Management of Osteonecrosis of the Humeral Head in the Pediatric Population: A Systematic Review

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Introduction

Osteonecrosis can present in the context of a variety of medical and iatrogenic abnormalities: trauma, hemoglobinopathies, and long term corticosteroid usage.[1-3] Although osteonecrosis of the proximal humerus is the second most common site after the femoral head, it is poorly understood and difficult to diagnose.[4, 5] Franceschi et al. (2017) conducted a systematic review of surgical management of osteonecrosis of the humeral head in the adult population, and found that whereas CD is effective for low-grade osteonecrosis, arthroplasty should be considered for high-grade osteonecrosis.[4] However, literature remains limited regarding the characteristics and management of humeral head AVN in younger populations.[4] The purpose of this study was to perform a systematic review to improve our understanding of the existing evidence regarding the prevalence and characteristics of proximal humeral AVN in young patients, the treatment modalities utilized, and the outcomes of these treatments in this population.

Methods

We searched PubMed, OVID Embase, and Scopus databases with terms "osteonecrosis", "pediatric", and "proximal humerus" on January 10, 2024. Two hundred and eighteen studies were screened, and 74 studies were evaluated for eligibility (Figure 1).

Studies that reported on the prevalence and/or management of pediatric humeral head osteonecrosis were included. The systematic review was conducted according to the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) guidelines. Clinical characteristics (etiology of osteonecrosis, imaging, grade of osteonecrosis, symptoms) and management characteristics (conservative vs. operative management, reported interventions, outcome of intervention) were collected as well. Prevalence was calculated as the total number of patients/shoulders with osteonecrosis of the humeral head divided by the total number of patients/shoulders at risk. Two independent reviewers assessed the risk of bias within each study using the Cochrane Risk of Bias Assessment Tool: for Non-Randomized Studies of Interventions for cohort and case control studies as well as the Joanna Briggs Institute (JBI) critical appraisal tool for case series.[6, 7]

Results

After initial screening and eligibility review, 12 studies remained eligible for inclusion in this systematic review. These studies included three prospective case series,[8-10] four retrospective case series,[11-14] one retrospective case-control study,[15] one retrospective cohort study,[16] and three case reports[17-19] (Table 1).

Prevalence and Clinical Characteristics

Across eight studies that presented data for the number of patients with humeral head osteonecrosis within a greater at-risk population, there were 106 shoulders (77 patients) that developed osteonecrosis of the humeral head, and an overall at-risk population of 5,226 shoulders (3,608 patients). Thus, we calculated the overall prevalence of osteonecrosis of the humeral head within an at-risk pediatric population to be 2.0%.

Conservative Management

Six studies reported on conservative management. For example, Kaste et al. used the National Cancer Institute's Common Terminology Criteria for Adverse Events (CTCAE) scoring system to show an improvement in the impact of osteonecrosis on activities of daily living (ADL) (2.61 to 1.76), pain (2.69 to 1.23), and ROM (2.15 to 1.69) after intra-articular steroid injection11 (Table 2a).

Surgical Management

Three studies reported on surgical management. For example, Kaste et al. found that among 12 shoulders with osteonecrosis, nine experienced resolution after core decompression11. Additionally, the mean CTCAE scores improved for pain and impact on ADL (2.91 to 1.66), and slightly

worsened for ROM (2.00 to 2.08) after undergoing core decompression11. Mean CTCAE scores improved for impact on ADL (2.75 to 1.75), pain (2.87 to 0.85), and ROM (2.37 to 1.87) after undergoing resurfacing hemiarthroplasty[11] (Table 2b).

Risk of Bias

Overall, the one retrospective cohort study and one retrospective case-control study had a low risk of bias. The four retrospective and three prospective case series had good methodological quality.

Discussion

Literature regarding the most effective management strategies for osteonecrosis of the humeral head in the pediatric population is limited.[4] The goal of this systematic review was to summarize published studies and current evidence on the prevalence and clinical characteristics, conservative management, and surgical management of osteonecrosis of the humeral head within the pediatric population. The overall prevalence of osteonecrosis of the humeral head across eight studies was about 2%. Intra-articular steroid injections, physical therapy, and activity modification are effective conservative management strategies. Additionally, core decompression and hemiarthroplasty are surgical treatment options.

