The surgical treatment of anterior knee pain due to infrapatellar fat pad pathology: A systematic review

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ABSTRACT

Background: Anterior knee pain (AKP) encompasses a range of pathologies. As a result, there are a number of therapeutic options used to treat AKP. The non-operative treatments have been analysed in a number of randomised controlled trials and systematic reviews. There is however a scarcity of such publications covering the surgical management of AKP. There are no systematic reviews that have investigated surgical interventions for AKP due to pathology of the infrapatellar fat pad (IFP). The aims of this study were to review the literature systematically, to establish which surgical procedures have been used to treat IFP disease and to determine their efficacy.

Methods: The review was conducted in accordance with the PRISMA reporting guidelines. A search of the literature was performed on 1st January 2014 using multiple databases including CENTRAL, MEDLINE, EMBASE, PubMed, and Google Scholar. The quality of the studies was assessed using Oxford Evidence-Based Medicine Levels of Evidence guidelines and the GRADE approach.

Results: Twenty-four eligible studies were found and included. The critical appraisal identified that the current evidence-base has low methodology quality. The clinical findings indicated that there is a positive trend towards the surgical management of IFP disease for AKP symptoms. Excision of IFP tumours and resection of the IFP in Hoffa’s disease can lead to improvements in symptoms and function.

Conclusions: Truly robust evidence to support the surgical management of IFP pathology requires randomised controlled trials; however the expenses involved to design such trials means that they are unlikely to be undertaken for this uncommon disorder. Consequently well-designed and well-reported case series need to be undertaken to improve our current understanding that includes recording quantitative measures such as range of knee motion, VAS Pain scores and a validated scoring system.

Level of evidence: Level IV.

PROSPERO registration: CRD42013006550.

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1. Introduction

Anterior knee pain (AKP) is an umbrella term, which encompasses symptoms, which can be the result of a wide range of pathologies. Consequentially there is much debate within the literature regarding the most effective way to manage it.

Many of the common conservative treatments have been well reported in the literature, and covered by a number of review papers [1–3]. The surgical treatment of AKP is not discussed in the literature with the same quality of studies as has been demonstrated for the conservative treatments [4–6]. Generally there are few randomised controlled trials (RCTs), and those that have been conducted have failed to prove that surgical therapy is more effective than nonsurgical treatments [7].

The infrapatellar fat pad (IFP) can be a cause of AKP, from two different pathologies; Hoffa’s disease [8] or benign tumours [9]. The various tumours [10–12] have been managed surgically, usually by excision biopsy to confirm the diagnosis histologically. Unfortunately, the published literature on the surgical management of IFP pathology is sparse and composed of case reports and small case series.

This study aims to review the literature systematically and to establish which surgical procedures have been used to treat IFP pathology, whilst determining the efficacy of these procedures in terms of symptom resolution, functional improvement, complications, and the need for further procedures.
2. Methods

This systematic review has been conducted using the guidelines published in the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement [13]. PROSPERO registration number CRD42013006550 [14].

2.1. Selection criteria

Due to a paucity of RCTs and systematic reviews found during the initial searches, all study designs were eligible. This therefore included any reviews, trials, case series, and case reports. Papers were included if all the participants had undergone an invasive procedure to treat any pathology of the IFP. There were no restrictions placed due to patient demographics, co-morbidities, year, or language of publication. Two publications identified which were not published in English were translated by medically qualified native speakers of that language. Studies were not included if they reported non-invasive management strategies.

2.2. Search strategy

The primary searches were performed using the following electronic databases: Cochrane Database of Systematic reviews, CENTRAL, MEDLINE (PMC), EMBASE, PubMed, and Google Scholar. In order to ensure that this review encompassed as much published work as possible, secondary searches included grey literature databases such as: the Open Grey (System for Information on Grey Literature in Europe) database. Further trials databases were also searched including: the US National Institute for Health Trials Registry and the WHO International Clinical Trials Registry Platform. Searches of all the databases were conducted on 1st January 2014, and no time limits were applied.

Multiple search strategies were used for differing databases due to their varying search engines. All of these have been based on the initial search strategy designed to be used for the PubMed database (Table 1). Finally, the reference lists of all the full-text articles accessed were hand searched and assessed to ensure that all relevant studies were included.

