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THE ROLE OF GENDER DIFFERENCES IN TISSUE BIOPHYSICAL PROPERTIES IN OSTEOARTHRITIS PROGRESSION

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ABSTRACT

Objectives

This study investigates gender differences in primary hip osteoarthritis (OA) progression through a prospective observational approach, analyzing functional, radiographic, and biophysical disparities between male and female patients. The findings aim to enhance patient treatment and management from clinical and biomechanical perspectives.

Materials and Methods

Patients undergoing total hip arthroplasty (THA) due to primary hip OA were divided into two cohorts based on gender. Preoperative evaluations included functional disability assessment and standard hip and pelvis X-rays graded by the Tönnis classification. During surgery, femoral heads were preserved for microstructural analysis. A subset (13 males, 12 females) underwent micro-computed tomography to assess bone volume fraction, porosity, trabecular thickness, and separation. Follow-ups at 6 and 12 months included postoperative X-rays and functional assessments.

Results

Both cohorts showed significant functional improvement postoperatively, consistent with literature. Return-to-work time ranged from 4 to 12 weeks, averaging 6 weeks. Statistically significant gender differences emerged in postoperative Harris Hip Score (HHS) and WOMAC scores at both follow-ups, as well as return-to-work time. Preoperatively, the HHS also showed a less pronounced difference. Analysis of 125 femoral head specimens revealed no significant gender differences in bone mineral density or bone volume fraction. However, trabecular anisotropy, thickness, and separation differed significantly. Correlation analysis indicated moderate preoperative associations between bone mineral density, anisotropy degree, and clinical scores, but these weakened postoperatively. Laboratory findings did not strongly correlate with clinical outcomes at 6 or 12 months.

Conclusions

While no significant gender disparities in clinical outcomes were identified, differences in microstructural tissue characteristics suggest the need for gender-specific considerations in managing end-stage OA. This study provides a rigorous and replicable framework for investigating osteoarthritis progression.

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INTRODUCTION

Hip osteoarthritis (Hip OA) affects millions of people worldwide, with an estimated 25% lifetime risk of symptomatic disease in those who live to age 85, and almost a 10% lifetime risk of undergoing a total hip replacement (THA) for end-stage OA [1–3]. Currently, there are no effective treatments for OA, and our limited knowledge of the disease's pathogenesis restricts our ability to perform early diagnoses [4].

Primary osteoarthritis exhibits significant sex-related differences in prevalence, severity, and degree of functional disability. Women often present with more advanced OA, experience more pain, and have increased disability, making them three times more likely to receive hip replacement surgery during their lifetime [1,2,5]. There is little evidence concerning the mechanisms underlying these differences. Despite new evidence on biophysical differences between males and females, the integration of sex and gender influences into medicine and surgery has been slow [6].

A simple explanation for this slow uptake is the lack of basic research on the topic. Most biomedical experiments are conducted exclusively on male animals, and women are significantly underrepresented in clinical trials. Consequently, many sex differences remain unexplored [7].

In this context, only a few studies have addressed the systemic, metabolic, and local effects of sex-related factors on the development and progression of primary hip OA. Observations have been made regarding sex differences in hip biomechanics and cartilage composition. For instance, Boyer et al. [8] found that females exhibit greater external hip adduction and internal rotation moments compared to males, with differences also noted in hip extension moments [8]. The authors hypothesized that these differences in gait characteristics, hip biomechanics, and bone structures may create unfavorable loading conditions, predisposing women to the development of idiopathic Hip OA.

Additionally, women have been found to have smaller cartilage volume and higher annual cartilage loss in both knee and hip joints, independent of body and bone size [9–11]. Studies on cartilage composition [12,13], specifically the concentration of glycosaminoglycans (GAGs) in human cartilage, have also revealed that females have lower GAG concentrations than males [13,14]. GAGs are crucial for joint lubrication and cartilage nutrition, and their concentration in articular cartilage is central to arthritic diseases [11].

In conclusion, sex-related differences in the progression of primary hip OA are a broad topic with significant diagnostic and therapeutic implications that needs to be explored through imaging, clinical, and biophysical studies.

The hypothesis of this research project is that different biophysical properties in the tissues of male and female patients influence the prevalence, clinical presentation, and progression of primary hip osteoarthritis. The objective of the research will be to study these properties from clinical, radiographical, and biophysical perspectives.

ANATOMY OF THE HIP

OSSEOUS ANATOMY OF THE HIP JOINT

The hip joint is classified as an enarthrodial joint. It is characterized by great intrinsic stability and the ability to move in all three planes of space. This joint is defined as a "ball and socket," which aptly describes the relationship between the proximal epiphysis of the femur and the acetabulum.

Femur

The femur is the longest and strongest bone in the human body. Its shaft is nearly cylindrical and is curved with an anterior convexity. It is narrow at the center and widens both proximally and distally. In its mid-third, the shaft has three faces and three margins: the anterior face, lateral face, and medial face. In the proximal epiphysis of the femur, the head, neck, greater trochanter, and lesser trochanter can be identified. The femoral head is spherical, smooth, and regular, covered by articular cartilage for articulation with the acetabulum. Articular cartilage covers the entire surface of the femoral head, except for the fovea capitis, a small pit located supero-medially, where the ligamentum teres attaches. The femoral neck connects the head with the intertrochanteric region, being narrower in the middle and wider distally and proximally. The greater trochanter develops laterally and superiorly to the cervico-diaphyseal junction, has a quadrangular profile, and its upper end medially borders the intertrochanteric fossa. The lesser trochanter is located medially, opposite the greater trochanter. The two trochanters are connected by the intertrochanteric line anteriorly and the intertrochanteric crest posteriorly, which are important sites for muscle attachment. The calcar is a dense bony ridge originating from the postero-medial endosteal surface of the proximal femur, near the lesser trochanter. It extends vertically and projects laterally towards the greater trochanter, providing crucial mechanical support, especially in flexion, and contributing to load distribution in the proximal femur.

On the frontal plane, the cervico-diaphyseal angle, formed by the axes of the femoral neck and shaft, averages 125°, with physiological variability between 120° and 135°. Variations beyond these values are termed coxa vara (angle $< 120°$) or coxa valga (angle $> 135°$), which may not necessarily be pathological. The cervico-diaphyseal angle varies by gender, with lower average values in females (129°) compared to males (133°). Additional variability can be observed based on geographic and phenotypic factors: populations from Northern

Europe tend to have a more valgus femoral neck compared to those from Southern Europe, and tall, slender individuals typically have a more valgus femoral neck compared to shorter stature individuals.

The average cervico-diaphyseal angle also changes during growth; at birth, it exceeds 140°, gradually decreasing by approximately 1° per year until the end of growth. High levels of physical activity and body mass index in children are associated with a relative reduction in the cervico-diaphyseal angle.

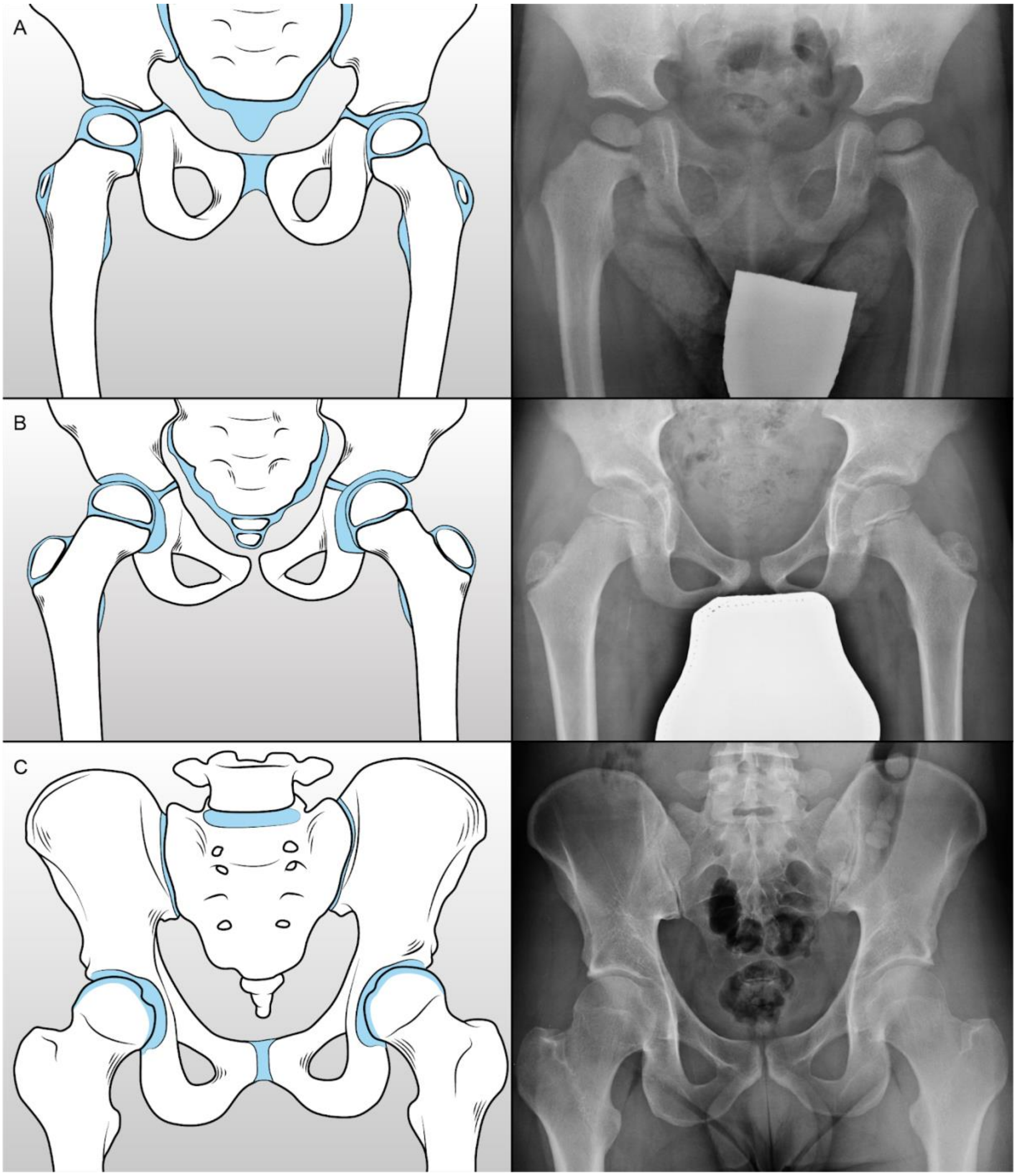

Figure 1. The cervico-diaphyseal angle decreases with skeletal maturity

The angle of declination (also known as the angle of anteversion) measures the angle formed between the plane tangent to the axis of the femoral neck and the plane tangent to the femoral condyles. It can open anteriorly (anteversion) or posteriorly (retroversion). Most individuals have a femoral neck anteverted by 15°, with physiological variability between 10° and 20°. There is a gender difference, with females generally having greater anteversion (16-20°) compared to males (10-15°).

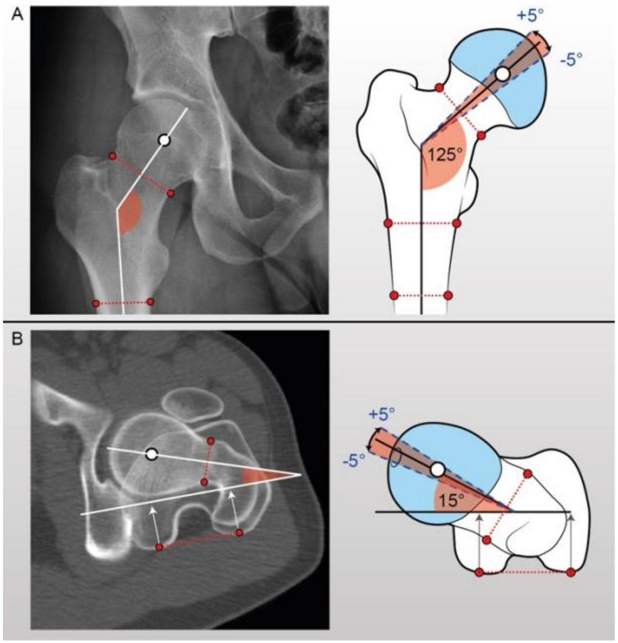

Figure 2. A. cervico-diaphyseal angle. B. Angle of declination

Anteversion also changes with age: at birth, it is higher (average 30°-40°), gradually decreasing by about 1.5° per year until 9-10 years of age. In some rare conditions (congenital coxa vara, post-traumatic outcomes), the angle may open posteriorly (coxa retroversa). The size of the diaphyseal canal varies based on cortical thickness. In 1993, Dorr proposed a classification of diaphyseal morphology based on femoral cortical thickness, defining the cortical index as the ratio between the internal cortical distance measured at the level of the lesser trochanter and the same distance 10 cm distal to it. Using these measurements, three distinct morphotypes can be classified: A (index less than 0.5), B (index between 0.5 and 0.75), and C (index greater than 0.75).

Morphotype A is more common in young men with a high BMI and is characterized by a narrow canal (also known as "champagne flute femur"). Type B femurs are typical in adult men and women, with higher cortical porosity compared to type A, resulting in a more flared endomedullary canal. Type C femurs are common in elderly women with low BMI and are characterized by an enlarged femoral canal (also known as "stovepipe femur"), typical in patients with osteoporosis.

These morphotypes are related to age, bone quality, and sex. Practically, this classification helps determine the most appropriate fixation method for the femoral component during hip replacement surgery, particularly regarding the use of cement.

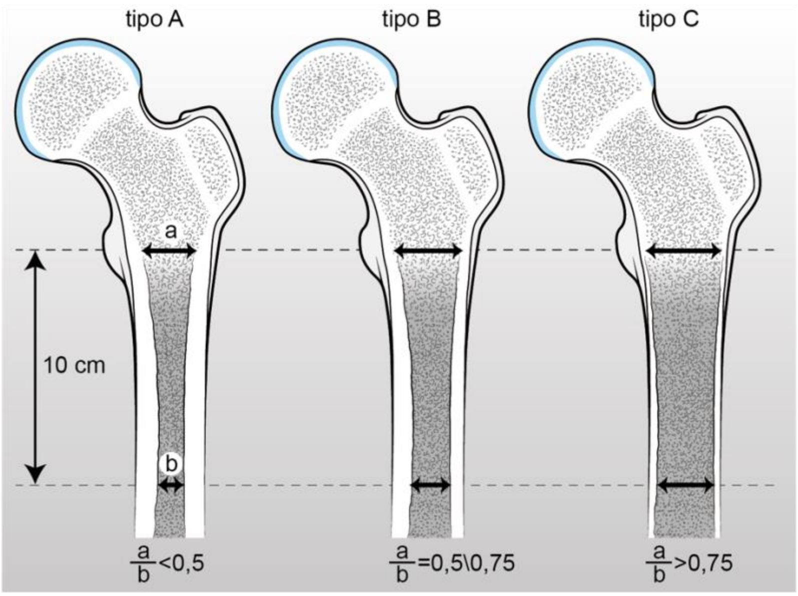

Figure 3. Dorr morphotypes

Pelvic Bone

The pelvis, also known as the bony pelvic girdle, is an osteoarticular structure comprising the right and left coxal bones (also referred to as hip or iliac bones), the sacrum, the coccyx, and their respective articulations.

This structure serves as the anatomical interface connecting the trunk to the lower limb through the coxofemoral joint.

The hip bone (also known as the innominate bone) is a flat, quadrilateral-shaped bone that is voluminous and irregular, wider at both the superior and inferior ends and narrowing at its central portion. The two contralateral bones articulate anteriorly at the pubic symphysis and posteriorly through the interposition of the sacrum at the sacroiliac joint, thereby forming the pelvic girdle. Each innominate bone consists of three distinct bones: the ilium, ischium, and pubis. In the young, these bones are connected by cartilage at the acetabular wall, a depression on the external surface that articulates with the femoral head; in adults, they are fused. Anteroinferior to the acetabulum is the obturator foramen, bounded by the ischiopubic rami.

The upper part of the hip bone is formed by the ilium, which narrows at its lower portion (ilium body) and contributes to the superior part of the acetabular cavity. It expands superiorly to form the iliac wing. Three surfaces can be distinguished: the gluteal (external), sacropelvic, and the iliac fossa (internal). The iliac fossa is separated from the sacropelvic surface by the arcuate line. The iliac tuberosity is a roughened surface situated below the posterior part of the iliac crest and is connected to the sacrum by the interosseous sacroiliac ligament. Antero-inferiorly, the auricular surface articulates with the lateral face of the sacrum.

The ischium forms the posteroinferior part of the hip bone and is divided into two portions: the body and the ramus. The body contributes to the inferior posterior part of the acetabulum and gives rise to the ramus, which proceeds anteromedially to fuse with the descending ramus of the pubis, thereby delineating the obturator foramen. The ischial tuberosity is a voluminous, roughened area on the posteroinferior aspect of the ischium, directed downward and medially. Below it lies the lesser sciatic notch.

The pubis forms the anterior part of the hip bone and articulates with its contralateral counterpart through the cartilaginous pubic symphysis. It consists of a body, a superior ramus extending posteroinferiorly to the acetabulum, and an inferior ramus, which extends inferiorly, posteriorly, and laterally to fuse with the ischial ramus. The body of the pubis has three surfaces: anterior, posterior, and symphyseal (or medial), which articulates with the contralateral pubic bone via the cartilaginous pubic symphysis. The obturator foramen is located antero-inferiorly to the acetabulum and is bounded by the ischium and the pubis. The shape varies between sexes, being wide and oval in males and smaller and almost triangular in females. It is almost completely obliterated by the obturator membrane, which is discontinuous in its upper part, allowing the passage of obturator vessels and nerves.

The acetabulum, also known as the cotyloid cavity, is a hemispherical cavity that articulates the femoral head. The acetabular rim is a ring interrupted antero-inferiorly by the acetabular notch, which is completed by the transverse acetabular ligament. The inner walls of the acetabulum are covered by semilunar articular cartilage, bordered by the acetabular rim, which articulates with the articular cartilage of the femoral head. The deepest part of the acetabulum, the acetabular fossa, lacks articular cartilage and comprise a pad of fatty tissue, the pulvinar. This structure includes the ligamentum teres, which aids in providing stability and vascularization to the femoral head through an artery that usually undergoes physiological obliteration in adulthood.

The spherical, convex articular surface of the femoral head articulates with the spherical, yet concave, surface of the acetabular cavity. However, the two surfaces are not equally extensive and not exactly congruent; they only fully match when the femur is in complete extension, slightly abducted, and internally rotated. The femoral head is contained within the bony component of the acetabulum for about 50% of its surface. The stability of the joint is further enhanced by the joint capsule and the acetabular labrum.

The joint capsule is a robust, richly vascularized fibrous structure that proximally attaches to the acetabular labrum and the transverse acetabular ligament. Distally, it attaches to the intertrochanteric line anteriorly and about one centimeter medial to the intertrochanteric crest posteriorly. The joint capsule is reinforced by three ligaments: the iliofemoral, ischiofemoral, and pubofemoral ligaments. The iliofemoral ligament is anterior and consists of two divergent bands forming a Y-shape. The ischiofemoral ligament reinforces the postero-inferior capsule, and the pubofemoral ligament reinforces the antero-inferior capsule.

The acetabular labrum is a fibrocartilaginous rim that attaches to the edge of the acetabulum. The anterior and posterior horns of the labrum are continuous with the transverse acetabular ligament. In the anterior portion, the labrum's cross-section is triangular, while in the posterior portion, it is roughly quadrangular and rounded. The outer edge of the acetabular labrum attaches to the bone, while the inner edge is continuous with the acetabular articular cartilage. The thickness of the labrum varies, from less than 2 mm in the thinnest postero-inferior part to more than 3 mm in the thickest antero-superior part, where it is also the widest due to the need to withstand greater stress in this area during loading. The acetabular labrum is supplied by arterial branches from the richly vascularized joint capsule. From the capsule, arteries enter the peripheral region of the labrum. Like the knee meniscus, the vessels are located only in the outer third, while the inner two-thirds of the labrum are nearly avascular. Consequently, peripheral labral lesions have some potential for repair, whereas central lesions have almost no repair capacity. The labrum is also richly innervated, which explains the significant pain symptoms in patients with labral lesions.

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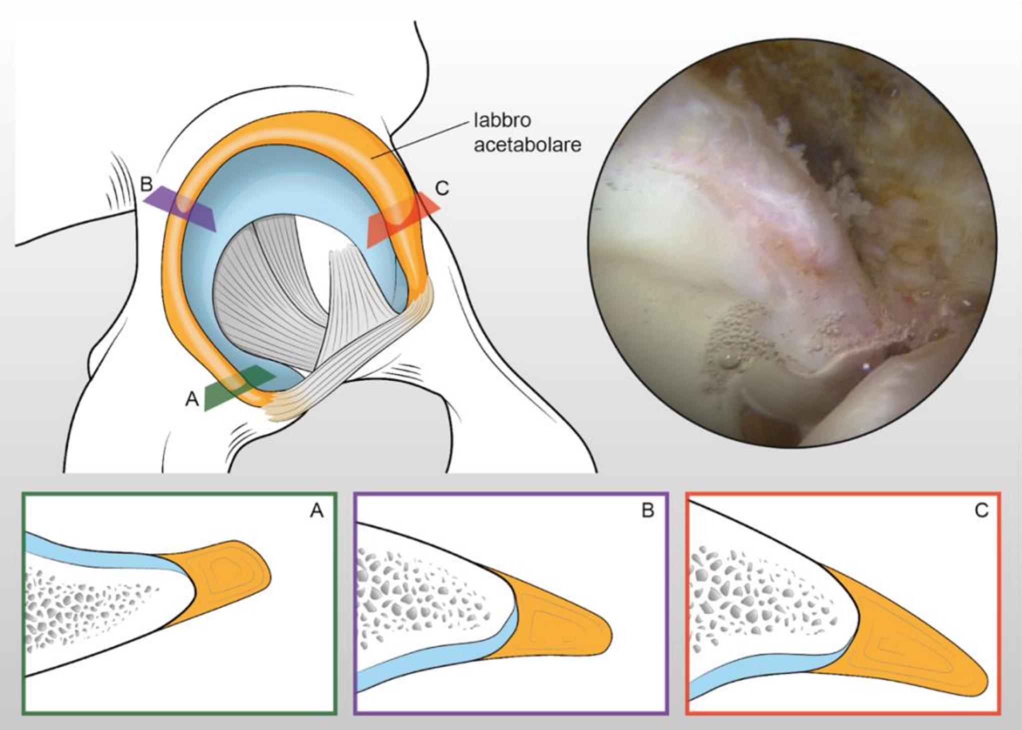

Figure 4. The acetabular labrum

The acetabular labrum, like the glenoid labrum in the shoulder, increases the depth of the acetabulum for better containment of the femoral head. However, its main function is to maintain negative pressure within the joint, preventing synovial fluid from escaping and acting as a sealant. This ensures uniform load distribution in the hip. Ultimately, the labrum contributes to effective joint biomechanics, and its damage can accelerate osteoarthritic degeneration.

MUSCLES OF THE HIP

The muscular structures of the thigh are contained within the fascia lata, a deep connective tissue structure. The fascia lata is not uniform throughout its extension. It includes the iliotibial band (a fibrous thickening that runs down to Gerdy's tubercle) and intermuscular septa connected to the periosteum, providing stability and protection to the muscle compartments.

The intermuscular septa identify six distinct muscle compartments based on anatomy and function:

1. iliac region
2. gluteal region
3. posterior region
4. external rotator region
5. anterior region
6. medial region

Muscles of the iliac region

The iliopsoas, the primary muscle of the iliac region, plays a crucial role in thigh flexion relative to the trunk and contributes to hip external rotation. This muscle group consists of two muscles: the major psoas, originating from the transverse processes and lateral surfaces of the vertebrae T12 to L4, and the iliacus, which arises from the upper two-thirds of the iliac fossa, the inner lip of the iliac crest, and the upper part of the sacral wing. Both muscles converge inferiorly to form a common tendon that inserts on the lesser trochanter of the femur. The major psoas muscle extends laterally to the lumbar segment of the spinal column and superior aperture of the pelvis, exiting through a notch on the anterior edge of the iliac bone before attaching to the femur. The iliacus muscle, originating from the iliac bone, joins the major psoas to form the iliopsoas muscle, which traverses the anterior surface of the joint capsule. Innervation of these muscles is provided by the ventral branches of lumbar spinal nerves L1, L2, and L3, while vascularization is derived from branches of the lumbar arteries, common iliac artery, external iliac artery, femoral artery, and medial circumflex artery. Additionally, a third muscle, the minor psoas, is present in about 60% of individuals. This muscle originates from the last lumbar vertebrae and attaches to the lumbosacral spine, but unlike the major psoas and iliacus, it does not act on the femur.

Muscles of the gluteal region and external rotator region

This region comprises nine muscles: the gluteus maximus, gluteus medius, gluteus minimus, piriformis, internal and external obturator, superior and inferior gemellus, and quadratus femoris. These muscles originate in the pelvic basin and insert onto the femur.

The gluteus maximus is the most superficial muscle, originating from the posterior gluteal line of the iliac wing, the sacrum, coccyx, and sacrotuberous ligament. Its fibers descend laterally, with superficial fibers continuing into the fascia lata and deeper fibers inserting onto the gluteal tuberosity of the femur. This muscle extends and externally rotates the femur, also extending the trunk by anchoring to the femur, playing a significant role in maintaining an upright posture. It is supplied by the superior and inferior gluteal arteries and innervated by the inferior gluteal nerve (L5 and S1).

The gluteus medius is a broad, thick muscle located beneath the gluteus maximus and covered by deep fascia anteriorly. It originates from the external surface of the iliac wing and inserts onto the upper and posterior part of the greater trochanter via a flat tendon. Vascularization is provided by the superior gluteal artery, with innervation from the superior gluteal nerve (L4 and L5).

The gluteus minimus, deep to the gluteus medius, is fan-shaped and originates from the external surface of the ilium between the anterior and inferior gluteal lines. Its fibers converge into a tendon that inserts onto the anterior surface of the greater trochanter. Like the gluteus medius, it is supplied by the superior gluteal artery and innervated by the superior gluteal nerve (L4 and L5). Both muscles abduct the thigh and internally rotate it when anchored to the pelvis, playing a crucial role in maintaining an erect trunk and horizontal pelvis during movement.

