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Diagnosis and Treatment of Avascular Necrosis of the Humeral Head: Current Concepts

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Pathogenesis and Treatment of Avascular Necrosis of the Humeral Head: Current Concepts
Abstract

Avascular necrosis (AVN) of the humeral head is an uncommon clinical entity which can result in significant morbidity for patients. Compared to femoral head AVN, the volume of literature concerning humeral head AVN is a distant second. This could be due to the relatively rarity of the condition and poorly understood nature. Despite being first described decades ago, the underlying pathophysiology leading to humeral head AVN is still poorly defined. Numerous causes have been identified, which only adds to the complexity of the condition. While the staging of humeral head AVN is well described, not much is known about prognosticating factors to predict the eventual course of the disease. Most of the management options so far are based on that of femoral head AVN, and even so, there is a paucity of good quality clinical trials in the literature. This current concept paper describes what is known about humeral head AVN from the literature thus far, and attempts to propose a possible management algorithm to guide clinicians.
Pathogenesis and Treatment of Avascular Necrosis of the Humeral Head: Current Concepts

- There are numerous causes of humeral head avascular necrosis (AVN), most commonly involving corticosteroids and hemoglobinopathies like sickle cell disease
- Humeral head AVN is usually insidious in onset, and often presents in the later stages
- Diagnosis and classification of humeral head AVN relies on plain radiographs and magnetic resonance imaging
- Management of humeral head AVN depends on the symptoms and stage of disease

Pathogenesis and Treatment of Avascular Necrosis of the Humeral Head: Future Perspectives

- While the classification of humeral head avascular necrosis (AVN) is relatively well described, there should be more focus on elucidating prognosticating factors for future progression to humeral head collapse
- Good quality randomised controlled trials comparing the efficacy of the various treatment methods, especially for early stage AVN, is needed
Introduction

Background

Osteonecrosis is the in-situ bone cell death following disruption to the blood supply [1]. Juxta-articular osteonecrosis can cause arthritis, resulting in significant morbidity for patients [1,2]. The humeral head is the second most common site of atraumatic avascular necrosis (AVN) after the femoral head [1]. To date, there is no clear guideline on the management of the condition. This paper aims to summarize some of the current concepts in the literature and suggest a possible management algorithm for humeral head AVN, with a focus on non-traumatic AVN.

Blood supply to the humeral head

The blood supply to the humeral head is by the anterior circumflex humeral artery (ACHA) and the posterior circumflex humeral artery [3] (PCHA). These two arteries have shown numerous variations in terms of their extra-osseous course and branches [3].

The ACHA traverses anteriorly towards the bicipital groove before giving off an ascending anterolateral branch, which follows the bicipital groove and enters the medial wall of the greater tuberosity as the arcuate artery of Laing [3,4]. The arcuate artery traverses medially towards the subchondral region of the humeral head.

In recent years, the PCHA is recognized as a critical source of blood supply to the subchondral region of the proximal humerus, with some showing that blood supply to majority of the humeral head comes from the PCHA [4-6]. The PCHA runs posterior to the humeral head, giving off branches which enter at the bone-cartilage border and greater tuberosity [3].

The circumflex arteries do not have clear extraosseous anastomoses [3], but the consensus is these arteries form an intraosseous network within the humeral head [4]. Of note, the superior aspect of the humeral head has been found to have the poorest blood supply [3].
**Etiology**

Traumatic causes of AVN include fractures and dislocations of the proximal humerus [1], with a 10-33% risk of avascular necrosis after a fracture [3]. There are also case reports of AVN following rotator cuff repair [2].

The most common non-traumatic etiology of humeral head AVN described in literature would be steroid use (see Figure 1 and 2). While prolonged use of high dose corticosteroids has been correlated with risk of AVN [7], there have been reports of AVN with small doses, such as intra-articular injections [1]. In addition, the diagnosis of AVN post-steroid use is variable, ranging from 6-24 months [1,8]. Of note, patients taking steroids often have underlying conditions which predispose to humeral head AVN, such as connective tissue disorders [7,8]. Increasingly applicable would be the recent Severe Acute Respiratory Syndrome (SARS) and Coronavirus disease 2019 (COVID-19) pandemics. Patients treated with corticosteroids eventually developed AVN of various sites, including the humeral head [9-11]. The incidence of humeral head AVN ranged from 3.9-14.1%, with a possible dose and duration-response relationship.

Sickle cell disease is an autosomal recessive hemoglobinopathy due to a mutation in the B-globin gene where red blood cells deform under low oxygen states and lose their elasticity, potentially occluding capillaries. The reported incidence of AVN in sickle cell disease is 5.6% [12]. In contrast to corticosteroid use, spontaneous regression of humeral head AVN caused by sickle cell disease is reportedly not observed even in early stage [13], and in fact the area of AVN increases sometimes, leading to the postulation of repeated bone infarcts caused by sickle cell disease.

