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Subchondroplasty in the lower extremity: A literature review

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Osteoarthritis is one of the most common and debilitating conditions encountered by foot and ankle surgeons. This osteoarthritis is often accompanied by a coinciding bone marrow lesion (BML) which has been shown to result in poorer patient outcomes. The subchondroplasty procedure was developed with the aim of targeting these painful BMLs in order to slow the progression of osteoarthritic changes. There has been a trend in both orthopedic and podiatric literature towards the use of this procedure in the lower extremity. This review is meant to bring forward the information most pertinent to the procedure to help inform the foot and ankle surgeon of its uses and potential, as well as to encourage future research into the procedure.

Keywords: subchondroplasty, bone marrow lesion, osteoarthritis, calcium phosphate, bone substitute material

Osteoarthritis (OA) remains one of most common and debilitating conditions encountered by foot and ankle surgeons. Whether the result of trauma or degenerative overuse, orthopedic and podiatric surgeons alike can agree that the sequelae of OA can be challenging to manage. The natural history of OA involves persistent joint pain, lack of normal function, and can include a vicious cycle which may progress to osteonecrosis of the affected bones. While the current body of evidence of *in vitro* cartilage repair and regenerative medicine is rapidly growing, there are perhaps other more readily available methods of treating OA which may ultimately demonstrate equal benefit to patients. Subchondroplasty® (SCP) (Zimmer Knee Creations, West Chester, PA) is a surgical system, developed in 2007, in which flowable bone substitute material (BSM) is injected into subchondral bone in order to fill a defect. The procedure acts to support the subchondral bone layer by providing a scaffold over which new, healthier osteochondral elements may be produced [1]. Although this technique has primarily been described in literature to treat bone marrow lesions (BMLs) in the knee joint, this technique has recently been applied to the foot and ankle with comparably successful outcomes.

This paper is not meant to serve as a technique guide, but a review of available relevant literature. As such, the use of the term subchondroplasty throughout the paper will be in reference to the procedure itself, not the proprietary system. The goal of this review is to benefit the foot and ankle surgeon by: first, providing a general understanding of the procedure and its expanding applications; second, by presenting the largely positive patient outcomes in both the orthopedic and podiatric literature in an attempt to encourage further study into a relatively new - yet promising - tool in the foot and ankle surgeon's array of treatments.

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Methods

An extensive search of available literature related to: 1) subchondral bone and the osteochondral unit; 2) lower extremity osteoarthritis; 3) bone substitute materials; 4) the subchondroplasty procedure, including its related radiographic findings and clinical outcomes in the lower extremity.

Background

Within joints, the subchondral bone layer is a supporting structure for the overlying articular cartilage. Subchondral bone is an underappreciated, yet vital component to the function of each osteochondral unit and overall joint health [2]. Bone metabolism is dynamic, in concert with Wolff's law, and a normal subchondral bone plate displays the same capacity to increase in thickness according to physiologic loading [3].

In osteoarthritis, this typically dynamic nature of the subchondral bone plate is disrupted. Increased and imbalanced dispersion of joint forces, combined with a concentration of stresses and synovial fluid infiltration into the subchondral bone, can lead to reduced healing capacity and abnormalities within the underlying cancellous bone. These abnormalities can be identified both histologically and on magnetic resonance imaging (MRI) as bone marrow lesions (BMLs) [4-7].

The mechanism of coinciding pain associated with these BMLs is currently under debate, but has been attributed to the healing response secondary to trauma and trabecular injury and/or impaired venous drainage [8-10]. Histologically, BMLs have been shown to be focal areas of demineralization, increased fibrosis, and vascular abnormalities. These abnormalities can mimic chronic stress fractures, which may then progress to areas of focal necrosis [6,11-15]. Clinically, it is of great importance that BMLs be identified and treated, as they have been linked to increased arthritic pain and may hasten the progression of joint deterioration [5,16-18].