Few studies have published on the prevalence of humeral head osteonecrosis, likely due to both the rare nature of the condition and its often-asymptomatic presentation in comparison to osteonecrosis in greater weight-bearing joints like the hip. Chung et al. found in a population of forty sickle cell patients that the prevalence of humeral head osteonecrosis was 3.8%, which was slightly higher than the current study's prevalence of 2.0% across both chemotherapy and sickle cell etiologies20. Regarding management of humeral head osteonecrosis, Franceschi et al. conducted a systematic review comparing core decompression, hemiarthroplasty, and TSA in adults with humeral head osteonecrosis, and found that while core decompression is effective for low grade osteonecrosis, arthroplasty should be utilized for high grade osteonecrosis.[4] However, comparing the efficacy of both conservative and surgical interventions for pediatric humeral head osteonecrosis is challenging given the limited existing prospective or comparative studies.

There are several limitations to this study. First, we were restricted by the available evidence on this topic. Given the rarity of humeral head osteonecrosis, especially in the pediatric population, many of the included studies were limited in sample size and did not include rigorous and robust analyses for the included interventions. Second, it is important to note that when comparing the results of the included studies, the patients were not standardized in demographic characteristics, osteonecrosis grade, and treatment protocols. Thus, the data provided is susceptible to selection, indication, and surveillance bias. Third, some of the studies included were case reports or published before the year 2000. While this may limit their quality or relevance, given the rareness of this condition, they were included in the screening process.

Conclusions

The prevalence of osteonecrosis of the humeral head is low even among at-risk populations with associated medical conditions. A variety of conservative and surgical treatment options have been described but no comparative evaluations of these modalities has been conducted.

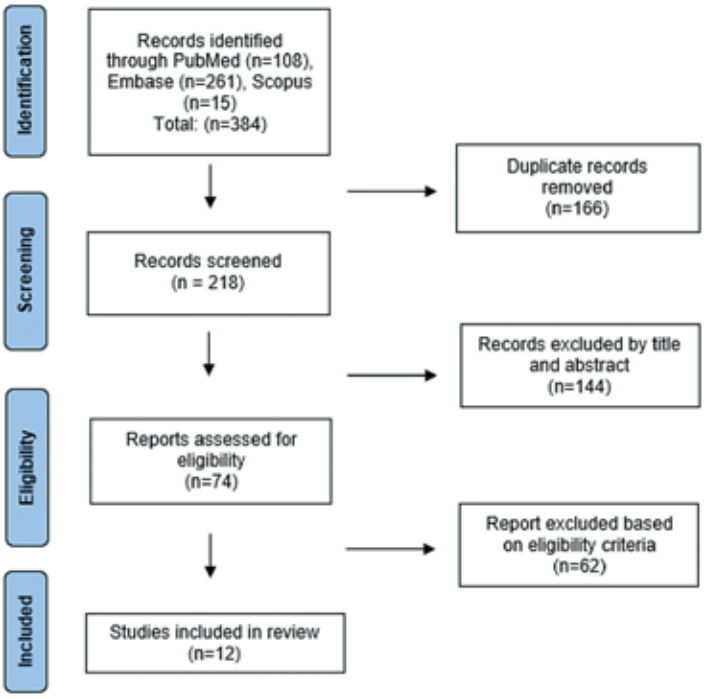

Figure 1. Study selection flowchart using PRISMA guidelines.

Table 1: Characteristics of Evaluated Studies included in Systematic Review (12)