2.3. Study identification

After the primary searches were completed the lead author (AR) reviewed the titles and abstracts of all the identified articles, and retrieved the full-text articles for those publications that initially met the inclusion criteria.

All possible studies that were identified in the primary and secondary searches had their title or abstract reviewed by the lead author (AR), and those that were deemed to have met the inclusion criteria so far had their full article retrieved. The full-text articles were then independently reviewed by two people (AR and AW) and were included in the systematic review when both reviewers had identified that the publication met the inclusion criteria. A third independent person (SD) was available to arbitrate if the two reviewers disagreed about the inclusion of an article.

2.4. Data analysis and critical appraisal

The primary outcomes were; the resolution of symptoms, functional improvement following the procedure, and the number of reported complications. The secondary outcome was the need for any additional procedures. Using these outcomes, data were extracted from the included studies, and have been analysed appropriately. The studies included report diverse pathologies and treatments, and as a result of this heterogeneity in these studies it has not been possible to perform a meta-analysis. Therefore a qualitative narrative analysis of the results was undertaken to assess the trends in findings for surgical management strategies for IFP-related APK.

The CASP (Critical Appraisal Skills Programme) tool was employed to aide analysis of the information gathered in this review [15]. The quality of the included studies has been assessed using the Oxford Centre for Evidence-Based Medicine (EBM) 2011 Levels of Evidence [16] and the GRADE approach [17]. This was undertaken by two reviewers (AA and AW). A third independent person (SD) was available to arbitrate if there was any disagreement in quality criteria on appraisal.

3. Results

A flow diagram (Fig. 1), based on the PRISMA protocols, illustrates how the various electronic databases contributed to the search, as well as why the final articles were covered in this systematic review. The included studies have been separated for analysis according to the level of evidence that they represent (Fig. 2). A total of 326 papers were identified. Following assessment of each citation, 24 papers were deemed eligible and included in the review.

3.1. Evidence-based medicine level V evidence articles

The greatest number of articles came from case reports, and these reported a number of separate pathologies that can be separated into two groups—isolated tumours of the IFP, and Hoffa’s disease. The summary of these case reports are presented in Table 2. The reports are of very low quality (as assessed using the GRADE approach) and carry a high risk of selection and reporting bias. This could have been partly remedied by the use of recognised scoring systems for knee function, visual analogue scales (VAS) for assessment of pain, and by pre- and postoperative comparisons of range of motion (ROM).

3.2. Evidence-based medicine evidence level IV articles

These studies are summarised in Table 3; they include a retrospective cohort study and five case series. All of these studies have also been classified as very low quality when assessed using the GRADE approach. All relevant publications, regardless of language or study size were included and therefore reflect all the available evidence relating to this subject. As the overall number of patients included was low (n = 146), and the reports were of multiple pathologies that were dealt with by different surgical techniques the limitations of this study come from the lack of published articles in this area, and the heterogeneity of these papers. These were therefore classified into two categories of IFP pathology: impingement (Hoffa’s disease); and tumours.
3.3. Infrapatellar fat pad impingement (Hoffa’s disease)

Hoffa’s disease was first described in 1904 [8]; in this paper Hoffa refers to an inflammatory fibrous hyperplasia of the articular adipose tissue. However since this point there has not been a refinement of this definition, or a clear radiological or histological description that identifies this specific diagnosis.

Clinically, the diagnosis of Hoffa’s disease can be made using the test originally described by Hoffa. The test is positive if pain is elicited when the knee is extended with direct pressure being applied to either side of the patella tendon. This test or variations of it have been used for diagnostic purposes in Kumar et al. [36], Adulkasem [34], House et al. [38], and Ogilvie-Harris et al. [35].

MRI is commonly used in the diagnosis of Hoffa’s disease, and the findings are a diffuse oedema-type signal within the Hoffa fat; hyposignal on T1-weighted images and hyper signal on PD fat sat signals [9,39]. The case report from Park et al. [21], and the House et al. study [38] report similar MRI findings.

