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Hip arthroplasty in Paget's disease of bone: literature review, clinical considerations, and current therapeutic recommendations

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Abstract

Paget's Disease of Bone (PDB) is a chronic condition characterized by abnormal bone resorption and formation, leading to deformities, pain, and an increased risk of fractures. When PBD affects the hip, it can cause severe dysfunction, making hip arthroplasty a critical intervention to restore function and relieve pain. This comprehensive review examines the current literature on hip arthroplasty in patients with PDB, covering preoperative assessment, long-term outcomes, and associated complications. Additionally, evidence-based therapeutic recommendations are provided to improve care and management for these patients.

Abbreviations:
ALP = ALkaline Phosphatase
HHS = Harris Hip Score
PDB = Paget's Disease of Bone
THA = Total Hip Arthroplasty
THA-R = Revision Total Hip Arthroplasty

INTRODUCTION

Paget's Disease of Bone (PDB) is the second most common metabolic bone disease after osteoporosis. With a greater incidence in men (3:2), the prevalence is about 1% in the population aged over 50 years, reaching 5% after 80 years. In the last two decades, a decrease in its prevalence has been reported worldwide; being estimated between 1.5 and 8.3%.[1,2] The disease was initially described in 1877 by Sir James Paget in San Bartolomé Hospital in London. He described a series of middle aged patients who presented altered bone structures and deformities that would worsen progressively. He named it «osteitis deformans» and noticed that various patients developed bone sarcomas that led them to death.[3]

PDB is a focal disorder of bone metabolism, with increased osteoblastic and osteoclastic activity that results in increased bone production that is more vascular, less compact, and mechanically weaker, making it more susceptible to fractures. The etiology is still unknown, but the most accepted hypothesis is that latent infection by viruses of the *Paramyxoviridae* family in genetically predisposed individuals can trigger the disease. This hypothesis is supported by in vivo research showing that

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co-expression of the measles virus nucleocapsid gene and mutation in sequestosome 1-p62P394L in mice is related to severe Paget's bone lesions. These results suggest that the p62P394L mutation and induction of IL-6 by the measles virus nucleocapsid gene play a significant role in PDB pathogenesis.[4-6]

Moreover, approximately 15% of patients have a family history of the disease, which follows an autosomal dominant inheritance pattern with incomplete penetrance. In 5-10% of cases with de novo disease, there is a mutation in the SQSTM1 gene, encoding p62, which is crucial in regulating osteoclast function.

Osteoclasts not only increase their activity nearly ninefold but also multiply (10 to 100 times more than normal), leading to the formation of approximately 100 nuclei of osteoclastic activity. This positive feedback loop increases osteoblast recruitment and subsequent bone matrix formation.[2]

The disease progresses through three well-defined stages: 1) osteolytic phase, characterized by increased bone resorption and hypervascularization; 2) mixed phase, where bone resorption and inadequate mineralization of new bone matrix coexist, leading to disordered bone tissue that appears as «cotton wool» areas; and 3) sclerotic or «burnt-out» phase, where osteoclastic activity decreases, resulting in dense, sclerotic bone tissue. All three phases can occur simultaneously in different parts of the skeletal system.[7]

PDB may affect a single bone (monostotic) or multiple bones (polyostotic), typically not spreading from one to another and new bones rarely become affected during the course of the disease. It asymmetrically affects the skeleton, with frequent involvement of the pelvis (60.3%), spine (35.1%), femur (32.3%), skull (22.2%), and tibia (15.5%). In long bones, osteolytic processes initially develop at the proximal epiphysis, spreading along the bone axis at a rate of 8 mm per year, which is visible on X-rays as a V-shaped «lytic wedge» progressing along the bone. 20-25% of cases are asymptomatic, while others present with nonspecific manifestations; commonly pain exacerbated at rest, predominantly nocturnal and relieved by activity. Fractures can be traumatic or pathological, occurring most commonly distal to the lesser trochanter of the femur (20-80%) and in the proximal third of the tibia.[4]

Advanced stages of PDB lead to deformities such as coxa vara, acetabular protrusion and anterolateral femoral bowing. Diagnosis is crucial for assessing disease extent and severity. Serum alkaline phosphatase (ALP) is the most reliable screening marker. Computed tomography (CT) scans or magnetic resonance imaging (MRI) are useful for investigating PDB complications such as spinal stenosis or osteosarcoma –the most common tumor in these patients–, with an incidence of 0.2-1%.[8]

