Treatment for unicameral bone cysts in long bones: an evidence based review

Sandra Donaldson,[1] Josie Chundamala,[2] Suzanne Yandow,[3] James G. Wright[2]

[1]Orthopaedic Surgery, The Hospital for Sick Children, Toronto, Ontario, Canada; [2]Department of Surgery, The Hospital for Sick Children, Toronto, Ontario, Canada; [3]Orthopaedic Surgery, Central Texas Pediatric Orthopedics, Austin, Texas, USA

Abstract

The purpose of this paper is to perform an evidence based review for treatment of unicameral bone cysts. A search of MEDLINE (1966 to 2009) was conducted and the studies were classified according to levels of evidence. This review includes only comparative Level I-III studies. The systematic review identified 16 studies. There is one level I study, one level II study and the remaining 14 studies are level III. Seven of the sixteen studies had statistically different results: three studies indicated that steroid injection was superior to bone marrow injection or curettage and bone grafting; one study indicated that cannulated screws were superior to steroid injections; one study indicated resection and myoplasty was superior to steroid injection; one study indicated a combination of steroid, demineralized bone matrix and bone marrow aspirate, and curettage and bone grafting were superior to steroid injection; and one study indicated that curettage and bone grafting was superior to non-operative immobilization. Based on one Level I study, including a limited number of individuals, steroid injection seems to be superior to bone marrow injection. As steroid injections have already demonstrated superiority over bone marrow injections in a randomized clinical trial, the next step would be a prospective trial comparing steroid injections with other treatments.

Introduction

Simple, or unicameral, bone cysts are a benign lesion in growing children. While the two terms are used interchangeably some would argue that bone cysts are not "simple", whereas the cysts are not always unicameral. Cysts are more common in males (70%) and typically present in the proximal humerus (70%) or femur (25%). While exact figures are unknown, it is estimated that approximately 75% of children present with pathological fracture.[1] Cysts heal in less than 15% of children following fracture.[2] Although unicameral bone cysts are believed to resolve with skeletal maturity, without treatment these children are at risk for pain, or recurrent fracture leading to activity restriction for many years.

Unicameral bone cysts may also lead to growth disturbance. Growth arrest, a relatively uncommon complication, may occur through many mechanisms. The disruptive, hydrodynamic assault of cyst fluid on the physis may in itself result in growth disturbances.[3] Other rare causes for growth arrest include multiple fractures through the cyst that damage the physis, direct extension of the cyst through the physis, or as a result of treatment of cysts adjacent to the physeal plate.[4-6] Regardless of the cause, growth retardation in the affected limb may lead to angular deformity and/or limb length discrepancy.[6]

Recurrent pathological fractures in children with unicameral bone cysts require immobilization, and/or internal fixation, and restriction of activities. Recurrent fractures, particularly in the lower limb, may also cause limb length discrepancy and deformity. In addition, children are often afraid of their usual play activities or are restricted from all sporting activities by their parents or physician because of the concern of fracture(s). Finally, some children with unhealed cysts complain of pain.[7] Although the origin of this pain is unclear, the pain seems to resolve with the healing of the cyst.[8] Thus despite the benign nature of these lesions, unicameral bone cyst can have significant detrimental effects on otherwise normal children and their families.

Many theories have been proposed to explain the pathogenesis of unicameral bone cysts. An early theory was that injury to the growth plate leads to abnormal endochondral bone formation.[9] Interest has also been drawn to the cyst lining and the presence of bone resorptive factors in the cyst fluid, including interleukin 1-B and prostaglandin E2[10] and oxygen free radicals and lysosomes.[11,2] Another theory suggests that vascular obstruction causes cyst fluid to accumulate under pressure and expand at the expense of the normal bone.[3,10-11] However, the uncertainty of the etiology has led to a wide variety of treatments.

Treatment strategies for unicameral bone cysts include injection, mechanical disruption of the cyst lining and/or wall, structural support, decompression, or mixed methods. Injections can include steroids,[13] bone marrow,[14] demineralized bone matrix,[15] calcium sulfate pellets,[16] and fibrin sealant.[17] Mechanical disruption of the cyst lining or wall is done by curettage. Structural support can be done with flexible intramedullary nailing.[18] Decompression can be done with multiple drill holes,[12] cannulated screws,[19] and different types of nails.[20] Many mixed methods approach the cyst on multiple levels such as percutaneous removal of cyst lining, curettage to break up septations, intramedullary decompression, and injection of calcium sulfate pellets.[16] To date, few comparative studies have been conducted (Table 1). The purpose of this study was to perform an evidence based review of treatment of unicameral bone cysts.

Correspondence: Sandra Donaldson, Orthopaedic Surgery, The Hospital for Sick Children, S107-555 University Ave, Toronto, Ontario, M5G 1X8, Canada.
E-mail: sandra.donaldson@sickkids.ca

Key words: unicameral bone cyst, pediatrics, treatment, levels of evidence.

Contributions: SD and JC, analysis and interpretation of data, drafting the article, final approval of the version to be published; SY, analysis and interpretation of data, revising article for important intellectual content, final approval of the version to be published; JGW, conception and design; analysis and interpretation of data, revising article for important intellectual content, final approval of the version to be published and funding.

Conflict of interest: the authors report no conflicts of interest.

Received for publication: 12 March 2010.
Revision received: 18 March 2010.
Accepted for publication: 19 March 2010.