Table 1 provides a non-exhaustive list of possible etiologies. The common link is disruption to the humeral head blood supply, with a few key sites [14]: Extra-osseous vascular (trauma resulting in transection of blood supply), intra-osseous extra-vascular (hypertrophic adipocytes and/or bone edema increasing intra-osseous pressure and leading to venous stasis), intra-osseous intra-vascular (intra-capillary fat emboli, hemoglobinopathies or air embolism).
Presentation

Symptoms and signs

Patients with humeral head AVN have an indolent course, with majority already in the later stages at initial presentation. Unlike the hip, the shoulder joint is rarely weightbearing and the glenoid is less encompassing compared to the acetabulum. Furthermore, the scapulothoracic joint allows for compensatory movement. Nevertheless, symptomatic patients often have a painful click accompanying certain shoulder movements, resulting from joint incongruity or a cartilage flap [8]. This can progress to rest pain and reduced range of motion (ROM), resulting in limitation of daily activities.

Disease staging

The superomedial part of the humeral head is often described to be where AVN initially sets in. This region articulates with the glenoid when the arm is in 90 degrees of abduction, where the greatest amount of stress is exerted on the humeral head [8]. This correlates with the area of poorest blood supply.

Plain radiograph is effective in evaluating osseous pathology. However, it may miss the pre-radiographic stage of AVN. Magnetic resonance imaging (MRI) of the shoulder is useful in detecting early AVN and for staging. The most widely known staging system would be Cruess, comprising of five stages (Table 2).

While disease staging helps to guide management, perhaps greater importance should be placed in prognosticating the risk of humeral head collapse for those in earlier stages, so there can be timely and sufficient intervention to minimize progression to later stages. This is critical since patients with humeral head AVN are usually young and those with radiological progression tend to have poorer outcomes [15].

The degree of subchondral involvement on diagnosis may predict the likelihood of future progression to humeral head collapse. Sakai et al. [16] found that if the area of subchondral necrosis on MRI was greater than 90 degrees on diagnosis, the chance of future collapse was up to 92%, whereas those less than that were unlikely to progress. Similarly, lesions involving less than 15% of the humeral head were less likely to collapse compared to those who had moderate (15-30% of humeral head) or severe (more than 30% of humeral head) involvement initially [7,13].
Aside from the degree of humeral head involvement on diagnosis, the presence of shoulder pain is another possible indicator for humeral head collapse. Between 49-60% of asymptomatic patients progressed to humeral head collapse [7], compared to 81-86% of symptomatic patients [7,13].
Management

Conservative therapy

Conservative management includes lifestyle modification, avoiding excessive active shoulder abduction and flexion while preventing stiffness through passive ROM. Modifiable etiologies such as alcohol and steroid use should be avoided where possible. Analgesia such as non-steroidal anti-inflammatory drugs (NSAIDs) and opioids may be considered for pain control. Conservative management has varying degrees of success, especially with regards to ROM and performing activities of daily living (ADLs) independently [8,17]. The consensus is that conservative management for stage III or more tend to have poorer outcomes [14,18].

Bisphosphonate is a class of anti-resorptive medication that inhibits osteoclast activity, thereby increasing bone density. Bisphosphonates may reduce pain and disease progression in early stage femoral AVN [19,20]. In a study [21] consisting of five early-stage humeral head AVN treated with bisphosphonate therapy, 80% progressed within four years. However, the sample size is small, and it remains unclear whether bisphosphonate therapy will be effective in humeral head AVN, especially for stage I.

Surgical intervention

Joint-preserving surgeries include arthroscopic debridement and core decompression with or without bone grafting. Joint-replacing options consist of humeral head re-surfacing, hemiarthroplasty (HA) and total shoulder replacement (TSA).

Arthroscopic debridement

The use of isolated arthroscopic debridement for humeral head AVN is mainly limited to case reports in the literature. Hardy [22] and Hayes [23] have reported doing arthroscopic debridement for stage III and above. Both studies had improved UCLA (University of California Los Angeles) scores and ROM post-operatively. The common thread is the presence of locking symptoms attributable to loose bodies or cartilage flaps. Arthroscopic debridement accords the advantages of low morbidity, rapid improvement in symptoms, and joint preservation. However, its utility in treating humeral head AVN aside from specific situations remains to be seen.

