruitment at the participating centres, which used a call from applications, with the only inclusion criteria being the ability to provide an equal number of records from patients considered as infected and non-infected with at least 1-year follow-up. We preferred working with centres familiar with this type of care as they would provide more homogeneous data, instead of expanding the recruitment to centres where prosthesis revision surgery – particularly infected ones – is not performed as often, as this could have created even greater bias. Since this was a retrospective study of patient records, a potential selection bias existed that could not be controlled. This bias may have affected the selection of participating centres, the selection of records by each of these centres and the representativeness of infected versus non-infected cases. An example of this bias is the large number of missing data for the CRP value, which is a factor known to discriminate between infected and non-infected cases [5]. But in our opinion, this is not a drawback; it is often when we are faced with ‘intermediate’ CRP results [15] that this type of infection score could be very valuable. In fact, other than in the case of infection, CRP levels can be altered and lead to diagnostic errors in obese patients who have a chronic inflammatory disease or have type 1 diabetes, and in smokers [16–18]. The second limitation cannot be ignored: there is no unequivocal, consensus definition of a PJ. Despite recent progress in this area, the current consensus definitions have no absolute value [19] and there continues to be variations between practitioners [20]. The serum assays proposed more recently (interleukin-6, procalcitonin, TNF-alpha) must be considered as experimental because they have not been formally validated, they are not universally available and they are difficult to use in routine practice because of their cost [17]. Thus it is possible that some of the records were incorrectly classified, despite the retrospective nature of the study allowing the postoperative follow-up to be integrated into the diagnostic reasoning. The potential impact of this bias cannot be evaluated. Unfortunately there is no way to limit its effect, even in a prospective study. As a consequence, our score must be used cautiously and we cannot recommend that it be used in routine practice at this point. A prospective study will be critical to validate the contribution of this score – this study is currently under way.

5. Conclusion

This study was able to define an infection score to use prior to THA revision. But it must be validated prospectively before being accepted and widely used within the orthopaedic community.

Disclosure of interest

Benjamin Adamczewski, Henri Bonfait, Emmanuel de Thomason, Julien Godet declare that they have no competing interest. Christian Delaunay declares that she has no competing interest, but is a consultant for Zimmer and receives payments from Orthorisq. Jean-Yves Jenny declares that he has no competing interest, but is a consultant for FH Orthopedics and Exatech and receives royalties from Aesculap.

Acknowledgements

The authors wish to thank François Gaucher, Henri Migaud, Jacques Tabutin, Michel Henry Fessy and Jean-Michel Laffosse for having provided and analysed records for this study.

References