These potential consequences have been attributed to both improper load transmission across the affected joints and an underlying imbalance in bone metabolism—favoring bone resorption when a BML is present [19]. A direct correlation between increasing size of BMLs and increased pain in the knee was identified in a study by Felson, et al., in 2007. Patients experiencing pain were found to have a 3.31-fold greater likelihood of significant findings on MRI compared to non-painful patients with the same radiologic degree of arthrosis [20]. Additionally, Saltzman and Kijowski found that BML prevalence, depth, and cross-sectional area under arthroscopy were each directly correlated with worsening grades of corresponding articular cartilage defects [2,21].

Osteoarthritis occurring in the hip and knee joints primarily occurs as a degenerative process. However, due to histological, anatomic, and biomechanical differences in the cartilage of the ankle joint, arthritis in the ankle most commonly occurs after significant trauma [22-24]. Due to the post-traumatic presentation of ankle joint arthritis, there exists a propensity for a wider range of ages at which osteoarthritis may present in the affected ankle, which has important implications with how these patients are definitively treated. Younger and more active patients with ankle joint arthritis are less tolerant of arthrodesis or arthroplasty procedures than are their elderly and less active counterparts. As such, it stands to reason that there should be a great deal of interest in the potential for joint sparing procedures in these patients.

The Procedure

In this procedure, BMLs are triangulated using fluoroscopy, and subsequently injected and filled with flowable, biologically-compatible ceramic materials. The injected bone substitute material (BSM) then undergoes an endothermic reaction, resulting in crystallization of the BSM which affords properties similar to that of cancellous bone. This is believed to assist in supporting the trabecular structure of the bone, and to slow or even halt the pathologic processes at work. Typically, this procedure has been performed with calcium phosphate (CaP), calcium sulfate (CaS) or hydroxyapatite (HA), with CaP being the more commonly used of the three [25]. However, in terms of osteobiology, these products only offer one component of the osteobiology triad: osteoconduction. As such, these products only function as a scaffolding upon which healing may take place.

In 2016, Hood et al proposed that the two remaining osteobiologic properties, osteogenesis and osteoinduction, could be imparted via the addition of bone marrow aspirate concentrate (BMAC) to the osteoconductive materials used during the procedure [25]. It had previously been shown that osseous regeneration occurs at a faster rate with the use of a combination of BMA and osteoconductive ceramic materials, as opposed to either alone [26]. The premise behind this is that replacing the 0.9% normal saline solution (NSS)—which is typically used for rehydration of the bone substitute material—with autogenous BMAC, bone healing potential can be improved.

The addition of BMACs, the osteoconductive CaP would have the theoretical benefit of mesenchymal stem cells (MSCs), osteoprogenitor cells (OPCs), hematopoietic stem cells (HSCs), platelets, vascular endothelial growth factor (VEGF) and transforming growth factor beta (TGF-β) to assist in the reparative process [26-29]. In patients with concomitant cartilaginous defects, particulated juvenile allograft cartilage (PJAC) can be used to address the overlying cartilaginous defect after hardening of the CaP scaffold [8].

Hood et al. presented a case report for a 26 year old female with two years of recalcitrant left ankle pain after a motor vehicle accident. This patient eventually underwent the modified SCP® technique with rehydration using BMAC for a talar dome BML [25]. It was reported that the patient's pain decreased from a preoperative VAS score of 9 to occasional 1-2/10 discomfort at 6 weeks postoperatively.

CaP with BMAC has since become a popular choice among bone and joint surgeons, though other orthobiologic combinations have also been reported with promising results: CaS with platelet-rich plasma (PRP), HA with BMAC, and HA-tri-CaP with MSC [30-32]. Subsequent studies have aimed to clarify the following: the ideal osteoinductive/osteogenic adjunct, the proper amount and consistency of adjunct, the effect on curing time and handling, and the adjunct's effect on the scaffolding material.