The piriformis is on the same plane as the gluteus medius, originating from the anterior sacrum and the gluteal surface of the ilium near the posterior-inferior iliac spine. It exits the pelvis through the greater sciatic foramen and inserts onto the superior margin of the greater trochanter. The piriformis externally rotates the thigh when the hip is extended and abducts it when flexed. It is innervated by branches from L5 and S1 and receives blood from the gluteal artery.

The internal obturator originates from the inner surface of the obturator membrane and the margins of the obturator foramen. Its fibers converge toward the lesser sciatic foramen and terminate in tendons that reflect at a right angle at the ischial notch. The muscle inserts, along with the superior and inferior gemelli, onto the medial surface of the greater trochanter. It functions as an external rotator of the thigh, like the gemelli, and is supplied by the obturator and ischiatic arteries, with innervation from L5 and S1.

The superior gemellus originates from the ischial spine and, along with the inferior gemellus (which originates from the ischial tuberosity), inserts onto the medial surface of the greater trochanter. These muscles, considered accessory to the internal obturator, externally rotate the thigh when extended and abduct it when flexed. The superior gemellus is innervated by the nerve to the internal obturator, and the inferior gemellus by the nerve to the quadratus femoris, with vascularization from the ischiatic and obturator arteries.

The quadratus femoris is a flat, quadrangular muscle located between the inferior gemellus and the superior margin of the adductor magnus. It originates from the external surface of the ischial tuberosity and inserts onto the intertrochanteric crest of the femur. This muscle also functions as an external rotator of the thigh, innervated by the nerve to the quadratus femoris (L5 and S1), and is vascularized by branches from the ischiatic artery and the deep femoral artery.

The external obturator is a flattened, triangular-shaped muscle originating from the external surface of the obturator membrane. Its tendon passes behind the articular capsule to insert into the trochanteric fossa of the femur, functioning as an external rotator of the thigh. It is vascularized by the obturator artery and innervated by the obturator nerve (L3 and L4).

The tensor fasciae latae is the most superficial and anterior muscle, aiding the gluteus medius and minimus in hip abduction. Posterior to it lies the gluteus maximus, which covers the other muscles in the compartment and is involved in trunk extension, maintaining posture, and extending and externally rotating the thigh. Beneath the gluteus maximus are the gluteus medius and gluteus minimus, which attach to the ilium and greater trochanter and are essential for hip abduction and maintaining an upright posture during walking.

Deep in the gluteal region are the short external rotators of the femur, which include the piriformis, the superior gemellus, the internal obturator, the inferior gemellus, the external obturator, and the quadratus femoris. These muscles run transversely from the pelvis to the proximal femur, providing external rotation and posterior stabilization of the hip joint.

Muscles of the posterior region

In the posterior region of the thigh, the muscles responsible for hip extension and leg flexion are the biceps femoris, semitendinosus, and semimembranosus—collectively known as the hamstrings. These muscles originate from the ischial tuberosity and insert distally onto the fibula and tibia via their tendons and ligamentous attachments, such as the pes anserinus. The hamstrings play a crucial role in protecting the hip and knee joints during movement.

The biceps femoris is situated in the posterolateral region of the thigh. It has two heads: the long head originates from the ischial tuberosity, sharing a common tendon with the semitendinosus, while the short head arises from the lateral lip of the linea aspera and the lateral supracondylar line. The long head forms a fusiform muscle belly that descends laterally, crossing the sciatic nerve, and continues into an aponeurosis that also receives fibers from the short head. The muscle then narrows into a tendon that bifurcates—one part wrapping around the lateral collateral ligament and attaching to the fibular head, and the other inserting into the lateral condyle of the tibia. It is innervated by the sciatic nerve (L5, S1) and vascularized by branches of the ischiatic artery, internal pudendal artery, circumflex femoral artery, and perforating arteries.

The semitendinosus is located in the posteromedial region of the thigh. It shares its origin with the long head of the biceps femoris at the ischial tuberosity. The muscle belly is fusiform and ends slightly below the midpoint of the thigh, where it transitions into a long tendon. This tendon courses along the surface of the semimembranosus, wraps around the medial condyle of the tibia, and inserts onto the upper part of the medial surface of the tibia, posterior to the sartorius and distal to the gracilis. The semitendinosus is innervated by the sciatic nerve (L5, S1) and receives blood supply from the ischiatic, internal pudendal, circumflex femoral, and perforating arteries.

The semimembranosus also lies in the posteromedial region of the thigh. It originates from a long, flat tendon at the ischial tuberosity, positioned laterally to the biceps femoris and semitendinosus tendons. The tendon runs medially alongside the adductor magnus, expanding into an aponeurosis that extends deep to the semitendinosus. Muscle fibers emerge from this tendon around the midpoint of the thigh, converging into another aponeurosis that narrows into a tendon, which inserts onto the posterior surface of the medial tibial condyle. The semimembranosus is innervated by the sciatic nerve (L5, S1) and vascularized by branches from the ischiatic, internal pudendal, circumflex femoral, and perforating arteries.

Functionally, the posterior thigh muscles flex the leg at the knee when the femur is fixed, and extend the hip when the pelvis is fixed, acting as antigravity muscles. In a semi-flexed knee position, the biceps femoris functions as an external rotator, while the semitendinosus and semimembranosus act as internal rotators.

Muscles of the anterior thigh region

The sartorius and the quadriceps femoris are key muscles in the thigh, contributing to complex movements of the hip and knee. The sartorius muscle is involved in flexion, abduction, and external rotation of the thigh and has an important relationship with the tensor fasciae latae, positioned anteriorly and medially. The space between these two muscles serves as an anterior approach to the hip during surgical procedures.

The quadriceps femoris is composed of four heads: the rectus femoris, vastus lateralis, vastus medialis, and vastus intermedius. This muscle group is the primary extensor of the leg at the knee joint. The rectus femoris, which originates from the pelvis, also assists in hip flexion. Among the quadriceps, the tensor fasciae latae, sartorius, and rectus femoris act on both the hip and knee joints, while the vastus medialis, vastus lateralis, and vastus intermedius act solely on the knee joint.

The tensor fasciae latae is a thin, flat muscle located in the upper external part of the thigh. It originates from the anterior edge of the lateral lip of the iliac crest, the lateral surface of the anterior superior iliac spine, and the underlying notch, inserting into the iliotibial tract between the middle and upper thirds of the thigh. It is innervated by the superior gluteal nerve (L4 and L5) and vascularized by the superior and inferior gluteal arteries. Through the iliotibial tract, it extends and externally rotates the leg, also participating in thigh abduction and internal rotation. In a standing posture, it contributes to pelvic stabilization.

The sartorius is a narrow, ribbon-like muscle originating from the anterior superior iliac spine and the upper half of the underlying notch. It crosses the thigh obliquely and descends vertically along the medial side of the knee. Its fibers continue into a flat tendon that expands into a broad aponeurosis, attaching to the upper part of the medial margin of the tibia, anterior to the gracilis and semitendinosus muscles, forming the pes anserinus. The sartorius aids in flexion of the leg at the knee and flexion of the thigh at the hip, as well as in abduction and external rotation of the thigh. It is innervated by the femoral nerve (L2 and L3) and receives blood supply from branches of the femoral artery.

The quadriceps femoris nearly covers the femur anteriorly, medially, and laterally. Its four components—rectus femoris, vastus lateralis, vastus medialis, and vastus intermedius—converge in the lower thigh to form the quadriceps tendon, which attaches to the patella and continues as the patellar ligament to the anterior tibial tuberosity.

The rectus femoris is the only biarticular muscle of the quadriceps, crossing both the hip and knee joints. It originates from the anterior inferior iliac spine via a direct tendon and from the acetabulum via a reflected tendon. The muscle ends in a broad, thick aponeurosis that narrows into a tendon, inserting at the base of the patella as part of the quadriceps tendon.

The vastus lateralis is the most voluminous of the quadriceps muscles, originating from the intertrochanteric line via a broad aponeurosis. Its muscle mass extends distally, forming a robust aponeurosis that narrows into a tendon and inserts onto the base and lateral margin of the patella.

The vastus medialis arises from the lower intertrochanteric line, the spiral line, and the medial lip of the linea aspera, with most fibers inserting onto the medial margin of the patella.

The vastus intermedius originates from the lateral and anterior surfaces of the proximal two-thirds of the femoral shaft, with bundles terminating in an aponeurosis that attaches to the lateral margin of the patella and the lateral condyle of the tibia. The articular muscle of the knee may be separate or fused with the vastus intermedius, consisting of bundles originating from the anterior surface of the distal femur and inserting into a superior recess of the synovial joint membrane of the knee.

Both the quadriceps femoris and the articular muscle of the knee are innervated by the femoral nerve (L3 and L4) and receive blood supply from the deep femoral artery, perforating arteries, and knee joint arteries. The primary function of the quadriceps is to extend the leg at the knee. Additionally, the rectus femoris contributes to flexing the thigh at the hip or, if the thigh is fixed, to flexing the pelvis.

Muscles of the medial thigh region

The medial thigh muscles, including the gracilis, pectineus, long adductor, short adductor, and large adductor, all traverse the hip joint. However, only the gracilis also crosses the knee joint.

The gracilis, the most superficial and thin muscle in this group, originates from a thin aponeurosis on the medial margin of the lower half of the pubic body and the adjacent ascending ramus of the ischium. Its fibers descend vertically, converge into a cylindrical tendon, cross the medial femoral condyle and medial tibial plateau, then fan out to insert on the upper part of the medial surface of the tibia. The gracilis is innervated by fibers from the obturator nerve (L2) and supplied with blood by the obturator artery. It functions to flex and internally rotate the leg and also contributes to thigh adduction

The pectineus is a flat, quadrangular muscle located in the femoral triangle. It originates from the pectineal crest of the pubis, with fibers running downward, backward, and laterally to insert along the line connecting the lesser trochanter to the linea aspera (pectineal line). It is innervated by the femoral nerve (L2 and L3) and receives blood supply from the obturator artery and the femoral circumflex artery. The pectineus adducts and flexes the thigh at the pelvis.

The long adductor is the most anterior of the adductor muscles, characterized by its broad, fan-shaped structure. It originates from the body of the pubis at the angle between the pubic crest and pubic symphysis, and expands into a broad belly that runs downward, backward, and laterally to insert via an aponeurosis on the linea aspera, at the middle third of the diaphysis. Its blood supply comes from the femoral artery, and it is innervated by the anterior branch of the obturator nerve (L2, L3).

The short adductor, a triangular muscle, originates from the external surface of the pubic bone and runs backward, laterally, and downward to insert onto the femur along a line from the lesser trochanter to the linea aspera. It is vascularized by the femoral artery and innervated by the obturator nerve (L2 and L3).

The large adductor is a robust, triangular muscle originating from the lower ramus of the pubis, the lower ramus of the ischium, and the inferior lateral aspect of the ischial tuberosity. The portion originating from the pubic ramus runs horizontally to insert on the femur's gluteal tuberosity, while fibers from the ischial ramus fan out downward and laterally to attach to the linea aspra and proximal part of the medial supracondylar line. The middle part of the muscle, arising from the ischial tuberosity, descends almost vertically and continues into a cylindrical tendon that inserts into the medial condyle. This long insertion is interrupted by fibrous arches attached to the bone. The large adductor is vascularized by the femoral artery and innervated by both the obturator nerve and the tibial component of the sciatic nerve (L2, L3, L4). Overall, the primary function of these muscles is thigh adduction, which aids in locomotion and posture. Additionally, the large adductor and long adductor also contribute to internal rotation of the thigh.

BLOOD SUPPLY TO THE HIP

The arterial blood supply to the musculoskeletal components of the hip joint is provided by the common iliac artery, a terminal branch of the abdominal aorta. The common iliac artery originates at the level of the L4 vertebra and runs downward and laterally to the sacroiliac joint, where it divides into the internal and external iliac arteries.

The internal iliac artery divides into an anterior trunk, giving rise to the obturator artery and the inferior gluteal artery, and a posterior trunk, giving rise to the iliolumbar artery and the superior gluteal artery:

- Obturator artery leaves the pelvic cavity through the obturator foramen to reach the thigh. It supplies the obturator internus and externus muscles, the pectineus, the adductors, and the quadratus femoris.

- Inferior gluteal artery passes between the first branches of the sacral plexus and the piriformis and coccygeus muscles, exiting the pelvis. It supplies the coccygeus, piriformis, gluteus maximus, obturator internus, gemelli, quadratus femoris, adductor magnus, and the sciatic nerve.

- Iliolumbar artery ascends into the iliac fossa and divides into lumbar and iliac branches. It supplies the iliopsoas, quadratus lumborum, and the lumbar spine. The iliac branch anastomoses with the deep iliac artery, a branch of the external iliac artery.

- Superior gluteal artery continues from the posterior trunk, running downward and posteriorly, exiting the pelvis through the greater sciatic foramen. It supplies the piriformis, obturator internus, gluteus minimus, and gluteus medius.

The external iliac artery, larger in caliber than the internal iliac artery, is the direct continuation of the common iliac artery. After passing the inguinal ligament, it enters the thigh as the femoral artery.

The femoral artery runs within a neurovascular bundle in the femoral triangle of Scarpa. As it continues, the femoral artery moves medially, passing through the adductor canal and becoming the popliteal artery. The main branch is the profunda femoris artery, which originates shortly after the inguinal ligament and runs between the muscles of the medial compartment, penetrating the adductor magnus with four perforating arteries and passing into the popliteal fossa. It supplies a vast territory, including the quadriceps femoris, adductor muscles, and the muscles of the posterior compartment.

The anastomotic circulation of the hip, important in relation to pathology, is established both at the level of the pelvis and the proximal femur. At the pelvis level, it occurs between the deep circumflex iliac artery (branch of the external iliac), the iliolumbar artery, and the superior gluteal artery superiorly, and between the obturator artery and the inferior epigastric artery (external iliac) inferiorly.
At the proximal femur level, it occurs between the lateral femoral circumflex artery, the first perforating branch of the profunda femoris, the inferior gluteal artery, the obturator artery, and the medial femoral circumflex artery. The terminal branches of this anastomotic network cross the capsule to reach the acetabulum and femoral head. The posterior and posterosuperior parts of the capsule are supplied by the superior and inferior gluteal arteries proximally, while the anterior part is supplied by the medial and lateral femoral circumflex arteries distally. The orientation and contribution of these vessels to the capsule's blood supply are significant

for surgical approaches, particularly in conservative surgery: the capsule should be cut medio-proximally for anterior approaches and latero-distally for posterior approaches.

Among all the vessels contributing to the anastomotic network of the hip, the medial femoral circumflex artery plays a crucial role. It provides terminal branches responsible for most of the blood supply to the femoral head at the posteromedial base of the femoral neck.

Understanding the blood supply to the hip joint is crucial from both clinical and surgical perspectives: various pathologies and treatments can disrupt blood flow to the femoral head, promoting femoral head necrosis and worsening pain symptoms. Furthermore, surgical damage to the blood supply of the pelvis and femur can be a severe, potentially lethal complication, given the large caliber and high flow rate of some of these vessels (e.g., iliac and femoral arteries).

Neuroanatomy of the hip

The neuroanatomy of the lower limb is characterized by the presence of two major nerve plexuses: the lumbar plexus, formed by the nerve roots from L1 to L4, with some fibers from T12, and the sacral plexus, which includes the roots from part of L4 to S3, with some contribution from S4.

The lumbar plexus is located posterior to the psoas major, anterior to the transverse processes of the lumbar vertebrae. It consists of a series of anastomotic arches that give rise to numerous nerves, among which the obturator and femoral nerves are the most significant, though other nerves also originate from this plexus.

In the anterior thigh, <u>the lateral femoral cutaneous nerve</u> (L2-L3) branches from the lumbar plexus roots, travels through the iliac fossa, and emerges in the thigh beneath the inguinal ligament near the anterior superior iliac spine. In the thigh, it lies between the subcutaneous tissue and the muscle fascia, providing sensory innervation to the lateral thigh and part of the buttock skin. This nerve is clinically important in anterior hip surgery.

The <u>obturator nerve</u> (L2-L3-L4, anterior roots) initially travels through the psoas major, emerges medially, and continues alongside the obturator internus, exiting the pelvis through the obturator foramen. It then divides into anterior and posterior branches in the thigh. It provides motor innervation to the obturator internus and adductor muscles of the medial thigh. Sensory-wise, it is responsible for the lower half of the medial thigh.

The <u>femoral nerve</u> (L2-L3-L4, posterior roots) descends laterally through the iliopsoas bundles, then enters the thigh beneath the inguinal ligament, lateral to the femoral artery. It innervates the iliopsoas muscle before dividing into four branches: two anterior, the lateral femoral cutaneous nerve, providing motor innervation to the sartorius muscle and sensory to the anterior thigh skin, and the medial femoral cutaneous nerve, providing motor innervation to the pectineus and adductor longus muscles and sensory to the upper-medial thigh skin; and two posterior, the saphenous nerve, providing sensory innervation to the patella, knee, medial leg, and dorsomedial foot skin, and the quadriceps nerve, providing motor innervation to the four heads of the quadriceps muscle.

The sacral plexus, initially ribbon-like, gives rise to numerous motor branches for the local muscles before exiting the pelvis through the greater sciatic foramen as the sciatic nerve. These include the nerve to the quadratus femoris and inferior gemellus (L4-L5), the nerve to the obturator internus and superior gemellus (L5-S1), the nerve to the piriformis (S1-S2), the superior gluteal nerve (L4-L5-S1), the inferior gluteal nerve (L5-S1-S2), and the posterior cutaneous nerve of the thigh (S1-S2-S3-S4).

The sciatic nerve (L4-L5-S1-S2-S3) is the largest and longest nerve in the body and is the direct continuation of the sacral plexus. It exits the pelvis through the greater sciatic foramen, passing between the piriformis and superior gemellus. It descends in the posterior thigh, passing between the greater trochanter and the ischial tuberosity, separated from the hip joint by the quadratus femoris muscle. It innervates the posterior compartment muscles and the adductor magnus muscle, with sensory branches to the hip joint, and innervates the posterior leg muscles, plantar muscles of the foot, and the skin of the posterior leg, plantar foot, and dorsal phalanges. The common peroneal nerve (or common fibular nerve) innervates the lateral and anterior leg muscles, the dorsal foot muscles, and the anterolateral leg and dorsal foot skin.

BIOMECHANICS OF THE HIP JOINT

The hip joint has a particularly complex muscular structure with several fundamental functions:

- Movement of the hip in all three planes of space

- Balance in both bipodal and monopodal stance

- Antigravity function for maintaining an upright posture

Hip movements

The hip joint is the most stable joint in the human body, with the lowest dislocation frequency due to the significant congruence of the joint surfaces. The movements allowed by the hip include flexion-extension in the sagittal plane, abduction-adduction in the coronal (frontal) plane, and internal-external rotation in the axial plane. The center of the femoral head serves as the pivot point for these movements. The hip's range of motion is influenced by the movements of adjacent joints and the position of the pelvis.

Flexion brings the anterior surface of the thigh closer to the trunk, facilitated by the iliopsoas, rectus femoris, sartorius, and tensor fasciae latae muscles. Extension is the opposite movement, taking the limb posteriorly, involving the hamstrings and the gluteus maximus. Hip mobility decreases with age, but the degree of functional limitation varies. For example, during normal walking, the hip moves from about 30° of flexion to 10° of extension. Therefore, a reduction in flexion is tolerated even at large degrees, while even a slight loss of extension can cause severe functional limitations.

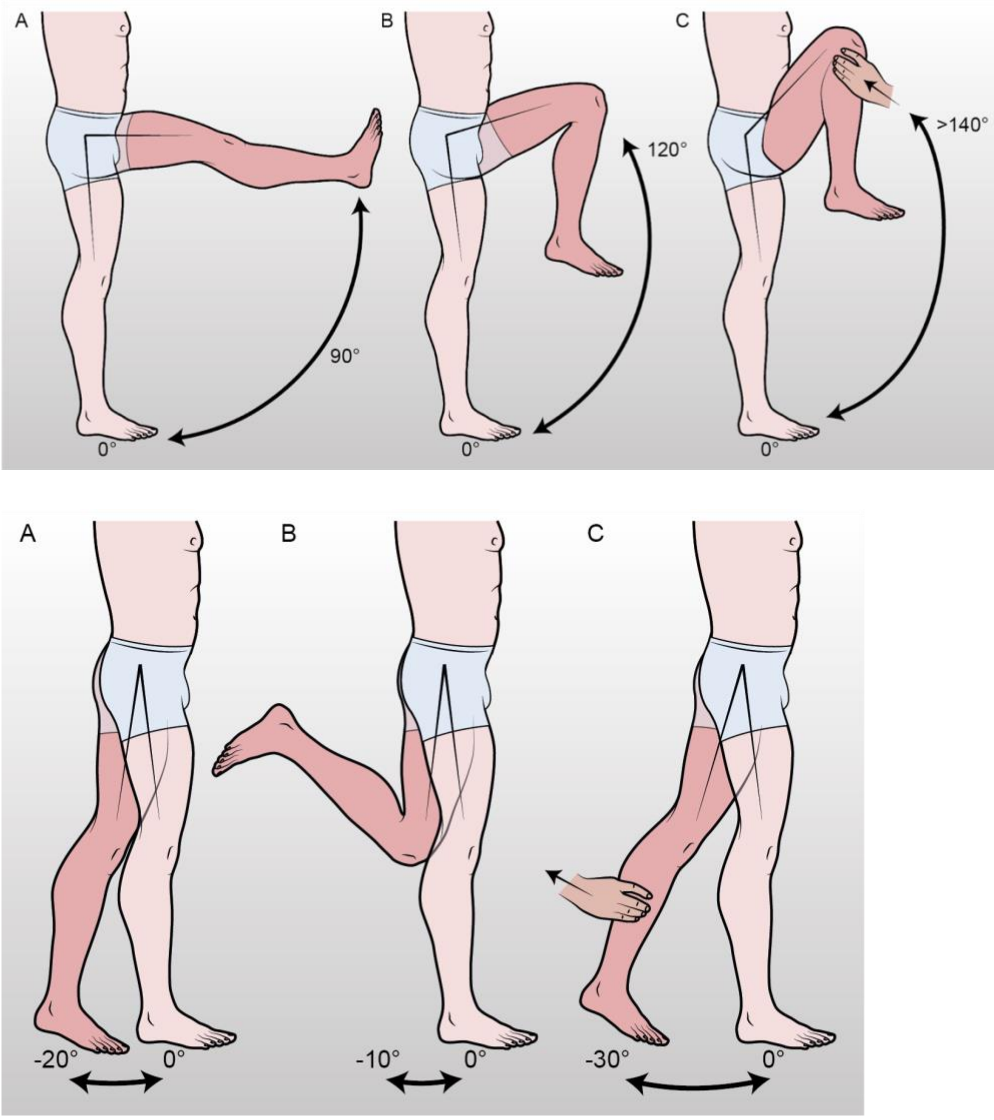

Figure 5. Hip mobility

Abduction is the movement of the limb away from the body's midline, mainly involving the gluteus medius, gluteus minimus, tensor fasciae latae, and piriformis muscles. Adduction brings the limb closer to the midline, sometimes even crossing it.

External rotation moves the foot outward when the patient is supine with an extended knee, while internal rotation is the opposite movement. In a seated patient, this rotation affects the entire leg.

The relationship between the hip, pelvis, and spine, and the changes that occur from standing to sitting, are particularly significant. In an erect posture, the pelvis is tilted forward, the spine is in lordosis, and the lower limbs are extended. This configuration balances the trunk on the pelvis and positions the acetabulum to cover the femoral head. When sitting, the pelvis tilts backward, reducing lumbar lordosis and causing the femur to flex only 55°-70° relative to the pelvis. Since the acetabulum is part of the pelvis, pelvic retroversion is accompanied by increased acetabular anteversion and inclination, allowing normal femoral flexion and internal rotation. These adjustments are crucial for spinal pathophysiology and surgery.

The stability of the hip joint is determined by the anatomical configuration of the skeleton and the action of surrounding soft tissues. Under load, gravity alone can maintain the femoral head in place, with the focal point of this balance being the contact between the acetabular roof and the femoral head. The orientation of the acetabulum plays a structural role in maintaining stability, with its normal antero-inferior and lateral inclination covering the femoral head. Femoral anatomy also plays a role, with physiological variations that favor either stability or mobility. For instance, a longer femoral neck, a femoral head larger than two-thirds of a sphere, and an increased cervico-diaphyseal angle provide greater mobility. Conversely, opposite characteristics reduce the joint's range of motion in favor of stability. Muscles and the joint capsule also contribute to the hip joint's stability.

Pelvic Balance in Bipodal and Unipodal stance

One of the main functions of the hip joint is to maintain pelvic balance in the frontal plane. This can occur in two conditions: bipodal stance, which is primarily seen in static standing, and unipodal stance, characteristic of the swing phase of the contralateral limb during the gait cycle.

In bipodal stance, with equal leg lengths, the pelvis is usually horizontal.

Anatomical leg length discrepancy can be either primary or acquired. Primary discrepancies include congenital developmental alterations or growth anomalies, with the frequency inversely proportional to the extent of the discrepancy.

- Discrepancies up to 9 mm are extremely common, seen in up to 70% of the general population without significant symptoms.

- Discrepancies between 1cm and 2 cm affect about 14% of the general population and are usually asymptomatic.

- Discrepancies over 2 cm occur in about 1 in 1000 people and are associated with gait alterations or compensatory postures. These are often congenital.

Acquired discrepancies include the results of fractures, degenerative orthopedic conditions, and post-surgical outcomes affecting the pelvis and lower limbs.

- Fracture-related discrepancies are classified by the type of defect. Shortening typically results from improper healing in adults, while lengthening may occur in growing children due to hyperactivation of growth cartilage stimulated by the fracture.

- Progressive cartilage degeneration in osteoarthritis leads to a gradual shortening of the limb.

- Surgical interventions, both replacement (prosthesis) and non-replacement (osteotomies), can alter overall limb length.

Anatomical discrepancies are typically compensated by pelvic obliquity within the first 10 mm and are asymptomatic. As the discrepancy exceeds one-centimeter, various compensatory mechanisms come into play, including knee flexion, which becomes noticeable beyond 2.5 cm. Pelvic balancing occurs in three ways:

1. Coronal plane rotation, where the pelvis drops on the shorter side.

2. Translation, where the pelvis shifts Antero posteriorly, moving the center of gravity toward the shorter limb, making the relatively shorter limb adducted and the longer limb abducted.

3. Sagittal plane rotation, with the pelvis making compensatory movements effective in limb length discrepancies, affecting both standing and walking. This leads to hip and knee flexion on the longer side and hip, knee, and ankle extension on the shorter side. Larger discrepancies often require shoe lifts for compensation.