When the diagnosis of Hoffa’s disease has not been made radiologically, it has been made either macroscopically at the time of surgery, or microscopically following histological analysis of the excised fat pad. The papers from Wu et al. [33], Ogilvie-Harris et al. [35], Adulkasem [34], and Kumar et al. [36] describe a macroscopic diagnosis by identification of inflammation and/or hypertrophy sometimes with evidence of fat pad impingement. Histologically the diagnosis is confirmed in Park et al. [21], Kumar et al. [36],
Table 2
Summary of EBM level V evidence.

<table>
<thead>
<tr>
<th>Study</th>
<th>n</th>
<th>Age</th>
<th>Pathology</th>
<th>Treatment</th>
<th>Follow-up</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Petersen et al. [18]</td>
<td>2</td>
<td>17 ± 18</td>
<td>Haemangioma</td>
<td>Open resection</td>
<td>1 + 2 years</td>
<td>Symptom resolution and improved ROM</td>
</tr>
<tr>
<td>Turhan et al. [10]</td>
<td>1</td>
<td>25</td>
<td>Osteochondroma</td>
<td>Open excision</td>
<td>1 year</td>
<td>Symptom resolution</td>
</tr>
<tr>
<td>Singh et al. [19]</td>
<td>1</td>
<td>55</td>
<td>Ossifying chondroma</td>
<td>Open excision of IFP</td>
<td>3 years</td>
<td>Symptom resolution</td>
</tr>
<tr>
<td>Osti et al. [20]</td>
<td>1</td>
<td>52</td>
<td>Synovial chondromatosis</td>
<td>Arthroscopic partial resection of IFP Open removal of mass following recurrence</td>
<td>10 years</td>
<td>Symptom resolution at 1 year, recurrence at 3 years Symptom resolution</td>
</tr>
<tr>
<td>Park et al. [21]</td>
<td>1</td>
<td>70</td>
<td>Hoffa's disease</td>
<td>Arthroscopic resection</td>
<td>20 months</td>
<td>Symptom resolution and improved ROM</td>
</tr>
<tr>
<td>Kelly et al. [22]</td>
<td>1</td>
<td>47</td>
<td>Neurofibroma</td>
<td>Open excision</td>
<td>4 months</td>
<td>Symptom resolution and improved ROM</td>
</tr>
<tr>
<td>Ogura et al. [23]</td>
<td>1</td>
<td>56</td>
<td>Osteochondroma</td>
<td>Open excision of mass</td>
<td>6 months</td>
<td>Symptom resolution and improved ROM</td>
</tr>
<tr>
<td>Rizzello et al. [24]</td>
<td>1</td>
<td>42</td>
<td>Osteochondroma</td>
<td>Open excision</td>
<td>3 weeks</td>
<td>Symptom resolution and improved ROM</td>
</tr>
<tr>
<td>Yoo et al. [25]</td>
<td>1</td>
<td>35</td>
<td>Localised nodular synovitis</td>
<td>Arthroscopic excision biopsy</td>
<td>1 year</td>
<td>Symptom resolution</td>
</tr>
<tr>
<td>Roth [26]</td>
<td>1</td>
<td>69</td>
<td>Ossifying synovial chondroma</td>
<td>Open excision</td>
<td>7 months</td>
<td>Symptom resolution and improved ROM</td>
</tr>
<tr>
<td>Park et al. [27]</td>
<td>1</td>
<td>24</td>
<td>Localised nodular synovitis</td>
<td>Arthroscopic excision biopsy</td>
<td>22 months</td>
<td>Symptom resolution and improved ROM</td>
</tr>
<tr>
<td>Nikolopoulos et al. [28]</td>
<td>1</td>
<td>37</td>
<td>Ganglionic cyst</td>
<td>Open excision</td>
<td>6 months</td>
<td>Symptom resolution and improved ROM</td>
</tr>
<tr>
<td>Krebs et al. [11]</td>
<td>1</td>
<td>52</td>
<td>Ossifying chondroma</td>
<td>Arthroscopic resection</td>
<td>1 year</td>
<td>Symptom resolution and improved ROM</td>
</tr>
<tr>
<td>De Maio et al. [29]</td>
<td>2</td>
<td>58 ± 71</td>
<td>Osteochondroma</td>
<td>Open marginal resection</td>
<td>4 + 8 years</td>
<td>Symptom resolution and improved ROM</td>
</tr>
<tr>
<td>Keser et al. [30]</td>
<td>1</td>
<td>42</td>
<td>Strangulated lipoma</td>
<td>Open resection</td>
<td>1 year</td>
<td>Symptom resolution and improved ROM</td>
</tr>
<tr>
<td>Emad et al. [31]</td>
<td>1</td>
<td>37</td>
<td>Liposynovitis prepatellaris</td>
<td>Arthroscopic resection of IFP</td>
<td>Not specified</td>
<td>Symptom resolution and improved function</td>
</tr>
<tr>
<td>Ghate et al. [32]</td>
<td>2</td>
<td>12 + 28</td>
<td>Ganglion Haemangioma or venous malformation</td>
<td>Open resection</td>
<td>1 + 2 years</td>
<td>Symptom resolution and improved Cincinnati Knee Scores</td>
</tr>
<tr>
<td>Palumbo et al. [12]</td>
<td>2</td>
<td>32 + 51</td>
<td>Localised pigmented nodular synovitis</td>
<td>Arthroscopic resection</td>
<td>Not specified</td>
<td>Symptom resolution</td>
</tr>
</tbody>
</table>