In 2015, Colon et al. evaluated in vitro injectability of common commercially available bone substitute materials (BSMs). Histologically, bone marrow lesions (BMLs) demonstrate micro-trabecular damage characteristic of stress fractures [15]. For injection of materials into these microtrabeculae to be considered possible, the materials must have the ability to be injected into a highly pressurized space. Eight of the most common commercially available BSMs were tested (AccuFill® (Zimmer, Inc.), Beta-BSM™ (Zimmer, Inc.), Cerament™ (Biomet, Inc.), HydroSet™ (Styker®), Norian™ SRS (DePuy Synthes®), Pro-Dense® (Wright Medical Inc.), StrucSure™ CP (Smith & Nephew plc), Simplex™ (Stryker®)) using the polyurethane block material, while three were additionally tested in femoral condyle cadaveric bone blocks from healthy donors (AccuFill®, Beta-BSM™ and StrucSure™). The results found that although these materials are all considered injectable BSMs, only three were able to flow into the closed structure of the polyurethane block (AccuFill®, Simplex™ and StrucSure™). Additionally, AccuFill® was shown to outperform the other BSMs in several areas: the ability to flow within micro-architecture without damage from the applied force, the lowest injection force, the highest volume injected, the greatest area covered by material injected, and the ability to set without an exothermic reaction. The knowledge that these commercial calcium phosphate (CaP) products have differing properties, and understanding how this may affect different aspects of the procedure, can help inform the decision making of the surgeon.

Imaging

In 2016, Agten, et al., and Nevalainen, et al., both published papers describing diagnostic imaging related to the subchondroplasty procedure in the knee. The goal was to educate radiologists and familiarize them with expected post-procedure findings. Agten, et al., reviewed the pre- and postoperative imaging for nine patients, with the first postoperative imaging at three months post-operatively. Nevalainen, et al., discussed two knee subchondroplasty case studies. Preoperative imaging revealed that insufficiency fracture was associated with a greater amount of bone marrow edema than osteoarthritis [33].

Following the procedure, postoperative radiographs should display an increased radiodensity at the site of calcium phosphate injection, which should correlate with the locations of bone marrow edema (BME) on preoperative imaging [33,34]. CaP extravasation into soft tissues may occur along the track of the injection, which predictably mimics the appearance of heterotopic ossification. Extra-articular extravasation of calcium phosphate may resolve over time, while intra-articular leakage is a complication that should be addressed intraoperatively.

When evaluating patients, it is important to identify the cause of bone marrow edema, as this is a relatively non-specific finding, particularly on MRI. Trauma, including bone contusions, is the most common cause of positive BME findings on MRI [35]. The remaining causes of BME on MRI are transient BME syndromes (including transient osteoporosis, regional migratory osteoporosis, and complex regional pain syndrome), repetitive microtrauma and stress fractures, and non-traumatic causes such as avascular necrosis, spontaneous osteonecrosis, reactive polyarthritis, and neoplasms [2].

Classic findings of BMLs include a focal area of BME appearing as high signal intensity on T2-weighted, fat-saturated images and low signal intensity on T1-weighted, fat sensitive images. The increased signal intensity of BMLs on T2-weighted, fat-saturated MRI sequences has been suggested to be a result of increased subchondral vascularity [1]. Additionally, a low-signal-intensity line in the subchondral region of T2-weighted, fat-saturated images may be present, corresponding to impaction of the trabecular bone [35]. If present, it has been shown that a length and thickness of this line greater than 14mm and 4mm, respectively, are risk factors for lesion progression and subchondral collapse [36]. This signal should change to a decreased signal intensity on both T1-weighted fat-sensitive and T2-weighted fat-saturated images following injection of the CaP [33,34]. On fat-saturated, fluid-sensitive images there may also be a fine rim of increased signal intensity surrounding the CaP, representing surrounding edema [33,34]. It should be noted that a direct correlation between increasing BME signal intensity and more advanced cartilage degradation on MRI has also been identified [37].

Preoperative CT scan may be useful in conjunction with MRI, especially in the case of concurrent cartilage injury, as this can be difficult to assess on MRI [38,39]. Concurrent evaluation of the cartilage portion of the osteochondral unit should be considered of utmost importance, as 60% of patients with surgically confirmed chondral degeneration in the knee have been shown to have associated BMLs [21]. Additionally, both cartilage thinning and bony edema can lead to over- or underestimation of cartilage and bone damage on MRI [40]. Postoperatively on CT scan, any drill holes will be seen as a hypodense track with the surrounding hyperdense CaP [33].