Core decompression
Core decompression (CD) aims to decrease intraosseous pressure and promote revascularization [24], and can be performed open [25,26], arthroscopic-assisted [27] or even percutaneously [28]. CD has mostly achieved good results especially for stage I and II humeral head AVN, where 88-100% [25,26,28] of patients showed good post-operative UCLA scores. In fact, a proportion of patients with early stage AVN who underwent CD showed no radiological progression after 5 years of follow-up. However, the efficacy of CD in the later stages plummets significantly, with good results obtained in only 70% and 14-16% of stage III and IV AVN respectively. L'Insalata [15] found that CD for stage III did not prevent clinical or radiological progression.

In contrast to steroid consumption, patients with humeral head AVN secondary to sickle cell disease who underwent CD often progressed to stage III and beyond [29]. The proposed explanation is that sickle cell disease is unmodifiable, therefore repeated vaso-occlusion will undermine any attempts at joint preservation. This is especially so if the patient is homozygous for the hemoglobin S trait (Hb SS) [13,29].

Grafting procedures

Various methods of grafting have been described, such as cartilage allograft [30] or autograft [31,32] to patch the chondral defect, deltoid muscle-pedicled bone graft [36] or vascularized scapular graft [36,30] and bone marrow grafting (often taken from iliac bone crest) [33-35]. The literature is heterogenous and includes stage III and above humeral head AVN [30-33], although most seem to report improvements in pain and ROM. These procedures are often paired with CD to enhance the chances of success. Hernigou et al. found that mesenchymal stem cell therapy was more effective in preventing progression for early stage (I/II) AVN, and the addition of cell therapy significantly reduced the chance of collapse (10% vs 74%) over a follow-up period of 7 years [34]. Similar to isolated CD, the addition of bone marrow grafting does not seem to halt radiological progression in patients with sickle cell disease [35].

Arthroplasty

Arthroplasty remains the treatment of choice for humeral head AVN in the arthritic stage (stage IV and V). The main categories for arthroplasty include partial re-surfacing (PS), HA and TSA. The key absolute contra-indication to arthroplasty is ongoing infection.
PS involves replacing the defect in the cartilage of the humeral head with a metal implant. There are a few common criteria for PS [36,37], including (1) a well-defined area of cartilage loss rather than diffuse arthritis, (2) area of cartilage loss is not excessively large (size of available metal implant is limited), (3) no glenoid wear, (4) good bone stock. These mean that PS is usually used for stage III or IV AVN. If careful patient selection is done, PS has shown to provide pain relief and improvements in ROM [36-38] at 2.5 to 3 years follow-up. The need for revision surgery in the reported literature is minimal, although the follow-up duration is short. Advancements in re-surfacing implants have resulted in the development of hemi-resurfacing or total re-surfacing, which have comparable results [39,40].

PS presents several advantages due to minimal resection of the native bone stock [36-38,41]. These include preservation of remaining healthy cartilage, maintaining the original biomechanics of the shoulder and easier conversion to other forms of arthroplasty if needed since most of the humeral head and neck remain intact. The operative duration and blood loss are also lower, with reduced risk of intra-operative peri-prosthetic fracture [36,37,41]. However, careful placement of the metal implant is required to prevent any step in the surface, which would present an opportunity for the implant to be caught and levered out [41].

HA and TSA are the mainstay of treatment for osteoarthritis secondary to AVN. HA is generally used for stage IV AVN, whereas TSA is performed when there is concurrent glenoid arthritis (stage V). The outcomes between the two types of surgery are similar [42-44] at a mean follow-up of 8-10 years, providing comparable pain relief and ROM. Glenoid wear is the most common complication for HA, with the need for revision surgery ranging from 2-10% [42-44]. Loosening of the glenoid component of TSA requiring revision is a relatively common complication, with a reported incidence of 5-21% [42-44].

The underlying etiology for AVN may affect the eventual outcomes for TSA. Burrus et al [45] found that TSA performed for traumatic AVN had a significantly higher risk of post-operative complication including infection, dislocation, revision surgery and stiffness. TSA for AVN secondary to steroid use also had increased risk of infection, revision surgery and fracture.

**Management algorithm**

Due to the rarity of humeral head AVN, there are few randomized controlled trials evaluating the efficacy of the various treatment options. The advent of MRI imaging potentially allows
greater number of early stage AVN to be diagnosed. Therefore, there is an increasing need to focus treatment on earlier stages, since patients are younger. Based on the review of literature, the following management algorithm is proposed (Figure 4).

The authors suggest that MRI be done for patients with shoulder pain and underlying risk factors for humeral head AVN with unremarkable or early stage AVN radiographs. This allows early stage (I/II) AVN to be detected and some form of prognostication of future progression. Conservative therapy should form the bedrock of treatment. The eventual management will then be guided by the stage of AVN on diagnosis and eventual progression.