ROM: Range of Movement; IFP: Infrapatellar Fat Pad.

Table 3
Summary of EBM level IV evidence.

<table>
<thead>
<tr>
<th>Study</th>
<th>Study type</th>
<th>Time period / Country</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wu et al. [33]</td>
<td>Retrospective cohort</td>
<td>20 (17–44) China</td>
</tr>
<tr>
<td>Adulkasem et al. [34]</td>
<td>Case series</td>
<td>20 (26–46) China</td>
</tr>
<tr>
<td>Ogilvie-Harris et al. [35]</td>
<td>Case series</td>
<td>11 (25–50) Canada</td>
</tr>
<tr>
<td>Kumar et al. [36]</td>
<td>Case series</td>
<td>32 (19–62) UK</td>
</tr>
<tr>
<td>Dean et al. [37]</td>
<td>Case series</td>
<td>19 (8–72) UK</td>
</tr>
<tr>
<td>House et al. [38]</td>
<td>Pilot study</td>
<td>12 (20–43) UK</td>
</tr>
</tbody>
</table>

Adulkasem [34], and Ogilvie-Harris et al. [35] by evidence of generalized inflammation, sometimes with accompanying fibrosis, and absence of another pathological process. There are no clear histological features that define Hoffa’s disease from a generalized inflammatory process.

3.3.1. Resolution of symptoms

The case reports only contributed one article to this specific pathology, Park et al. [21], and even though it does report that the patient was pain free after follow-up at 20 months it fails to provide any more information with regards to this, including the baseline pain score. The case series from Adulkasem [34], which measured the outcomes of 30 patients undergoing a subtotal excision of the IFP, also only contributes a qualitative assessment of symptom improvement, reporting relief of AKP and no recurrence at the time of final follow-up. Again this is without a report of the baseline pain scores, or an objective measurement of the reported relief from AKP.

The quantitative measures in improvement of symptoms come from the cohort study and the other case series [33,35,36,38]. Between them they have shown that surgical intervention has been reported to reduce AKP in those that have had an invasive intervention to treat IFP disease.

Wu et al. [33] examined outcome differences between those treated with a partial excision of the IFP, and those following a total excision. Using the Larson Rating Scale [40] to assess the difference in pre- and postoperative function they found that arthroscopic resection of the IFP was effective for the management of Hoffa’s disease, and demonstrated that the improvement in the Larson score was highly significant (p < 0.001) when comparing the preoperative score 78.65 (range: 66–88) to the postoperative score 95.45 (range: 80–100). However, they did not find a statistically significant difference in outcomes between the partial resection group 17.25 (range: 0–26) and the total resection group 15.38 (range: 92–20) (p > 0.5).

Ogilvie-Harris et al. [35] reported on 11 patients who underwent arthroscopic resection of the IFP. The Cincinnati Rating System [41] was employed to measure the postoperative results. When analysing symptoms they reported an improvement from the average preoperative score of 32 to a postoperative score of 46. Mean paired difference was 14 with a standard deviation of 6.3 (95% confidence intervals (CI); 9 to 18; p < 0.001).