The hip is commonly affected, with osteoarthritis being the most frequent clinical manifestation, occurring in up to 50% of cases. Deformity alters mechanical loads, leading to early joint degeneration. A study by Van Staa et al., evaluated 2,465 PDB patients and found a relative rate of 3.1 hip arthroplasties compared to controls.[9]

The altered bone morphology and quality make total hip arthroplasty (THA) challenging. Preoperative localization of pathological bone and deformity is critical for surgical planning and implant selection. Although THA generally improves patient's quality of life, it carries risks and complications. Patients with PDB pose various surgical challenges due to extremely dense bone that complicates medullary canal preparation and implant integration. Selection of implant type remains debated; initially, cemented implants were used, but studies reported higher rates of complications such as aseptic loosening. Hypervascularity in Paget's disease may hinder achieving a dry cancellous bed, limiting cement interdigitation and long-term implant durability. Moreover, additional components and procedures have been suggested for better functional outcomes, such as corrective osteotomy, medial acetabular bone grafting, antiprotrusio cage, and the use of locking or compression screws.[10]

MATERIAL AND METHODS

A comprehensive literature search was conducted in February 2024 using Google Scholar, PubMed, Scopus, Embase and Cochrane Central Register of Controlled Trials. The search aimed to identify all studies published between January 1st 2020 to January 31st 2024; that evaluated outcomes of patients with PDB undergoing THA or revision total hip arthroplasty (THA-R), this, in order to focus on the most recent evidence and minimize overlap with previous reviews.

The search strategy included the following keywords and MeSH terms: «Paget's Disease of Bone», «Osteitis Deformans», «Coxarthrosis», «Total Hip Arthroplasty», «Joint Replacement», «Osteopathy», «Revision Total Hip Arthroplasty».

Inclusion criteria

We included all articles published in Spanish or English describing outcomes of THA/THA-R in skeletally mature patients with PDB. Exclusion criteria comprised studies in languages other than Spanish or English, narrative reviews, conference abstracts, and patients undergoing partial knee/hip arthroplasty or arthroplasty of any joint other than the hip.

Data selection

Abstracts and titles of all works were screened. Articles not meeting criteria based on title and abstract were excluded through consensus. Full texts of all eligible articles were independently reviewed. Data regarding publication, subjects, implants used, complications, and functional outcomes from all included studies were recorded in a spreadsheet.

Data analysis

Evaluated clinical outcomes included revision rates, medical complications (venous thromboembolism [VTE], cardiovascular events, renal impairment, non-surgical site infections, and respiratory complications), surgical complications (heterotopic ossification (HO), aseptic loosening, dislocation, fracture, and periacetabular osteolysis) and postoperative Harris Hip Score (HHS) results.

RESULTS

Five relevant studies evaluating outcomes of hip arthroplasty in heterogeneous populations, including patients with Paget's disease of bone, were identified. A comparative analysis revealed important variations in patient characteristics, implant types used, perioperative complications, and functional outcomes *(Table 1)*.

D'Ambrosi et al., reported a single case of a 57-year-old male patient with bilateral disease, managed with a custom-made implant composed of a 55 mm femoral stem, a 56 mm uncemented cup, a 56/36 mm polyethylene liner, two screws, and vitamin E additives. No medical complications, significant blood loss, or need for revision surgery were documented during the reported follow-up.

In contrast, Arif et al., presented a large series involving 4,211 patients, with a mean age of 72.9 years (range 49-92) and an even sex distribution. At a mean follow-up of 7.2 years, the cumulative revision rate was 1.4% at one year and 4.4% overall. The mean intraoperative blood loss was 880 mL (range 100-3,500 mL). A high incidence of medical complications was observed, including urinary tract infections (11.8%), respiratory complications (7.7%), and venous thromboembolic events (7.3%). The postoperative functional outcome, assessed through the HHS, was 85.2 points.

Giaretta et al., reported a single case of an 82-year-old female patient with a follow-up of three months. Heterotopic ossification prophylaxis was administered with indomethacin (50 mg every 12 hours for 15 days). The patient achieved an HHS of 82 points, with no significant postoperative complications reported.