For stage I and II AVN, aside from conservative therapy, CD with or without grafting may be considered, especially when there are risk factors such as pain or a large area of involvement on MRI. This is because such procedures may help the patient symptomatically and potentially delay progression to later stages.

Stage III AVN straddles the boundary between early and late stage AVN, as there is disruption in the articulating surface with no gross arthritis. CD with or without grafting may be attempted, although it is likely a temporizing measure to delay the need for joint replacement. Arthroscopic debridement can be done in the same setting or in isolation if there are identifiable cartilage flaps or loose bodies which may contribute to patients’ symptoms. Finally, PS can be considered in a select group of patients, although there is also a need to inform patients of the possibility of revision surgery in the future.

The management of stage IV and V AVN is generally not contentious as there is gross arthritis of the glenohumeral joint, with the main differentiating factor being the presence of glenoid arthritis. Where possible, HA should be performed patients with stage IV AVN as compared to TSA due to its lower risk for revision surgery.

Overall, patient involvement in the decision-making process is key as patients are young and regardless of the treatment given, there is always a chance of disease progression or need for repeated surgeries. This is especially if there are known risk factors for poorer outcomes such as underlying non-modifiable risk factors like sickle cell anemia.
Conclusion

Humeral head AVN can lead to destruction of the glenohumeral joint and result in significant patient morbidity. The current literature is not sufficiently robust to definitively prove which treatment methods are superior. However, with careful patient selection taking into account the patient’s symptoms, stage of disease and underlying etiology, the authors propose the aforementioned management algorithm to help guide the decision-making process.
References


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<td>Sclerosis of humeral head</td>
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<td>III</td>
<td>Osteochondral lesion (crescent sign) with no collapse of the humeral head</td>
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<td>IV</td>
<td>Collapse of the humeral head with loss of joint congruity</td>
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<td>V</td>
<td>Osteoarthritis of the humeral head, with extension to the glenoid</td>
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Figure 1: X-rays of Cruess stage III-IV

This 82 year old male with type 2 diabetes mellitus, hypertension, and STEMI 10 years prior with persistent heart block, presented with left shoulder pain. Ultrasound showed rotator cuff tendinosis. A subacromial steroid injection was performed, which initially relieved the pain. Several years later, he presented with intractable left shoulder pain. X-rays showed sclerosis of the humeral head with flattening of the humeral head and erosive changes. The glenoid is spared, making this Cruess stage III-IV. Acknowledgement to Dr Lim Chee Yeong for providing the images.
Figure 2: X-rays and MRI of AVN Cruess stage IV

This patient is a 38 year old female who presented with pain and weakness of her right shoulder. She had an 8 year history of SLE, with three relapses in the past year. She has been on high dose steroids since her diagnosis. Examination of the right shoulder demonstrated crepitus and weakness of rotator cuff and deltoid muscles. X-rays and MRI (A, B) showed sclerosis and collapse of the supero-medial aspect of the humeral head with loss of congruity (Cruess stage IV). Hemiarthroplasty has been offered. Acknowledgement to Dr Lim Chee Yeong for providing the images.
The patient is a 31 year old lifeguard with a background of hemophilia A, presenting with several years of right shoulder pain. X-ray (A) showed subchondral sclerosis of the superomedial humeral head, with subchondral cysts noted on MRI (B) at the same region (Cruess stage II). Core decompression was initially offered but the patient elected to proceed with conservative treatment. Nine years later, the patient's X-ray and MRI (C, D) showed extensive glenohumeral arthritis (Cruess stage V), and despite his age, arthroplasty was offered. However, the patient deferred surgical intervention.

**Figure 3: X-rays and MRI of progressive AVN of the humeral head**

The patient is a 31 year old lifeguard with a background of hemophilia A, presenting with several years of right shoulder pain. X-ray (A) showed subchondral sclerosis of the superomedial humeral head, with subchondral cysts noted on MRI (B) at the same region (Cruess stage II). Core decompression was initially offered but the patient elected to proceed with conservative treatment. Nine years later, the patient's X-ray and MRI (C, D) showed extensive glenohumeral arthritis (Cruess stage V), and despite his age, arthroplasty was offered. However, the patient deferred surgical intervention.
Figure 4. Management Algorithm for Humeral Head AVN

1. Observation
2. Core decompression +/- grafting

1. Core decompression +/- grafting
2. Arthroscopic debridement
3. Partial humeral head re-surfacing

1. Shoulder hemi-arthroplasty
2. Total shoulder arthroplasty
Declaration of interests

☒ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

☐ The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: