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CLINICAL RESEARCH

Does Bone Wax Induce a Chronic Inflammatory Articular Reaction?

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Abstract

Background Bone wax is used to control femoral neck bleeding during open femoroacetabular impingement (FAI) surgery. Despite its widespread use, only a few case reports and small case series describe side effects after extraarticular use. It is unclear whether intraarticular use of bone wax leads to such complications. However, during revision FAI surgery, we have observed various degrees of articular inflammatory reactions.

Questions/Purposes We therefore investigated whether the bone wax used intraarticularly to control femoral neck bleeding during FAI surgery could be associated with the inflammatory reactions observed at revision surgery.

Methods We visually inspected the area and analyzed biopsy specimens from all 14 patients undergoing revision surgery from March 2005 to March 2006, 11 of whom had bone wax used at the time of original surgery. The three patients who did not have bone wax were used as controls.

Results Bone wax was identified macroscopically on the femoral neck at the time of the revision surgery in all 11 patients. In all 11 patients, biopsy results indicated a foreign body-type chronic synovial inflammation. Five patients also had an associated synovial lymphoplasmacytic inflammatory reaction. No inflammatory reaction was observed in the biopsy specimens obtained from the three patients in whom bone wax was not originally used.

Conclusions Our findings suggest a synovial foreign body reaction, with or without an associated lymphoplasmacytic chronic inflammatory reaction, may be associated with intraarticular use of bone wax.

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Each author certifies that his or her institution approved the human protocol for this investigation, that all investigations were conducted in conformity with ethical principles of research, and that informed consent for participation in the study was obtained.
The work was performed at the Royal Adelaide Hospital (Adelaide, Australia), The University of Adelaide (Adelaide, Australia), University of Bern (Bern, Switzerland), and Luzerner Kantonsspital (Luzern, Switzerland).

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Introduction

Resection of the cam deformity at the femoral head-neck junction during femoroacetabular impingement surgery (FAI) exposes the cancellous bone of the femoral neck and often is accompanied by profuse bleeding. Bone wax, a sterile mixture of beeswax softened with paraffin or isopropyl palmitate, is recommended and used in this setting to stop intraarticular bleeding and to reduce the formation of adhesions between the cancellous bone and the overlying joint capsule [7, 16]. Although bone wax achieves bone hemostasis [22] and has the beneficial effect of suppressing new bone formation in the resection area [13], side effects have been reported. A foreign body reaction to bone wax has been reported after its use in orthopaedics [6, 11, 15, 19, 23], neurosurgery [20], dental surgery [12], and cardiothoracic surgery [1, 3, 25]. Despite this apparent large number of publications, the relative number of adverse reactions to bone wax that have been reported is small as all other studies, with two exceptions reporting on case series [23, 25], were single case reports. Additionally, we identified only one publication [23] reporting on the severity, not just the occurrence, of the foreign body reaction to bone wax. In that study, the authors investigated 12 patients who had bone wax used to prevent bleeding during surgery on the tibial tuberosity and reported a foreign body inflammatory reaction ranging from mild to severe in five of the 12 patients. They also noted, with the passage of time, the specimens progressed toward a marked fibrous reaction [23].

Although bone wax is widely used to control bleeding during open FAI surgery, we identified only one case study reporting on side effects associated with intraarticular use of bone wax [15]. In that study, the authors reported a foreign body reaction to bone wax used to control cancellous bone bleeding from the anterior femoral neck during FAI surgery. Thus, it is unclear whether and to what extent intraarticular bone wax causes a foreign body reaction.

During revision surgery for persistent hip pain after open FAI surgery, we have observed bone wax in the area of the original cam deformity resection, even though many years may have passed since the original surgery, and it has been associated with varying degrees of local inflammatory reaction. Based on these clinical observations, we questioned whether bone wax used intraarticularly is inducing routinely a pathologic reaction in the synovial membrane and capsular soft tissue. As a synovial and capsular inflammatory reaction to bone wax may be responsible for a poor outcome, we believed it was important to investigate this topic and disseminate the results to the increasing number of surgeons who perform surgical hip dislocation and use bone wax to control bleeding.

