Meta-Analysis of Unexpected Findings in Routine Histopathology during Total Joint Replacement

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ABSTRACT: Background: Routine histopathological analysis of bone extracted during total joint replacement is controversial.

Objectives: To evaluate the utility of routine histopathological analysis in total joint replacement.

Methods: We calculated the risk for discrepant diagnosis between the pre- and postoperative histopathological results by performing a meta-analysis of 11 studies (including our data). We also calculated the risk for significant discrepancies.

Results: The discrepant diagnoses analysis showed a random effect of 3% discrepancies (95% confidence interval 1.2–3.7%). Funnel plot indicates a publication bias; consequently, the conclusions from this analysis should be interpreted with caution. Regarding the significant discrepancy in diagnosis, we performed a meta-analysis of nine studies. Fixed-effects analysis of all the studies resulted in 0.16% significant discrepancies (95% CI 0.02–0.30%) with no heterogeneity (Q = 3.93, degrees of freedom = 9, P = 0.14, I² = 49.2%), and appropriate fixed-effects models.

Conclusions: We recommend no further routine histological examination, reserving this tool for cases with a controversial primary diagnosis and unexpected findings during the operation.

Joint arthroplasty, occult malignancy, meta-analysis, unexpected diagnosis

KEY WORDS:

In order to confirm the preoperative clinical diagnosis many surgeons send the removed bone for pathological examination. This option is debatable due to cost and effectiveness; however, the results sometimes reveal unexpected findings with different clinical significance. In order to assess the risk for discrepancy between pre- and postoperative histopathological results we performed a meta-analysis of bones sent for histopathologic examinations following joint replacement in addition to those described in the literature. The clinical significant discrepancy percentage was calculated.

MATERIALS AND METHODS

IDENTIFICATION AND SELECTION OF STUDIES
We performed a literature search using the MEDLINE computerized database for articles published from 1966 to 2008. Our purpose was to identify all the pertinent publications including the key words: joint, hip, knee, arthroplasty, joint replacement, unexpected diagnosis, and unexpected malignancy. We also performed a search of our patients’ files and the bibliographies of all the included articles. We discovered 10 pertinent abstracts or full-text articles during our literature search, which we reviewed and included in our meta-analysis. Studies were selected for inclusion on the basis of strict methodological criteria: a) the patients had to have been treated with elective primary total joint arthroplasty, b) only studies that described results of routine histopathological examinations were selected, c) case reports were excluded, and d) a consecutive series of 67 femoral heads retrieved during elective total hip arthroplasty in our department were included.

ANALYSIS
The log odds of a discrepancy were calculated and logistic regression was performed since many of the studies had a small number of discrepancies. Wherever there were 0 discrepancies 0.5 was added in order to calculate the odds. To accommodate for the pooling of multiple trials, the 95% confidence interval for each risk was calculated using a logistic regression model. With this approach, the width of the estimated confidence interval is increased as compared to the standard approach, ignoring the correlation between observations within a study [4,5].
Table 1. Discrepant diagnoses in 11 studies