Orthopedic Reviews 2010; 2:e13
doi:10.4081/or.2010.e13

Materials and Methods

A search of MEDLINE (1966 to 2009) was conducted using the following search string: Bone cysts/ and (unicameral or multi-cameral or simple). The search was limited to English language, humans and children aged 0 to 18 years. The studies had the following inclusion criteria: sample size greater than one; randomized controlled trial or comparative study; cysts located in long bones; and all forms of treatment including observation or fracture immobilization. Studies were excluded if the cysts were located in areas other than long bones, i.e. calcaneus or pelvis. Studies with mixed populations of cyst location were included, but studies focusing exclusively on calcaneal cysts were excluded. Studies of mixed populations

Table 1. Summary of Levels of Evidence I -III [N=1340].

Author Year	Level of evidence	Study design	Age of population years	Follow-Up years	Definition of healed	Intervention	Complications	Outcome
Wright *et al.* 2007[7]	I	RCT	Mean: 9.5 Range: 2.8 to 17.1	Mean: 2.2 Range: 1.5 to 3.3	Modified Neer / Cole classification 4 grade scale, healing defined as grades 3 or 4: 3) sclerosis around or within a partially visible cyst; 4) complete healing with obliteration of cyst	Steroid injection [n=38] Autologous bone marrow injection [n=39]	Fractures: 11 Complications: 0 Fractures: 9 Complications: 2 superficial infections	Steroid superior to bone marrow (P=0.01)
Brecelj *et al.* 2007[18]	II	Prospective comparative	Mean: 9.8 Range: 2.7 to 16	Mean: 5.8 Range: 1 to 13.1	Chang classification 4 grade scale, healing defined as grades 1 or 2: 1) Healed: cyst filled by formation of new bone with or without small static radiolucent area(s) less than 1 cm in size; 2) Healing with defect: static radiolucent area(s), less than 50% of the diameter of the bone with adequate cortical thickness to resist fracture.	Steroid injection [n=33] Curettage + bone grafting [n=8] Cannulated screw [n=28]	Fractures: none reported Complications: none reported Fractures: none reported Complications: none reported Fractures: complications: 3 broken screws (left in place)	Cannulated screw superior to steroid (P=0.001)
Sung *et al.* 2008[21]	III	Retrospective comparative	Mean: 11.2 Range: not provided	Mean: 4.7 Range: 0.08 to 27	Outcome defined as: Treatment failure (defined clinically as subsequent pathological fracture or need for retreatment to prevent pathological fracture) or complications.	Steroid injection [n=94] Curettage and bone grafting [n=39] SDB: Combination injection of steroid, demineralized bone matrix, and bone marrow aspirate [n=34]	Fractures: 17 Complications: 5 deformity/ growth disturbance Fractures: 1 Complications: 3 deformity/ growth disturbance Fractures: 4 Complications: 1 deformity/ growth disturbance	SDB superior to steroid injection (P<0.001) Curettage and bone grafting superior to steroid (P=0.01) No difference between curettage and SDB (P=0.23)
Cho *et al.* 2007[22]	III	Retrospective comparative	Mean: 11.2 Range: 2 to 18	Mean: 4.7 Range: 2 to 15.5	Modified Neer classification 4 grade scale, healing defined as 1 or 2: 1) Healed: cyst filled by new bone, with or without small radiolucent area(s) <1 cm in size; 2) Healed with defects: radiolucent area(s)<50% of the diameter of bone, with enough cortical thickness to prevent fracture.	Steroid injection [n=30] Autologous bone marrow injection [n=28]	Fractures: 0 Complications: none reported Fractures: 3 Complications: none reported	No difference between treatment groups (P>0.05)
Chuo *et al.* 2003[23]	III	Retrospective comparative	Mean: 11.9 Range: 6 to 21	Mean 5.7 Range 2 to 12	Modified Neer / Capanna classification 4 grade scale, healing not defined beyond grades. 1) Completely healed 2) Healed with residue 3) Recurred 4) No response	Observation [n=6] Curettage + bone grafting + ORIF [n=4] Cannulated screw [n=7]	Fractures: 0 Complications: 1 malunion (humerus) Fractures: 0 Complications: none reported Fractures: 0 Complications: none reported	No difference between treatment groups (P=0.42)
Chang *et al.* 2002[24]	III	Retrospective comparative	Mean: 9.1 Range: Not provided	Mean: 3.7 Range: 1 to 9	Modified Neer classification 4 grade scale, healing defined as 1 or 2: 1) Healed: cyst filled by formation of new bone with or without small static, radiolucent area(s) less than 1 cm in size; 2) Healed with defect: static, radiolucent area(s) greater than 50% of the diameter of bone with enough cortical thickness to prevent fracture.	Steroid injection [n=65] Autologous bone marrow injection [n=14]	Fractures: 26 Complications: none reported Fractures: none reported Complications: none reported	No difference between groups (P>0.05)
Tsuchiya *et al.* 2002[25]	III	Retrospective comparative	Mean: 15.2 Range: 8 to 22	Mean: 6.8 Range: 0.7 to 12.3	Not defined	Curettage, multiple drilling + titanium cannulated screws [n=15] Curettage, multiple drilling + cannulated hydroxyapatite pin [n=11]	Fractures: 2 Complications: none reported Fractures: 0 Complications: none reported	No difference between treatment groups (P=0.12)

Continued next page

Table 1. Continued from previous page.