We determined whether patients in whom bone wax had been used intraarticularly during original FAI surgery had an associated inflammatory reaction in the hip capsule and synovial membrane at the time of revision surgery.

Patients and Methods

Ninety-six patients underwent open FAI surgery in our institutions during a 1-year period from March 2005 to March 2006; 14 of these were revision surgeries and were included in this prospective case series. The reason for revision surgery was persistent anterior hip pain exacerbated by hip movement. The demographic and surgical details of the 14 patients are shown (Table 1). This study was approved by our institutions' ethics committees.

The original surgical procedure for 12 of the 14 patients requiring revision surgery involved surgical hip dislocation with an osteochondroplasty of the femoral head-neck junction (Table 1). Another patient initially underwent a periacetabular osteotomy combined with osteochondroplasty of the femoral head-neck junction. For the remaining patient, the original surgery was open reduction and internal fixation of a femoral neck fracture, with osteochondroplasty of the femoral neck for associated FAI. Eleven of the 14 patients had bone wax (Ethicon Inc, Somerville, NJ, USA) used at the time of the original surgery. The amount of bone wax used per patient was not specifically recorded at the time of the original FAI surgery. However, clinical practice across our institutions at the time was for the bone wax to be thinly applied to the bleeding surfaces and then excess wax was removed once bleeding had ceased; therefore, it is estimated 0.5 to 1 g or less bone wax would have been applied during the original FAI surgery.

Prerevision MR images showed capsular (synovial) adhesions (Fig. 1) in all 14 patients, persistent labral disorders in four patients, and incomplete osteochondral resection of the femoral head-neck junction in three patients. The revision surgery involved repeat open osteochondroplasty in six of the 14 patients, arthroscopic osteochondroplasty in four patients, and revision to primary THA in four patients who had radiographic signs of secondary arthritic degeneration. In addition, one of the patients who underwent repeat open osteochondroplasty has since had additional revision surgery to a THA. Four of these 14 patients had undergone additional hip arthroscopy between their original and revision osteochondroplasties to treat postoperative adhesions.

At the time of revision surgery, the hip synovial membrane was visually inspected for the presence of residual bone wax, edema, hyperemia, adhesions, and hypertrophy of the synovial membrane over the area of the former osteochondroplasty. In all cases, synovial membrane

Table 1. Patient demographic and surgical details

Patient	Age (years)	Sex	Index surgery	Intermediate surgery	Revision surgery	Interval between initial and revision surgeries (years)
1	25	Female	PAO		SHD	1.56
2	50	Female	SHD		Arthroscopy	1.19
3	36	Male	ORIF NOF		SHD	1.08
4	53	Male	SHD		THA	0.62
5	24	Female	SHD	Arthroscopy × 2	Re-SHD	2.55
6	50	Female	SHD	Arthroscopy	THA	1.04
7	28	Female	SHD	Arthroscopy × 2	Re-SHD	1.92
8	32	Male	SHD		THA	0.89
9	28	Male	SHD		Arthroscopy	1.08
10	37	Male	SHD	Arthroscopy	THA	5.88
11	29	Female	SHD		Arthroscopy	0.36
12	22	Male	SHD		Re-SHD	1.3
13	40	Male	SHD		Re-SHD	0.5
14	15	Female	SHD		Arthroscopy	4.6

PAO = periacetabular osteotomy; SHD = surgical hip dislocation; ORIF NOF = open reduction and internal fixation of neck of femur fracture; re-SHD = revision surgical hip dislocation.