Study	Level of Evidence and Study Type		Year	Study Period	Study Population	No. of patients		Median Age in years	Mean Length of Follow-Up in years
					Total (No. of shoulders)	Humeral Head Osteonecrosis (No. of shoulders)		(Range)	(Range)
Milner et al.*	IV	Prospective Case Series	1993	1979-1981	SCD	1,019 (2,038)	19 (NR)	NR (5-14)	5.6 (NR)
Inaba et al.	IV	Prospective Case Series	2020	2012-2017	ALL/L	15 (30)	8 (15)	14 (9-17)	NR
Kaste et al.	IV	Retrospective Case Series	2019	1996-2014	ALL/NHL	1,478 (2,956)	33 (62)	14.2 (4.3-19)	6.4 (0-12.7)
Mesleh Shayeb et al.	III	Retrospective Case-Control	2018	1998-2014	SCD	612 (1,224)	6 (8)	NR (6-18)	NR
Littooij, et al.	IV	Prospective Case Series	2017	2012-2015	HL	24 (48)	NR (2)	15.1 (10.1-17.9)	1.0 (0.48–3.6)
Heneghan et al.	III	Retrospective Cohort	2016	2004-2012	ALL	10,729 (21,458)	NR	7.04 (2.02 – 21.2)	NR
Kuhlen et al.	IV	Retrospective Case Series	2014	2003-2009	ALL	124 (248)	5 (8)	12.6 (2.4-19.9)	2.3 (0.1-6.2)
Miettunen et al.	IV	Retrospective Case Series	2012	2006-2008	ALL	32 (64)	5 (9)	5.4 (4.8–11.9)	NR
Riccio et al.	IV	Retrospective Case Series	2016	1982-2003	ALL	328 (656)	1 (2)	Mean: 7.2 SD: 0.1-14.3	NR
Wong et al.	IV	Case report	2022	-	SCD	1 (2)	1 (1)	12	0.2
Solarino et al.	IV	Case report	2008	-	ALL	1 (2)	1 (2)	12	5.3
Martin et al.	IV	Case report	1997	-	Salter-Harris II fracture	1 (2)	1 (1)	14	1
Total (of reported)**						3,608 (5,226)	77 (106)		

*Only information regarding patient group 5-14y included. **NR:** Not reported; **SCD:** Sickle Cell Disease; **ALL:** Acute Lymphoblastic Leukemia; **ALL/L:** Acute Lymphoblastic Leukemia/Lymphoma; **NHL:** Non-Hodgkin's Lymphoma; **HL:** Hodgkin's Lymphoma

**Does not include data from case reports or Heneghan et al.

Table 2: (A) Conservative Management of humeral head osteonecrosis in evaluated studies

Study	Shoulders	Reported Interventions	Outcome
Inaba et al.	NR	Reduction or cessation of chemotherapy	>30% epiphyseal involvement: 3/9 shoulder regressed <30% epiphyseal involvement: 1 shoulder resolved
Kaste et al.	13	Intra-articular steroid injections	7/13 shoulders resolved; Mean CTCAE score for ROM improved from 2.15 to 1.69; Mean CTCA score for pain improved from 2.69 to 1.23
	NR	Physical therapy; Anti-inflammatory agents	NR
Kuhlen et al.	8	Physiotherapy; Activity modification; Anti-inflammatory agents; bisphosphonates; Iloprost	NR
Riccio et al.	2	Activity modification; Physical therapy	Good ROM; residual humeral head deformity
Wong et al.	1	Physical therapy; Psychotherapy; Acupuncture; Intraarticular steroid injections; pain medication (pregabalin, meloxicam, methadone; hydrocodone as needed)	No improvement in pain
		Intra-articular Hyaluronic Acid injections	50% reduction in pain (6/10 to 0/10 at rest, 10/10 to 5/10 with activity); improvement in function
Martin et al.	1	Activity Modification	Asymptomatic

NR: Not reported; CTCAE: National Cancer Institute's Common Terminology Criteria for Adverse Events; ROM: range of motion

Table 2: (B) Surgical Management of humeral head osteonecrosis in evaluated studies

Study	Shoulders	Procedure	Outcome
Inaba et al.	3	Core Decompression: 2	No shoulders resolved
		Bone Resurfacing: 1	NR
Kaste et al.	20	Core Decompression: 12	9/12 shoulders resolved; Mean CTCAE score for ROM worsened from 2.00 to 2.08; Mean CTCAE score for pain improved from 2.75 to 1.00
		Hemiarthroplasty (Resurfacing): 8	Mean CTCAE score for ROM improved from 2.37 to 1.87; Mean CTCAE score for pain improved from 2.87 to 0.75
Heneghan et al.	8	NR	NR
		Total Shoulder Arthroplasty: 1	NR

NR: Not reported; CTCAE: National Cancer Institute's Common Terminology Criteria for Adverse Events; ROM: range of motion

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