Notably, the changes described correlating to post-procedure imaging have been shown to regress over time. Still, the specific time-frame is currently unclear and likely variable. In canine models, the majority of BSM has been found to be absorbed by two years postoperatively [41].

Use for OA/BML in the knee

Subchondroplasty was originally described for use in the treatment of moderate to severe osteoarthritic knee pain present for more than 2-6 months, with concomitant presence of a BML localized to the area of pain [42]. The presence of a BML in these patients is particularly concerning, as patients with knee OA compounded with a BML have a highly predictable progression to total knee arthroplasty (TKA). In fact, this occurs approximately nine times more frequently over a three year period when compared to OA in patients without a coinciding BML [4,43-45]. Previous treatment of cartilaginous defects in the knee by arthroscopic debridement alone has not been shown to yield success for patients suffering from moderate to end stage osteoarthritis, with several studies showing either no improvement or minor improvement at six months, and no improvement at two years. [4,45-48].

In 2016, a study by Cohen, et al., evaluated the combined treatment of subchondroplasty and arthroscopy in the knee in 66 patients who initially presented for TKA consultation [4]. Pain was significantly decreased and function significantly improved in all groups, including at both 6 and 24 months post-op. Notably, there was a 70% 2-year joint preservation survivorship. Patients who ultimately received TKA were significantly older and were more likely to have had a history of prior meniscectomy. A follow-up study from Brazil also noted positive results, with improvement on both VAS and knee injury and osteoarthritis outcome scores (KOOS) at 24 weeks postoperatively [14]. Longer-term outcomes of treatment with CaP in post-traumatic, impact-induced BMLs in a medial femoral condyle canine model have also shown symptomatic and functional benefits for up to two years [41].

The effect on TKA

Logically, the next question to address is whether the technique of treating BML using CaP bone substitutes affects outcomes in patients who fail this joint preserving technique and require knee replacement. It has previously been reported that the complexity of knee arthroplasty increases in patients who have had previous knee surgery, resulting in the potential for more complications and poorer outcomes [49-52]. In 2016, Yoo, et al., evaluated the effect of prior BML treatment on the complexity and outcomes of future knee arthroplasty procedures [53]. A total of 22 patients who had undergone prior arthroscopic repair of BMLs were demographically matched in a 1:2 ratio to a group of controls undergoing knee arthroplasty, either unicompartmental knee arthroplasty (UKA) or total knee arthroplasty (TKA). Patients were followed up for an average of 23.5 months (ranging from 12-52 months), with no significant differences identified between the groups. There were no cases of intra-operative UKA conversion to TKA, no differences in surgical complications or technical challenges between groups, and no cases of non-standard primary components required. Additionally, on intraoperative inspection of the CaP bone substitute, it was reported to be consistently well incorporated without signs of compromise or inconsistencies from the subchondral bone. Based on their findings, Yoo, et al., concluded that previous treatment of BMLs using CaP bone substitute did not compromise knee arthroplasty outcomes or surgical performance.

Functional/Subjective outcomes in the knee

Functional and subjective outcomes have been generally favorable following subchondroplasty. In 2018, a literature review of 8 articles and 164 total patients treated with CaP injection for BMLs in the femoral condyles or tibial plateau noted significant improvement in symptoms, few complications, and return to activity at an average of three months [42]. Of the articles reviewed, only a single paper reported a subgroup of patients who experienced poor outcomes from the procedure. Chatterjee, et al., identified an inverse relationship between the subjective postoperative Tegner-Lysholm knee scoring scale and preoperative Kellgren-Lawrence osteoarthritis grade [54]. In other words, a correlation was identified between poorer subjective outcomes and more severe preoperative osteoarthritis. Despite this, other studies have failed to report similar correlation between OA grade and outcomes. As such, future prospective studies would be valuable in confirming this finding.