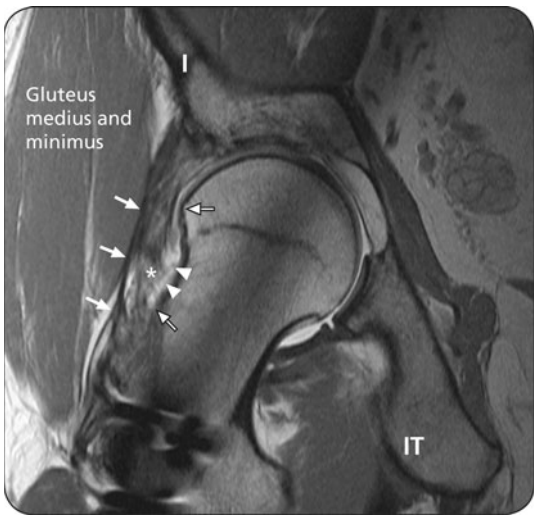

Fig. 1 A prerevision T2-weighted coronal MR image shows anterior hip capsular adhesions to the femoral neck in the presence of an inflammatory reaction at the site of the femoral neck footprint of the adhesions. There is an absence of joint effusion. IT - ischial tuberosity; I - ilium; white arrows = anterior hip capsule; * capsular adhesions to the anterior femoral neck; arrowheads = synovitis at the femoral neck footprint of the capsular adhesions; black line arrows = limits of previous cam resection on the femoral neck.

biopsy specimens were collected from the femoral neck areas where the femoral neck resection had been performed. If abnormalities were identified on visual inspection of the synovial membrane covering the femoral neck areas, these were the areas that underwent biopsy. Biopsy specimens also were taken from the hip area where bone wax was identified at the time of revision surgery.

All specimens were fixed in 10% neutral-buffered formalin, dehydrated through graded alcohols, immersed in xylene, embedded in paraffin, microtomed, mounted, and stained with hematoxylin and eosin (H&E) and all specimens were examined independently by two pathologists (CG, RWB) using plain light and polarized light microscopy on an Olympus BH-2 microscope (Olympus Optical Co, Tokyo, Japan). The findings were analyzed descriptively and the agreement between the two pathologists compared. There was no disagreement between the two pathologists with respect to the presence and type of the inflammatory reactions.

Results

At the time of the revision surgery, bone wax was identified macroscopically in the area of femoral neck resection in all 11 patients in whom bone wax had been used at the original surgery (Table 2). In addition to visual identification of bone wax in these 11 hips, the synovial membrane covering the bone wax appeared thickened, hyperemic, and inflamed in all hips (Fig. 2) and capsular adhesions were documented in every hip. In all 11 patients, a foreign body reaction was confirmed histologically in the biopsy specimens, with five of the 11 patients also having an associated lymphoplasmacytic inflammatory reaction (Fig. 3) (Table 2). In all three hips where no bone wax had been used at the time of the original surgery, capsular adhesions to the femoral neck were present, but the synovial membrane otherwise had a normal appearance. In these three hips, no

Table 2. Summary of clinical and histopathologic findings

Patient	Bone wax used at index surgery	Bone wax identified macroscopically at revision surgery	Chronic inflammatory responses	
			Foreign body giant cell	Lymphoplasmacytic
1	Yes	Yes	+	−
2	No	Not applicable	−	−
3	Yes	Yes	+	−
4	Yes	Yes	+	+
5	Yes	Yes	+	+
6	No	Not applicable	−	−
7	Yes	Yes	+	−
8	Yes	Yes	+	−
9	Yes	Yes	+	+
10	Yes	Yes	+	+
11	No	Not applicable	−	−
12	Yes	Yes	+	−
13	Yes	Yes	+	+
14	Yes	Yes	+	−

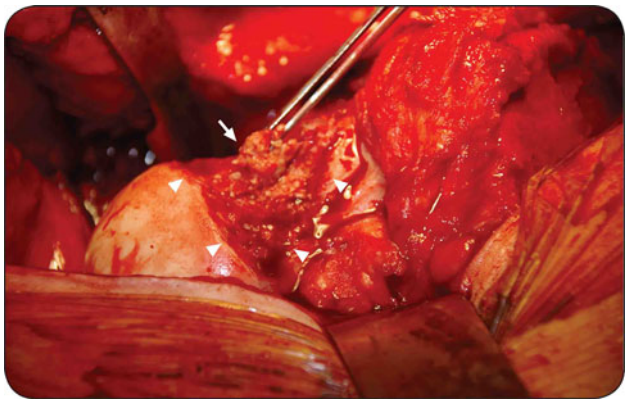

Fig. 2 An intraoperative image shows a thickened inflamed synovial lining on the anterior aspect of the femoral neck at the site of a previous cam resection in a patient who had bone wax at the initial FAI surgery. Arrowheads = previous cam resection area; arrow = a thickened inflamed synovial biopsy harvested from the previous area of cam resection.