Author Year	Level of evidence	Study design	Age of population years	Follow-Up years	Definition of healed	Intervention	Complications	Outcome
Bensahel *et al.* 1998[26]	III	Retrospective comparative	Mean: 7 Range: 2 to14	Mean: 9 Range: 3 to 15	Not defined	Steroid injection [n=55] Resection + myoplasty [n=50]	Fractures: 0 Complications: 0 Fractures: 0 Complications: 0	Resection and myoplasty superior to steroid injection (P=0.02)
Gennari *et al.* 1995[27]	III	Retrospective comparative	Mean: 7 Range: 3 to 13	Mean: 6 Range: Not provided	Not defined	Steroid injection [n=3] Curettage + bone grafting + ostesynthesis [n=10] Rupture of cyst w/o osteosynthesis [n=5] Orthopedic treatment [n=2]	Fractures: 0 Complications: 0 Fractures: 2 Complications: 2 limb shortenings Fractures: 2 Complications: 3 limb shortenings Fractures: 0 Complications: 1 limb lengthening	No difference between treatment groups (P=0.08)
Mylle *et al.* 1992[28]	III	Retrospective comparative	Mean: 15 Range: Not provided	Mean: 8.5 Range: Not provided	Neer/Campanacci Classification 4 grade scale, healed defined as 2 or 3: 2) Incomplete healing: new bone formation fills the area previously occupied by the cyst. Small sites of osteolysis remain visible in the boundaries of the cyst; 3) Complete healing: the space occupied by the SBC is completely filled by new bone or by hydroxyapatite.	Steroid injection [n=20] Curettage +/- bone grafting [n=21] Curettage + steroid injection [n=6] No treatment [n=12]	Fractures: 0 Complications: 1 superficial infection Fractures: 0 Complications: 3 superficial infection Fractures: 0 Complications: 1 superficial infection Fractures: 10 Complications: 1 growth disturbance	Steroid injection superior to curettage + bone grafting (P=0.03)
Farber *et al.* 1990[29]	III	Retrospective comparative	Mean: 8.1 Range: Not provided	Mean: 6.7 Range: Not provided	Not defined	Steroid injection [n=17] Curettage + bone grafting [n=19]	Fractures: none reported Complications: 0 Fractures: none reported Complications: 0	No difference between treatment groups (P=0.27)
Bovill *et al.* 1989[30]	III	Retrospective comparative	Mean: 8.9 Range: 0.75 to 30	Mean: 5.6 Range: Not provided	Oppenheim and Galleno Modification 4 grade scale, healing defined as 1 or 2: 1) Resolution: 70-100% obliteration and renewed cortical thickening on serial X-ray; 2) Incomplete resolution: 50-70% obliteration with renewed cortical thickening.	Steroid injection [n=12] Surgical treatment (multiple) [n=15] Non-surgical treatment (orthopedic) [n=5]	Fractures: 3 Complications: 0 Fractures: 1 Complications: 3 limb deformity, 1 infection, 1 median nerve palsy, and 1 keloid. Fractures: 0 Complications: 0	No difference between treatment groups (P=0.11)
Pentimalli *et al.* 1987[31]	III	Retrospective comparative	Mean: 9.1 Range: 4-15	Mean: 7 Range: (3 to 20)	3 grade scale: healing not defined further 1) Good: cyst had completely disappeared, the thickness of cortical bone was normal, and no irregularity was present in the medullary canal; 2) Fair: cyst had disappeared, but the cortical bone was thinner than normal and some irregularities were evident inside the medullary canal; 3) Poor: cyst was still present, although reduced in volume, and/or there was shortening of the affected bone by more than 2 cm, with the bone slightly deformed at the site of the cyst.	Steroid injection [n=20] Curettage + bone grafting [n=20]	Fractures: none reported Complications: none reported Fractures: none reported Complications: none reported	No difference between treatment groups (P=0.29)

Continued next page

Table 1. Continued from previous page.

Author Year	Level of evidence	Study design	Age of population years	Follow-Up years	Definition of healed	Intervention	Complications	Outcome
Campanacci *et al.* 1986[32]	III	Retrospective comparative	The majority of these cases were under the age of 15 years.	C + BG Mean: not provided Range: 1-35 SI Mean: Not provided Range: 1-8	Modified Neer classification 4 grade scale, healing not defined further: 1) Complete healing – the space occupied by cyst was completely filled by new bone formation; 2) Incomplete healing – new bone formation did fill the area previously occupied by the cyst; small sites of osteolysis were seen within the boundaries of the cyst; 3) Recurrence – initially the cyst was consolidated with new bone, and areas of osteolysis with definite cortical thinning appeared; 4) No response – no clinical or radiographic evidence of amelioration was noted.	Steroid injection [n=141] Curettage + bone grafting [n=178]	Fractures: 13 Complications: 28 limb length discrepancies, 1 avascular necrosis Fractures: none reported Complications: 25 limb length discrepancies	Steroid injection superior to curettage and bone grafting (P=<0.001)
Oppenheim *et al.* 1984[33]	III	Retrospective comparative	Mean: 74% of cases presenting between the ages of 5 and 15 years. Range: 1.5 to 26	Mean: 3.8 Range: 0.5 to 12	4 grade scale, healed defined as 1 or 2: 1) Healed: complete obliteration of the cyst, or at most a 1 cm non progressive radiolucent area and a serial increase in cortical bone thickness; 2) Improved: Non progressive, radiolucent areas 1-3 cm in diameter and enough cortical thickness to prevent fractures.	Steroid injection [n=20] Curettage or excision + grafting [n=37]	Fractures: none reported Complications: 1 mild steroid flush, 1 shortening of humerus Fractures: none reported Complications: 6, including coxa vara, wound infection, physeal arrest and extremity shortening	No difference between treatment groups (P=0.22)
Neer *et al.* 1946	III	Retrospective comparative	Mean: 12.02 Range: 1.5 to 54	Mean: not provided Range: non- operative 1 to 10	3 grade scale 1) excellent: complete obliteration of the cyst during the period of observation; 2) Residual defect: one or more static, cyst-like residua with good bone strength by the appearance of roentgenogram; 3) Re-operation: subsequent operation required by recurrence.	Curettage + bone grafting [n=125] Non-operative immobilization after fracture [n=45]	Fractures: 3 femoral Complications: 1 wound infection, 4 premature epiphyseal closures Fractures: 32 humeral, 4 femoral Complications: 4 growth disturbance/ deformity	Curettage + bone grafting superior to non operative immobilization (P<0.001)