<table>
<thead>
<tr>
<th>Study</th>
<th>No. of cases</th>
<th>No. of discrepancies</th>
<th>% of discrepant diagnoses</th>
<th>Odds</th>
<th>Log odds</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sugihara et al., 1999 [6]</td>
<td>137</td>
<td>5</td>
<td>3.65%</td>
<td>0.038</td>
<td>-3.273</td>
</tr>
<tr>
<td>Kocher et al., 2000 [7]</td>
<td>1234</td>
<td>28</td>
<td>2.27%</td>
<td>0.023</td>
<td>-3.763</td>
</tr>
<tr>
<td>Raab et al., 1998 [8]</td>
<td>168</td>
<td>16</td>
<td>9.52%</td>
<td>0.105</td>
<td>-2.251</td>
</tr>
<tr>
<td>Lawrence et al., 1999 [9]</td>
<td>1388</td>
<td>0</td>
<td>0.00%</td>
<td>0.000</td>
<td>-7.236</td>
</tr>
<tr>
<td>Campbell et al., 1997 [10]</td>
<td>715</td>
<td>6</td>
<td>0.84%</td>
<td>0.008</td>
<td>-4.772</td>
</tr>
<tr>
<td>Meding et al., 2000 [11]</td>
<td>951</td>
<td>27</td>
<td>2.84%</td>
<td>0.029</td>
<td>-3.533</td>
</tr>
<tr>
<td>Pagnano et al., 1998 [12]</td>
<td>2289</td>
<td>10</td>
<td>0.44%</td>
<td>0.004</td>
<td>-5.429</td>
</tr>
<tr>
<td>Di Carlo, 1992 [13]</td>
<td>1794</td>
<td>97</td>
<td>5.41%</td>
<td>0.057</td>
<td>-2.862</td>
</tr>
<tr>
<td>Fornasier and Battigia, 2005 [14]</td>
<td>460</td>
<td>3</td>
<td>0.65%</td>
<td>0.007</td>
<td>-5.027</td>
</tr>
<tr>
<td>Palmer et al., 1999 [15]</td>
<td>1146</td>
<td>91</td>
<td>7.94%</td>
<td>0.086</td>
<td>-2.450</td>
</tr>
<tr>
<td>Rubin et al. (present study)</td>
<td>67</td>
<td>5</td>
<td>7.46%</td>
<td>0.075</td>
<td>-2.584</td>
</tr>
<tr>
<td>Fixed effects</td>
<td></td>
<td></td>
<td></td>
<td>0.048</td>
<td>-3.03</td>
</tr>
<tr>
<td>Random effects</td>
<td></td>
<td></td>
<td></td>
<td>0.024</td>
<td>-3.72</td>
</tr>
</tbody>
</table>

RESULTS

OUR DATA

A total of 67 consecutive cases were included in this study. Of the 67 patients we found 5 incidental diagnoses that did not concur with the primary diagnosis (6%). Of the five cases, there were three low-grade, B cell, non-Hodgkin’s lymphoma, one enchochroma and one avascular necrosis. The lymphoma pathology specimens showed focal infiltration with nodules of small B lymphocytes. Immunohistochemical staining was positive for CD20. A thorough hematological evaluation was performed in patients including image staging with isotope imaging positron emission tomography-FDG, which was negative. Abdominal ultrasonography demonstrated normal spleen and liver amplitudes. Lactate dehydrogenase and beta-2-microglobulin were in the normal range. The patients were asymptomatic and it was concluded that non-Hodgkin’s lymphoma was an incidental finding.

DISCREPANT DIAGNOSES

We identified ten studies that met the entry criteria [6-15]. From a total of 10,349 patients (including our study) there were 287 discrepancies (2.7%). The percentage of discrepant diagnoses ranged from 0.0 to 9.5 [Table 1]. In all but one of these studies the percentage of discrepancies was significantly different from 0. Fixed-effects analysis of all the studies revealed a value of 1.12% discrepancies (95% confidence interval 0.9–1.3%). Random-effects analysis demonstrated a value of 3.0% discrepancies (95% CI 1.7–4.4%). Figure 1 shows the Forest plot of the data. The Forest plot reveals few non-overlapping intervals, indicating a possible lack of heterogeneity. Formal tests for heterogeneity indicate the presence of high heterogeneity (Q=178.4, degrees of freedom = 10, P < 0.01, I² = 94%), suggesting that fixed-effects models should not be used. The Funnel plot shows asymmetry (a linear decreasing trend), which is an indication of publication bias [Figure 2]; therefore, conclusions from this analysis need to be interpreted with caution.

SIGNIFICANT DISCREPANCIES

As shown in Table 2, 10 of the 11 studies showed significant discrepancies, 9 of which resulted in a change in treatment. Fixed-effects analysis of all the studies showed 0.16% signifi-
significant discrepancies (95% CI 0.02–0.30). A Forest plot of the data [Figure 3] indicates homogeneity among the studies. No heterogeneity was found in a heterogeneity test (Q = 15.29, degrees of freedom = 9, P = 0.08, I² = 41%) and fixed-effects models are appropriate. Random-effects analysis revealed a value of 0.04% (95% CI -0.07–0.15) for significant discrepancies in all studies. The Funnel plot indicates no publication bias [Figure 4].