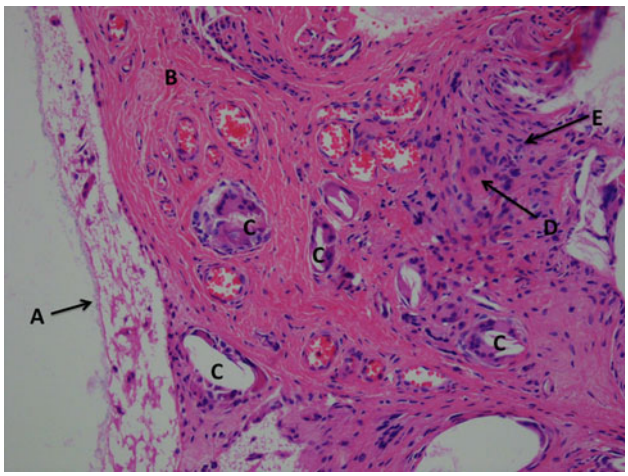

Fig. 3A–E A photomicrograph of the synovial lining shown in Fig. 2 from a patient who had wax at the initial FAI surgery shows multinucleated foreign body giant cells surrounding bone wax particles (Stain, hematoxylin and eosin; original magnification, ×20). **A** = synovial lining; **B** = fibrosis surrounding the foreign body reaction = **C**; with associated lymphoplasmacytic inflammatory reaction; **D** = plasma cell; **E** = lymphocyte.

foreign body or inflammatory reaction was present in the biopsy specimens (Fig. 4).

Discussion

Although there is considerable low-level evidence that extraarticular use of bone wax can cause a foreign body reaction of various degrees in between 40% (five of 12 patients [23]) and 100% (17 of 17 patients [25]) of patients, the effect of intraarticular bone wax is less clear, with only one case report published to date [15]. We therefore investigated histologically, at the time of revision surgery, the reaction of the hip synovial membrane to intraarticular use of bone wax during open FAI surgery.

We acknowledge limitations to this study. First, we had a relatively small number of cases. However, our study comprised of 14 patients undergoing revision surgery was considerably larger than the single case studies that have comprised the majority of publications in this area [1–4, 6, 10–12, 14, 19, 20, 24]. Second, owing to the nature of our study, we were unable to show whether intraarticular use of bone wax resulted in any clinical consequences, only that

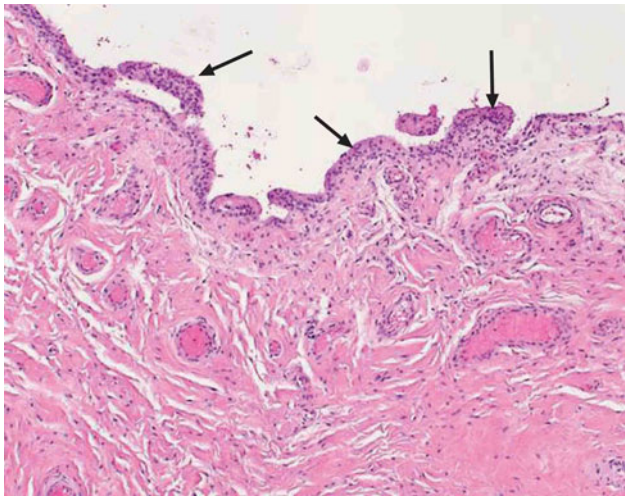

Fig. 4 A photomicrograph of a synovial biopsy specimen from a patient undergoing revision who did not have bone wax at the initial FAI surgery shows the absence of any signs of inflammation (Stain, hematoxylin and eosin; original magnification, ×10). Arrows = synovial lining.

synovial membrane inflammation was present at the time of revision surgery. Furthermore, we do not know whether patients not undergoing revision surgery would have shown similar levels of inflammation. Despite these limitations, the study provides evidence that intraarticular bone wax is associated with synovial inflammation; although such inflammation has the potential to generate clinically important symptoms, we cannot say whether the inflammation seen was related directly to the symptoms in these patients. Third, it would have been advantageous if we could have looked for clinical and radiographic signs of articular and periarticular soft tissue inflammation in all patients who had undergone FAI surgery in our institutions, not just those undergoing revision surgery, to look for an association between the use of intraarticular bone wax and inflammatory sequelae. However, this was deemed beyond the scope of this study.