including children and adults were included as long as the mean age of patients ranged between 0 and 18 years.

The following information was collected from each of the studies: year of publication, study design, age of patients, duration of follow-up, definition/grading system for cyst healing, treatment(s), sample size, and outcome. The studies were classified according to levels of evidence as described in the Journal of Bone and Joint Surgery, where therapeutic studies are classified into five levels based on study design.[34] This review includes levels I-III only.[35] Level I evidence consists of high quality randomized controlled trials and systematic reviews of level I studies with consistent results. Level II evidence includes lesser quality randomized controlled trials, prospective comparative studies, and systematic reviews of level II studies or level I studies with inconsistent results. Level III evidence consists of case-control studies, retrospective comparative studies, and systematic review of level III studies.[34]

P values were obtained in two ways. First, if statistical analysis was performed in the original study then the associated P value was used. Second, if a P value was not provided but statistical data (absolute or relative) on cyst healing was available, then a χ^2 *test* was used to calculate a P value. Cyst "healing" was defined as "complete healing or partial healing (with small residual cyst)" when a cyst graded scale was specified. When cyst healing index was not specified, the author's description of "healed" was used.

Results

The literature search yielded 263 articles (Figure 1). Of these, 247 were excluded for the following reasons: 99 were levels IV or V (case series, editorial, or review article); 53 were focused on non-long bones (calcaneal, mandible, pelvis); 36 were not therapeutic (diagnostic or prognostic); 28 were differential diagnosis (benign lesions or malignant tumors); 18 focused on treatment of complications (pathological fractures, growth arrest, limb length discrepancy); and 13 had an English abstract but the paper was written in another language. This review included the results of 16 identified studies as listed in Table 1. Years of publication span 1966 to 2009 and include a total number of 1,340 patients and 13 different types of treatment. Table 2 provides ranges of treatment success. There is one level I study, one level II study and the remaining 14 studies are level III. Studies are presented chronologically by level, starting with the most current publications.

Level I studies

In the one level I study, Wright *et al.*[7] reported a randomized clinical trial comparing intralesional bone marrow [n=39] and methylprednisolone [n=38] injections. This trial involved 24 centers and 47 surgeons across North America and India with follow-up of 2.2 years. Results of the trial indicated that steroid injection (42% healed) was significantly better than bone marrow (23% healed) for healing

bone cysts (P=0.01). The authors also found that both subsequent fracture (P=0.04) and increased cyst area (P=0.03) were significantly associated with non-healing of the cyst. Complications included 9 subsequent fractures and 2infections in the bone marrow injection group, and 11 fractures and no infections in the steroid group (P=0.12).

Level II studies

In the one level II study, Brecelj *et al.*[19] compared steroid injection (n=33), curettage and bone grafting (n=8), and a specially designed cannulated screw (n=28) in a prospective comparative study with a follow-up of 5.8 years. All three groups required multiple courses of treatment. The cannulated screw group, after two attempts, demonstrated the highest rate of healing (P=0.001) at 65% compared to 50% and 19% for open curettage and methylprednisolone injections, respectively. Complications included three screws that broke during removal and were left in place. None of the following factors were related to treatment success: sex, cyst size ratio, cyst activity, age at first treatment, pathological fractures or number of humeral cysts (with exception of second steroid injection, there were a higher number of humeral cysts in the failed treatment group [P=0.017]).

Level III studies

The remaining 14 studies were level III. A retrospective study by Sung *et al.*[21] compared steroid (n=94), curettage and bone grafting (n=39), and a combination injection (SDB) of steroid, demineralized bone matrix, and bone marrow aspirate. Results indicate that both curettage and bone grafting and the combination injection (SBD) were superior to steroid, P=0.01 and P<0.001 respectively. However, there was no difference between curettage and bone grafting and the combination injection (SBD) (P=0.23). Subsequent pathological fractures were reported in 18% (17/94) of patients treated with steroid injection, 2.6% (1/39) of patients treated with curettage, and 12% (4/34) of patients treated with the combination injection SDB. Other complications, such as deformity or growth disturbance, were reported in 5.3% (5/94) of patients treated with steroid injection, 7.7% (3/39) of patients treated with curettage and 2.9% (1/34) of patients treated with SDB.