High-portal arthroscopic resection of the IFP was described in Kumar et al. [36]. They studied patients in which other knee pathologies had been excluded, and in whom at least 4 weeks of physiotherapy had been undertaken preoperatively, but had failed to manage their symptoms. The outcomes were measured using the Lysholm score [42]. The preoperative scores were compared to scores measured at 3 months, 12 months, and at final follow-up (average 68 months, range 49–95). The gains measured at these time points were 44.76, 55.59, and 53.97 points respectively, and all of these were highly significant (p < 0.001). Preoperative Tegner scores [43] were reached by 13 patients after 3 months, and by 30 in total at 4 months; the remaining two were reported to have a reduced sporting level for other medical reasons. The two patients
that were lost to follow-up had not returned to their preoperative Tegner scores; one had improved temporarily and one did not improve at all, but it is unclear when this was assessed postoperatively. The Lysholm scores were further analysed and the gain was inversely proportional to the duration of the symptoms prior to surgery (Pearson $r = -0.53, p = 0.001$). The histological analysis of the resected samples identified three morphological types, albeit with only a fairly non-specific histological definition; Type 1 was an acute lesion, Type 2 a chronic lesion without fibrosis, and Type 3 a chronic lesion with fibrosis. The Type 1 lesions were found to have a better prognosis than the Type 2 lesions ($p = 0.05$), and a significantly better prognosis than the Type 3 lesions ($p = 0.03$). As the histological analysis would suggest, the patients with Type 3 lesions had longer preoperative symptoms, and this necessitated a prolonged period of postoperative physiotherapy.

Using a different approach to treating Hoffa’s disease, House et al. [38] demonstrated a statistically significant reduction in AKP with improvement in the VAS score following ablation of the IFP with ethanol in bupivacaine. The participants in this study were enrolled after they had been clinically diagnosed with IFP impingement; the diagnosis was confirmed on MRI, and other pathologies were excluded. However, the MRI scans identified three patients that had scar tracts present from a previous arthroscopy. These injections were repeated at 3-weekly intervals; the mean number of injections was four (range: 2–6). The post-procedure VAS scores were measured at 6 weeks following the final injection, and the average was 2.92 (standard deviation [SD]: 2.61), reduced from a pre-procedure average of 7.75 (SD: 1.14), a 62% reduction ($p < 0.001$). There were two patients in this study that did not do well, both had post-procedure VAS scores of 8 with pre-treatment scores of 8 and 10; both of these had scar tracts identified on MRI but the authors comment that the numbers are too low to draw any conclusions about the significance of this.

3.3.2. Restoration of function

Assessing restoration of function has been carried out in a number of ways including validated knee scores, improvements in postoperative range of movement, and some articles have commented on a return to activities that were not possible preoperatively.

As with the reports of symptom resolution some papers have shown a quantitative improvement, but the same papers only provided subjective measurements of functional improvement. The Park et al. case report [21] described full ROM at 20 months follow-up, and the Adulkasem article [34] reported that all 30 patients were full weight bearing 1 day after their operation, and had a full ROM. Preoperative ROM measurements were not reported for these patients, and so an objective improvement cannot be demonstrated.

Wu et al. [33], and Kumar et al. [36] used scoring systems, which simultaneously measured symptoms and function, so a separate analysis of these outcomes is not possible. The function scores measured using the Cincinnati Rating System in the Ogilvie-Harris et al. study [35] improved from an average of 31 preoperatively to a score of 46 following the operation; the mean paired difference was 13 (95% CI: 9 to 18; $p < 0.001$).

3.3.3. Peri-operative complications

None of the articles reported any major peri-operative complications. Adulkasem [34] and House et al. [38] reported post-procedure pain, but this was short-lived resolving within a few days. Kumar et al. [36] reported one patient had temporary paraesthesia, and another had quadriiceps atrophy requiring a longer period of rehabilitation.

3.3.4. Additional procedures

None of the papers reported the need for an additional procedure after the first intervention.

3.4. Tumours of the infrapatellar fat pad

Only one of the level IV evidence studies, Dean et al. [37], dealt with the treatment of tumours of the IFP, Table 4, but nearly all of the case reports reviewed covered this topic.