DISCUSSION

Based on the literature review, histopathological examination of bone removed during total joint replacement is controversial for two reasons: the cost-effectiveness of this procedure when performed routinely, and the recipient's safety when examination is not performed prior to arrival at the bone bank. We found ten articles that compared the pre- and postoperative diagnoses. From among the 10,349 patients (including those in our study) who participated in these studies, 287 discrepancies (2.7%) were found. Significant discrepancies that resulted in a change in the patients' treatment include one case with osteomyelitis (Raab et al. [8]) and seven cases described by DiCarlo et al. [13] who did not report the clinical outcome. In addition, Sugihara and co-researchers [6] found four cases of asymptomatic non-Hodgkin's lymphoma and claimed that since the possibility of disease transmission is not clear, pathological examination is justified. Palmer et al. [15] found 91 discrepancies but did not describe their clinical significance.

The meta-analysis showed values of 3.0% (95% CI 1.7–4.4%) for random effects of discrepant diagnoses and 0.16% for fixed effects of significant discrepancies (95% CI 0.02–0.30%). This meta-analysis reinforces most of the authors' conclusions, namely, not to perform routine histopathology examinations [7,9–12].

In accordance with the literature, we recommend reserving the tool of histological examination exclusively for cases with a controversial primary diagnosis, unexpected findings during surgery, and/or cases where the femoral head will be used as an allograft even though the possibility of malignancy transmission is not yet determined.

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References

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Human social interactions crucially depend on the ability to represent other agents’ beliefs even when these contradict our own beliefs, leading to the potentially complex problem of simultaneously holding two conflicting representations in mind. Kovacs and co-researchers show that adults and 7 month olds automatically encode others’ beliefs, and that, surprisingly, others’ beliefs have similar effects as the participants’ own beliefs. In a visual object-detection task, participants’ beliefs and the beliefs of an agent (whose beliefs were irrelevant to performing the task) both modulated adults’ reaction times and infants’ looking times. Moreover, the agent’s beliefs influenced participants’ behavior even after the agent had left the scene, suggesting that participants computed the agent’s beliefs online and sustained them, possibly for future predictions about the agent’s behavior. Hence, the mere presence of an agent automatically triggers powerful processes of belief computation that may be part of a “social sense” crucial to human societies.

Science 2010; 330: 1830
Eitan Israeli

What’s next for disease eradication?

Two days after the 30th anniversary of the eradication of smallpox, 30 scientists and public health experts from around the world gathered for a week-long meeting in the German city of Frankfurt am Main to try to chart a new path for disease eradication in the 21st century. Their meeting was triggered by several developments. Interest in tackling global health problems has surged in the past decade, as has funding, but the two ongoing eradication campaigns – against guinea worm disease and polio – have proven far more difficult than predicted. Meanwhile, a key rationale for past eradication efforts – the promised financial windfall from stopping all control measures once a disease is gone – all but disappeared as a result of 9/11 and the 2001 anthrax letters. Wealthy countries in particular are determined never to let their guard down against diseases like smallpox, polio or measles. Meanwhile, developing countries have their own questions: Why should they keep spending inordinate amounts of time and money on a disease such as polio — now down to fewer than 2000 cases a year – while their health systems are struggling with far more devastating diseases such as AIDS and TB?

Science 2010; 330: 1736
Eitan Israeli

Electrical synapses control hippocampal contributions to fear learning and memory

The role of electrical synapses in synchronizing neuronal assemblies in the adult mammalian brain is well documented. However, their role in learning and memory processes remains unclear. By combining Pavlovian fear conditioning, activity-dependent immediate early gene expression, and in vivo electrophysiology, Bissiere et al. discovered that blocking neuronal gap junctions within the dorsal hippocampus impaired context-dependent fear learning, memory, and extinction. Theta rhythms in freely moving rats were also disrupted. These results show that gap junction-mediated neuronal transmission is a prominent feature underlying emotional memories.

Science 2011; 331: 87
Eitan Israeli