A retrospective study by Cho *et al.*[22] compared bone marrow (n=28) and steroid (n=30) injections with a follow-up of 4.7 years. The overall success rates were 86.7% after 2.5 injections in the steroid group and 92.0% after 1.8 injections in the bone marrow group (P>0.05). Despite this lack of difference between treatment groups in the final outcome, they found that the steroid group had a higher recurrence rate after one injection (P<0.05) and needed more injections to complete healing (P<0.05). Cho *et al.* indicated there was no association between healing after the initial procedure and age, gender, location of the cyst, cyst activity or previous pathological fracture in either the bone marrow or steroid group (P>0.05). Complications included three fractures after bone marrow injections in patients who did not follow postoperative immobilization instructions.

A retrospective study by Chuo *et al.*[23] compared cannulated screws (n=7), curettage and bone grafting with ORIF (n=4), and observation (n=6) with a follow-up of 5.7 years. Although the authors concluded cannulated screws were preferred, the difference in rates of healing between treatment groups (P=0.42) was not statistically different. There was one complication of a malunion in the observation group.

A retrospective study by Chang *et al.*[24] compared steroid (n=65) and bone marrow injections (n=14) with a follow-up of 3.7 years. Although there was no statistical difference between treatment groups (P>0.05), the rate of healing after 2 injections in the bone marrow group and 1.5 injections in the steroid group was 37% and 56%, respectively. No complications were reported in either group. Cysts that healed after one injection (of either bone marrow or steroid) compared with those that didn't heal, had a significant difference in the

Table 2. Rates of success by treatment.

Treatment: N=1340 [n]	Range of success (%)
Steroid injection [563]	15-100[7,19,21,22,24,26-33]
Bone marrow injection [81]	23-92[22,24]
Curettage and bone grafting [447]	36-85 [2,7, 19,21,28,29,31-33]
Cannulated screw [35]	46-100[19,23]
Steroid injection + DBM + bone marrow aspirate[34]	29-5[021]
Curettage + bone grafting + ORIF [4]	75[23]
Curettage + multiple drilling + titanium cannulated screw [15]	80[25]
Curettage + multiple drilling + hydroxyapatite pin [11]	100[25]
Resection + myoplasty [50]	72[26]
Curettage + bone grafting + osteosynthesis [10]	100[27]
Cyst rupture + osteosynthesis [5]	60[27]
Orthopedic treatment [70]	4-100[2,27,30]
Mixed surgical treatment [15]	87[30]

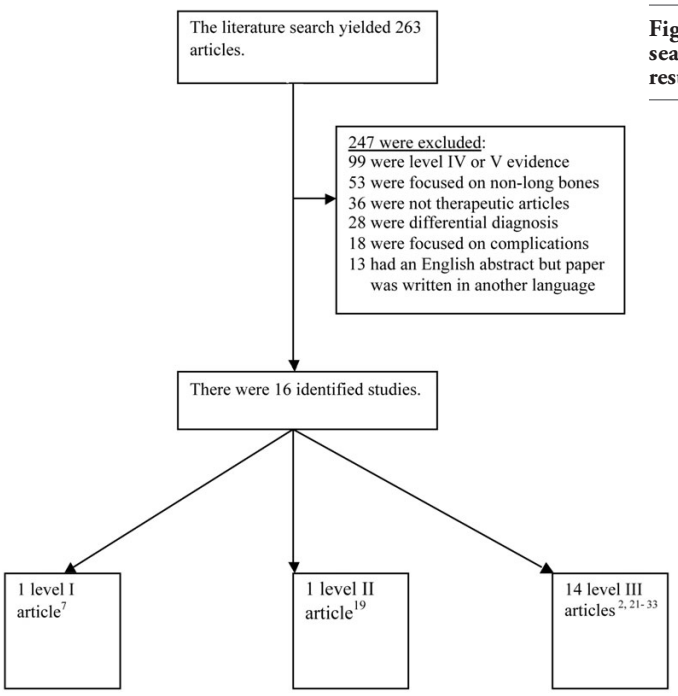

Figure 1. Literature search and review results.

size of the cyst (P<0.01). Sex, cyst activity, previous pathological fracture, and site of the cyst had no affect on healing.

In 2002, Tsuchiya *et al.*[25] retrospectively compared curettage, multiple drilling and titanium cannulated screws (n=15) and curettage, multiple drilling and cannulated hydroxyapatite pins (n=11) with a follow-up of 6.8 years. The authors recommended the hydroxyapatite pins because the pins didn't require removal. Although all patients receiving cannulated titanium screws healed, there was no difference in healing between treatment groups (P=0.12). There were two complications in the cannulated screw group (one fracture and one fissure fracture) and no complications in the hydroxyapatite pin group.

Bensahel *et al.*[26] retrospectively compared resection and myoplasty using a local muscle flap (n=50) and steroid injections (n=55) with a follow-up of nine years. Resection and myoplasty compared with steroids had a higher rate of healing of 71% and 50%, respectively (P=0.02). There were no complications reported in either group.

Gennari *et al.*[27] retrospectively compared steroid injection (n=3), curettage and bone grafting and osteosynthesis (n=10), rupture of cyst without osteosynthesis (n=5), and observation (or "orthopedic treatment") (n=2) in cysts in the upper third of the femur with a follow-up of six years. There was no difference in rates of healing between treatment groups (P=0.08). There were two limb shortenings (<2 cm) in the curettage group, three shortenings (≥2 cm) in the cyst rupture group, and one lengthening (>2 cm) in the observation group.