Functional leg length discrepancy results from pelvic obliquity due to a hip joint stiffness, perceived as a discrepancy even when the legs are equal in length. The perceived longer limb is in abduction, while the perceived shorter limb is in adduction. This can be secondary to altered joint mechanics, such as joint contractures, mechanical axis deviations of the lower limbs, and muscle weakness or tightness leading to alignment changes.

Distinguishing between anatomical and functional discrepancies is crucial for treatment strategies. Anatomical discrepancies are compensated with shoe lifts, while functional discrepancies worsen with lifts and require restoring the balance between hip abduction and adduction. Identifying and correcting the cause of the blockage, whether muscular or mechanical, is necessary. Physiotherapy is often required to balance muscle action, typically involving stretching the adductors on the perceived shorter side and the abductors on the perceived longer side.

The patient's perception of discrepancy varies and depends on its onset. Primary or degenerative discrepancies allow time for compensatory mechanisms to develop, leading to better tolerance. However, post-traumatic or iatrogenic discrepancies arise quickly, limiting the development of compensation and resulting in poor tolerance.

The pelvis's position in space is secondary to the forces acting on it and closely related to hip joint biomechanics. The hip acts as a first-type lever with the fulcrum at the joint's center of rotation, with forces from body weight medially and abductor muscle tension laterally. This system, traditionally known as Pauwels' balance, honors the scholar who first described it mechanically.

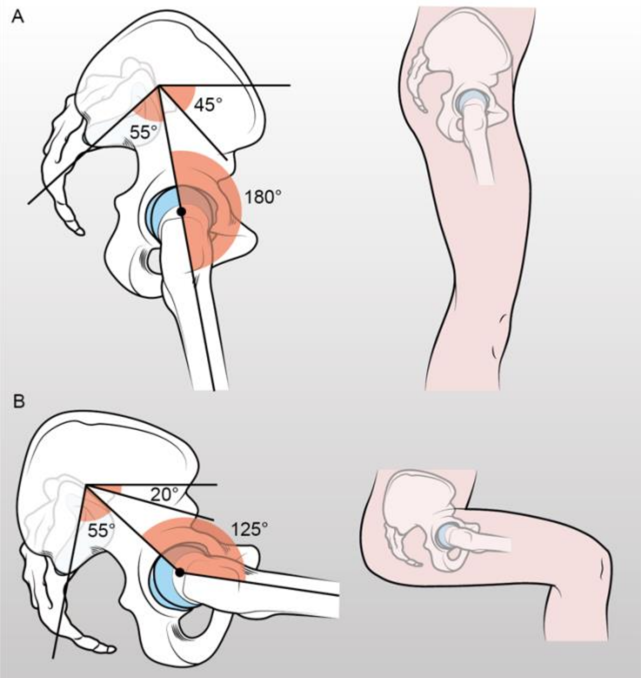

Figure 6. Pelvis and acetabular position when standing (A) and sitting (B)

Biomechanics of Bipodal Stance

In bipodal stance, the balance is maintained by the abductor and adductor muscles of the hip, whose forces counterbalance each other to keep the pelvis stable. Any alteration in one of the components of Pauwels' balance affects the pelvic equilibrium. Significant changes in this balance mechanism are determined by factors such as the position of the center of rotation (the fulcrum of the lever), femoral offset (proportional to the abductor muscle lever arm length), and the tension of the adductor and abductor muscles (which depends on the limb length). Alterations in these parameters are fundamental to the development of anatomical and functional discrepancies, particularly after hip surgeries:

<u>1. Changes in the Center of Rotation:</u>

- The hip's center of rotation is influenced by both the femoral and acetabular components. It is the fulcrum for all hip movements, particularly for the abductor lever. Its position can be altered by hip joint pathologies (such as congenital hip dysplasia, Legg-Calvé-Perthes disease, epiphysiolysis, severe coxarthrosis) or by corrective (femoral and acetabular osteotomies) or replacement (hip prosthesis) surgeries.

- Lateralization: Reduces the abductor muscle lever arm, decreasing its contractile effectiveness and causing abductor insufficiency symptoms. This is typically seen in dysplastic hips.

- Medialization: Increases the abductor muscle lever arm, enhancing its contractile effectiveness. While sometimes desirable (in cases of preoperative abductor insufficiency), it can cause an abducted hip posture. This is a complication in hip replacement surgery in patients with coxa profunda, where the hip center is medialized.

- Proximalization: Causes progressive retraction and contracture of the adductor muscles on the affected side, leading to an adducted limb and pelvic translation toward the affected side during bipodal stance. This elevation of the rotation center is seen in congenital hip dislocation; restoring a physiological rotation center with a prosthesis may result in a functional limb length discrepancy.

- Distalization: Occurs after surgeries such as pelvic osteotomies that can restore a proximally and laterally displaced pathological rotation center to a physiological position.

2. Changes in Femoral Offset:

- Femoral offset determines the abductor muscle lever arm (Bm), and increasing it enhances the muscles' efficiency. In a normal hip, the offset is dependent on the cervico-diaphyseal angle of the femur. An angle below 120° (coxa vara) is associated with an increased offset, while an angle above 135° (coxa valga) is associated with a decreased offset. Evaluating and restoring the offset is crucial in hip replacement surgery. Some prosthetic designs allow for an increased offset to compensate for abductor muscle hypofunction or excessive medialization of the rotation center.

3. Muscle Tension:

- The reciprocal positions of the femur and pelvis in space result from the balance of the abductor and adductor muscles. This tension is closely related to any discrepancies in leg lengths. Shortening of the lower limb (as seen in hip osteoarthritis) leads to shortening of the abductor muscles and contracture of the adductor muscles. This imbalance causes compensatory pelvic obliquity through rotation and translation in the coronal plane. Restoring limb length through surgery can lead to two distinct situations:

  - Adductor Prevalence: In cases of adductor prevalence, with no significant discrepancy (<2.0cm), the patient has limited active and passive hip abduction. In bipodal stance, the center of gravity shifts toward the adductor-prevalent side, with the limb presenting an adducted posture and apparent limb shortening.

  - Abductor Prevalence: In cases of abductor prevalence, with no significant discrepancy (<2.0cm), the patient has limited active and passive hip adduction. In bipodal stance, the center of gravity shifts toward the contralateral side, with the limb presenting an abducted posture and apparent limb lengthening.

Achieving balance in unipodal stance results from the balance of muscle levers acting on the hip fulcrum. Gravity pulls the contralateral hemipelvis downward in the absence of abductor muscle forces. Consequently, reconstructing the gluteal muscles is crucial in surgical approaches that detach or weaken these muscle groups (such as the direct lateral approach to the hip and surgeries involving greater trochanter osteotomy that require osteosynthesis).

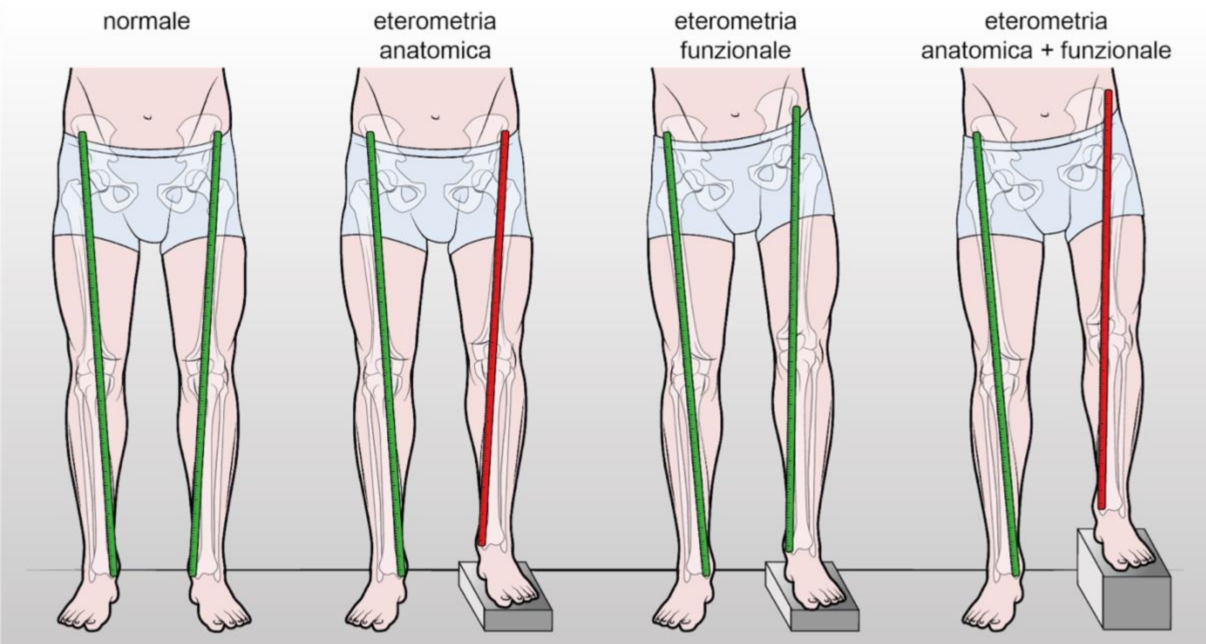

Figure 7. The pelvis is horizontal when there is no legs length discrepancy (A). When there is anatomical discrepancy (B), the shorter limb needs to be compensated in order to maintain the pelvis horizontal. In functional discrepancy, there is not actual legs length discrepancy, but the abducted limb is perceived as longer (or the adducted limb as shorter), therefore if the functional discrepancy is compensated, the pelvis is not horizontal (C). When both anatomical and functional discrepancy are present (D), compensating the defect requires a higher heel and the pelvis remains inclinated.

HIP OSTEOARTHRITIS

Definition

Osteoarthritis of the hip, or coxarthrosis, is characterized by a combination of symptoms and radiographic changes due to the degeneration of articular cartilage. It typically involves both the femoral and acetabular components of the hip. The onset of symptoms is usually insidious, with a progressive worsening of the clinical condition. Coxarthrosis can be primary or secondary, with primary coxarthrosis diagnosed by excluding all secondary causes.

Epidemiology

The hip is the third most commonly affected joint by osteoarthritis[15], following the knee and the lumbar spine, mainly due to the high loads it endures during daily activities, its significant intrinsic mobility, and the high congruence of the articular surfaces. It has a slightly higher prevalence in females, and the incidence increases proportionally with age, with about 60% of individuals over 65 showing radiographic signs of osteoarthritis. The prevalence is higher in Caucasians of European origin compared to Hispanics, African Americans, and Asians, suggesting a possible genetic etiology.

Pathogenesis

The development of primary coxarthrosis is influenced by genetic predisposition, hormonal factors, and lifestyle. Estrogens have a protective effect, which explains the increased incidence of coxarthrosis in women post-menopause. Conversely, an excess of growth hormone (GH) can promote early onset. Other predisposing factors include high body weight, heavy labor, and sports involving running and jumping.

Secondary coxarthrosis can result from various hip conditions. The main causes include deformities and post-traumatic conditions. Deformities lead to abnormal load distribution and subsequent degenerative lesions, while post-traumatic causes often involve impaired blood supply to the femoral head or damage to the articular cartilage.

Pathological Anatomy

The damage initially affects the articular cartilage, which has limited regenerative capacity, leading to progressive degeneration and exposure of the underlying subchondral bone. Cartilage damage usually starts in the anterolateral acetabular region, the area subjected to the highest load, and progresses centripetally. In early stages, the acetabular labrum undergoes metaplastic calcification, contributing to altered joint mechanics and the formation of large peri-acetabular osteophytes in advanced stages.

The degenerative process also affects the capsular ligaments, leading to thickening and fibrosis, which can involve the hip's external rotators, causing the affected limb to assume an externally rotated position. The joint capsule is richly innervated, particularly in the posterior-inferior region. When affected by pathology, abduction and internal rotation movements can cause tension and muscle spasms, further limiting internal rotation and promoting an adducted-external rotation posture.

Anterior capsule thickening and fibrotic involvement of the iliocapsular and iliopsoas muscles result in irreducible flexion, adduction, and external rotation of the hip. This flexion contracture impairs functional movement since, during weight-bearing, the hip is normally extended and internally rotated, providing maximum contact surface and stability. Inability to fully extend the hip accelerates degeneration due to reduced contact area and increased mechanical wear.

Clinical Presentation

The typical age of clinical onset is over 55, although the degenerative process begins much earlier and progresses asymptomatically. The late onset of pain has anatomical and pathophysiological reasons. The structures with the most sensory afferents in the hip joint are the acetabular labrum and the posterior-inferior capsule, which are rarely stressed in daily movements. Early calcification of the labrum further reduces sensory input, delaying the onset of pain.

Patients with primary coxarthrosis often present with advanced radiographic osteoarthritis, reduced range of motion due to mechanical block (sometimes leading to sub-ankylosis), but with minimal or recent pain onset. When symptomatic, pain is usually localized to the groin and trochanteric region, radiating to the anteromedial thigh and knee. Initially, pain occurs upon waking or after inactivity, improves with movement, and subsides with rest. In advanced stages, pain becomes constant, worsened by weight-bearing, posture changes, and walking.

Functional limitation is characterized by progressively decreased joint movements due to anatomical alterations and reflexive muscle contractures. Disease progression leads to increased deformity and loss of joint sphericity, reducing movement in all planes, with abduction and internal rotation being the first to be lost, followed by flexion-extension.

At rest, the lower limb typically appears slightly adducted, externally rotated, and moderately flexed. Clinically, the hip is very painful during movement, with significant reduction in passive abduction and blocked internal rotation. Crepitus and joint irregularities may be felt during examination.

These pathological changes result in altered gait, often with an antalgic limp, where the swing phase is increased, and the stance phase is reduced to minimize weight-bearing on the affected hip. Progressive deformity and pain lead to muscle atrophy in the pelvic girdle, particularly the hip abductors, resulting in a positive Trendelenburg sign. Decreased joint function impairs simple tasks like climbing stairs and putting on socks.

Differential diagnosis should exclude lumbar spine issues (cruralgia or sciatica), which can refer pain to the trochanteric, inguinal, and crural regions. This is challenging as coxarthrosis often coexists with polyarticular osteoarthritis. Other conditions like inguinal hernias, renal colic, pelvic tumors, and adnexitis must also be considered.

Osteoarthritis typically progresses with recurring chronic symptoms, alternating between remission and exacerbation. However, the slow progression invariably leads to worsening disability. This process accelerates with multiple risk factors, particularly in older, osteoporotic, obese females, and those with chondrocalcinosis, leading to severe, destructive osteoarthritis ("rapidly destructive arthrosis").

Radiologic assessment

The first-level investigation, often sufficient for diagnosing coxarthrosis, is the X-ray. This should be performed on the pelvis to evaluate both the affected and the contralateral hip, as well as the sacroiliac joints, which can be inflamed in the case of osteoarthritis and act as a confounding factor clinically.

Along with the pelvic X-ray, axial X-rays of the hip should be performed to assess the anatomical changes of the femoral head on the lateral plane. Typical changes observed in X-rays characteristic of osteoarthritis include:

- Reduction of the joint space
- Subchondral bone sclerosis
- Presence of subchondral cysts (geodes)
- Osteophytes
- Joint deformities

Figure 8. A. X-ray of the pelvis, showing a severe osteoarthritis of the right hip. B and C. MRI and CT scan of the same patient

In cases of severe deformities or significant bone loss, a CT scan can be useful to complete the diagnostic process, especially for surgical planning purposes.

MRI is considered a third-level examination in osteoarthritis to evaluate muscle trophism and exclude secondary causes of pain, such as neoplastic lesions of the soft tissues, early or undiagnosable conditions with conventional radiology (such as osteonecrosis and synovitis), or to exclude potential differential diagnoses (such as complex regional pain syndrome, osteoid osteoma) that are not visible with conventional radiology.

Classification

Coxarthrosis can be classified based on radiographic findings. The most commonly used classifications are the Kellgren and Lawrence classification and the Tönnis classification.

The Lawrence classification, published in 1957, identifies four degrees of severity based on radiographic findings in the anteroposterior projection.

The Tönnis classification, more recent and dating back to 1972, identifies only three degrees of severity:

<u>Lawrence Classification</u>

- 0: No radiographic signs of osteoarthritis
- 1: Initial joint space narrowing (<2 mm) and possible osteophytes
- 2: Presence of osteophytes with initial joint space narrowing
- 3: Multiple osteophytes, joint space narrowing, subchondral sclerosis, and initial bone deformity
- 4: Large osteophytes, severe joint space narrowing, severe subchondral sclerosis, and marked bone deformities

Tönnis Classification

- 0: No signs of osteoarthritis
- 1: Mild
  - Subchondral bone sclerosis
  - Slight joint space narrowing
  - No or slight loss of sphericity of the femoral head
- 2: Moderate
  - Small cysts (geodes)
  - Moderate joint space narrowing
  - Moderate loss of sphericity of the femoral head
- 3: Severe
  - Large cysts (geodes)
  - Severe joint space narrowing or disappearance
  - Severe deformity of the femoral head

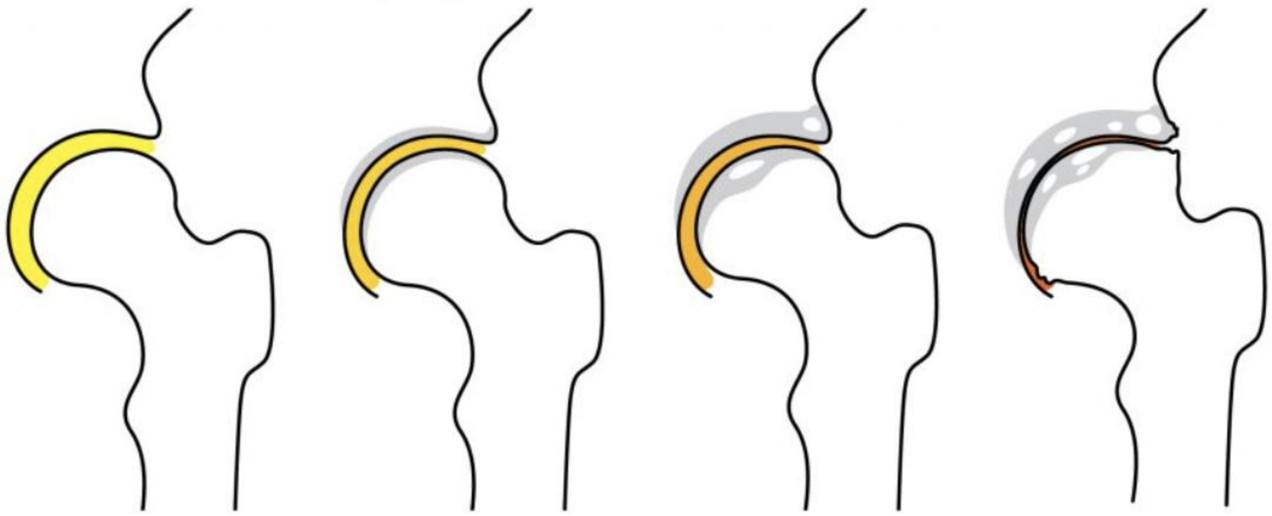

Figure 9. Tonnis classification of hip OA

Treatment

The treatment of hip osteoarthritis in the early stages is typically conservative and based on weight control, strengthening the pelvic girdle muscles with exercises that do not overload the joint (biking, swimming, bodyweight exercises), physical therapy for pain relief and anti-inflammatory purposes, postural exercises, and pharmacological treatment with anti-inflammatories (NSAIDs or corticosteroids) or pain relievers (opioids, acetaminophen). Patients should be informed about the progressive nature of primary coxarthrosis; symptom reduction is possible, but altering the natural course of the disease is not. Coxarthrosis is thus destined to worsen progressively until the joint deformity and pain become intolerable.

When symptoms become intolerable, surgical intervention is indicated. In the early, minimally symptomatic stages, in young patients (under 40) and selected cases, an arthroscopic treatment of cheiloplasty (removal of osteophytes), capsulotomy, and synovectomy may be indicated; however, this treatment only addresses symptoms. In more advanced stages, the only effective treatment to restore function and alleviate pain is total hip replacement surgery.

HIP REPLACEMENT

The prosthetic replacement of the hip joint is heralded as the surgical intervention of the century, owing to its high success rates and significant improvement in the patients' quality of life who undergo this treatment. Hip arthroplasty remains the treatment of choice for patients with severe joint destruction accompanied by limitations in movement and functional disability.

Three principal types of hip prostheses exist:

- **Hemiarthroplasties or partial prostheses**, which only replace the proximal epiphysis of the femur. They consist of a femoral stem and a hemispherical head articulating directly within the acetabulum (unipolar hemiarthroplasty) or a head articulating within a cup lodged in the acetabular cavity (bipolar hemiarthroplasties).

- **Total hip arthroplasties**, which replace both articular surfaces—namely the proximal epiphysis of the femur and the acetabulum.

- **Resurfacing prostheses**, which also replace both articular surfaces but conserve the proximal femoral bone, merely "resurfacing" it.

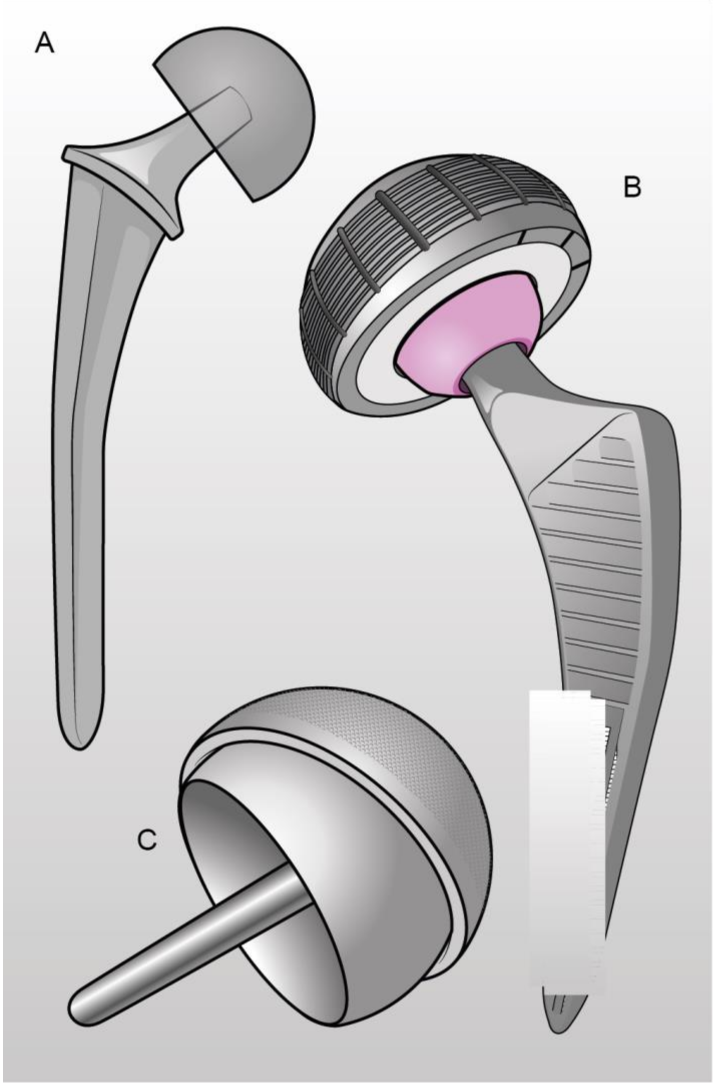

Figure 10. Hemiarthroplasty (A), total hip replacement (B), resurfacing (C)

Hemiarthroplasties, also known as partial prostheses, replace only the proximal epiphysis of the femur. Structured as a stem inserted into the femur and a hemispherical head replacing the bony head of the femur, the surface may articulate either with the native acetabulum or within a cup lodged in the acetabulum. The primary drawback of this type lies in the joint's limited stability, making it unsuitable for younger patients with high functional demands. It is not recommended for patients with primary hip osteoarthritis, as advanced-stage patients often already have compromised acetabula. However, it remains the preferred choice for elderly patients with femoral neck fractures, offering shorter surgical time and quicker postoperative recovery.

Total hip arthroplasties aim to replace both articulating surfaces of the hip. The prosthesis consists of an acetabular cup, liner, femoral head, and stem. The acetabular component is usually hemispherical or elliptical and is affixed using screws, cement, or a press-fit technique. Between the cup and the head lies the liner, a prosthetic structure made from various materials like ceramic, metal, or polyethylene, enhancing the prosthesis's overall stability.

Resurfacing prostheses preserve the proximal epiphysis of the femur and involve metal surfaces covering both the femoral and acetabular articulating surfaces. They offer advantages in load distribution, thus reducing the risk of dislocation. However, from a surgical standpoint, a larger incision is required for implantation, and there is an increased risk of femoral neck fractures.

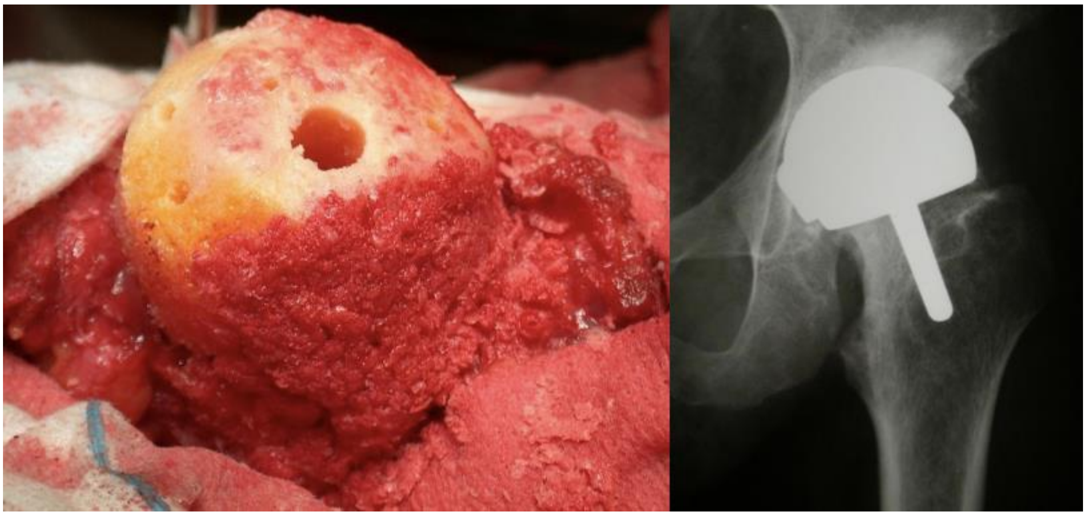

Figure 11. Resurfacing prosthesis.