3.4.1. Resolution of symptoms

Dean et al. [37] demonstrated that a limited open surgical excision of IFP tumours lead to improvement in AKP. Cases were identified using a regional tumour registry, consisting of 19 cases reported, containing 11 different tumour types. All the tumours described were benign in nature, and all were managed with an open excision. American Knee Society Scores [44] were used to assess operative success, and found an improvement from 76 (range: 17–100) to 96 (range: 46–100) following the operation; however, no statistical tests have been applied to this data in order to judge its significance.

In the case reports the resolution of AKP has generally been reported in a qualitative fashion, and all of them have reported improvement. This improvement is quoted as from “pain nearly resolved” in Kelly et al. [22] to “resolution of symptoms/pain free” in nearly all the other papers. Chate et al. [32] reported two cases that involved open resection of IFP tumours which were asymptomatic at follow-up, but also showed improvement using the Cincinnati Knee Score. This was the only case report that demonstrated a quantitative improvement following the operation.

3.4.2. Restoration of function

Function had been reported mainly as an improvement in ROM, but it has also been described as “return-to-work” or “usual activities”. The time at which function improved was very variable depending on when the patient was followed up; between 2–3 weeks and 8 years. Range of motion was reported as full or improved in all that mentioned this as an outcome, but the papers did not report a quantitative assessment of this improvement. Only six of the articles reported return to activities or work as an outcome, and all of these had a positive improvement. None of the articles reported that the patients were unable to return to work or to their usual activities following the operation. In the case reports there was no quantitative measure of function, apart from the aforementioned Ghate et al. [32] article reporting the Cincinnati Knee Score.

Dean et al. [37] demonstrated improvements following excision of solitary tumours using the American Knee Score, with functional scores improving from 92 (range: 60–100) to 100, but again they did not comment on the statistical significance of this result.

Table 4

<table>
<thead>
<tr>
<th>Tumours reported in Dean et al. [37].</th>
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<tbody>
<tr>
<td>Number of cases</td>
</tr>
<tr>
<td>-----------------</td>
</tr>
<tr>
<td>5</td>
</tr>
<tr>
<td>4</td>
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</table>

3.4.3. Peri-operative complications
There were no reports of any peri-operative complications in this group of patients.

3.4.4. Additional procedures
There were two articles that reported recurrence of IFP tumours, [20,37]. Osti et al. [20] reported a recurrence following an arthroscopic partial resection of the IFP to remove synovial chondromatosis. The patient was symptom-free at 1 year following the initial operation, and an MRI performed at this time did not identify any residual disease, but recurrence of symptoms occurred at 3 years post-operation. Following an open excision of the new mass the patient had a good recovery and was still symptom-free 10 years after the second procedure. Dean et al. [37] reported that one of the patients in their series had a recurrence of pigmented villonodular synovitis after 5 years that required a re-operation.

4. Discussion
This systematic review has shown some favourable results for the surgical management of AKP due to IFP pathology. Surgical excision of solitary tumours of the IFP are associated with good outcomes and a low incidence of recurrence; recurrence only being reported for benign synovial tumours affecting the fat pad. For those patients with Hoffa’s disease in whom conservative treatment failed, surgery may be beneficial, but the more favourable results in those being treated for solitary tumours indicates that a clear diagnosis with a distinct underlying pathological process will lead to a better outcome. If a diagnosis of Hoffa’s disease is made it is important to have excluded other causes; indeed Hoffa’s disease is often a diagnosis of exclusion. When excision of the IFP was performed, arthroscopic partial resection produced outcomes similar to total resection.

Given the low incidence of Hoffa’s disease, the difficulty in diagnosing this condition, and its tendency to be well managed with conservative measures, it would not be possible to recruit the numbers needed for an appropriately powered RCT to confirm the benefit of surgical management. Therefore improving our knowledge can only be provided by well-designed cohort studies. In order to gain more information on the management of solitary tumours of the IFP it would be desirable for authors to report quantitative information that includes pre- and postoperative measurement of ROM, andVAS Pain scores; ideally this would be in addition to the use of a validated scoring system.

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Disclosure of interest
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