Mylle *et al.*[28] retrospectively compared steroid injection (n=20), curettage and bone grafting (n=21), curettage and steroid injection (n=6), and no treatment (n=12) with a follow-up of 8.5 years. Steroid injection was found to be superior to curettage and bone grafting (P=0.03) with 90% and 43% healing, respectively. Complications included one superficial infection in the steroid group, three in the curettage and bone grafting group, and one in the curettage and steroid injection group. There were ten subsequent fractures and one growth disturbance in the 'no treatment' group.

Farber *et al.*[29] retrospectively compared steroid injections (n=17) and curettage and bone grafting (n=19) with a follow-up of 6.7 years. Although methylprednisolone has higher rates of healing of 70% compared with 53% in the curettage group, the difference was not statistically different (P=0.27). No complications were reported.

Bovill *et al.*[30] retrospectively compared steroid injections (n=12), multiple surgical techniques (n=15), and observation (n=5) with a follow-up of 5.6 years. No difference was found between rates of healing in the treatment groups (P=0.11). There were eight complications in the surgical group: three leg length deformities, one infection, one transient median nerve palsy, one subsequent fracture, and one keloid. There were three subsequent fractures in the steroid group.

Pentimalli *et al.*[31] retrospectively compared steroid injections (n=20) and curettage and bone grafting (n=20) with a follow-up of seven years. Although the authors recommend steroid injections because the radiographic results were better with a lower recurrence rate, the rates of healing for steroid injections (95%) and curettage and bone grafting (85%) were not statistically different (P=0.29). No complications were reported.

Campanacci *et al.*[32] retrospectively compared steroid injections (n=141) and curettage and bone grafting (n=178) with a follow-up of one to 35 years (mean not provided). Although the authors indicated the end results were comparable in both groups, the steroid group had higher rates of healing than curettage on bone grafting (P<0.0001), 91% and 68%, respectively. The steroid group had 28 limb length discrepancies, 13 subsequent fractures, and one avascular necrosis. The curettage and bone grafting group had 25 limb length discrepancies.

Oppenheim *et al.*[33] retrospectively compared steroid injections (n=20) and curettage or excision with or without grafting (n=37) with a follow-up of 3.8 years. There was no difference in rates of healing between steroid injection (40%) and the curettage group (57%) (P=0.22), although the authors recommended the steroid injection due to its simplicity and reduced morbidity. Complications included one mild steroid flush (2.4 g dose of Depo Medrol was inadvertently given) and one shortening of the humerus in the steroid group. There were 6 complications in the curettage group which included coxa vara, wound infection, physeal arrest, and extremity shortening.

Neer *et al.*[2] retrospectively compared curettage and bone grafting (n=125) with immobilization after fracture (n=45) with a minimum 2-year follow-up. Curettage and bone grafting had higher rates of healing than the non-operative treatment (P<0.001), 77% and 4%, respectively. Complications for the non-operative group included subsequent fractures in 36 patients and 4 growth disturbances and deformity. Complications for the curettage group were 3 subsequent fractures, one wound infection, and 4 premature epiphyseal closures which led to shortening of 1-3 cms.

Discussion

Seven of the sixteen studies had statistically different results: three studies indicated that steroid injection was superior to bone marrow injection or curettage and bone grafting;[7,28,32] one study indicated that cannulated screws were superior to steroid injections;[19] one study indicated resection and myoplasty was superior to steroid injection;[30] one study indicated a combination of steroid, demineralized bone matrix and bone marrow aspirate, and curettage and bone grafting were superior to steroid injection;[21] and one study indicated that curettage and bone grafting was superior to non-operative immobilization.[2] In interpreting the literature the different treatments have different pros and cons. The treatments range from simple injections to open treatments to internal fixation. The invasiveness must be contrasted with the need for repeat treatment such as steroids which may require multiple injections. These factors must all be balanced against risk of fracture and probability of success.

The literature has several shortcomings. First, the outcome for almost all studies (15/16) was based on radiographic healing rather than patient based outcomes such as fracture, pain or function. Second, there was variability in the type of radiographic healing scale or index used. Eight of the sixteer studies used a modification of the Neer criteria, four did not define the scale or index used, and four used their own original criteria. Third, there was a wide variation in treatment protocols. For example, although all steroid injection protocols used methylprednisolone acetate, the dosage ranged from 40 to 250 mg and number of injections ranged from one to 6. Bone marrow injection protocols also varied including amount withdrawn from each harvest site (2-8 mL), amount injected into cyst (9-50 ml), and number of injections (1-4). Fourth, there was different duration of follow-up with the mean ranging from 2.2 to 9.0 years and overall range from one to 35 years. Finally, the studies had a variety of sample sizes, ranging from very small (n=2) to 178.