All prostheses are constructed from metallic alloys designed to withstand loading forces. They adhere to the bone to achieve implant fixation, which can be either biological or cemented.

Biological fixation necessitates that the bone cavity for the prosthesis closely mirrors the implant's shape and is slightly smaller to promote primary stability (press-fit). The material must not only be biocompatible but also osteoconductive, facilitating osteointegration and subsequent secondary stability achieved within approximately six weeks.

Cemented fixation requires the bone cavity to correspond to the implant's shape but be slightly larger to accommodate a layer of cement.

The cement is a polymethylmethacrylate (PMMA) acrylic resin that, when mixed with a catalyst, initially assumes a viscous consistency. It subsequently hardens due to an exothermic reaction, permanently fixing the prosthesis to the bone.

Articular movement in total and resurfacing hip arthroplasties is facilitated by the head sliding within the acetabular insert or liner. Prosthetic coupling can be "hard-on-soft," where a hard head made of metal or ceramic articulates with a soft liner made of polyethylene, or "hard-on-hard," where both the head and liner are made of hard materials. Hard-on-hard couplings (Metal-on-Metal, Ceramic-on-Ceramic) have high resistance to wear but are prone to brittleness, while hard-on-soft couplings are less likely to break but may undergo more wear over time.

HISTORY OF PROSTHETIC REPLACEMENT AND CURRENT DEVELOPMENTS

The modern conception of hip prosthesis was introduced by Sir John Charnley in the 1960s. He pioneered the use of the metal-polyethylene pairing with small-sized heads and the cementation of prosthetic components using an acrylic cement, polymethylmethacrylate (PMMA). These innovations overcame the limitations of previous technologies, increasing implant longevity and substantially improving clinical outcomes. The prosthetic fixation to the bone was achieved.

Charnley's prosthesis was also characterized by the use of a monoblock femoral stem made of a metallic alloy, resulting in a low-friction metal-polyethylene prosthesis, conceptually identical to those used today.

From the 1960s to the present, numerous innovations have rendered the technologies introduced by Charnley obsolete. The development of ultra-high molecular weight polyethylenes, cross-linked and added with Vitamin E, as well as the introduction of new surfaces like ceramic, have virtually resolved the wear issue. Moreover, the study of osteointegration capabilities and biocompatibility of various materials, in the form of coatings or surface treatments, has reserved cementation for specific cases where the patient's biological potential is irreparably compromised. Recently, the assistance of 3D printers has allowed for the additive technology reproduction of the characteristic porosity of cancellous bone.

In recent years, innovations have been directed not only at prosthetic design but also in the search for minimally invasive surgical approaches to minimize soft tissue damage, reduce perioperative complications, and expedite functional recovery of the operated lower limb.

Indications for Hip Arthroplasty and Clinical-Diagnostic Evaluations

Hip arthroplasty serves as the treatment of choice for various pathological conditions of the hip joint, including primary hip osteoarthritis, avascular osteonecrosis of the femoral head, congenital hip dysplasia, slipped capital femoral epiphysis, rheumatoid arthritis, and other seronegative autoimmune arthritides. These conditions are characterized by arthritic degeneration of the joint. Another significant indication for hip replacement is medial femoral neck fractures. The primary aim of the surgical procedure is to alleviate pain, enhance joint mobility, and improve overall function, thereby elevating the patient's quality of life.

Absolute contraindications encompass local or systemic infectious states or severe comorbidities such as multi-organ failure, severe cardiovascular, respiratory, renal, and metabolic diseases. Neuromuscular disorders often constitute a relative contraindication for hip arthroplasty due to the elevated risk of postoperative complications like prosthetic dislocation.

Clinical Evaluation

Once the decision for hip arthroplasty is made, a comprehensive preoperative assessment of the patient is imperative. A detailed remote pathological history should seek to identify any absolute contraindications to the surgery, such as severe multi-organ insufficiencies that heighten perioperative mortality risk. The presence of significant cardiovascular, respiratory, renal, and metabolic conditions may necessitate a pre-admission anesthesiologic evaluation and specialized consultations. Furthermore, it is critical to examine any history of generalized or localized infections (e.g., urological, dental) that are either episodic or recurrent. Moreover, it is vital to investigate previous orthopedic conditions like fractures or joint deformities that might complicate the surgical procedure.

Physiological anamnesis should assess the patient's body habitus, potential presence of obesity, and muscular status. Information about the patient's profession, involvement in sports, and lifestyle habits will aid in understanding functional demands and surgical expectations. It is useful to inquire about ongoing pharmacological treatments (particularly anticoagulants or immunosuppressants requiring cessation or substitution before surgery) and lifestyle habits like smoking and alcohol consumption, as hospitalization could exacerbate withdrawal symptoms.

Recent pathological anamnesis should focus on the clinical condition of the hip to be operated upon the onset of pain, duration of limping, and previous unsuccessful conservative treatments. Surgical indications are typically reserved for patients with chronic pain persisting for at least six months and unresponsive to pharmacological conservative therapy. Additionally, it is essential to ascertain that the patient has not undergone intra-articular hip injections within the preceding three months to minimize the risk of local infection.

The general physical examination should evaluate the patient's posture while standing and walking. The type of limp (escape or ankylosis), any anatomical, functional, or perceived leg-length discrepancies should be determined. The potential for correcting such discrepancies should be communicated to the patient, noting that corrections exceeding 2 cm in lengthening substantially increase the risk of neurovascular stretching complications, and shortening beyond 1 cm significantly elevates the risk of dislocation.

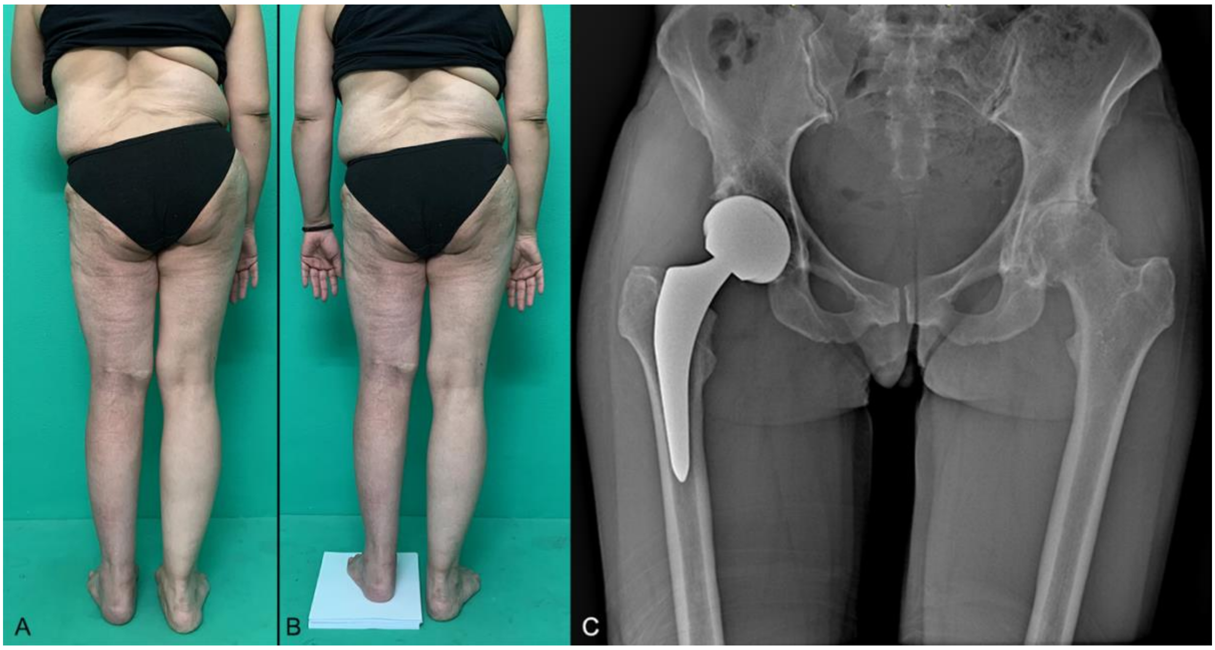

Figure 12. Hip osteoarthritis can cause shortening of the affected limb and therefore inclination of the pelvis

Lastly, the assessment should include spinal alignment, especially on the sagittal plane, and pelvic anteversion. Concerning muscle tone and trophism, alterations (particularly in the gluteal muscles) can severely compromise implant stability. The range of motion should be assessed in all planes and communicated to the patient, explaining that greater motion restriction implies a lengthier rehabilitation process. Severe articular stiffness, as observed in advanced osteoarthritis, can complicate intraoperative dislocation maneuvers. Patient's functional requirements must be considered in light of their age, muscle state, body mass, profession, and sports activities. The patient should be questioned about the duration of pain and/or disability, particularly the duration of symptoms, any conservative therapy, or intra-articular injections.

RADIOLOGICAL ASSESSMENT

Instrumental evaluation is crucial for the proper diagnostic framing of the patient and for preoperative planning. During the diagnostic pathway, the patient often presents at the orthopedic consultation already in possession of a radiographic report. For the purposes of preoperative evaluation, it is essential to visualize the hip in an anteroposterior radiograph.

In this manner, one can not only elucidate the etiology but also assess the surface of both joint ends, detect any acetabular dysmorphisms, and proactively plan for the ideal prosthetic implant to restore the geometric integrity of the pelvis.

Preoperative planning is executed on an anteroposterior pelvis radiograph: if the hip to be operated on is fixed in an incongruous position, planning can be conducted on the contralateral hip. Planning involves measuring the osseous surfaces of the acetabular cavity and the proximal femur to select the most suitable prosthetic implant for restoring the correct articular geometry of the hip. At the acetabular level, one must observe any dysmorphisms, deficiencies in the acetabular walls (crossover sign, center of rotation-to- posterior wall ratio), osteophytosis, and degree of acetabular protrusion. The radiographic teardrop serves as the reference marker, which in vivo is identifiable through the transverse acetabular ligament.

The acetabular component should approximate the size of the native socket as closely as possible, following adequate removal of sclerosis: this generally corresponds to one, or at most two, sizes larger than the diameter of the femoral head. Additional considerations on measurements can be made based on the implant (choice of a larger diameter head, resurfacing prostheses). The socket should be positioned at 40-45° of inclination relative to a line passing through the radiographic teardrops; it should not be uncovered by bone for more than one-third of its surface and should restore the physiological center of rotation as much as possible.

At the femoral level, the osteotomy of the neck should be planned according to the type of stem: the typical section is 1 cm proximal to the lesser trochanter and inclined at 45° relative to the longitudinal axis of the femur, although some prosthetic designs require more conservative cuts. The implant should be positioned with the junction between the neck of the prosthesis and the stem at the level of the femoral head osteotomy, selecting the most appropriate size to ensure optimal filling of the femoral canal.

If variable neck geometry implants or modular prostheses are available (with options to select designs with standard or lateralized geometry), it is necessary to monitor the

cervico-diaphyseal angle of the femur to be operated on by calculating the offset. One then tests the various components, assessing the offset, the center of rotation of the acetabulum, and the limb length, with the aim of selecting the most suitable type of implant.

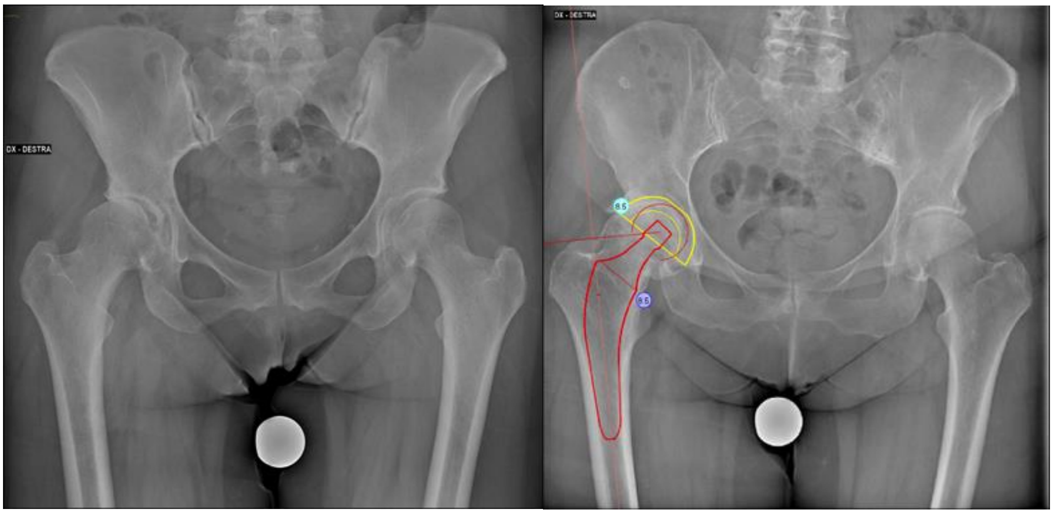

Figure 13. Preoperative planning is typically based on an anteroposterior x-ray of the pelvis.

FIXATION TYPE: CEMENTED AND UNCEMENTED PROSTHESES

The selection of the implant is made based on the pathological anatomy of the hip, the general characteristics (age, medical history, functional requirements) of the patient, and the preferences of the surgeon. Foremost, it is essential to choose the type of fixation to employ biological or cemented. To date, no clear superiority of one implant type over the other has been demonstrated. On one hand, cemented prostheses ensure immediate fixation of the implant, allowing the patient to ambulate without any load protection immediately postoperatively. On the other hand, uncemented prostheses, although requiring a biological adhesion process to the bone, have achieved better long-term survival outcomes. While uncemented prostheses offer some advantages over cemented ones, such as reduced surgical time and lesser biological impact due to the absence of the cementation process, it is important to note that their osseointegration is mediated by the same mechanisms that facilitate fracture healing. Consequently, biologically high-risk local situations, such as irradiated bone, or systemic conditions (chemotherapy aftermath) or other medications that slow cellular turnover, are exposed to the risk of delayed osteointegration of the implant.

Another contraindication to uncemented prostheses is severe osteopenia (Dorr C) due to the high risk of intraoperative fractures (see chapter on hip prosthesis complications).

Although the choice between cemented and uncemented implants remains tied to a comprehensive clinical evaluation and the preferences of the surgeon, the preferential indication for uncemented implants can be considered in young patients with higher functional demands and longer life expectations, and good bone quality.

CEMENTED HIP PROSTHESES

In cemented hip prostheses, the femoral and acetabular implants are slightly smaller in size compared to the osseous site where they are to be implanted. This is because the primary stability of the implant is entrusted to a layer of acrylic cement (PMMA) between the prosthesis and the bone; this can be employed for both the acetabular and femoral components, or a hybrid fixation implant can be performed (only one cemented component). Acrylic cement was developed in the early 20th century in the aeronautical field. Its biocompatibility characteristics were accidentally discovered during the Second World War and were initially used in dentistry until the 1950s when the English orthopedic surgeon John Charnley first used it for cementing an orthopedic prosthesis at the hip level. This insight revolutionized prosthetic surgery, providing a reliable fixation methodology between the prosthesis and bone, and presenting itself as an alternative to uncemented implants, which at the time due to deficiencies in prosthetic design, limited availability of sizes, and non-biocompatible materials, were associated with a high rate of mobilization.

The introduction of cementation enabled immediate, reliable, and reproducible fixation, paving the way for the widespread dissemination of orthopedic prosthetic implants. Since then, numerous types and designs of implants have been proposed and used, and cementation of both acetabular and femoral components remains a valid and widely used option with short- and medium-term satisfactory results that justify its use.

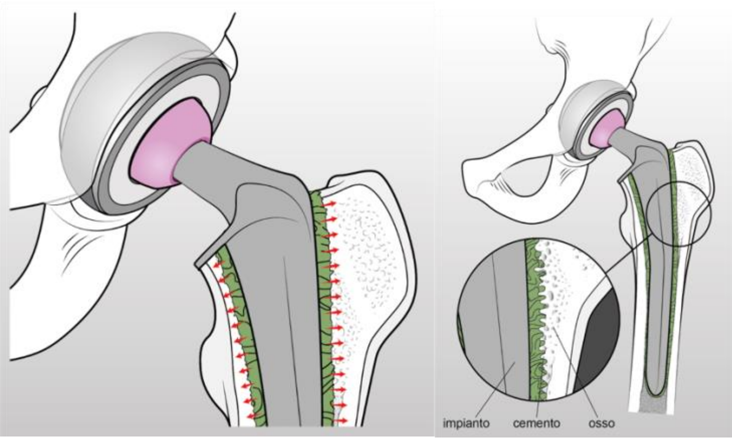

Figure 14. Cementation of the femoral component allow primary stability. Moreover, cement interdigitation with the trabeculae provides a solid bone-cement interface.

Acrylic Cement in Orthopedic Surgery

Acrylic cement is constituted by two primary components: polymethyl methacrylate (PMMA) powder and a liquid catalyst, which includes a radiopaque agent for radiographic identification. Recent market offerings also include antibiotic-infused cements; prevalent formulations comprise either 1 gram of clindamycin and 1 gram of gentamicin per 50 grams of cement, or 1 gram of vancomycin and 1 gram of gentamicin per 50 grams of cement. Upon mixing these primary components, polymerization initiates. Initially, the cement displays a viscous liquid consistency, which facilitates its injection into a bony cavity. Within minutes, it attains a malleable state, ultimately reaching full hardness in approximately 12 to 15 minutes through an exothermic reaction.

The polymerization process can reach temperatures upwards of 100°C, leading to a slight expansion in volume, thereby enhancing the cement's osteo-implant gap-filling capabilities. However, this elevated temperature introduces the risk of cellular necrosis in adjacent osseous tissue. Furthermore, it presents a non-negligible risk (with an intraoperative mortality incidence of 0.11%) of post-cementation embolism. The estimated mortality rate for cemented and non-cemented hip prostheses is 2.3% and 1.6%, respectively, although the generally older patient population for cemented prostheses may contribute to the higher mortality rate.

In addition to increased mortality, the bone cement implantation syndrome (BCIS) is characterized by hypoxia, hypotension, and/or unexpected loss of consciousness during the cementation period, prosthesis insertion, and joint reduction. The etiology and pathophysiology of BCIS remain incompletely understood.

Various mechanisms have been proposed, including monomer release into the bloodstream during cementation, embolism formation during cementation and prosthesis insertion, histamine release, complement activation, and vasodilation mediated by endogenous cannabinoids. Embolism usually occurs due to elevated intramedullary pressures during the cementation and prosthesis insertion processes. The cement undergoes an exothermic reaction and expands between the prosthesis and the bone, trapping air and medullary cells, and forcing them into the bloodstream.

Mechanically, the cement functions by filling the cavities in the cancellous bone, thereby creating a 'mold' effect that leads to gap-filling, rather than adhesive fixation. Besides fixation, the cement serves the purpose of transmitting mechanical forces to the bone-prosthesis interface. Mechanical forces acting on the cement mantle are particularly complex in hip prostheses, as they are the summation of various stresses combined in bending, tension, shear, and torsion. Laboratory simulation of this complex situation is highly challenging; thus, to determine the cement’s compressive and bending strength as well as its elastic modulus (or Young's modulus), strength tests have been simplified to two potential scenarios, i.e., in compression and in four-point bending, using both static and dynamic stresses. According to ISO standards (ISO5833), the minimum compressive strength requirement is 70 MPa. All commercial cements meet this criterion, with no significant difference in compressive strength between regular and antibiotic-added cements. The same ISO standard prescribes a minimum bending strength of 50 MPa and a minimum elastic modulus of 1800 MPa. Once again, all commercial cements meet these requirements, and the addition of antibiotics causes a reduction in bending strength, but not significantly so.

Cementation in orthopedic surgery offers the distinct advantage of providing immediate primary stability to the implant. This enables the implant to tolerate full loading without any restrictions. Additionally, the use of cement eliminates the need for specific sizing of the acetabulum and femoral canal, as the cement does not require bone interference for stabilization. Consequently, this minimizes the risk of intraoperative fractures, particularly in osteoporotic bone, and reduces the variety of implant sizes that need to be kept readily available.

Economically, cementation is a cost-effective technique. Furthermore, it exhibits a high medium-to-long-term survival rate (up to 15 years), which, in many cases, is reported to be equal to or greater than that of non-cemented fixation. However, a limitation compared to non-cemented implants lies in the higher rate of long-term loosening (20 years), especially concerning the acetabular component.

Uncemented Hip Prostheses

In the setting of uncemented hip prostheses, both the femoral and acetabular components are slightly oversized relative to the corresponding osseous sites to achieve primary stability via "press fit." This entails close contact between the bone and the implant. Secondary stability is achieved biologically through osseointegration over a period of 4-8 weeks, dependent on the bone quality, material of the implant, and the level of primary stability attained during the surgical procedure. Uncemented fixation can be used for both components, or a hybrid implant can be employed, which utilizes a non-cemented acetabular cup and a cemented stem.

Although uncemented implants were developed prior to their cemented counterparts, early outcomes were unsatisfactory. Numerous failures were attributed to inadequate prosthetic design and smooth surfaces, which were unable to achieve either primary or secondary stability.

A major milestone in the development of modern uncemented hip prostheses was set by Konstantin Mitrophanovich Sivash, who presented his results at a conference on osteoarticular tuberculosis in Moscow in 1963. His design featured a titanium press-fit acetabulum, a non-cemented stem, and a cobalt-chromium (MoM) articulating couple. Unfortunately, geopolitical conditions at the time prevented the dissemination of his innovative ideas in the West for approximately 15 years.

In the Western context, the concept of biological fixation, or osseointegration, was first introduced by Robert Judet in 1971, who proposed a prosthesis with a highly porous "porometal" surface composed of a chromium-cobalt-nickel-molybdenum alloy. By the mid- 1980s, a biomaterials research group from Leiden, Netherlands, led by Prof. Geesink, along with Prof. Furlong of London, Dr. Manley of Osteonics, and Prof. Epinette of Bruay- Labuissiere, France, had introduced the use of a bioactive coating for secondary implant integration—hydroxyapatite. Prof. Lord's concept that "living bone, undergoing remodeling, ensures stable implant fixation" was foundational to this innovation.

Since then, continual advancements have been made both in prosthetic design and materials. These advances have made the application of uncemented implants a reliable and reproducible procedure with encouraging long-term outcomes. This scientific treatise aims to provide an in-depth understanding of the development, mechanisms, and clinical applications of uncemented hip prostheses, grounded in historical background and current evidence-based practices.

MATERIALS EMPLOYED IN ARTICULAR COUPLING

Polyethylene

It was Sir John Charnley who, in the 1960s, pioneered the use of high molecular weight polyethylene (HMWPE) in hip arthroplasty to construct the acetabular component. Polyethylene is a semicrystalline polymer of ethylene, specifically organized in a reticular pattern when utilized in orthopedic applications. The high molecular weight enhances both wear and impact resistance without sacrificing ductility. Initial implementations of this material displayed unsatisfactory long-term wear rates, which led to the introduction of cross-linked polyethylene in the 1990s. This newer form underwent irradiation processes to induce new interchain bonds, offering increased wear resistance but greater susceptibility to oxidation, resulting in the deterioration of its tribological characteristics over extended periods. Further evolution in the 2000s saw the introduction of Vitamin E as an antioxidant to augment long-term wear resistance further. The material's ductility and mechanical strength have enabled the design of raised edges (anti-dislocation rims) or retentive head mechanisms to minimize dislocation risks. Polyethylene remains the most globally employed material for acetabular liners and, in its latest formulations when paired with ceramic heads, has shown excellent long-term survival rates. The initial drawbacks, such as premature aseptic mobilizations from osteolysis due to wear debris, have been largely overcome. The singular limitation of modern polyethylene is its elevated wear rate compared to ceramic when used with larger diameter heads.

Metal

In the context of metallic components in articular coupling, reference is typically made to articular surfaces composed of a crystalline alloy of Chromium-Cobalt-Molybdenum (CrCoMo), characterized by high mechanical strength and resistance to corrosion and wear. These metallic components can either be utilized solely at the femoral head to form a metal- on-polyethylene (MOP) coupling or at the acetabular liner level to create metal-on-metal (MOM) pairings.

The effective functioning of metallic articular surfaces is contingent on their self-lubricating capabilities. Usually, the thickness of the surface lubricating film exceeds the asperities of

the metal surface by a factor proportionally related to the dimensions of the cup and head as well as the radial clearance.

Thus, a high radius value of the head (large diameter head) coupled with low radial clearance facilitates the dragging of lubricant into a gradually converging space between the surfaces, thereby reducing polar stress. Conversely, small head sizes, erroneous component placements, and an increase in radial clearance can compromise the fluid film dimensions. It is believed that acetabular inclination angles greater than 50 degrees and extreme combined anteversions are negative predictive factors, inducing material wear and the subsequent release of debris and ions.

The allure of metal-on-metal (MoM) articular coupling has consistently resided in its ability to offer younger and active patients low wear rates in combination with large-diameter heads, bordering on anatomical reconstruction. Despite this, MoM implants are not without complications. Notably, several such devices have been withdrawn from the market due to unacceptable medium-term failure rates, prompting some manufacturers to impose restrictions on indications. Specifically, total hip arthroplasties employing MoM couplings have demonstrated suboptimal long-term results due to wear at the neck-head interface (known as "trunnionosis") and cases of inflammatory reactions arising from metal wear (termed "metallosis"), resulting in both local and systemic ion-induced damage.

All MoM joints are subject to wear from dynamic loading and corrosion from biological fluids, synergistically resulting in a phenomenon known as tribocorrosion. Normally, metal corrosion resistance is maintained by the continuous repassivation of surfaces, facilitated by the presence of body fluids. When this repassivation layer is disrupted due to excessive pressure between surfaces, friction occurs, leading to progressive wear and the release of metal ions and toxic debris into surrounding tissues. These debris particles further exacerbate the situation by causing additional surface damage through foreign body abrasive wear.

The risks associated with surface wear and adverse reactions to metallic ions have reduced the viable indications for the use of MoM couplings. Such utilization is no longer justifiable in light of the excellent outcomes and reduced complications guaranteed by other coupling mechanisms. The use of MoM coupling now remains a limited indication for select cases involving resurfacing implants. Although these implants come with specific issues related to their unique design, they are less susceptible to the surface-induced damage common to MoM and may be considered for younger, active patients. However, it should be noted that female gender and femoral resurfacing heads smaller than 50 mm are correlated with higher failure rates.

Ceramic

Since 2005, the ceramic material employed for articular couplings in orthopedics is primarily composed of alumina oxide reinforced by zirconia. This formulation enhances the material's hardness and hydrothermal stability. Ceramics are known for their excellent tribological properties, combined with high biocompatibility, but they are also characterized by fragility when subjected to repeated microtrauma—a limitation particularly relevant to older generation ceramics with a low zirconia content.