Described use in the Foot and Ankle

At this time, the literature regarding treatment of BMLs using flowable calcium phosphate (CaP) has been primarily directed to cases in the knee. However, due to the need for joint-sparing procedures for ankle osteoarthritis and for the treatment of symptomatic BMLs, there has been growing interest in its application in the foot and ankle. Since subchondroplasty was first introduced into the field of foot and ankle surgery in 2015, more than six thousand foot and ankle subchondroplasty procedures have been performed [55]. The first reported subchondroplasty procedures performed in the foot and ankle were from Miller, et al., [56]. Two cases were reported, the first in a 48 year old male with complaints of chronic left ankle pain and instability, and the second in a 28 year old male with chronic ankle pain following a fibular non-union. In both cases, the patients exhibited talar BMLs on MRI that were recalcitrant to conservative treatments. Each patient underwent a subchondroplasty procedure, combined with other indicated procedures. The first patient was able to return to full activity at 12 weeks post-operatively, while the second sustained a tibial fracture due to a syncopal event at 13 weeks post-op. Miller, et al., reported minimal subjective pain in both cases at 10-month follow-up with no activity restrictions.

Shortly thereafter in 2018, Chan, et al., reported an 11-patient retrospective cohort study of symptomatic talar osteochondral defects (OCDs) treated with subchondroplasty with bone marrow aspirate concentrate (BMAC) injection [57]. In this cohort, the mean talar OCD size was 1.3 cm x 1.4 cm. All subjective outcomes improved from preoperative baseline to final one year follow-up, including visual analog pain scale and Foot and Ankle Outcome Score, with 10 out of the 11 patients reporting they would undergo the procedure again. There was a single reported complication in the cohort, with a talar neck stress fracture at bone-BSM interface after the patient had previously experienced full resolution of symptoms. All patients, except for the aforementioned complication, returned to full activity between three and nine weeks postoperatively.

Barp, et al., published two case reports, including a 25 year-old male tennis player and a 53 year-old female, treated with percutaneous injection of CaP into the 2nd metatarsal head (Frieberg's infraction) and cuboid (stress fracture), respectively. Both patients were allowed protected weightbearing as tolerated at one week postoperatively, returned to full activity without pain at four weeks, and remained free of related complaints at final follow-up at one and three years, respectively [58].

BMLs in the foot have also been found to be associated with plantar fasciitis, specifically patients requiring surgical intervention [59]. This may have significant clinical implications. In a report by Bernhard, et al., a single case of recalcitrant plantar fasciitis was shown to have a concomitant calcaneal BML on MRI [60]. This patient was treated with repeat plantar fasciotomy and CaP injection of the BML, successfully resulting in full return to activity and pain-free follow-up at 3 and 10 months.

Complications

Perhaps due to the minimally invasive nature of the procedure, few complications of subchondroplasty have been reported in the literature. While rare, the surgeon should be aware of the following potential complications: pain secondary to overfilling with CaP, intra- or extra-articular extravasation of CaP, deep vein thrombosis of the operative limb, subsequent soft tissue or bone infection, stress fracture at the bone-BSM interface, and avascular necrosis [8,57,61].

Pain secondary to overfilling with CaP has been identified as the most common complication of the subchondroplasty procedure, and has been described clinically as a disproportionate pain which often resolves completely within 72 hours postoperatively [42]. Over-pressurization and failure to completely fill a BML have both been associated with poorer outcomes in the orthopedic knee literature and are highly preventable with increased surgeon experience [62]. A single case of osteomyelitis secondary to subchondroplasty in the medial femoral condyle was reported by Dold, et al. In their report, the authors considered that this procedure may have a predisposition for infectious complications due to direct seeding and the hydrophilic nature of CaP, which can result in prolonged wound drainage, poor healing, and eventual sinus tract formation [61]. In a series of 11 patients receiving CaP injection in the talus for painful osteochondral defects, Chan, et al., reported a single complication in a patient with a BMI of 34 kg/m² who experienced a talar neck stress fracture at the bone-BSM interface [57].

Conclusion

Overall, subchondroplasty for the treatment of BMLs has led to promising outcomes and infrequent complications. The range of potential applications of the technique is constantly expanding, with increasing use in the treatment of foot and ankle pathology. Additional studies may help clarify the potential benefits in the setting of osteoarthritis of the foot and ankle, including the procedures potential in delaying and/or preventing total ankle arthroplasty.

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