Di Martino et al.,[11] evaluated 26 patients (29 hips) with a mean age of 69 years (range 53-85). The mean clinical follow-up was 84.2 months, and the radiographic follow-up was 30.7 months. Most implants were uncemented (69%), hybrid (27.6%), or fully cemented (3.4%). The revision rate was 6.9% at seven years, with femoral head fracture and acetabular cup loosening as the primary causes. Approximately 45% of patients received bisphosphonate therapy. Heterotopic ossification was reported in 51.7% of cases at two years, predominantly Brooker grades I and II. Periacetabular osteolysis was observed in 13.8% of patients. The mean postoperative HHS was 89 (range 70.8-99.8).

Makaram et al., described a cohort of 144 patients (152 hips) with a mean age of 76.6 years. The revision rate was 2.8% at five years. Within the first 30 postoperative days, several acute medical complications were reported, including cardiovascular events, acute renal impairment, non-surgical site infections, atelectasis, and paralytic ileus. During the first year, additional complications such as severe anemia, congestive heart failure, and cerebrovascular accidents were documented. Surgical complications included hemorrhage (1.4%), prosthetic joint dislocation (1.4%), and the need for revision arthroplasty (1.4%).

Comparatively, the larger series[12] reported relatively low revision rates but a higher incidence of medical complications, possibly attributable to the older patient population and associated comorbidities. In contrast, the smaller series and isolated case reports (D'Ambrosi, Giaretta, Di Martino) demonstrated fewer complications, although the limited sample size introduces a risk of bias. Functional outcomes, as measured by HHS, were consistently high across all studies, suggesting favorable postoperative function despite the observed complication rates.

Table 1: Comparative analysis of literature on hip arthroplasty in Paget's Disease of Bone.

Author	Patients	Hips	Age (range)	Sex	Follow-up	Implant	Revision rate	Revision cause	Bleeding	Meds	Med complications	C. qx	PO scores
D'Ambrosi R	1	2	57	M		Custom-made (55 mm stem, 56 mm cementless cup, 56/36 mm poly insert, 2 screws, vit E)							
Arif M	4,211		72.9 (49-92)	50% F	7.2 y (0-20)		1.4% at 1 y 4.4% overall		880 mL (100-3,500)		UTIs 11.8% (285) Respiratory complications 7.7% (185) VTE 7.3% (175)	HO 4% (168) Aseptic loosening 3.1% (129) SSI 3% (125) Dislocation 2.4% (103) Fracture 1.1% (47) Other 0.6% (25)	HHS 85.2
Giaretta S	1	1	82	F	3 m					Indomethacin 50 mg/12 h 15 d			HHS 82
Di Martino A	26	29 (14 R 48% / 15 L 52%)	69 (53-85)	14 M (54%) 12 F (46%)	Clinical 84.2 m (1-195 m) / Rx 30.7 m (1-132 m)	Cementless 20 (69%) 3 (15%) aug screw Cemented 9 (31%) 1 (3.4%) full 8 (27.6%) hybrid 3 (37.5%) screw Cer-cer 25 (86.2%) Cer-poliet 3 (10.3%) Met-poliet 1 (3.5%)	6.9% at 7 y	One femoral head fracture, one cup mobilization		Bisph 13 (45%)	HO 15 (51.7%) 2 y Brooker I 6 (40%), II 6 (40%), III 3 (20%)	Periacet osteolysis 4 (13.8%)	HHS 89 (70.8-99.8)
Makaram N	144	152	76.6 (52-97)	76 M (53%) 68 F			4 at 5 y (2.8%)				< 30 days 4 acute cardiovasc events 1 acute renal impairment 1 non surgical site infection 1 atelectasia 1 paralytic ileus 1 year 3 anaemia for transfusion 8 ACE 1 congestive heart failure 7 NSSI 1 cerebrovascular accident 1 atelectasia 1 pleural effusion	< 1 y 2 haemorrhage (1.4%) 2 dislocation of prosthetic joint (1.4%) 2 revision arthroplasty (1.4%)	

C. qx = Complications. F = Female. HHS = Harris Hip Score. HO = Heterotopic Ossification. L = Left. M = Male. m = months. NSSI = Non Surgical Site Infection. PO = postoperative. R = right. Rx = radiologic. SSI = surgical site infection. UTI = urinary tract infection. VTE = venous thromboembolism. y = years.