New-generation ceramics have demonstrated excellent 15-year survival rates, even in younger patients, with robust clinical and radiographic outcomes. Osteolysis is largely anecdotal in the context of ceramic couplings. The wear debris of ceramics is biologically inert and well-tolerated, inducing only minimal granulomatous response. Given their outstanding tribological attributes, ceramic femoral heads have become the gold standard in Western countries, replacing metal heads.

Nevertheless, ceramics are not without specific complications that must be recognized and considered (see related chapter). Component fracture is a rare but potential complication, most often occurring suddenly and acutely.

Most such events are of traumatic or iatrogenic origin, due to imperfect surgical techniques. Noise represents another typical ceramic- related complication. This can manifest as a squeaking or clicking sound, evoked by certain hip movements, and may become frequent and intense enough to cause patient concern and discomfort. The genesis of this noise remains poorly defined but is likely the result of imperfect surface lubrication under load. Noise is more common in male, young, active, and overweight patients, as well as in those with anteverted acetabular components and suboptimal positioning. Although not a pathological condition per se, this complication is associated with an increased risk of component breakage, typically occurring within five years of noise onset, which serves in this instance as a prodromal symptom. Suboptimal positioning is also correlated with premature ceramic wear, known as stripe wear. This phenomenon is related to component micro-instability arising from incorrect soft tissue tensioning or imprecise positioning (excessive acetabular abduction and/or extreme combined anteversion). In essence, these predisposing conditions cause the components to articulate over short surface segments, resulting in localized overload and subsequent wear.

SURGICAL APPROACHES

Multiple surgical approaches have been developed for the execution of hip arthroplasty, each with its specific advantages and disadvantages. The most employed surgical pathways for hip arthroplasty include the posterolateral approach, the direct lateral approach, and the direct anterior approach. Over the years, and with the advent of novel surgical instruments, each of these approaches has undergone modifications to minimize invasiveness, thus reducing biological damage to the patient and facilitating early rehabilitation.

The posterolateral approach, also known as the Southern or Moore approach, aims to access the articular plane from the posterior, by spreading the distal fibers of the gluteus maximus muscle and dissecting the external rotator muscles (piriformis, superior and inferior gemellus, external and internal obturator, and quadratus femoris), followed by posterior hip dislocation. This access provides good visualization of the posterior capsule and the entire acetabulum, although managing fractures of the anterior acetabular wall may be challenging. Femoral exposure is straightforward, facilitating good visualization of the lesser trochanter, an important intraoperative landmark.

The primary advantages of this approach include the sparing of abductor musculature, with resultant biomechanical benefits, ease of distal extension of the surgical route in case of femoral intraoperative complications, reduced incidence of heterotopic ossifications compared to the lateral approach (due to sparing of the abductor muscles), relative simplicity of the surgical technique, and rapidity of execution. The main disadvantage lies in the necessity to perform the surgery with the patient in the lateral decubitus position, which results in the loss of key anatomical landmarks that can be assessed in the supine position, leading to difficulties in positioning the acetabular component, especially in terms of anteversion, and in intraoperative limb-length assessment. The most vulnerable structure in this approach is the sciatic nerve, due to its relationship with the piriformis muscle.

The principal complication associated with this approach, in comparison to others, is post- operative dislocation, generally posterior, due to weakening of the containment structures (articular capsule, external rotators) of the posterior wall. Minimizing this risk necessitates meticulous reconstruction of the posterior capsule and the short external rotator musculature, particularly the piriformis tendon.

The direct lateral approach, also known as the Hardinge or Charnley approach, allows access to the articular plane by partially detaching the medius and minimus glutei from their insertion on the greater trochanter, followed by anterior femoral dislocation.

The patient can be positioned either in lateral or supine decubitus; the latter is usually preferable for superior visualization of anatomical landmarks to be used during the procedure.

Advantages include excellent exposure of both the acetabulum and femur, easy extension of the surgical route at both the proximal and distal levels and sparing of posterior containment structures of the hip (reduction in post-operative dislocation rates). Additionally, major vascular and neural structures are relatively distant from the surgical field (except for the inferior gluteal artery, which must be preserved in case of proximal extension of the incision). However, the necessity to partially detach the minimus and medius glutei from the greater trochanter compromises the abductor and antigravity function of these muscles, leading to post-operative limp (termed gluteal limp) and a positive Trendelenburg sign, reported in the literature in up to 10% of cases. This is also the surgical approach with the highest incidence of heterotopic ossifications, mainly due to the abductor musculature's tendency to calcify in response to surgical stress.

To minimize the risk of gluteal insufficiency, it is imperative to perform a meticulous suture of the medius gluteus tendon, ensuring its continuity and that the suture guarantees good strength. In the initial post-operative weeks, patients are prescribed a rehabilitation protocol that includes partial weight-bearing on the operated limb to allow tendon healing.

The direct anterior approach, also known as the Smith-Petersen or Heuter approach, has regained popularity among surgeons in recent years for prosthetic replacements as well. This surgical access exploits the intermuscular interval between the tensor fasciae latae and the sartorius muscle, thus allowing the articular plane to be reached and the arthroplasty to be performed without detaching any muscle. The main vascular and neural structure at risk with this approach is a sensory nerve, the lateral femoral cutaneous nerve.

The main advantages of this approach include excellent visualization of the acetabulum, reduced bleeding, and reduced post-operative pain, facilitating early rehabilitation. The major limitation is the challenging exposure of the femur, which increases the risk for intraoperative fractures. Moreover, this approach requires a more complex distal extension than the others, necessitating a greater learning curve and the utility of specialized instruments and limb positioning tables.

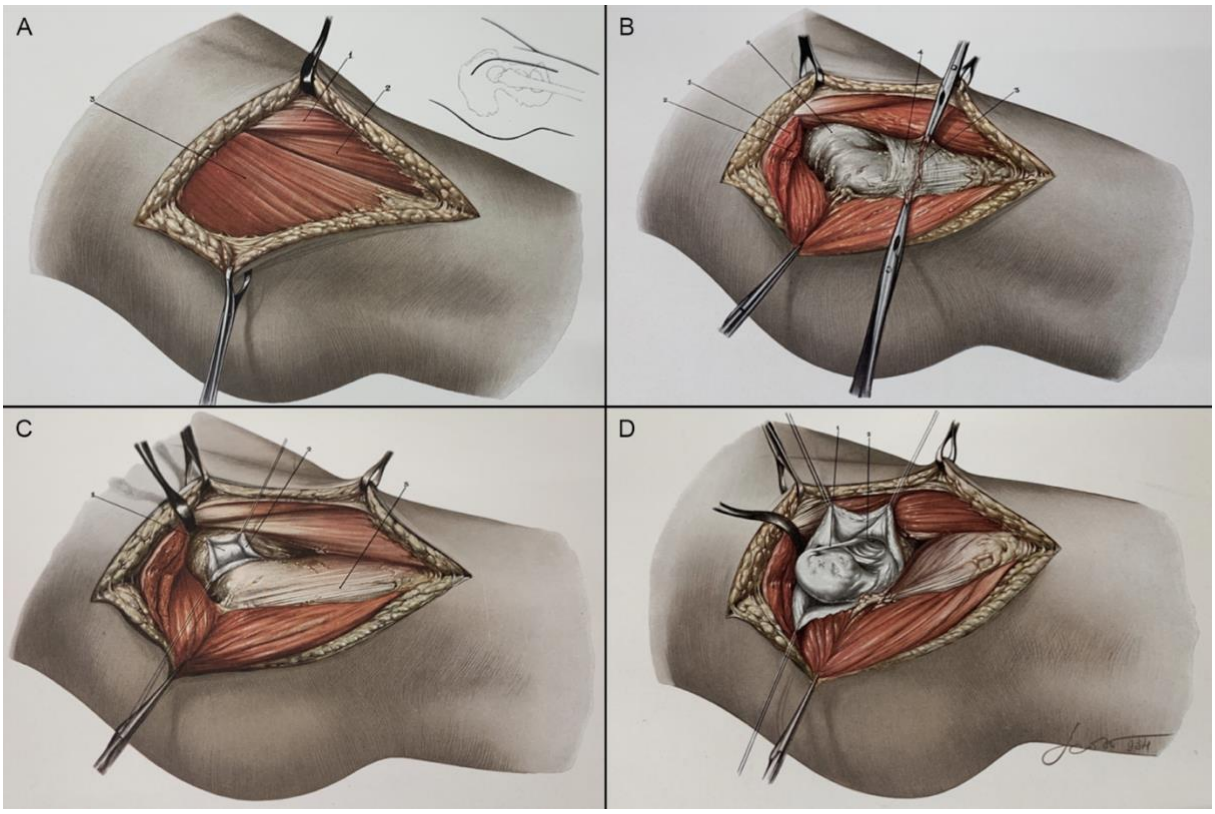

Figure 15. Direct anterior approach, described by Vittorio Putti and painted by Remo Scoto

Rehabilitation and Recovery Timeframes Following Total Hip Arthroplasty

Achieving an excellent clinical outcome following total hip arthroplasty (THA) requires an optimal postoperative rehabilitation program. The program should be individualized, taking into consideration preoperative activity levels, postoperative expectations, preoperative anatomical anomalies, surgical approach employed, prosthesis components, and any intraoperative or perioperative complications. Advances in surgical techniques, minimally invasive approaches, and improved pain management protocols have facilitated increasingly accelerated rehabilitation timelines. Anesthesia and pain control techniques should be aligned with postoperative functional recovery goals.

The rehabilitation program can be divided into three phases:

- Preoperative Phase: This phase involves educating the patient about recovery timeframes, rehabilitation modalities, and potential implant-related complications and their prevention. It may also be beneficial to instruct the patient on using crutches and gait patterns with assistive devices.

- Immediate Postoperative Phase: Commencing immediately after the return of voluntary motor function, this phase includes isometric exercises (active knee extension) and antithromboembolic exercises (ankle dorsiflexion and plantar flexion). These exercises can be performed autonomously while in bed. Under the guidance of a physiotherapist, the patient may also be mobilized, be made to assume a sitting and even standing position on the same day as part of an intensive rehabilitation program.

Alternatively, these activities can be delayed to the subsequent days (first and second postoperative days). Pain management, improving patient autonomy, initiating muscle strengthening exercises, achieving a joint range of motion between 0° and 80°, and introducing partial weight-bearing ambulation with forearm crutches are crucial during this phase. Contractures causing apparent limb length discrepancies should be corrected. The patient should also be educated about movements that risk dislocation, with precautions tailored to the specific surgical approach. For all approaches, adduction is generally avoided, but specific caution against hyperextension-external rotation is advised for anterior approaches, whereas flexion-external rotation is avoided in direct lateral approaches. For posterolateral approaches, flexion-internal rotation is discouraged. The patient can be considered for discharge when clinically stable, able to walk independently with crutches over short distances, ascend and descend stairs with aids, and perform self-care tasks.

- Post-discharge Phase: The physiotherapy program should include a gradual increase in joint range of motion up to 90°, muscle strengthening exercises focusing on abductors, flexors, and extensors, stretching of the adductor muscles, and optimization of ambulation with crutches. Once a balanced pelvic gait is achieved, ambulation without crutches may be permitted for extended distances. Subsequently, exercises to further strengthen muscles, increase joint range, and optimize gait should be encouraged. Water-based exercises, cycling with gradual saddle lowering, independent ambulation, and resistance exercises targeting abductors are beneficial. Complete recovery typically occurs around 40 days post-surgery. Anti-dislocation precautions can generally be lifted 25 days post-surgery with soft tissues adequately healed. However, patients must continue to avoid extreme movements that pose a risk of dislocation or impingement and maintain sufficient muscle strength, particularly focusing on abductor muscle trophism.

Postoperative Assessment of a Hip Prosthesis

The postoperative evaluations of a hip prosthesis are tailored to the individual patient's specific characteristics and those of the implant. As best practice, an initial assessment should be conducted within 20-30 days, followed by additional evaluations at 3-6 months, 12-18 months, and subsequently biennially. It is advisable to maintain a high level of vigilance during the first 1-2 months to identify and treat potential early complications (infections, early dislocations). Subsequent assessments should focus on monitoring osteointegration around 6-12 months to identify early mobilizations, typically occurring within the first two years. As time progresses, the frequency of follow-up visits may be lengthened, although periodic clinical and radiographic evaluations should never be entirely discontinued.

The follow-up assessments consist of a clinical evaluation combined with recent anteroposterior and axial radiographs of the operated hip. Clinical assessment aims to verify the presence of newly emerged pain or limping, the condition of the skin around the scar, painless passive mobilization of the hip in flexion rotation, and active mobilization with a focus on active flexion and abduction. Particular attention should be given to autonomous ambulation, specifically to pelvic obliquity, gluteal insufficiency limp, or escape limping.

Radiographic evaluation is critically important since some complications, such as polyethylene wear or adverse metal reactions, may manifest as early radiographic anomalies in asymptomatic or minimally symptomatic patients. Radiographic assessment should be compared to the initial postoperative radiograph and all subsequent radiographs. Reviewing the preoperative radiograph may also provide insights into surgical choices, residual leg length discrepancies, and the accuracy of biomechanical parameter reconstruction.

In postoperative radiographs, attention must be directed to the centering of the head, movement of the prosthetic components compared to immediate postoperative radiographic control (movement is unequivocally a sign of prosthesis failure termed "mobilization"), osteolysis, radiolucent lines, and periosteal reactions. These signs could indicate dislocations, wear, aseptic or septic failures.

On the acetabular side, a well-integrated cup shows the absence of radiolucent lines, radial bony trabeculae, superolateral and inferomedial buttresses, and medial areas of bone rarefaction (stress shielding). Mobilized acetabular components demonstrate progressive movement (rising or rotating) of more than 2 mm in two consecutive radiographs. Moreover, radiolucent lines greater than 2 mm, circumferential to the acetabulum, are frequent.

On the femoral side, a well-integrated stem shows the absence of diffuse radiolucent lines and multiple radial trabeculae. No varus-valgus or sinking mobilizations relative to a fixed point should be evident. A certain degree of sinking may be immediately evident postoperatively; however, it must be clinically contextualized and should progress to stabilization in subsequent assessments. Differentiated diagnoses (primarily infection) should not be neglected. For cemented stems, the uniformity of cementation, absence of radiolucent lines at the prosthesis-cement interface, and absence of cement mantle fractures must be evaluated.

Articular surfaces should be scrutinized carefully. Polyethylene liners undergo normal wear, manifesting as an eccentric femoral head and liner thickness reduction in the superolateral quadrant compared to the inferomedial quadrant. They often accompany periprosthetic osteolysis and changes in the shape of soft tissues (foreign body reactions, see complications). Similarly, metal-on-metal surfaces, which show no gross signs at the joint level, may accompany periprosthetic osteolysis and pseudotumors. Failures in ceramic- ceramic pairings can result in the release of radiopaque intracapsular particles and liner malpositioning relative to the acetabular cup.

Radiographic anomalies must always be clinically contextualized, compared to subsequent radiographic controls, and further investigated through secondary-level tests.

COMPLICATIONS

Total hip arthroplasty demonstrates exceedingly high success rates; complications are relatively rare. However, due to the increasing prevalence of prosthetic replacements, complications are becoming a progressively more significant issue. Complications can be general in nature, arising as a consequence of major surgical intervention (see medical and anesthetic complications of surgery), or they can specifically pertain to total hip arthroplasty. They can be categorized as intraoperative and postoperative, with the latter further subdivided into early and late complications.

Unstable Hip Prosthesis: Diagnosis and Treatment

Instability is defined as the temporary and incomplete loss of articular contact between prosthetic components, with variable but generally benign clinical outcomes. In contrast, dislocation refers to a clinically significant event characterized by the complete loss of articular contact between the femoral head and the acetabular cup.

These complications represent a major cause of implant failure, with an incidence reported in the literature of up to 5%, particularly during the first postoperative year. Key risk factors for instability and dislocation include female sex, advanced age, neuromuscular disorders, abductor muscle insufficiency, and alcohol abuse. The dislocation can be either posterior or anterior, based on the position of the femoral head relative to the acetabular cup. Posterior dislocation typically occurs following a posterior-lateral approach due to hip flexion, adduction, and internal rotation; whereas anterior dislocation can follow an anterior approach due to hyperextension, adduction, and external rotation.

The etiological factors for dislocation may involve malpositioning of the prosthetic components (see combined anteversion), inadequate function and tension of periarticular muscles, lack of patient cooperation during the immediate postoperative period, excessive wear of the acetabular liner (polyethylene), or its breakage (ceramic). The incidence of prosthetic dislocation is higher during the first 60 postoperative days due to reduced muscle tone and/or the pathway created by the surgical approach, which generates a zone of lesser resistance not adequately protective against dislocation. In subsequent weeks and months, a scar tissue capsule forms around the prosthetic implant, limiting extreme joint movements and providing adequate protection against potential dislocation (Figure 14.265). Late dislocation (beyond 90 days) usually occurs due to excessive motion, post-traumatic events (sprains, falls), or polyethylene wear.

Clinical presentation of unstable hip is typically insidious; upon physical examination, patients may report a sensation of snapping or internal movement within the hip, a feeling of discomfort at extreme ranges of motion, sometimes accompanied by pain or a sense of apprehension. Clinical manifestations of hip prosthesis dislocation are more apparent; patients typically present in an emergency setting in a supine position, with severe pain, complete functional impairment of the limb, and extreme pain upon any attempt at movement. Peripheral neurological examination is essential, testing active and passive ankle and foot movements, and a valid quadriceps muscle contraction to identify potential sciatic or femoral nerve involvement. Anamnestic data collection is crucial, including any previous dislocations or instabilities, and the reconstruction of the event that led to the dislocation.

Initial assessment should include a thorough history; documenting the timing of the surgical procedure, the surgical approach used, the type of prosthetic model, the postoperative course, and any prior dislocations or subluxations. The patient should be queried regarding any comorbidities (neuromuscular disorders) and previous treatments (surgical interventions, medical therapies). Radiographic evaluation is indispensable; conventional radiography allows, within certain limitations, for the estimation of implant position and orientation, and any wear of the polyethylene liner. However, dislocation usually occurs predominantly due to incorrect combined positioning of the acetabulum and femur on the axial plane (combined anteversion of the femur and acetabulum), necessitating CT scans for precise measurement of these parameters.

Early dislocation (within the first month post-implantation) can be effectively managed conservatively with strict functional limitations and anti-dislocation devices maintained for six weeks, the time needed for soft tissue healing around the prosthesis. When conservative measures fail to achieve a stable implant or nonsurgical treatment fails, surgical intervention is warranted. The goal of revision surgery is to replace the malpositioned prosthesis with components adequately oriented. Combined anteversion should be a minimum of 30º and not exceed 50º. When the dislocating condition is not solely attributable to prosthetic malpositioning but has a multifactorial etiology, primarily muscular, alternative surgical strategies should be employed, involving special acetabular components (dual-mobility cups); larger prosthetic heads (increased jump-distance); anti-dislocation liners (Figure 14.266) properly oriented to protect against dislocation; distalization of the greater trochanter or lateralized prosthetic stems (with increased offset to amplify joint reaction forces by placing periarticular muscles under appropriate tension); retentive components (that lock the prosthetic head within the acetabulum); and muscle plastic surgery (reconstruction of the abductor musculature).

The treatment strategy must be predicated upon the accurate etiological characterization of the instability. The table presents the primary parameters potentially responsible for the instability and dislocation of the implant. (Tab 1)

Type of Instability	**Acetabular Orientation**	**Stem Orientation**	**Abductor Mechanism**	**Impingement**	**Wear**	**Recommended Type of Revision**
Acetabular Malpositioning	Incorrect	Correct	Intact	Absent	Absent	Revision of the Acetabulum
Stem Malpositioning	Correct	Incorrect	Intact	Absent	Absent	Isolated Revision of the Stem
Abductory deficiency	Correct	Correct	Damaged	Absent	Absent	Repair of the Abductor Complex. Incorporate Dual Mobility or Retentive Acetabulum
Impingement	Correct	Correct	Intact	Present	Absent	Remove the Cause of Impingement, Dual Mobility Acetabulum or Revision of Modular Parts
Wear	Correct	Correct	Intact	Absent	Present	Revision of the liner or the Acetabulum

Unknown cause	Correct	Correct	Intact	Absent	Absent	Dual Mobility, Retentive Acetabulum

Table 1

: Parameters of Instability and Implant Dislocation

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THE CARTILAGE

STRUCTURE OF CARTILAGE

The cartilage is a load-bearing connective tissue that plays essential roles in skeletal support, facilitates joint movement, and significantly contributes to bone development and growth. Its ability to perform various functions is determined by its composition and location. The primary characteristics of cartilage include its high resistance to compression and tension, coupled with inherent flexibility. It has a low metabolic activity and is limited in vascularization, which is confined to its surface or large perforating canals. Cartilage is covered by the perichondrium, except on the surfaces of synovial joints.

This tissue is composed of an extracellular matrix, in which cartilage cells are embedded. Depending on the appearance and composition of the matrix, cartilage is classified into hyaline, elastic, and fibrous types. Elastic collagen fibers provide resistance to tension, bending, and twisting, while the composition of the ground substance contributes to its compression resistance.

The specialized cells of cartilage include chondroblasts, chondrocytes, and chondroclasts. These cells are responsible for the synthesis and turnover of the extracellular matrix. Chondroblasts are globular in shape, with small nuclei and cytoplasm rich in ribosomes; they can divide and are responsible for synthesizing various components of the cartilage ground substance, such as proteoglycans. As the production of ground substance increases, the cells move apart and become enclosed within the matrix in cavities known as "cartilage lacunae." The ability to synthesize and divide gradually diminishes, and the cells transform into chondrocytes, which cluster within the individual lacunae in small groups called "isogenous groups," each representing the progeny of a single chondroblast. These cells continue to divide and produce matrix until they are enveloped by the matrix they produce, eventually ceasing to divide and entering a quiescent phase. In response to external stimuli, chondrocytes can resume their synthetic and cellular division activities. Lastly, chondroclasts are giant cells with phagocytic activity, responsible for the resorption of cartilage tissue during the

process of ossification by substitution.

The cartilage matrix consists of collagen fibers embedded in a dense gel-like ground substance composed of water, dissolved salts, proteoglycans, proteins, and lipids. Water is the major component of the extracellular matrix, comprising 65% to 80% of its total weight. Among the more than 10 different collagen macromolecules with varying characteristics, type II collagen is present in all types of cartilage and provides strength and tensile resistance to the tissue. Proteoglycans are complex macromolecules produced by chondroblasts and chondrocytes, consisting of a central protein portion to which several glycosaminoglycan chains are attached, themselves formed from repetitive saccharide units. The central protein portion is divided into three regions: one capable of binding hyaluronic acid, a more distal region rich in keratan sulfate, and an even more distal region rich in chondroitin sulfate. The sulfate and uronic groups confer a high concentration of negative charges to the proteoglycan molecules, which are linked together through a long hyaluronic acid filament. Each proteoglycan macromolecule represents an incompressible structure, providing resistance to compressive forces. This is a direct result of the intramolecular interactions between the negative charges of the glycosaminoglycans, which tend to repel each other when subjected to pressure. Finally, proteoglycans act like a porous sponge, highly hydrated due to their intrinsic ability to retain significant amounts of fluid, allowing cartilage to adapt to and resist compressive stimuli.

Bound water is released when the tissue is under load and is reabsorbed when the compressive force ceases. For these reasons, the ability to withstand compressive loads is directly related to the levels of proteoglycans within the cartilage tissue; a reduction in their levels can lead to stresses that may result in structural collapse.

Cartilage is avascular, which is crucial in understanding diseases that affect this tissue. Chondrocytes receive nourishment through diffusion from the surrounding environment, a process enhanced by the compressive forces regularly acting on cartilage. This indirect nutrient delivery contributes to the slow turnover of the extracellular matrix and the tissue's limited repair capabilities. Vascularization is confined to the surface, primarily in the perichondrium, where the exchange of nutrients and waste products occurs solely by diffusion through the extracellular matrix. This characteristic underlies the poor healing and regenerative capacity of cartilage, leading to its degeneration.
Cartilage is also aneural. When pain is present in conditions affecting cartilage, it usually arises from the inflammation of nearby structures, such as joint and bone inflammation in osteoarthritis.

Hyaline Cartilage

Hyaline cartilage is the most widespread type of cartilage tissue in the body, forming part of the skeleton of the nose, larynx, and bronchial rings, covering articular surfaces, and forming costal cartilages. Macroscopically, articular hyaline cartilage appears tightly adhered to the cortical bone and creates a smooth, uniform load-bearing surface that minimizes friction during joint movements.

The etymology of the term "hyaline" comes from the ancient Greek word ὕαλους (hyalos = glass), which describes the white, translucent, and pearly appearance of this tissue in young adults. Immature cartilage has a bluish hue, while cartilage in older individuals tends to have a yellowish color. Its matrix contains tightly packed collagen fibers and is relatively homogeneous, with a soft consistency and elasticity due to the richness of chondroitin sulfate and hyaluronic acid, which ensure its hydration.

Articular cartilage is separated from surrounding tissues by a fibrous membrane known as the perichondrium. This is composed of two layers: an outer layer made up of dense irregular connective tissue, called the fibrous layer, and an inner layer called the cellular layer. The fibrous layer provides support and protection and allows the cartilage to adhere better to surrounding structures. The inner, or cellular, layer enables cartilage growth.

Articular cartilage is divided into different zones, each with varying thickness, composition, and structure. The superficial layer accounts for approximately 10-20% of the total thickness, the intermediate layer for 40-60%, and the deep layer for about 30-40%. The superficial layer contains the highest amount of water (about 80%) and collagen (about 85%); collagen fibrils in this layer are small in diameter and are arranged parallel to the direction of joint movement, making this layer particularly resistant to shear forces resulting from joint movement. The percentages of collagen and water gradually decrease in the intermediate layer, where fibrils are larger in diameter and lack a preferential orientation. In the deep layer, the content of collagen and water remains constant, the fibrils orient perpendicularly to the surface of the subchondral bone, and partially merge with it. Physiologically, articular cartilage is an avascular, aneural, and alymphatic tissue. Cellular density is lower than in other tissues, and mitogenic potential is very low, resulting in minimal regenerative capacity following injury.

Elastic Cartilage

Elastic cartilage is found in more limited areas compared to hyaline cartilage. It is present in the external auditory canal, the auricle, the auditory tubes, the larynx, the epiglottis, and partially in the nose. This cartilage has a more opaque and yellowish appearance due to the high number of elastic fibers within it, making it extremely resilient and flexible.