We found all patients in whom bone wax had been used intraarticularly at the time of original FAI surgery had macroscopic evidence of synovial membrane swelling and inflammation at the time of revision surgery, with histologic confirmation of a foreign body reaction in all samples and a lymphoplasmacytic inflammatory reaction in ½ of the biopsy specimens. Thus, although bone wax had the desired effect of providing bone hemostasis at the time of initial FAI surgery and also may have had the beneficial effect of suppressing new bone formation in the resection area, it appeared to be associated with an inflammatory reaction that was not only more extensive than we had anticipated but also was present in all cases where bone wax had been used, at least in this sample of patients undergoing revision surgery.

Not only did we find a foreign body reaction to the bone wax in all 11 patients in whom bone wax was used, but also in five of the 11 hips in our study, we found an additional lymphoplasmacytic infiltration. Dysynchrony between the degree of granulomatous and lymphocytic inflammation is a well-recognized phenomenon [5], with, for example, some patients in our study having marked granulomatous inflammation but a negligible lymphoplasmacytic infiltrate. This finding presumably relates to underlying differences in the nature of the response of macrophages and lymphocytes and plasma cells to foreign body irritation. It is possible a more pronounced lymphoplasmacytic and plasma cell reaction may have enhanced the fibroblastic response through cytokine activation with resultant capsular adhesions. All 14 patients in this case series had capsular adhesions at the time of revision surgery, between the area of the femoral neck osteochondroplasty and the overlapping hip, even though bone wax had been used at the time of the initial surgery to prevent bleeding and formation of such adhesions in 11 of the 14 patients. Given that all 14 hips (ie, not just the 11 who had bone wax used at the time of initial surgery) had capsular adhesions and that ½ had additional disorders showed it is not possible to delineate the exact role that intraarticular bone wax played in the development of capsular adhesions and symptoms before revision surgery. However, previous research has identified increasing fibrosis around bone wax, with or without a foreign body-type reaction, with the passage of time [23]. Even though the contribution of the bone wax to the symptoms of the patients remains unclear, the presence of a chronic lymphoplasmacytic inflammatory reaction in the presence of bone wax, identified for the first time in this study, is worrisome. We speculate a chronic inflammatory reaction may induce a symptomatic synovitis of the hip. Even though not all hips in which bone wax has been used may have symptoms develop, the observation of an inflammatory reaction in all 11 hips with bone wax should be considered a complication that may lead to an undesired clinical result. Intraarticular use of bone wax during FAI surgery therefore should be omitted.

Although numerous studies have reported multiple adverse effects associated with extraarticular use of bone wax across various clinical settings as noted earlier [1–4, 6, 10–12, 14, 19, 20, 23–25], none of these studies reported on the intraarticular use of bone wax. Although serious clinical consequences associated with the use of bone wax appear to be unusual, with most studies being single case reports only [1–4, 6, 10–12, 14, 19, 20, 24], these side effects can be devastating in some nonorthopaedic applications (eg, sternal pseudarthrosis [1], paraplegia [2, 11, 14, 24], venous sinus thrombosis [4], and cerebrospinal fluid leak [20]). There is also evidence that bone wax can cause allergic reactions [10], impairs the ability of bone to

clear bacteria [9], and is associated with an increased risk of surgical site infection [8, 22].

Although our study cannot confirm a direct link between the use of intraarticular bone wax during FAI surgery and the occurrence of subsequent clinically important symptoms, we did observe chronic inflammatory reactions to its use at the time of revision surgery. Thus, although bone wax may have had the desired effect of stopping bleeding at the time of the initial FAI surgery, our findings should caution surgeons against intraarticular use of bone wax during FAI surgery. Based on our findings, we have abandoned the use of intraarticular bone wax during FAI surgery. Alternatives to bone wax, including absorbable copolymers and gelatin-based agents that do not provoke adverse tissue response or interfere with bone healing [17, 18, 21, 26–29], may be preferable absorbable hemostatic agents for treating bone bleeding.

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