DISCUSSION

The diagnosis of PDB is often incidental, typically identified through elevated levels in routine blood tests or characteristic radiographic findings observed during imaging performed for non-Paget-related musculoskeletal or systemic examinations. Serum ALP is the most consistently elevated biochemical marker, reflecting increased osteoblastic activity and bone turnover. Elevated ALP levels have been associated with a higher incidence of implant loosening following arthroplasty. Moreover, revision failure rates with cemented prostheses have been reported to reach up to 15% in patients with elevated ALP, highlighting its role as a surrogate marker of disease activity and a potential predictor of adverse surgical outcomes.[13]

Preoperative evaluation

A meticulous preoperative evaluation is critical in patients with PDB scheduled for THA. This assessment should evaluate the current phase of disease activity, the extent of bone involvement, any deformities, and the patient's overall health. Imaging modalities including plain radiographs, computed tomography (CT), and magnetic resonance imaging, are essential to assess bone morphology and deformities, assisting the surgeon in planning the surgery and selecting the most appropriate implant.

In CT scans, similar findings are often observed to those seen in classic radiographs, but defining anatomically complex regions of the skeleton. It is important to note that radiographic patterns vary depending on the disease phase. However, the most sensitive method of detecting Paget's lesions is through bone scintigraphy, which is recommended for determining the extent of the disease.[13]

Careful preoperative evaluation for anemia and coagulopathy is essential due to increased intraoperative bleeding associated with bone hypervascularity. Bisphosphonates are the treatment of choice in Paget's management. Evidence supports bisphosphonate therapy effectively suppresses bone turnover, healing radiological lesions and restoring normal bone histology. Late disease activity can lead to rapid periprosthetic osteolysis and premature implant failure. To reduce this risk, pretreatment with bisphosphonates should start six weeks before surgery. Whether asymptomatic patients benefit from treatment remains debated.

The trial «Intensive Treatment vs. Symptomatic Treatment (PRISM)» included 1,324 PDB patients, comparing outcomes after bisphosphonate treatment in symptomatic vs asymptomatic patients. Symptomatic treatment group used bisphosphonates if analgesics and anti-inflammatory drugs were ineffective for bone pain. Intensive treatment group used bisphosphonates regardless of symptoms, aiming for normal ALP levels. Results showed no clinical advantage to intensive treatment over symptom-based therapy.[14]

Common bisphosphonate side effects include gastrointestinal symptoms (oral) and acute phase reactions (intravenous). Severe adverse effects include atypical femoral fractures and osteonecrosis of the jaw, which presents a very low incidence that increases with treatment duration.

Surgical considerations

Some patients may require surgery for fractures, deformities, compression neuropathies, osteoarthritis or neoplasms.

The femur is the second most common site affected by PDB (25-46%) after the pelvis (21-75%). Monostotic cases are less common (10-35%) than asymmetrical polyostotic (65-90%) presentations.[15]

Important considerations for surgical approach, implant selection and intraoperative techniques include altered bone quality requiring adjunct techniques like bone grafting or cement reinforcement. Correcting pre-existing deformities and managing increased vascularity during surgery are also critical.

Sclerotic bone and protrusion can be challenging while working the acetabular component. High-speed burs are suggested to avoid sclerosis and cages aid stabilize the acetabulum to prevent protrusion.[16] Femoral component risks primarily relate to stem malposition, necessitating careful preoperative planning for optimal osteotomy height.[16]

Non-cemented components are preferred for most hip arthroplasties due to higher survival and lower loosening rates compared to cemented components.[17] However, concerns arise regarding non-cemented implants in Pagetic bone, remaining uncertain whether altered bone quality and morphology adversely affects implant integration.[17]

Outcomes and complications

Hip arthroplasty outcomes in Paget's patients generally show significant pain/function

improvements. Wilson et al., evaluated 37 hips in Paget's hip arthroplasty with cemented THA; no revisions occurred over 7.8 years.

Complications may include implant loosening causing pain, joint instability, and loss of function. Loosening can result from implant material wear, initial poor fixation, or common osteolysis in these patients.