Fibrocartilage

Fibrocartilage is a transitional form between hyaline cartilage and dense connective tissue. It is primarily found in intervertebral discs, the synchondrosis between the first rib and sternum, the glenoid and acetabular labrum, the ligament of the femoral head, the pubic symphysis, and the menisci of joints. Fibrocartilage has a sparse ground substance, and a matrix mainly composed of collagen fibers, and it may sometimes lack a perichondrium. The collagen fibers in fibrocartilage align with the lines of tension, making them more orderly than those in hyaline or elastic cartilage. This alignment provides resistance to compression, especially in intervertebral discs, and allows the cartilage to act as a shock absorber, preventing contact injuries between bones. Fibrocartilage is also major component of entheses, defined as the connective tissue between muscle tendon or ligament and bone. The fibrocartilaginous enthesis consists of 4 transition zones as it progresses from tendon to bone.
These transition zones are listed in order of progression from muscle to bone.

1. Longitudinal fibroblasts and a parallel arrangement of collagen fibers are found in the tendinous area.
2. A fibrocartilaginous region where the main type of cells presents transitions from fibroblast to chondrocytes
3. A region called the "blue line" or "tide mark" due to an abrupt transition from cartilaginous to calcified fibrocartilage.
4. Bone

CLINICAL SIGNIFICANCE

There are numerous clinical conditions involving cartilage, including osteoarthritis, spinal disc herniation, traumatic rupture or detachment, achondroplasia, costochondritis, neoplasms, and others. These conditions stem from a range of degenerative, inflammatory, and congenital factors.

Osteoarthritis impacts the entire joint, with articular cartilage (a type of hyaline cartilage) being the most affected. It is often referred to as a "wear and tear" condition because it predominantly affects joints subjected to higher stress levels. This results in the thinning and erosion of articular cartilage, leading to a reduced range of motion, direct bone-to-bone contact within the joint, and pain. Initial treatment typically involves anti-inflammatory medications and intra-articular corticosteroid injections, which help reduce the inflammatory response triggered by cytokine release from degenerating cartilage. Patients may also benefit from weight loss, exercise, and efforts to minimize joint stress through rest and the use of assistive devices like a cane. However, as symptoms progress and interfere with daily life, joint replacement or resurfacing may become necessary. Arthroscopic surgery is no longer recommended for knee osteoarthritis due to a lack of efficacy and potential for harm.

Spinal disc herniation is another common degenerative cartilage disorder, arising from degenerative changes in the annulus fibrosus, the outer ring of the intervertebral disc composed of fibrocartilage. Trauma, strain, and lifting injuries can weaken the annulus fibrosus, making it prone to disc herniation. When the annulus fibrosus is damaged, the nucleus pulposus within the disc can herniate into the spinal canal, causing nerve impingement and triggering inflammatory changes due to damaged fibrocartilage. Diagnosis is based on history, symptoms, and physical examination, often supplemented by imaging studies to rule out other conditions like tumors, spondylolisthesis, or space-occupying lesions. While some severe cases may require surgery, most resolve with conservative treatment, including anti-inflammatory medications and lifestyle modifications.

In contrast to degenerative cartilage diseases, achondroplasia is a genetic disorder affecting cartilage formation and is the most common cause of dwarfism. It results from a mutation on chromosome 4 affecting the fibroblast growth factor receptor 3 (FGFR3) gene, which typically acts as a negative regulator of bone and cartilage growth. This mutation leads to a truncated, dysfunctional protein that remains active, inhibiting cartilage growth by suppressing chondrocyte proliferation and calcification. Achondroplasia is usually diagnosed during pregnancy through prenatal ultrasound. Currently, there is no cure for achondroplasia, as it does not involve a hormone pathway that can be targeted pharmacologically, and corrective surgery remains controversial.

RADIOLOGIC ASSESSMENT

X-ray

Cartilage is typically radiolucent, so X-rays do not directly depict cartilage morphology. In a conventional joint X-ray, cartilage appears as a translucent space separating the opposing bone ends. In growing bones, the growth plate cartilage is visible at the metaphysis, indicating active longitudinal bone growth. In cases of cartilage pathology, such as osteoarthritis, indirect signs like a narrowed joint space can be observed, indicating secondary chondropathy with cartilage thinning, which may cause bones to come into contact. Additionally, calcified lesions like meniscal calcifications and chondrocalcinosis may be visible.

Computed Tomography (CT)

CT also uses X-rays, and due to the density characteristics of cartilage tissue, its use is limited. In CT scans, cartilage appears as a hypodense line at the growth plates and as a grayish band in joint regions. Contrast agents can enhance the visualization of articular cartilage, and this method is used in studying cartilage tumors and for patients contraindicated for MRI.

Magnetic Resonance Imaging (MRI)

MRI is the most commonly used imaging technique for studying cartilage. MRI images of cartilage vary depending on the sequence used. T2-weighted sequences are particularly useful for evaluating cartilage integrity, showing areas of cartilage swelling or contour defects with high sensitivity. Conversely, T1-weighted sequences provide lower contrast between cartilage, joint fluid, and surrounding soft tissues. MRI can reveal anatomical details of cartilage structures, highlight lesions, and assess conditions ranging from simple chondropathy to full-thickness osteochondral injuries. MRI is also the basis for various cartilage injury classifications, describing lesion location and characteristics. The ability to detect fluids makes MRI useful in identifying joint effusions or bone edema. A specific variant, arthro-MRI, involves the injection of contrast material into the joint for evaluating pathologies in large joints. The contrast agent used is gadolinium, which significantly enhances the contrast between intra-articular fluid and articular cartilage. However, the sensitivity of this method can be limited by digital image reconstruction processes that may obscure small cartilage lesions, such as fissures or cartilage flaps.

Ultrasound

Ultrasound is rarely used for studying cartilage but can appropriately assess joint spaces. In some cases, it can detect mobile bodies within the joint, which may result from cartilage injuries.

CARTILAGE GROWTH

Cartilage grows during development through two mechanisms: interstitial growth and appositional growth. These mechanisms ensure the proper development and physiological growth of cartilage, as well as the various body segments during the growth period. During this time, cartilage remains in the metaphyses, facilitating longitudinal bone growth.

- Interstitial growth: is typical of immature cartilage tissue. Chondroblasts within the cartilage tissue undergo cell division, creating isogenic groups that separate as extracellular matrix is deposited.
- Appositional growth: occurs in both immature and mature cartilage tissue. Stem cells from the inner layer of the perichondrium undergo multiple cycles of division and differentiate into chondroblasts, which begin to produce cartilage matrix. Once fully surrounded by matrix, they differentiate into chondrocytes. This mechanism gradually increases the size of cartilage through the addition of new material on the surface.

FUNCTION AND HOMEOSTATIC MECHANISMS

In joints, cartilage plays several key mechanical roles:

- It reduces stress from loads and strains by distributing them over a wider contact area.

- It facilitates the smooth movement of opposing joint surfaces.

- It enhances the congruence between joint surfaces.

- It reduces friction and thus minimizes wear on the joint surfaces.

These functions depend on the biochemical composition of cartilage, its specific architecture, and the geometry of the joint surfaces. Mechanically, cartilage can be considered a deformable solid with viscoelastic properties, consisting of a fluid component (due to water and free mobile ions) and a solid component (collagen fibers and proteoglycans).

Cartilage tends to swell due to the hydrophilic nature of proteoglycan-hyaluronic acid complexes, which absorb water and increase its volume. During periods of loading (compression) and unloading (rest), driven by body weight and movement, the structure deforms as interstitial fluid moves from the stressed area to the resting area. Under non-maximal load conditions, about 75% of the total stress is borne by the fluid component of the cartilage, with only 25% borne by the solid component, primarily the proteoglycans. As load and deformation increase, tissue permeability decreases, halting interstitial fluid flow, so mechanical resistance is ensured only by the properties of the solid component. During these periods of loading and unloading, the articular cartilage also functions like a pump: during loading, interstitial fluid moves from the cartilage to the joint space, and during unloading, the cartilage re-expands, absorbing water and nutrients.

The second mechanical function of articular cartilage is to ensure the smooth gliding of joint surfaces through a lubrication mechanism, facilitated by interactions between synovial fluid and cartilage structure. The formation of a fluid film between the two surfaces allows the synovial fluid to enhance load-bearing capacity and improve lubrication, thus protecting the joint. Physiological mechanical stresses are essential for stimulating chondrocyte activity, as mechanical factors and joint movement help maintain cartilage metabolic homeostasis.

In conclusion, the function of articular cartilage is influenced by three factors: synovial fluid, joint biomechanical balance, and adherence to subchondral bone. Permeability, which regulates the exchange of essential nutrients through positive and negative pumping mechanisms, deformability, lubrication, degradation and synthesis processes, and mechanical adherence to subchondral bone, are all crucial for cartilage vitality.

REPAIR AND DEGENERATION OF ARTICULAR CARTILAGE

Due to the lack of significant vascularization, adult cartilage tissue has limited repair capacity under physiological conditions. Moreover, mature chondrocytes, once differentiated, have a limited ability to produce extracellular matrix. As a result, the natural history of cartilage lesions often involves the development of secondary osteoarthritis. Cartilage tissue responds to external insults by increasing extracellular matrix production. When matrix production is insufficient relative to the severity of the injury, degeneration begins, characterized by cartilage thinning, surface fissures, cell death, structural changes with increased type X collagen and decreased type II collagen, and vascular invasion of the basal layer.

The prognosis depends on the patient’s age: it is better in younger patients and worse in older ones. In younger patients, more effective repair mechanisms are observed, similar to those that ensure physiological cartilage growth during development. However, the reparative tissue formed in articular cartilage lesions is limited by the poor proliferative capacity and extracellular matrix production of chondrocytes. Therefore, other types of connective cells are recruited in an attempt to repair the damage, but the resulting scar tissue, typically fibrocartilage, does not possess the same physiological and mechanical properties as native articular cartilage. Additionally, vascular invasion of the deep layers of cartilage can alter its properties, leading to ossification and subsequent loss of function.

GENDER MEDICINE IN ORTHOPAEDICS

A considerable number of diseases or conditions affecting the musculoskeletal (MSK) system show sex differences. These conditions can occur at various stages of life, including before puberty, after puberty, and, in women, during the post-menopausal period. While many of these conditions are idiopathic (with unknown causes), some are secondarily related to autoimmune diseases, and others are linked to differences in injury risk to MSK tissues.

Sex differences have been observed in the risk of injuries to the MSK system. For instance, injuries to the anterior cruciate ligament (ACL) of the knee are more common in young females participating in certain sports, with a female-to-male ratio of up to 5:1 in some cases[16] .

Some of this risk is attributed to changes in joint laxity during the menstrual cycle[17], while other factors may relate to muscle function differences between females and males[18]. However, the underlying causes of all injury-related risks that show sex differences in incidence have not been fully characterized.

In several other conditions or diseases, MSK involvement may be secondary to immune dysfunction and subsequent localization within a joint, either generally or in specific joints. Many autoimmune diseases disproportionately affect females, leading to conditions that impact joints and other connective tissues, predominantly in females. Rheumatoid arthritis (RA) is an example, which can begin before puberty (e.g., Juvenile Idiopathic Arthritis; Juvenile Inflammatory Arthritis; JIA)[19], in adulthood, or even in post-menopausal women[20]. JIA shows sex differences in incidence, with a female-to-male ratio of 3-6.6:1[19]. However, sex hormones alone cannot explain these disparities, given the early onset of JIA in many patients. Additionally, some JIA patients exhibit involvement of other tissues, which also appear to be sex-associated. For example, females with JIA often experience knee involvement and chronic anterior uveitis[19].

A third category of MSK conditions showing sex differences in incidence/prevalence includes those not linked to immune dysfunction or obvious injury events[21]. An example is adolescent idiopathic scoliosis, affecting 1%–4% of adolescents[22], resulting in varying degrees of spinal deformities, typically manifesting in the post-puberty phase of growth and maturation[23]. This condition primarily occurs in young females[23], with a female-to-male ratio of up to 10:1 for those with spinal curvatures exceeding 30°[24]. While some cases can be managed with braces, others require surgery to correct deformities that severely impair function and quality of life[25].

Although scoliosis progression may slow after skeletal maturity, in some individuals, it may "re-activate" post-menopause, necessitating surgery later in life.

Other examples of this third category include the development of osteoarthritis (OA), osteoporosis (OP), and sarcopenia in post-menopausal women (reviewed in 21). Before menopause, the incidence of idiopathic OA is approximately equal in females and males (~1:1), but post-menopause, the ratio increases to >2:1 (discussed in 21). While osteoporosis can occur in younger individuals due to certain drug treatments or surgeries, most osteoporosis cases develop post-menopause, with approximately 70%–75% of patients being female and ~25% male. However, there is significant variability in bone loss rates among OP patients, indicating disease heterogeneity. Sarcopenia, the loss of muscle mass and function, can also occur with aging, contributing to the decline of the "muscle-bone" unit[26].

From the discussion above, several key points regarding sex differences and MSK disease risk emerge:

1. Sex differences are relative, not absolute, affecting only a subset of the total population.
2. Sex differences in MSK conditions may manifest during hormone level changes at their onset (puberty) and loss (menopause), as well as during development. Thus, MSK conditions are evident across the lifespan, often occurring during or as a result of transitional phases such as puberty and menopause.
3. There is heterogeneity within each sex in terms of risk, suggesting that factors other than just sex hormones contribute to risk.
4. Different MSK conditions that show sex differences likely involve different molecular mechanisms, and not all can be directly attributed to sex hormones.
5. MSK involvement in diseases with sex differences may be primary or secondary.

The purpose of this review is to explore in detail a limited but representative range of MSK system diseases and conditions concerning their onset and progression that show sex-dependent differences. The goal is to better understand the similarities and differences in the molecular mechanisms involved and their potential relationship to sex hormones and their receptors across the lifespan. Given the large number of MSK diseases and conditions exhibiting sex differences, the selected subset for discussion represents different tissues, life cycle phases, and possible mechanisms. As discussed, studying sex differences and the role of sex hormones and their receptors is complex, partly due to human heterogeneity and the specific circumstances surrounding different life cycle stages.

SEX DIFFERENCES IN RISK FOR INJURY TO MSK TISSUES DURING DEVELOPMENT, GROWTH, AND MATURATION

Neonatal Hip Dysplasia: Development

Sex differences in the risk of musculoskeletal (MSK) dysfunction can emerge as early as fetal development. A pertinent example of this is hip dysplasia in newborns. Research has consistently shown that the incidence of neonatal hip dysplasia is higher in females than in males, with commonly reported Odds Ratios for female-to-male (F/M) of 3.8-4 [27]. Within this group, several factors have been identified that contribute to the risk, including family history and genetic predisposition[28].

The rate of unilateral hip dysplasia is higher on the left side compared to the right, with only a small percentage (~10%) of patients experiencing bilateral hip dysplasia[29]. When identified, this condition can often be corrected using noninvasive methods like braces or a Pavlik harness to keep the femoral head within the acetabulum[30]. Failure to address this condition early in life can make conservative treatment ineffective, leading to the early onset of osteoarthritis (OA) and potentially requiring arthroplasty at a young age. Therefore, maintaining correct biomechanics during hip growth and maturation necessitates proper alignment of the joint components. Notably, whether increased hip laxity occurs in this population post-puberty, when sex hormones fluctuate with the menstrual cycle, has not been well-documented. If tissues affected by developmental hip dysplasia exhibit unique responsiveness to sex hormones, there might be a resurgence of hip laxity, altering biomechanics and increasing the risk for early OA.

The mechanisms underlying sex-dependent differences in the development of hip dysplasia are not well understood. Noninvasive treatments are usually short-term interventions aimed at keeping the hip joint stable, and since hip dysplasia is not a permanent developmental issue, neonates can "correct" the deficiency once removed from the intrauterine environment. Ligaments, which contribute to the stability of the femoral head in the socket, were once considered significant in this developmental issue. However, studies did not find substantial differences in the gross characteristics of the ligamentum teres between patients and controls[31]. These studies did not explore ligament function, so the possibility remains that maternal hormones might have temporarily affected the laxity of connective tissues during hip development, with this influence being self-corrected after birth. It is noteworthy that elevated estrogen receptor levels have been found in the hip tissues of babies with developmental dysplasia[32], as well as higher levels of receptors for relaxin—a protein related to

IGF-1— which increases late in pregnancy and in some species' milk, including humans[33]. However, this hormonal influence does not explain the difference in hip dysplasia between the left and right sides. The extent of hip dysplasia varies (i.e., severity), indicating that factors beyond hormone levels might be at play, potentially at the cellular level, involving sex hormone receptors or genetic factors[34]. Thus, any left-right differences within a sex may involve other variables. This conclusion is supported by findings in pregnant women, where joint laxity occurs but does not correlate with serum relaxin levels[33]

Improvements in imaging techniques have enhanced the detection of hip dysplasia[35], leading to greater sensitivity in diagnosing the condition[36]. These advancements may also help to identify sex differences in patients with borderline dysplasia[37]. Further advancements might be achieved through the use of machine learning and artificial intelligence, along with improved training[38]. Additionally, some reports suggest that it may be possible to detect the condition prenatally[39]. These are significant developments as even subtle forms of hip dysplasia could contribute to the development of hip osteoarthritis later in life and might help explain the higher incidence of osteoarthritis in post-menopausal women[26] . This is relevant because, despite early detection and treatment, many patients still exhibit altered gait patterns[40,41] .

The idea that ligament laxity may play a role in developmental hip dysplasia should not be dismissed, as it might also contribute to the risk of knee injuries during adolescence and beyond, as discussed later. It is also worth considering whether women with neonatal hip dysfunction might be predisposed to developing hip issues after pregnancy, where laxity reoccurs, potentially affecting hip biomechanics again.

Some individuals, predominantly females, are diagnosed with acetabular dysplasia during adolescence or adulthood[41]. This condition also exhibits a left hip predisposition and can lead to osteoarthritis. While very young infants with hip instability can develop acetabular dysplasia[42], some researchers suggest that acetabular dysplasia is a distinct condition from developmental dysplasia [41]. Further research is required to understand the underlying mechanisms, but both conditions seem to show sex differences.

Sex differences in risk for ACL rupture postpuberty

Sex differences in the risk of ACL rupture after puberty have been observed in various sports injuries, with distinctions occurring either before or after skeletal maturity[43]. ACL injuries are particularly prevalent, especially among young athletes, with over 200,000 cases annually in the United States[44]. Notably, most ACL injuries are non-contact and occur in sports requiring cutting maneuvers[44] . Females are more prone to ACL injuries than males, with some sports like soccer showing a female-to-male injury ratio of up to 5:1[16]. An ACL rupture often necessitates reconstruction to stabilize the knee, yet even post-reconstruction, approximately 50% of individuals may develop osteoarthritis (OA) within 10–15 years[45]. While some patients manage unreconstructed injuries well, others [46]. Post-reconstruction, males and females continue to exhibit different gait and muscle patterns, with persistent quadricep muscle integrity loss contributing to OA risk[47].

Given the significant impact of ACL injuries and the evident sex differences, extensive research has focused on understanding risk factors[48] and developing prevention strategies[49] to reduce the injury incidence, particularly in females. Neuromuscular training programs designed to address muscle imbalances have been shown to significantly reduce ACL injuries in Norwegian female handball players, although their adoption outside of clinical trials remains low, and the broader population may not fully embrace these programs despite their success in controlled settings[49]. Consequently, changing behavior remains a challenge even with strong scientific and clinical evidence.

Sex differences in risk for development of adolescent onset scoliosis post-puberty

In the context of adolescent-onset scoliosis post-puberty, Adolescent Idiopathic Scoliosis (AIS) typically begins after puberty, characterized by a lateral spinal curvature of at least 10°. As the curvature severity increases, the female-to-male ratio of affected individuals rises, reaching approximately 10:1 for curvatures exceeding 30°[50]. The incidence of AIS is about 1%–4% of the adolescent population, with similar rates across geographically diverse countries like the USA, China, and Brazil[22].

The majority of the curvature develops before skeletal maturity, and progression typically slows after this point, despite continued hormonal cycling in females. No evidence suggests that AIS progression differs between males and females concerning disease progression and skeletal maturity.

Given the correlation between AIS onset and puberty-associated hormonal changes, some researchers have examined the effects of subsequent pregnancy on women with a history of AIS. Studies by Betz et al. (1987[51]) and Dewan et al. (2018)[52] found minimal effects of AIS on pregnancy and outcomes, indicating that pregnancy-related hormonal changes do not significantly "re-activate" AIS in affected females.

The coordinated growth required after puberty implies that all system components must work in harmony. Based on this concept, some researchers have suggested that muscle imbalances during growth may contribute to AIS development and progression[53,54]. Whether muscle asymmetry existed before puberty and was only exacerbated by puberty and rapid growth remains an open question[54]. Additionally, paravertebral muscle analysis has revealed potentially relevant molecular differences in AIS patients[55]. Methylation of an estrogen receptor (ESR 2) has been reported more frequently in AIS patients, though it does not correlate with disease severity[56]. Kudo et al. (2015)[57] also reported higher levels of nerve growth factor (NGF) and estrogen receptor-alpha in AIS patients, with NGF levels correlating with curvature severity. However, other studies have found that estrogen receptor 2 levels in such muscles correlate with Cobb angle in AIS patients[55]. Further studies have explored potential roles for growth-related hormones[58] and sex hormone levels[59] in AIS development and progression. Nonetheless, the data in this area remain limited and require further study.

Given the incidence of AIS is only ~1%–4% of the population, other factors beyond puberty-related sex and growth-related hormone levels must be involved. It is also unclear whether muscle involvement is primary or secondary in terms of causality. To address these gaps, numerous studies and reviews have examined the possibility of genetic or epigenetic factors influencing AIS initiation and progression[60]. Various genes and gene families have been implicated in AIS, including Fibrillin-1[61], Fibrillin-1 and Fibrillin-2 variants associated with severe disease[62], estrogen receptor variants and polymorphisms, the NUCKS1 gene in Chinese adolescents[63], and the helicase DNA-binding protein 7 (CHD7)[64]. While additional studies are necessary, the heterogeneity in genetic contributions observed so far suggests that AIS may be an umbrella term for multiple subsets of the disease, or more research is needed to better understand the molecular basis for a common set of pathways.

INFLUENCE OF SEX ON MSK TISSUES AS AN ADULT

Sex differences in spondyloarthritis

Spondyloarthritis refers to a diverse group of conditions that affect various tissues, including joints and the spine, particularly the sacroiliac joints[65]. These immune-mediated inflammatory diseases often target the spinal tissues, especially the supportive tissues such as ligaments and their entheses in the axial skeleton[66]. Although ankylosing spondylitis, a form of spondyloarthritis, was traditionally considered a male-dominated disease, recent findings suggest that it also affects a subset of females[67]. Studies have reported sex differences in the presentation and disease activity, with females often experiencing higher disease activity compared to males and responding differently to clinical interventions[68].

The genetic basis of axial spondyloarthritis is well established, with strong associations with the HLA-B27 allele[69]. The sex differences in spondyloarthritis are notable in that the majority of patients are male, contrasting with many other autoimmune diseases where females are more commonly affected. This suggests that females with spondyloarthritis-related conditions may represent a unique subpopulation. The molecular and cellular mechanisms underlying these sex differences have yet to be fully elucidated, but ongoing research aims to provide greater clarity on these issues in the near future.

Sex differences in osteoporosis

Osteoporosis (OP) is characterized by a loss of bone integrity and an increased risk of low-energy fractures[70]. Although OP is often associated with post-menopausal females, it affects only a subset of this population, with a female-to-male ratio of approximately 3:1. The treatment of OP in males is relatively understudied[71]. Furthermore, sex differences exist in the timing of fractures, with males generally experiencing fractures about 10 years later in life than females [71]. The variability in bone loss between individuals of either sex suggests that multiple factors influence the underlying mechanisms. While there are known sex differences in skeletal growth[72], correlations between early-life bone growth, the rate of bone loss with aging, and the onset of menopause have not been established.

For many years, hormone replacement therapy (HRT) was an effective treatment for OP in females, but concerns about associated risks (e.g., cardiovascular disease, breast cancer, venous thromboembolism, endometrial cancer) have led to a decline in its use[73]. However, HRT is now being reconsidered as a treatment option. Nevertheless, OP often remains a "silent disease" until a fracture occurs, resulting in many individuals, particularly men, going untreated as OP is typically viewed as a female disease.

The molecular basis for why only a subset of females develop OP following menopause, and why a subset of males also develops the condition, remains largely undefined. It is also unclear whether the mechanisms involved in OP are similar or different between sexes. Despite this, males do respond to treatments such as bisphosphonates, indicating potential commonalities in the disease's underlying mechanisms[74].

Sex differences in osteoarthritis

Osteoarthritis (OA) is a degenerative condition that affects joints such as the knee, hip, shoulder, and fingers. Traditionally, it was viewed as a disease of the articular cartilage, the tissue most affected by OA. However, it is now understood as a disease of the entire joint, with the joint considered an organ system[75]. As recently reviewed by Hart[76], OA is currently recognized as an inflammatory disease, with sex differences observed in some inflammatory markers associated with OA[77].

Before menopause, the ratio of females to males with OA is approximately 1:1, but post-menopause, this ratio increases to more than 2:1[78,79]. This indicates a higher incidence of OA in females after menopause compared to males. It has been suggested that this subset of post-menopausal females, who primarily develop knee and hip OA, represents a distinct subtype of OA[76]. Currently, conservative treatment options, such as exercise, pain medications, and bracing, are not sex specific. However, in the future, treatments may be tailored to address the potentially unique mechanisms involved in OA in post-menopausal females, as suggested by Hart[76] and Hart et al.[26]. Despite this, progress in conservative treatment for OA has been slow, leading many patients to eventually undergo total joint replacement.

In this subset of post-menopausal females, the loss of sex hormones results in alterations in joint regulatory mechanisms, contributing to OA[80]. The precise mechanisms by which sex hormone loss leads to OA in this subset remain largely unexplored.

Sex differences in Sarcopenia

Sarcopenia is the age-related loss of muscle structure and function, including muscle mass and strength, and it can occur in both males and females. However, there are sex-associated differences in the onset and progression of muscle loss[81]. Sarcopenia can also be influenced by associated obesity in some patients [82]. In older individuals, sarcopenia and sarcopenic obesity can impact other age- and sex-related conditions, such as osteoporosis[83] , cardiovascular fitness[84], osteoarthritis[85], and cognitive performance[86], all of which affect different subsets of post-menopausal females compared to age-matched males.