As unicameral bone cysts and corresponding pathological fractures present in different locations, variations in treatment may result. Pathological fractures in the lower extremities, particularly in the proximal femur, have greater potential for complications. Fracture(s) in this area may result in physeal damage, coxa vara, extremity shortening or avascular necrosis.[27,36] As cysts rarely heal following fracture,[36,37] risk of refracture leads to restriction of physical activities. As failure to achieve radiographic healing within the first year following presentation increases the risk of refracture,[38] the goal of treatment is to stabilize the fracture and treat the cyst simultaneously. Flexible intramedullary nails have been promoted as they stabilize the fracture (or pending pathological fracture) and provide

treatment of the cyst through continuous decompression.[39-45] Advantages of this treatment include stability to the bone and early mobilization of the patient. Complications include nail revisions due to bone growth and difficulty of anchoring nails due to lack of bone in the femoral neck.[41]

There are few reports in the literature on prophylactic internal fixation of bone cysts at risk for pathological fracture in the proximal femur.[39,41,44,45] These reports are case series with the majority of patients presenting with pathological fractures. The authors acknowledge the numbers for cysts treated prophylactically with internal fixation are small but indicate they see no difference in rates of cyst healing when compared to cysts treated with concurrent pathological fracture.

Treatment for unicameral bone cysts has evolved over the years. Curettage and bone grafting was used for many years.[5] Unfortunately, this aggressive approach had high recurrence rates of 40-50% with the associated scar and morbidity of surgery.[32] A less intrusive technique, intralesional steroid injections,[13] became a common treatment modality for many years with rates of healing ranging from 41-90%.[8,13,27,32,33,46] In 1996, Lokiec *et al.*[14] published a preliminary study on bone marrow injections reporting that all ten cysts demonstrated radiographic healing. Subsequent reported rates of healing using bone marrow injections ranged from 42-100%.[14,22,24,47-49] Based on early promising results, many surgeons shifted from steroid injection to bone marrow. Based on the levels of evidence analysis, this may have been a premature shift in clinical practice.

In conclusion, based on one level I study, including a limited number of individuals, steroid injection seems to be superior to bone marrow injection. As steroid injections have already demonstrated superiority over bone marrow injections in a randomized clinical trial, the next step would be a prospective trial comparing steroid injections to other treatments.

References

1. Beaty JH, Kasser JR. Rockwood & Wilkins' Fractures in Children, 6th Edition; Chapter 6: Pathologic fractures associated with tumors and unique conditions of the musculoskeletal system by John P. Dormans and John M. Flynn. Lippincott, Williams & Wilkins 2001.
2. Neer CS, Francis KC, Marcove RC, et al. Treatment of unicameral bone cyst. J Bone Joint Surg Am 1966;48:731-45.
3. Stantor RP, Abdel-Mota'al MM. Growth arrest resulting from unicameral bone cyst. J Pediatr Orthop 1998;18:198-201.
4. Cohen J. Unicameral bone cysts. A current synthesis of reported cases. Orthop Clin North Am 1977;8:715-36.
5. Tachdjian MO. Pediatric Orthopaedics 1990,1271-1. Philadelphia, W.B. Saunders.
6. Haims AH, Desai P, Present D, Beltran J. Epiphyseal extension of a unicameral bone cyst. Skeletal Radiol 1997;26:51-4.
7. Wright JG, Yandow S, Donaldson S, Marley L. A randomized clinical trial comparing intralesional bone marrow and steroid injections for simple bone cysts. J Bone Joint Surg Am 2008;90:722-30.
8. Hashemi-Nejad A, Cole WG. Incomplete healing of simple bone cysts after steroid injections. J Bone Joint Surg Br 1997;79:727-30.
9. Jaffe H, Lichtenstein L. Solitary unicameral bone cyst, with emphasis on the roentgen picture, pathologic appearance and pathogenesis. Arch Surg 1942;44:1001-25.
10. Watanabe H, Arita S, Chigira M. A etiology of a simple bone cyst. Int Orthop 1994;18:16-9.
11. Chigira M, Maehara S. The Aetiology and treatment of simple bone cysts. J Bone Joint Surg 1986;42:609-15.
12. Komiya S, Minamitani K, Sasguri Y, et al. Simple bone cyst. Treatment by trepanation and studies on bone resorptive factors in cyst fluid with a theory of its pathogenesis. Clin Orthop Relat Res 1993;287:204-11.
13. Campanacci M, De Sessa L, Trentani C. Scaglietti's method for conservative treatment of simple bone cysts with local injections of methylprednisolone acetate. Ital J Orthop Traumatol 1977;3:27-36.
14. Lokiec F, Ezra E, Khermosh O, Weintroub S. Simple bone cyst treated by percutaneous autologous marrow grafting. J Bone Joint Surg 1996;78:934-7.
15. Rougraff BT, Kling TJ. Treatment of active unicameral bone cysts with percutaneous injection of demineralized bone matrix and autogenous bone marrow. J Bone Joint Surg Am 2002;84-A:921-9.
16. Dormans JP, Sankar WN, Moroz L, Erol B. Percutaneous intramedullary decompression, curettage, and grafting with medical-grade calcium sulfate pellets for unicameral bone cysts in children: a new minimally invasive technique. J Pediatr Orthop 2005;25:804-11.
17. Tang XY, Liu LJ, Peng MX, Xiang B. Simple bone cysts in children treated with intracystic fibrin sealant injection. Chin Med J (Engl) 2006;119:523-5.
18. Roposch A, Saraph V, Linhart WE. Flexible intramedullary nailing for the treatment of unicameral bone cysts in long bones. J Bone Joint Surg Am 2000;82-A:1447-53.
19. Brecelj J, Suhodolcan L. Continuous decompression of unicameral bone cyst with cannulated screws: a comparative study. J Pediatr Orthop B 2007;16:367-72.
20. Bumci I, Vlahovic T. Significance of opening the medullar canal in surgical treatment of simple bone cyst. J Pediatr Orthop 2002,22:125-9.
21. Sung AD, Anderson ME, Zurakowski D, et al. Unicameral bone cyst: a retrospective study of three surgical treatments. Clin Orthop Relat Res 2008;466:2519-26.
22. Cho HS, Oh JH, Kim H-S, et al. Unicameral bone cysts: a comparison of injection of steroid and grafting with autologous bone marrow. J Bone Joint Surg Br 2007;89:222-6
23. Chuo CY, Fu YC, Chien SH, et al. Management strategy for unicameral bone cyst. Kaohsiung J Med Sci 2003;19:289-95.
24. Chang CH, Stanton RP, Glutting J. Unicameral bone cysts treated by injection of bone marrow or methylprednisolone. J Bone Joint Surg 2002;84-B;3:407-12.
25. Tsuchiya H, Abdel-Wanis ME, Uehara K, et al. Cannulation of simple bone cysts. J Bone Joint Surg Br 2002;84:245-8.
26. Bensahel H, Jehanno P, Descrippes Y, Pennecot GF. Solitary bone cyst: controversies and treatment. J Pediatr Orthop B 1998;7:257-61.
27. Gennari JM, Merrot Th, Piclet-Legre B, Bergoin M. The choice of treatment for simple bone cysts of the upper third of the femur in children. Eur J Pediatr Surg 1996;6:95-9.
28. Mylle J, Burssens A, Fabry G. Simple bone cysts: a review of 59 cases with special reference to their treatment. Arch Orthop Trauma Surg 1992;111:297-300.
29. Farber JM, Stanton RP. Treatment options in unicameral bone cysts. Orthopedics 1990;13:25-32.
30. Bovill DF, Skinner HB. Unicameral bone cysts: a comparison of treatment options. Orthop Rev 1989;18:420-7.
31. Pentimalli G, Tudisco C, Scola E, et al. Unicameral bone cyst: comparison between surgical and steroid injection treatment. Arch Orthop Trauma Surg 1987;106:251-6.
32. Campanacci M, Capanna R, Picci P. Unicameral and aneurysmal bone cysts. Clin Orthop Relat Res 1986;204:25-36.
33. Oppenheim WL, Galleno H. Operative treatment versus steroid injection in the management of unicameral bone cysts. J Prosth Orthotics 1984;4:1-7.
34. Wright JG, Swiontkowski MF, Heckman JD. Introducing levels of evidence to the journal. J Bone Joint Surg Am 2003;85-A:1-3.
35. Chundamala J, Wright JG. The efficacy and risks of utilizing povidone-iodine irrigation to prevent surgical site infection: an evidence-based review. Can J Surg