Several studies noted higher rates of symptomatic/asymptomatic radiolucencies around bone-cement interfaces in Pagetic bone. THA revision may correct implant loosening.[12]

Ludkowski et al., found good outcomes with cemented THA but reported higher aseptic loosening revision rates in Paget's patients. Hozack et al., reviewed five patients with non-cemented acetabular components during THA, reporting no acetabular loosening over 5.8 years on radiographic checks.[18]

Parvizi et al., evaluated 19 hips with Paget's undergoing non-cemented THA; no revisions for aseptic loosening occurred over seven years. Lusty et al., assessed 33 non-cemented THAs; three required revision (one aseptic loosening, two periprosthetic femoral fractures).[19]

Ludkowski et al., reviewed 37 THA patients, noting 70% had good/excellent outcomes over 7.8 years with no dislocations or revisions but intraoperative difficulties in nine patients.[18] Sochart studied 98 hips in 76 Paget's patients undergoing THA, noting 10% acetabular and 8% femoral stem aseptic loosening.[20]

Hanna SA et al., reviewed eight studies (358 hips, mean 8.3 years); 19 aseptic loosening cases (5%) occurred. Non-cemented group had three cases (3%) over 15.3 years vs. cemented 16 cases (6%) over 7.5 years. 27 revisions (8%) occurred; non-cemented six revisions (6%) over 8.6 years vs. cemented 21 (6%) over 7.5 years.[21]

Hurley TE et al., 2017 systematic review showed similar functional/survival outcomes with both components but lower aseptic loosening/revisions with non-cemented.[17] Lusty et al., studied 33 uncemented prostheses; three revised in 6.7 years, Harris hip scores improved from 56/100 pre-op to 90/100 post-op.[22]

Other common complications include infection, periprosthetic fracture, and disease recurrence. Long-term follow-up detects and treats these early. Previous THA studies in Paget's report coxa vara, acetabular protrusion, and femoral bowing. Increased intraoperative blood loss occurs; preoperative bisphosphonates reduce blood loss. Concern for increased heterotopic ossification post-THA in Paget's is valid, with rates up to 32%.[23]

Hernández et al., studied tranexamic acid use in THA, suggesting contemporary practice may lower transfusion rates. More studies are needed on heterotopic ossification prophylaxis and functional outcomes.[24]

Patients with Paget's may present neurologic symptoms from nerve compression by bone deformities; perioperative management should address these for better long-term outcomes.

Therapeutic recommendations

Based on available evidence, multidisciplinary management is recommended for Paget's patients needing THA. Comprehensive preoperative evaluation, meticulous surgical planning, specific surgical techniques, and long-term follow-up are essential for early complication detection and management.[25,26]

The reviewed studies consistently reported favorable functional outcomes following THA in patients with PDB, as reflected by high HHS across heterogeneous cohorts and case series. Despite the variations in patient demographics, implant types, and surgical approaches, all studies documented significant pain relief and functional improvement postoperatively.

However, notable differences emerged regarding complication rates. Larger cohort studies[12] demonstrated higher incidences of medical complications, likely related to the older age and comorbidities of their populations, whereas smaller series and isolated case reports exhibited fewer complications, though potentially underreported due to smaller sample sizes.

Revision rates were generally low across all studies, with slightly better outcomes observed in patients treated with non-cemented components, aligning with previous literature suggesting superior implant longevity in PDB when cementless fixation is used. Additionally, a high prevalence of heterotopic ossification (up to 51.7%) was noted, emphasizing the importance of prophylactic measures such as indomethacin therapy.

These findings collectively informed the conclusions that, although THA is effective in PDB, meticulous preoperative evaluation, surgical planning, management of disease activity (particularly through bisphosphonate therapy), and long-term monitoring are essential to optimize outcomes and manage potential complications.

CONCLUSIONS

THA effectively improves function/pain relief in Paget's patients but requires careful disease consideration for optimal results. Interdisciplinary collaboration and long-term follow-up enhance patient care/outcomes.

THA remains the optimal treatment for advanced coxarthrosis in Paget's patients, with literature showing significant clinical/functional improvements post-surgery and high implant survival rates. However, Pagetic bone alterations pose therapeutic challenges, necessitating more long-term studies on survival/revision rates compared to the general population, particularly comparing outcomes of cemented vs. non-cemented implants.

Limited literature exists on THA outcomes in Paget's; further research on cemented vs. non-cemented hip prostheses is needed to determine optimal complication rates.

Furthermore, PDB patients undergoing THA have a 46% prevalence of heterotopic ossification, which can be prevented with postoperative use of indomethacin. Preserving as much bone stock as possible is mandatory for potential future revision procedures.

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