Thus, sarcopenia, as an age-related loss of muscle integrity, appears to interact with other post-menopausal conditions, influencing disease activity and progression. As some post-menopausal females tend to gain weight, likely due to the loss of estrogen's effect on energy balance[87], sarcopenic obesity is prevalent in this population, potentially exacerbating the impact of the conditions mentioned above.

Sex differences in Intervertebral Disc Degeneration

Estrogen is believed to play a role in intervertebral disc (IVD) degeneration[88]. In the post-menopausal state, the primary symptom is often pain[89]. Types of IVD degeneration include adult-onset lumbar scoliosis[90] or spondylolisthesis[91]. The causes of these conditions in post-menopausal women are largely unknown, although some associations with parity have been made[92]. Risk factors for pregnancy-related pelvic girdle pain have also been investigated[93], along with pregnancy-associated changes in spinal motor control[94].

Evidence has emerged indicating that hormone replacement therapy (HRT) may prevent the development of post-menopausal spondylolisthesis [95], implicating estrogen loss in the condition's development rather than solely pregnancy-related factors.

In summary, several musculoskeletal (MSK) conditions occur at higher rates in subsets of post-menopausal females compared to age-matched males or are associated with conditions unique to females, such as pregnancy. Some of these conditions can be more directly linked to the loss of sex hormones than others, but significant sex differences have been observed. Notably, adolescent idiopathic scoliosis, which arises in the thoracic spine post-puberty and is associated with increased sex hormone levels, differs from adult scoliosis, which occurs in the lumbar spine and emerges post-menopause following sex hormone loss. Adult scoliosis may be a "reactivation" of somewhat quiescent adolescent idiopathic scoliosis or a new development, but it appears to progress rapidly in the post-menopausal state in a subset of patients [95.] The reasons for its occurrence in this particular subset are currently unknown. A recent clinical case series of 187 patients with Adult Symptomatic Lumbar Scoliosis (ASLS) found that over 90% were female[96]. Thus, the majority of ASLS patients are post-menopausal females with a mean age of over 58 years [96]. Details regarding the characteristics of males with ASLS are not readily available.

On the surface, these differences may be difficult to reconcile, but it is evident that many epigenetic changes occur during puberty[76] and as a result of life experiences. Therefore, the loss of sex hormones following menopause likely does not return females to a pre-puberty state. The development of post-menopausal conditions is likely complex and multifactorial.

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GENDER-SPECIFIC DIFFERENCES IN TISSUE COMPOSITION AND IN OSTEOARTHRITIS PROGRESSION

Despite ongoing research, the mechanisms underlying the onset, progression, and treatment of osteoarthrosis (OA) remain largely unknown. Identified risk factors such as age, genetic predispositions, obesity, and traumatic injury vary in their impact, with women disproportionately affected[97–100] .

The role of gender in OA has often been underestimated[101,102] , yet there are clear sex/gender differences in the prevalence, incidence, and severity of OA. Studies consistently show that men generally have higher quality and greater quantities of knee cartilage compared to women, particularly after menopause, which corresponds with more severe clinical symptoms[98].

Research examining gender as a risk factor for knee OA found that women have almost double odds compared to men [103]. This disparity may stem from differences in cartilage composition between the sexes, potentially leading to earlier joint degeneration in women[104,105]. Imaging techniques, such as magnetic resonance imaging (MRI), enable non-invasive assessments of cartilage composition, including collagen matrix loss, proteoglycans, and water content variations[106,107]. Literature shows how knee morphometry varies with gender[108–117] as MRIs have revealed the disparities in cartilage quantity, with men typically having more than women. These differences in cartilage thickness and volume have been observed across several stages of life, even starting as early as childhood.

Research from the early 2000s[110] highlighted that variations in cartilage formation could account for sex- and joint-compartment-related differences in the risk of knee OA. A study of 92 children revealed that males had significantly more knee cartilage than females, with variations in cartilage thickness and volume being statistically significant at all measured locations, attributable to gender in 6–36% of cases. These differences remained significant even after accounting for bone density, age, BMI, bone area, and physical activity. This last factor is very important, as physical activity was a significant explanatory factor for cartilage volume at all sites, however, it did not explain the observed sex differences. Therefore, although boys may be more active than girls, on average, physical activity is not sufficient to explain sex-related differences in cartilage volume. A study of 200 healthy Taiwanese children (5–13 years old) found that for all the joints studied (knee, ankle, wrist, metacarpophalangeal, and proximal interphalangeal joints), cartilage was thicker in boys compared to girls[118]. Of note, these results are across both weight and non-weight bearing joints. Similar results were observed in 394 healthy Danish children, 7–16 years old, where boys had thicker cartilage than girls on the same joints mentioned above[119]. Remarkably, these sex differences remain constant throughout puberty[110] and no significant changes in cartilage volume were observed between pre- and post-menarchical girls[110], which questions the role of sex hormones in the observed dimorphism. Indeed, in prepubescent children as young as 4–9 years old, boys still have a thicker cartilage at the medial epicondyle compared to girls[120].

Gender differences in cartilage thickness and volumes were also observed in healthy participants who underwent MRIs to quantify articular surface area, cartilage thickness, and volume. Women had 19.9% smaller patellar cartilage, and 46.6% smaller medial tibial cartilage compared to men, though these differences were less pronounced when body weight and BMI were considered[111].

Two studies[112,113] examining the relationship between gender, BMI, age, bone size, and cartilage degeneration rate found that men had significantly higher (33–42%) knee cartilage volume than women, and that the rate of cartilage deterioration in women increased significantly after age 40, with annual cartilage loss in the medial tibia, lateral tibia, and patella at 3.5%, 2.6%, and 0.8%, respectively. An average atlas of femoral knee cartilage morphology was produced[108], showing that after adjusting for joint surface area, women's cartilage was thicker than men's. The cartilage was normalized to an atlas for overall size; therefore, if the cartilage scaled nonlinearly with body size, a linear global correction resulted in a larger cartilage volume. Additionally, gender disparities were noted in post-matrix-associated autologous chondrocyte transplantation (MACT) zones and healthy cartilage[117], with women showing lower cartilage quality and less healing capacity than men. MRI findings indicated that T2 values, a measure of cartilage quality, were significantly shorter in men than women. Using 3T MRI, the knee cartilage of three patient cohorts was quantitatively described[109] : young active individuals, middle-aged without OA, and middle-aged with OA. Women had higher levels of lateral articular and patellofemoral cartilage on T1ρ (T1rho), indicative of lower proteoglycan content and lower tissue quality.

Gender-based morphological variations in femoral condyle architecture were also observed, even in patients of the same height[114]. A stratified study of patient height and medial/lateral condylar width revealed significant differences in condylar widths for each stratum, with a statistically significant difference in articular cartilage width between males and females (31.62 ± 3.54 for males and 26.53 ± 3.70)[114].

In comparison to the knee, the morphometric differences in cartilage within the hip joint between the two genders have been less extensively studied and described, however, it was noted that men had better cartilage quality compared to women. Longitudinal studies combining hip cartilage volume measures and standard radiographic measures may provide more definitive answers in this regard. Few data are available in the published literature to explain the sex differences observed in hip OA, with conflicting reports about associations of systemic factors such as hormonal status and obesity with hip OA in males and females

In a randomly selected population-based cohort, was found that female sex was independently associated with lower hip cartilage volume in MRI assessment[121]. Another, MRI analysis of the hip in asymptomatic participants revealed higher T1ρ values in women, unaffected by age, BMI, or sports activity levels. Women's T1ρ value standard deviations were notably larger than those for men[116].

Histological analysis suggests that women tend to have lower cartilage quality than men. Studies focusing on osteoarthritic cartilage have shown that women often have more cartilage cracks, particularly in moderate to severe OA cases. Cracks in the subchondral bone were more frequent in severe OA, and women with severe histological grades exhibited a higher frequency of cracks[122].

The literature consistently underscores that men typically have significantly higher cartilage volumes than women, who are more predisposed to developing OA, especially with advancing age. Women over 50 are particularly vulnerable to developing OA in various joints, often presenting at a more advanced clinical stage. While the exact reasons for these gender differences remain unclear, understanding the underlying processes and the role of gender in OA development is crucial for epidemiological, diagnostic, and treatment purposes. Recognizing these gender-based disparities may lead to more tailored diagnostic approaches and personalized treatments.

Significant variability in cartilage width and structure between genders is evident. Although histological analyses of cartilage composition were not conducted, imaging studies have illustrated these variations. MRI assessments have documented both qualitative and quantitative differences, with males frequently showing larger cartilage volumes in the hip and knee compared to females, even after adjusting for height and body weight. Some studies attribute variations in cartilage volume to differences in joint size rather than cartilage thickness. Moreover, differences in cartilage composition have been linked to lower proteoglycan concentrations in women's cartilage.

Research into gender differences in cartilage has also highlighted that these disparities become more pronounced with age, particularly after 50, suggesting a link between developmental changes in cartilage and its loss in adulthood. The significant reduction in estrogen levels in postmenopausal women is hypothesized to contribute to the initiation of OA. Studies have shown that women begin losing cartilage around age 40, with a notable increase after menopause. The specific reasons behind these age-related differences are not fully understood, but they may reflect earlier effects of estrogen deficiency and menopause. Hormone replacement therapy has been associated with a reduced rate of cartilage degeneration in women, indicating potential preventive measures for OA. Nonetheless, the reasons for the observed gender disparity in cartilage quality and quantity remain complex and require further investigation.

Recent advancements suggest that gender-specific customized prosthetic implants, considering morphological and biomechanical differences between genders, have achieved very favorable outcomes. This progress points towards a deeper understanding of the biological mechanisms underlying diseases, aiming for more personalized and effective treatments.

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EXPERIMENTAL STUDY

INTRODUCTION

This study arises from the need to investigate whether the biophysical properties of tissues in male and female patients influence the clinical and radiological presentation of primary hip osteoarthritis. It aims to enhance the understanding of primary hip osteoarthritis progression in both sexes from clinical and biomechanical perspectives by examining differences in preoperative cartilage thickness, glucosaminoglycan (GAG) content, and postoperative outcomes between males and females.

The biomechanical and histological studies currently available in the literature do not sufficiently address the well-documented sex-related differences in the prevalence, severity, and functional disability associated with primary osteoarthritis. Although some biomechanical differences between males and females have been reported, most biomedical studies have been conducted exclusively on male animals, and many clinical trials have excluded women. This selection bias may have led to the underreporting of sex-related differences.

Existing experimental studies do not offer a comprehensive analysis of how biophysical properties can influence clinical outcomes. Most studies rely on histological analysis, imaging assessments, or biomechanical differences, which hinders the generalization of these results.

The cartilage structure of the hip joint is highly variable, as demonstrated by the wide variability in current studies. These variations can be attributed to the limitations of studying cartilage structure using MRI assessments alone. First, the difficulty in distinguishing femoral head cartilage from acetabular cartilage may lead to measurement errors, and MRI results are heavily dependent on the contrast relative to adjacent tissues. Second, MRI scans are typically performed at specific times of the day, which may not account for diurnal variations in hip cartilage volume due to compression over the course of the day. Third, cartilage thickness has often been used as a marker in studies of hip cartilage morphology, but since it is usually measured in the central sagittal section, and thickness distribution may be inhomogeneous in patients with osteoarthritis, this could contribute to lower reproducibility of these techniques. Additionally, most MRI cartilage morphology studies have been conducted in specific ethnic populations (e.g., Tasmanian), which further limits the generalizability of the findings.

Limitations were also identified in histological and biomedical studies where differences in cartilage composition and GAG concentration were described. Firstly, joint tissues other than articular cartilage may contribute to the GAG concentration in synovial fluid. Furthermore, interpreting the analysis of GAG in synovial fluid can be challenging, as the sources of GAG are unknown. Additionally, the clinical stage of joint disease undoubtedly has a differential effect on each tissue surrounding the joint, further complicating the interpretation.

With a robust and representative scientific model, it is possible to precisely and comprehensively assess how the biophysical properties of tissues in male and female patients influence the clinical and radiological presentation of primary hip osteoarthritis. Moreover, the selection of specific results allows for better data interpretation, facilitating the generation of recommendations that are directly applicable to clinical practice, with the potential to either modify or confirm current medical practices.

Through this comprehensive approach, the study aims to make a meaningful contribution to the existing body of knowledge regarding how the biophysical properties of tissues in male and female patients influence the clinical and radiological presentation of primary hip osteoarthritis.

MATERIALS AND METHODS

We designed a scientific workflow model that does not interfere with the routine clinical and surgical activities dedicated to patients requiring total hip replacement for primary osteoarthritis. Patients were carefully selected using exclusion criteria to avoid selection biases, and each patient underwent a clinical evaluation using validated clinical and functional scores.

Subsequently, patients were assessed radiographically with standard preoperative hip and pelvis X-rays to facilitate preoperative planning and to grade the osteoarthritis. During surgery, the resection of the femoral head, a well-documented standard procedure in total hip replacement, was performed. This tissue collection for study purposes does not represent an additional invasive procedure. The resected femoral heads were preserved to obtain tissue specimens for microstructural analysis.

The study protocol employed a series of specialized techniques and methodologies to ensure both the reliability and reproducibility of our results. Each step was meticulously conducted in accordance with recognized standards, ensuring that the findings would not only hold scientific credibility but also offer clinically relevant insights.

Various microstructural features were assessed, including bone mineral density, bone volume fraction, tissue anisotropy, trabecular thickness, and trabecular spacing.

Study sample

After Institutional Review Board approval, and in accordance with Declaration of Helsinki for medical research involving human subjects[123], patients aged >18 affected by primary hip ostheoarthritis were prospectively included in the study.

Patients with an history of specific hip conditions leading to secondary OA, such as hip fractures, Perthes's disease, femoral-acetabular impingement, hip dysplasia, those who had already received hip surgery in the were excluded in order to avoid selection biases. Patients with diagnosis of rheumatologic disease, connective tissue disease and malabsorptive disorder were also excluded, because these conditions can affect the bone and cartilage quality confounding the results. Subjects with non-available imaging or without a minimum 1-year follow-up were also excluded.

Data collection

Medical charts of included patients were obtained and analyzed from our institutional database. Demographic data, age, gender, laterality, intraoperative complications, and follow-up complications were collected.

The functional disability and symptoms of enrolled patients was evaluated by validated clinical scores such as the Harris Hip Score (HHS)[124] and WOMAC score[125]. These indices were calculated in keeping with existing hip surgery literature[124–126]. Both are formulated assuming the results of hip surgeries could be measured and could be used to evaluate various hip disabilities and methods of treatment for different hip pathologies treated with total hip replacement.

The radiological data were measured via standard preoperative hip and pelvis x-ray, in order to perform an adequate preoperative planning for prosthesis implantation and to grade the osteoarthritis according to the Tonnis classification. The Tonnis classification groups the patients into three separate grades of osteoarthritis based on the evaluation of a standard AP pelvis radiograph[127].

The femoral heads specimens collected during surgery, were adequately stored and sent to the experimental biomechanics laboratory of the Istituto Ortopedico Rizzoli research Center, for microstructural characterization. Here five specimens were collected for each femoral head and analyzed for bone mineral density, bone volume fraction, tissue anisotropy, trabecular thickness, and trabecular spacing.

The primary outcomes were the description of postoperative outcomes, radiographical grading of osteoarthritis and microstructural characterization differences between female and male patients. Then all pre and postoperative data were analyzed and preoperative and postoperative gender differences in hip joint degeneration, cartilage composition, pain, disability and functional performance were highlighted.

Moreover, adverse events during surgery and the 30-days postoperative period and return to work time were collected.

The diagnosis of any postoperative adverse event was postulated by an experienced surgeon or based on intraoperative findings, clinical data, radiographic findings, blood tests, and/or a documented positive culture obtained at the time of revision or debridement surgery.

All the measurements were evaluated independently by the candidate and one another member of the working group (FB, MB), both blinded to their respective measurements and to the patient's name. After checking for data accuracy and inconsistent results, any disagreement was solved by senior surgeon (CF).

Functional disability assessment

The Harris Hip Score (HHS) was developed to assess the outcomes of hip surgery and is designed to evaluate various hip disabilities and treatment methods in an adult population. The original version was published in 1969, where thirty-eight individuals who had undergone total hip replacement (THR) operations due to traumatic arthritis were the first patients evaluated using the HHS. The items were generated based on expert opinion, emphasizing that pain and functional capacity are the two primary considerations for hip surgery, hence these factors were given the most significant weight: 91 out of 100 points.

The HHS covers four domains: pain, function, absence of deformity, and range of motion. The pain domain assesses the severity of pain, its impact on activities, and the need for pain medication. The function domain includes daily activities (such as stair use, using public transportation, sitting, and managing shoes and socks) and gait (including limp, support needed, and walking distance). The deformity domain considers hip flexion, adduction, internal rotation, and extremity length discrepancy. The range of motion domain measures hip flexion, abduction, external and internal rotation, and adduction.

Therefore, the HHS consists of 10 items, with a maximum score of 100 points (indicating the best possible outcome). These points are distributed across pain (1 item, 0–44 points), function (7 items, 0–47 points), absence of deformity (1 item, 4 points), and range of motion (2 items, 5 points).

The HHS was originally developed for evaluating outcomes in patients undergoing surgery for femoral and/or acetabular fractures. Today, its most common use is for patients undergoing total hip replacement and conservative treatment for osteoarthritis.

Each item on the HHS has a unique numerical scale corresponding to descriptive response options, with the number of response options and points assigned varying by item. The range of motion item consists of 6 motions that are graded based on the possible arc of motion. Each range of motion gradation is assigned an index factor and a maximum possible value, which are used to calculate the arc of motion points. These points are summed and multiplied by 0.05 to determine the total points for the range of motion. The total HHS score is calculated by summing the scores for the four domains.

The HHS provides a maximum of 100 points, distributed as follows: pain receives 44 points, function 47 points, range of motion 5 points, and deformity 4 points. Function is further subdivided into activities of daily living (14 points) and gait (33 points).

A higher HHS indicates less dysfunction. A total score of 70 is considered poor; 70–80 is fair; 80–90 is good; and 90–100 is an excellent result. No normative values are currently available.

The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) is a widely used tool for assessing symptoms and physical disability, originally developed for individuals with osteoarthritis (OA) of the hip and/or knee. The WOMAC has also been applied to evaluate conditions such as back pain, rheumatoid arthritis, juvenile rheumatoid arthritis, systemic lupus erythematosus, and fibromyalgia. It was developed at Western Ontario and McMaster Universities in 1982.

The WOMAC was designed to assess clinically significant, patient-relevant changes in health status resulting from treatment interventions. Higher scores indicate greater pain, stiffness, and functional limitations. The WOMAC includes five items for pain (score range 0–20), two for stiffness (score range 0–8), and 17 for functional limitations (score range 0–68). The physical functioning section covers daily activities such as stair use, standing up from a sitting or lying position, standing, bending, walking, getting in and out of a car, shopping, putting on or taking off socks, lying in bed, getting in or out of a bath, sitting, and performing heavy and light household duties.

The questionnaire is self-administered and takes approximately 5 to 10 minutes to complete.

Radiographical assessment

The Tönnis classification originated from a series of research articles published in 1972 by Professor Dietrich Tönnis and his colleagues in Dortmund, Germany. The goal of these studies was to develop a quantitative method to differentiate between normal and dysplastic juvenile hips. In their article titled "A New Method for Roentgenologic Evaluation of the Hip Joint—The Hip Factor," the authors evaluated 817 adult hip radiographs (patients aged 21-50 years, excluding those who had undergone hip surgery) to develop a quantitative measurement for assessing hip dysplasia, referred to as "the hip factor."

As part of their analysis, the authors categorized the patients into three distinct grades of osteoarthritis based on the evaluation of a standard AP pelvis radiograph, forming the foundation of what is now known as the Tönnis classification.

- Grade 1 indicates slight narrowing of the joint space, slight lipping at the joint margin, and slight sclerosis of the femoral head or acetabulum.
- Grade 2 indicates the presence of small bony cysts, further narrowing of the joint space, and moderate loss of femoral head sphericity.
- Grade 3 is the most severe, indicating large cysts, severe narrowing of the joint space, severe femoral head deformity, and avascular necrosis.

The Tönnis classification system was specifically developed for the hip joint and is most directly applicable to a spheroidal (ball-and-socket) synovial joint reinforced by a fibrocartilaginous lip (the acetabular labrum). Because other diarthrodial joints have different anatomies and play different roles in weight-bearing and motion, the Tönnis grading system cannot be broadly applied to all joints.

Some studies suggest that the Tönnis classification may be less valid in its lower grades. Research involving a high number of low-grade osteoarthritis (OA) cases has demonstrated lower validity for the Tönnis classification. This is particularly important in one common application of the Tönnis classification, which is to help determine whether a patient might be a good candidate for hip preservation surgery—a procedure known to be less effective in patients with even mild arthritis. Moreover, because the Tönnis classification relies exclusively on radiographic findings, it does not consider other factors that might influence the success of hip preservation surgery, such as articular cartilage health, three-dimensional femoroacetabular anatomy, and labral integrity, which often require advanced imaging for proper evaluation.

A significant criticism of the Tönnis classification system is its subjectivity. The classification has been criticized for unclear terminology and overlapping parameters. Five major radiographic findings are used in the classification: presence of sclerosis, joint space width, head sphericity, cyst size, and osteophyte formation (described as "lipping at the joint margins"). However, none of these parameters includes quantitative definitions. For example, Tönnis Grade 2 arthritis includes "small" subchondral cysts, while Grade 3 is defined by "large" cysts, but no specific sizes are designated in the original article.

Additionally, Tönnis' original article does not provide guidance on which grade to assign if findings from different grades are present in a single radiograph. For instance, if a patient has moderate loss of femoral head sphericity (a Grade 2 finding) alongside only slight joint space narrowing (a Grade 1 finding)—as might occur in a patient with early Legg-Calvé-Perthes disease—the classification does not clarify whether this would be considered Grade 1 or Grade 2 arthritis. The classification assumes a stepwise progression in which all parameters worsen radiographically over time in accordance with the described grades, which is not always the case. Although femoral head sphericity is one of the more reliably reproducible parameters, it could lead to confusion in grading, particularly in patients with non-degenerative cam deformity and no radiographic signs of OA.

Although the Tönnis classification has limitations, it remains a simple system that provides a qualitative description of commonly obtained radiographic imaging of the hip. It continues to be widely used in both clinical practice and research. The classification relies on the visual assessment of an AP pelvis radiograph and does not require additional time or resources for digital or manual measurements.

Several studies have found that patients with higher Tönnis grades who undergo hip preservation surgery have poorer patient-reported outcome scores and are more likely to undergo premature conversion to total hip arthroplasty (THA). This suggests that despite its reliability issues, the Tönnis classification can be an effective tool for communication, prognosis, and research when used appropriately.

Surgical technique

All patients underwent standing antero-posterior X-rays of the pelvis and frog-leg X-rays of the affected hip. Digital pre-operative planning was performed using specialized software. During surgery, the patient was positioned supine with the foot of the operated leg secured by a boot on a specialized traction table, allowing for control of traction, flexion, rotation, adduction, and abduction. The lower limb was positioned with 10° of internal rotation and slight abduction, maintained at approximately 15° of hip flexion using a step. The surgical incision was made starting 2 cm distally and 2 cm laterally from the anterior superior iliac spine and extended distally by about 7–8 cm. Dissection of the subcutaneous plane was carried out down to the fascia of the tensor fascia latae muscle, which was then incised longitudinally to avoid damage to the lateral femoral cutaneous nerve. The tensor fascia latae was retracted laterally and the sartorius muscle medially. Branches of the lateral circumflex artery were isolated and ligated in every case. The capsule was fully exposed and gently opened with a seven-shaped incision, resulting in a thick proximally reflected flap suspended by a stitch. The femoral neck was osteotomized according to preoperative planning, 5 mm proximal to the trochanteric tubercle. The leg was then placed under modest traction and external rotation to enlarge the osteotomy area before the head was extracted using a corkscrew. Acetabular preparation was carried out using a chamfered reamer to limit impingement on soft tissues. Two screws were used if necessary. To prepare the femur, the leg was progressively externally rotated, extended, and adducted. Simultaneously, a release of the pubofemoral and ileofemoral ligaments, as well as the posterior-medial capsule, was performed to facilitate the elevation and external rotation of the femur. The capsule was sutured, and intra-articular drainage was applied in every case. A final X-ray check was performed at the end of the surgery.

The same implant design and type of instruments were used for all the surgeries: a hydroxyapatite-coated elliptical cup for the cup, and a straight, triple tapered, hydroxyapatite-coated non-cemented stem for the femur.

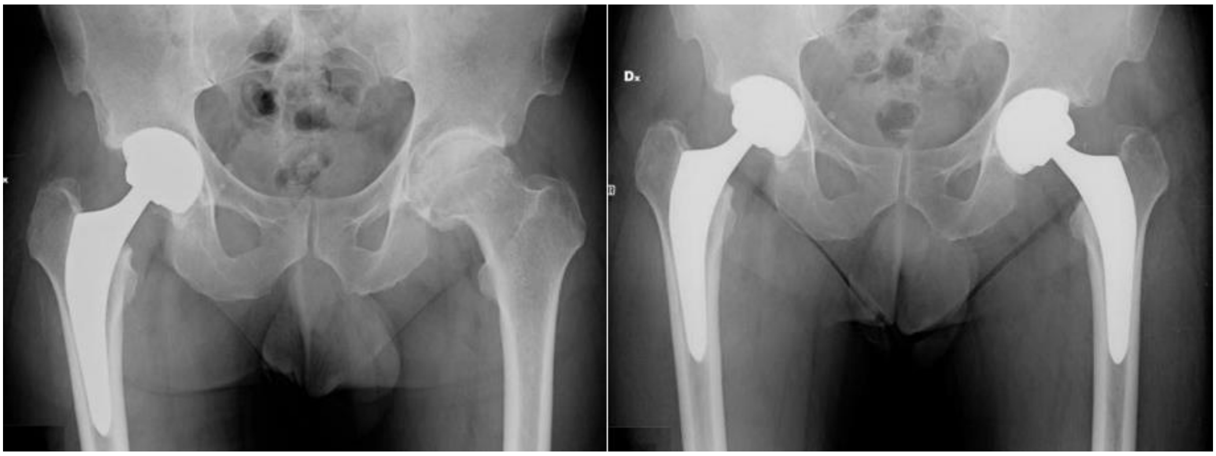

Figure 12. Pre and postoperative x-ray of a patient operated for left primary osteoarthritis

Microstructural characterization

The heads were stored in a 70% ethanol solution for at least four weeks before testing to prevent the transmission of infectious diseases during laboratory handling. It has been demonstrated that this treatment does not affect the elastic properties of cancellous bone, although it does increase viscoelastic properties such as hysteresis energy and loss tangent.