2007;50;6:473-81.
36. Ahn JI, Park JS. Pathological fractures secondary to unicameral bone cysts. Int Orthop 1994;18:20-2.
37. Garceau GJ, Gregory CF. Solitary unicameral bone cyst. J Bone Joint Surg Am 1954;36:267-80.
38. Norman-Taylor FH, Hashemi-Nejad A, Gillingham BL, et al. Risk of refracture through unicameral bone cysts of the proximal femur. J Pediatr Orthop 2002;22:249-54.
39. Roposch A, Saraph V, Linhart WE. Flexible intramedullary nailing for the treatment of unicameral bone cysts in long bones. J Bone Joint Surg Am 2000;82-A:1447-53.
40. Knorr P, Schmittenbecher PP, Dietz HG. Elastic stable intramedullary nailing for the treatment of complicated juvenile bone cysts of the humerus. Eur J Pediatr Surg 2003;13:44-9.
41. Roposch A, Saraph V, Linhart WE. Treatment of femoral neck and trochanteric simple bone cysts. Arch Orthop Trauma Surg 2004;124:437-42.
42. Givon U, Sher-Lurie N, Schindler A, Ganel A. Titanium elastic nail – a useful instrument for the treatment of simple bone cyst. J Pediatr Orthop 2004;24:317-8.
43. Vigler M, Weigl D, Schwarz M, et al. Subtrochanteric femoral fractures due to simple bone cysts in children. J Pediatr Orthop B 2006;15:439-42.
44. de Sanctis N, Andreacchio A. Elastic stable intramedullary nailing is the best treatment of unicameral bone cysts of the long bones in children? J Pediatr Orthop 2006;26:520-5.
45. Kanellopoulos AD, Mavrogenis AF, Papagelopoulos PJ, Soucacos PN. Elastic intramedullary nailing and DBM-bone marrow injection for the treatment of simple bone cysts. World J Sug Oncol 2007;5:111.
46. Capanna R, Dal Monte A, Gitelis S, Campanacci M. The natural history of unicameral bone cyst after steroid injection. Clin Orthop Relat Res 1982;166:204-11.
47. Docquier PL. Delloye C. Autologous bone marrow injection in the management of simple bone cysts in children. Acta Orthop Belg 2004;70:204-13.
48. Yandow SM, Lundeen G, Scott SM, Coffin C. Autogenous bone marrow injection as a treatment for simple bone cyst. J Pediatr Orthop 1998;18:161-620.
49. Köse N, Göktürk E, Turgut A, et al. Percutaneous autologous bone marrow grafting for simple bone cyst. Bull Hosp Jt Dis 1999;58:105-10.