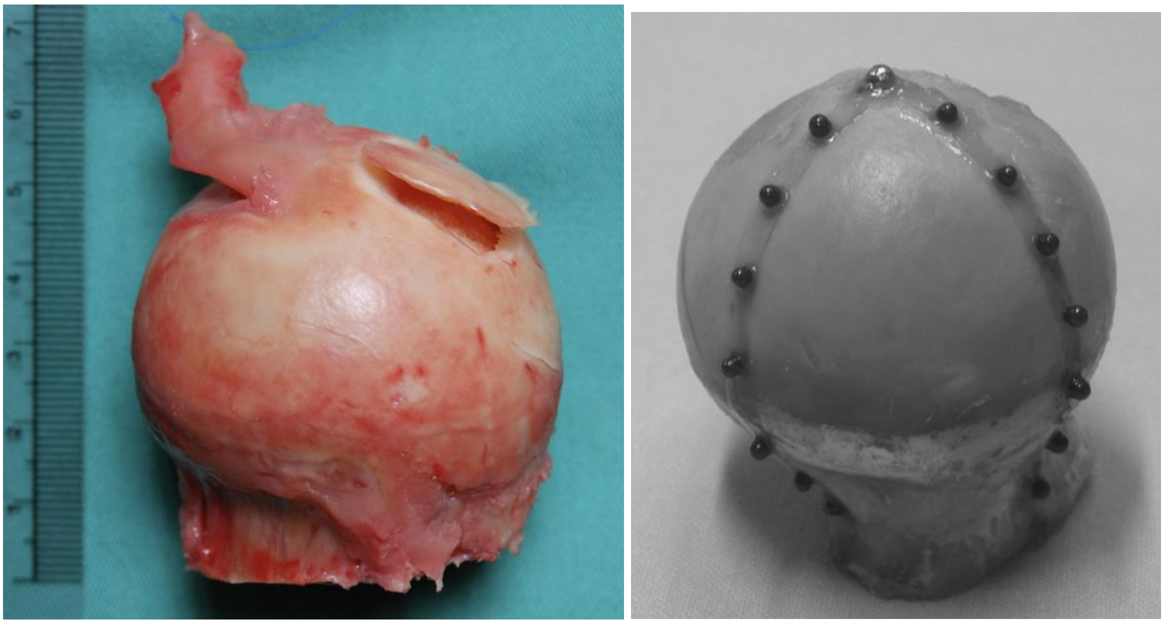

Figure 13. The intraoperatively resected femoral head was collected (A). Each head was divided in 4 quadrants by 2 orthogonal lines (the center was the fovea), B. From each of the quadrants and from the fovea, 1 specimen was obtained. So 5 specimens were obtained from each head.

Finally, a 10mm cylinder was extracted from the head slice using a holed diamond-coated milling cutter with the slice immersed in water. The specimen's height and diameter were measured.

The cylindrical specimens underwent micro-tomographic analysis. During microCT scanning, each sample was placed vertically into a polyethylene cylinder filled with Ringer’s solution. The scanner operated at a voltage of 50 kVp, a current of 200 mA, and used a 1-mm-thick aluminum filter to reduce beam hardening. The image acquisition process involved a rotation over 185°. For each specimen, 1024 microCT cross-sections (total height 20mm) were reconstructed using a filtered back-projection algorithm. Each reconstructed cross-section was saved as an 8-bit greyscale image, 1024 × 1024 pixels in size, with an isotropic voxel size of 19.5 μm.

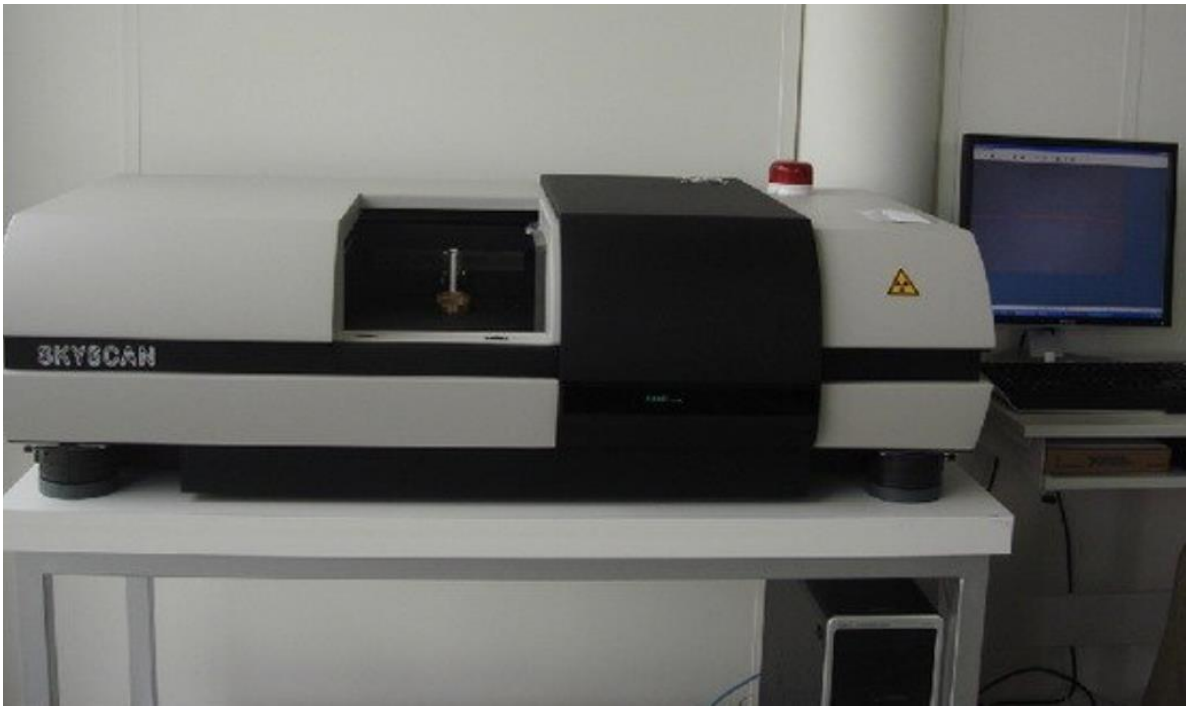

Figure 14. Micro CT scan, model Skyscan 1072, Skyscan, Aartselaar, Belgium

For each bone sample, the stack of microCT cross-sections was then binarized using a global threshold procedure. The following structural parameters were calculated for each specimen: bone volume fraction, trabecular thickness, trabecular separation, bone mineral density and anisotropy degree following the recommendations of the American Society of Bone and Mineral Research.

Statistical analysis

After collection of baseline demographics and outcomes our cohort was subdivided in different cohorts. Indeed, we evaluated gender status and subdivided our cohort into female and male groups.

The differences between the various groups were assessed using hypothesis testing based on an unpaired t-test or Person's chi-square distribution test used to investigate whether there were significant differences in the measured continuous or categorical parameters, respectively, between the two groups. Subsequently, to verify differences among samples collected from the two genders a Friedman test was used.

Missing data, if present, were handled using complete case analysis, discarding units with incomplete information. However, if the elimination of units with incomplete data resulted in a significantly reduced sample size, missing data was addressed using multiple imputation, generating simulated values for the missing data, considering the uncertainty associated with the missing data.

All statistical analyses were conducted with Jamovi version 2.2 (The Jamovi Project, Sydney, Australia) software. *P* value <.05 was considered significant.

RESULTS

Demographic Data

A total of 58 patients were included in this study, with a near-equal distribution between genders, comprising 31 females (53.3%) and 27 males (46.5%). The mean age at the time of surgery was 65.64 years, with a range of 45 to 80 years. The majority of the patients (72.4%) were over the age of 60, reflecting a predominantly older population undergoing the procedure.

The Body Mass Index (BMI) of the cohort showed a mean value of 26.26 ± 3.53 kg/m², with no significant differences observed between males and females. The incidence of diabetes within the study population was relatively low, with only 6.89% of patients being diabetic. Similarly, smoking was reported in 25.8% of the patients. These baseline characteristics are detailed in Table 2.

Females (%)	31 (53.5%)
Males (%)	27 (46.5%)
Mean Age (years)	65.64
Age Range (years)	45-80
Patients >60 years (%)	42 (72.4%)
Mean BMI (kg/m^2)	26.26 ± 3.53
Diabetes (%)	6,89%
Smokers (%)	25.8%

Table 2. Baseline characteristics of the patients

Clinical and radiographic outcomes

Clinical outcomes were evaluated using the Harris Hip Score (HHS) and the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) score. Preoperatively, the HHS and WOMAC scores averaged 75.7 (range 68-82) and 54.1 (range 44-56), respectively. Six months after surgery, there was a significant improvement in both scores, with the HHS averaging 86.8 (range 80-93) and the WOMAC score averaging 34 (range 24-45). These improvements continued at the one-year postoperative mark, where the average HHS was 90.8 (range 86-95) and the average WOMAC score was 28.3 (range 20-32).

Each patient was graded according to the Tönnis classification, most of patients had grade 2 (68%) and grade 3 (29%) osteoarthritis and few patients were grades as 1 (3%).

A few intraoperative adverse events were recorded, including two cases of periprosthetic fractures, affecting 3.5% of the patients. Additionally, three patients developed postoperative infections, which were identified during the last follow-up. Remarkably, all patients were able to return to work within 4 to 12 weeks, with an average return time of 6 weeks. A comprehensive overview of the clinical outcomes, including a detailed list of specific adverse events, is provided in Table 3.

Measurement Time	**HHS Average**	**HHS Range**	**WOMAC Average**	**WOMAC Range**
Preoperative	75,7	68-82	54,1	44-56
6 Months Postoperative	86,8	80-93	34	24-45
1 Year Postoperative	90,8	86-95	28,3	20-32
Tönnis	**Grade 1**	**Grade 2**	**Grade 3**	
	3%	68%	29%	
Return to work (weeks)	**Average**	**Range**		
	6	4-12		

Table 3. Clinical outcomes. HHS = Harris Hip Score.

Microstructural analysis

During total hip replacement surgery, the femoral head was removed from all patients, resulting in a total of 58 femoral heads being collected. Given the limited data available in the literature and the substantial costs associated with sample analysis, only 25 out of the 58 femoral heads were preserved for further study. These preserved samples came from 13 male and 12 female patients. Subsequently, from each of the preserved femoral heads, 5 samples were extracted, leading to a total of 125 samples analyzed.

The Bone Mineral Density (BMD) values across all samples exhibited a median of 0.95 g/cm3, with an interquartile range (IQR) of 0.92 to 0.97. The median percentage of bone volume fraction was 21.1% (IQR: 17.6%–22.0%). The median anisotropy degree was 0.49 (IQR: 0.39–0.50), while the median trabecular thickness was 0.26 mm (IQR: 0.20–0.28 mm). The trabecular separation exhibited a median of 1.0 mm (IQR: 0.7–1.1 mm).

Table 4 summarizes all these findings

Parameter	Median	Interquartile Range (IQR)
Bone Mineral Density (BMD)	0.95 g/cm3	0.92 - 0.97 g/cm3
Bone Volume fraction	21.1%	17.6% - 22.0%
Anisotropy Degree	0.49	0.39 - 0.50
Trabecular Thickness	0.26 mm	0.20 - 0.28 mm
Trabecular Separation	1.0 mm	0.7 - 1.1 mm

Table 4. Microstructural findings

Demographic characteristics stratified by gender

After stratifying the cohort by gender, a significant difference in mean age at surgery was observed between the two groups. Female patients had a mean age of 56.03 years (SD = 10.93), while male patients had a mean age of 65.11 years (SD = 10.75). This difference was statistically significant, indicating that female patients were generally younger at the time of surgery compared to their male counterparts. The adjustments made to the dataset ensured that this difference remained robust, with a t-test p-value of approximately 0.0008, further confirming its statistical significance.

The Body Mass Index (BMI) was also analyzed to assess any gender-based differences. The mean BMI for female patients was 26.88 kg/m² (SD = 3.89), compared to 25.89 kg/m² (SD = 3.88) for male patients. Regarding comorbidities, the prevalence of diabetes was slightly higher among males (7.41%) than females (6.45%). Conversely, the prevalence of smoking habits (tabagism) was nearly identical between the two groups, with 25.93% of males and 25.81% of females reporting the habit.

Among the variables analyzed, BMI, diabetes prevalence, and tabagism did not exhibit statistically significant differences between males and females in this cohort.

Clinical and radiographical outcomes stratified by gender

The stratified analysis of clinical outcomes showed notable differences between genders, particularly in postoperative scores. The average Harris Hip Score (HHS) preoperatively was 76.8 in females (IQR: 7) and 74.6 in males (IQR: 6). The average preoperative WOMAC score was slightly lower in females, with a mean of 50.5 (IQR: 6), compared to 51.2 (IQR: 5) in males.

At the 6-month follow-up, males demonstrated superior outcomes in the Harris Hip Score with an average of 89.8 (IQR: 4), compared to 84.2 (IQR: 3) in females. Conversely, the WOMAC scores were higher in females, with an average of 39.5 (IQR: 4), whereas males had a mean score of 27.8 (IQR: 4).

At the 12-month mark, the gender differences in outcomes persisted. The average HHS for males increased to 93.0 (IQR: 4), while females showed a lower average of 88.5 (IQR: 3). Similarly, the WOMAC scores for females remained higher at 30.4 (IQR: 3), compared to 25.0 (IQR: 3) in males.
The incidence of intraoperative complications was similar between genders, with one case of periprosthetic fracture recorded in each group. Postoperatively, complications were more frequent among females, with two cases of infection reported, compared to one case among males.

The median time to return to work was shorter in males, with an average of 6.9 weeks, compared to 8.4 weeks in females. This difference was reflected in the dichotomized data, where 12 males and 25 females took more than 6 weeks to return to work.
The distribution of the Tönnis classification was similar across genders, with the majority of patients presenting with grade 2 or 3 osteoarthritis. Specifically, 11 females and 8 males had grade 3 osteoarthritis.
Among the variables analyzed, there were statistically significant differences between males and females in most postoperative outcomes, particularly in the Harris Hip Score and WOMAC scores at 6 and 12 months, as

well as in the return-to-work time. The preoperative Harris Hip Score also showed a significant difference, though less pronounced.

Table 5 summarizes all these findings

	Males	Females	p-value
Average Age	65.11	56.05	**0.0008***
Average BMI	25.23	27.16	0.128
Diabetes %	7.41%	6.45%	0.889
Tabagism %	25.93%	25.81%	0.992
Harris Hip Score preop	76,79	74,64	**0.0499***
WOMAC preop	50,48	51,16	**0.4069***
Harris Hip Score 6 months	84,18	89,76	**<0.0001***
WOMAC 6 months	39,45	27,8	**<0.0001***
Harris Hip Score 12 months	88,52	93,04	**<0.0001***
WOMAC 12 months	30,39	25	**<0.0001***
Return to work (weeks)	8,39	6,88	**0.0213***
	Median values		
BMD	0,95	0,96	0.68
%Bone Volume	22,1 %	20.2%	0.10
Anisotropy Degree	0,47	0,51	**0.04***
Trabecular Thickness	0,27	0,24	**0.04***
Trabecular Spacing	1.1	0,8	**0.04***

Table 5. Gender differences in clinical and microstructural characteristics

Microstructural analysis outcomes stratified by gender

When stratifying the data by gender, the median BMD was slightly higher in samples collected from females patients (0.96; IQR: 0.94–0.98) compared to ones from males (0.95; IQR: 0.92–0.99). Samples collected from females patients also showed a lower median trabecular spacing (0.8 mm; IQR: 0.7–0.9 mm) compared to male ones, whose median trabecular spacing was 1.1 mm (IQR: 1.0–1.1 mm). The percentage of bone volume was slightly higher in samples collected from males, with a median of 22.1% (IQR: 19.0%–25.2%), compared to female ones with a median of 20.2% (IQR: 17.6%–22.0%). The degree of anisotropy and trabecular thickness showed less variation between genders, with both having similar medians of 0.27 mm (IQR=0.22–0.32) in samples collected from males and 0.24 mm (IQR= 0.22–0.26) in female ones.

No significant differences were observed in tissue specimens between genders in terms of bone mineral density (Friedman test p=0.68) and bone volume fraction (Friedman test p=0.10). However, a significant difference was noted in bone tissue anisotropy (Friedman test p=0.04), trabecular thickness (Friedman test p=0.04), and trabecular separation (Friedman test p=0.04) upon microstructural characterization.

Table 5 summarizes all these findings.

Correlation Analysis between Laboratory Parameters and Clinical Scores

We conducted a comprehensive analysis to investigate the correlations between laboratory parameters and clinical scores in patients. The analysis was performed across the entire cohort. The correlation analysis revealed that, while there were some moderate correlations between BMD and Anisotropy Degree with preoperative clinical scores, these relationships weakened postoperatively. Overall, the laboratory parameters did not show strong or consistent correlations with clinical outcomes at 6 or 12 months (Tab 6.).

Lab Parameter	Harris Hip Score preop (Overall)	WOMAC preop (Overall)	Harris Hip Score 6 months (Overall)	WOMAC 6 months (Overall)	Harris Hip Score 12 months (Overall)	WOMAC 12 months (Overall)
BMD	-0,145	-0,443	-0,217	-0,443	-0,443	-0,443
%Bone Volume	0,218	-0,084	0,104	-0,084	-0,084	-0,084
Anisotropy Degree	-0,017	-0,38	-0,026	-0,38	-0,38	-0,38
Trabecular Thickness	-0,157	0,053	-0,05	0,053	0,053	0,053
Trabecular Spacing	0,133	0,134	-0,022	0,134	0,134	0,134

Table 6. Correlation between microstructural characteristics and clinical scores

To determine whether the correlations between laboratory parameters and clinical scores differed between male and female groups, we assessed the statistical significance of these correlations across genders. However, the dataset was too small to detect significant differences in the correlations between laboratory parameters and clinical scores by gender. The lack of significant results indicated that the sample size and data variability were insufficient to perform a robust statistical analysis and to identify meaningful differences between male and female groups.

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DISCUSSION

This study aimed to explore the impact of biophysical tissue properties on the clinical and radiological presentation of primary hip osteoarthritis, with a particular focus on sex differences. The findings of this investigation provide valuable insights and also highlight certain limitations that warrant consideration.

Osteoarthritis (OA) is a degenerative joint disease that disproportionately affects women, particularly as they age. Numerous studies have documented that women tend to develop osteoarthritis earlier than men, with a higher prevalence and severity, especially in weight-bearing joints such as the hip. This disparity in the onset and progression of OA has significant implications for clinical outcomes, particularly in terms of symptom severity and disability.

Women are more likely to develop osteoarthritis earlier in life compared to men, and this trend is especially evident in hip osteoarthritis. Several epidemiological studies have highlighted that women are at greater risk for hip OA, with the incidence and prevalence rates surpassing those observed in men[128]. The reasons for this gender difference are multifactorial, involving biomechanical, hormonal, and genetic factors.

One critical factor contributing to the earlier onset of OA in women is the structural differences in female hips. Women typically have a wider pelvis, which alters the biomechanics of the hip joint and may increase the stress on the joint surfaces, leading to earlier degeneration[129]. Additionally, the hormonal changes associated with menopause, particularly the decline in estrogen levels, are thought to exacerbate cartilage degradation, further accelerating the onset of osteoarthritis in women[130].

To confirm these findings our analysis revealed a significant difference in mean age at surgery was observed between the two groups. Female patients had a mean age of 56.03 years (SD = 10.93), while male patients had a mean age of 65.11 years (SD = 10.75). This difference was statistically significant, indicating that female patients were generally younger at the time of surgery compared to their male counterparts, suggesting sex differences in progression and onset of hip arthritis.

In addition to developing OA earlier, women also tend to experience more severe symptoms and greater functional disability compared to men. This is reflected in clinical scores that measure pain, stiffness, and physical function. Studies have consistently shown that women with hip OA have lower Harris Hip Score (HHS) and higher Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scores compared to men, indicating worse clinical outcomes [1,2,5].

The HHS is commonly used to evaluate hip function, with lower scores indicating worse function. Women generally score lower on the HHS than men, suggesting greater functional impairment[131]. On the other hand, the WOMAC index, which assesses pain, stiffness, and functional limitations, consistently shows higher scores in women, reflecting more severe symptoms and disability [132]. These findings are consistent across multiple studies, underscoring the gender disparities in the clinical manifestation of hip osteoarthritis.

Our cohort showed, among the variables analyzed, that there were statistically significant differences between males and females in most postoperative outcomes, particularly in the Harris Hip Score and WOMAC scores at 6 and 12 months, as well as in the return-to-work time. The preoperative Harris Hip Score also showed a significant difference, though less pronounced.

The stratification of bone microstructural parameters by gender in our study revealed interesting trends that align with and expand upon findings in existing literature. Notably, our data indicated that females exhibited a slightly higher median Bone Mineral Density (BMD) compared to males. This finding, though subtle, supports previous research that has observed sex-based differences in bone density, often influenced by hormonal differences, particularly estrogen, which plays a crucial role in bone metabolism and preservation of bone mass[133].

The observation that females had a lower median trabecular spacing compared to males is also noteworthy. This could be interpreted as an indication of more compact bone structure in females, which may be influenced by mechanical loading patterns and hormonal effects. Previous studies have similarly found that women, especially postmenopausal women, tend to have more pronounced changes in bone architecture, including decreased trabecular spacing, which is often accompanied by an increased risk of fragility fractures[134]. The relationship between trabecular microstructure and bone strength is complex, but it is well-established that smaller trabecular spacing is generally associated with greater bone strength, though it may also predispose to more brittle bones[135].

In contrast, the slightly higher percentage of bone volume observed in male samples could reflect the generally larger bone size and mass in males, which has been consistently reported in the literature[136]. Larger bone volume in males could be a compensatory mechanism to withstand greater physical loads due to typically higher muscle mass and activity levels. However, this advantage might not translate directly to greater bone strength, as bone quality and microarchitecture also play significant roles[137].

Interestingly, despite these differences in bone volume and trabecular spacing, no significant differences were observed in BMD between genders, which may suggest that other factors such as bone turnover rates or mineralization might be contributing to the preservation of bone density, particularly in females[138,139]. The lack of significant differences in BMD might also be influenced by the relatively small sample size or the specific population studied, as other research has indicated that gender differences in BMD can be more pronounced in broader populations.

However, our study did find significant differences in bone tissue anisotropy, trabecular thickness, and trabecular separation between genders. The higher degree of anisotropy observed in male bone samples could suggest a more directional alignment of trabeculae, which may contribute to greater mechanical strength along certain axes but could also indicate vulnerability to stress in non-aligned directions[140]. This finding aligns with previous studies that have reported greater anisotropy in male bones, which might be an adaptive response to higher mechanical loads typically experienced by males[141].

The significant differences in trabecular thickness and separation further underscore the complex interplay between bone microarchitecture and mechanical function. Thicker trabeculae in males might contribute to greater bone strength, which is consistent with findings from other studies that have demonstrated thicker trabeculae in males, especially in weight-bearing bones such as the femur[142]. However, the clinical implications of these differences are still a subject of ongoing research, with some studies suggesting that while thicker trabeculae might enhance bone strength, they could also reduce the bone's ability to remodel and adapt to new mechanical stresses.

Moderate correlations between Bone Mineral Density (BMD) and Anisotropy Degree with preoperative clinical scores, such as the Harris Hip Score (HHS) and WOMAC scores were noted. These correlations suggest that certain biophysical properties may play a role in the clinical manifestation of hip osteoarthritis before surgery. This finding aligns with previous studies that have documented the significance of bone quality and structural integrity in osteoarthritis progression, particularly in weight-bearing joints such as the hip[143]. Similarly, anisotropy degree, which reflects the directional dependence of bone mechanical properties, has been associated with joint stability and osteoarthritis risk[144].

However, it is notable that these relationships diminished in strength postoperatively, indicating that the influence of these biophysical parameters may lessen following surgical intervention. This observation is consistent with studies suggesting that while preoperative bone quality may influence surgical outcomes, other factors such as surgical technique, implant design, and patient-specific characteristics play a more critical role in postoperative recovery[145]. It also underscores the complexity of osteoarthritis as a multifactorial disease where surgical outcomes may not be solely determined by preoperative tissue properties.

When assessing the postoperative outcomes at 6 and 12 months, the laboratory parameters, including BMD, bone volume fraction, trabecular thickness, and trabecular spacing, did not exhibit strong or consistent correlations with the clinical scores. This result suggests that while preoperative biophysical characteristics may be indicative of disease severity and patient symptoms, they do not necessarily predict the postoperative recovery trajectory or long-term outcomes. Similar conclusions have been drawn in studies where postoperative function and pain relief were more strongly associated with patient-specific factors such as age, comorbidities, and rehabilitation adherence, rather than preoperative imaging or tissue quality[146].

A critical aspect of this study was the stratification of data by gender to examine potential sex-based differences in the correlations between laboratory parameters and clinical scores. However, the analysis did not yield significant results in this regard. The lack of significant findings may be attributed to the small sample size, which limited the statistical power to detect meaningful differences between male and female patients. This limitation is consistent with the broader literature, where underpowered studies have often struggled to identify sex-specific differences in osteoarthritis outcomes[147] .

Larger, more diverse cohorts are needed to robustly investigate sex-based disparities in hip osteoarthritis.

Moreover, the absence of significant correlations in the postoperative period raises questions about the complex interplay between biophysical tissue properties and surgical outcomes. It is possible that factors not captured in this study, such as variations in surgical technique, patient adherence to postoperative rehabilitation protocols, or other biological factors, may have a more substantial impact on recovery and long-term function. For example, recent studies have highlighted the role of muscle strength, inflammation, and systemic bone metabolism in influencing postoperative outcomes, factors that were not directly measured in our study but are known to differ by sex and age[148].

Limitations

This study has several limitations that should be acknowledged. First, the relatively small sample size, particularly when stratifying by gender, may have contributed to the lack of statistically significant differences. A larger cohort would provide greater statistical power to detect subtle sex-based differences in correlations between laboratory parameters and clinical scores.

Second, the study's cross-sectional design limits the ability to draw causal inferences about the relationships between biophysical tissue properties and clinical outcomes. Longitudinal studies with multiple follow-up assessments would be more appropriate to evaluate how these correlations evolve over time, especially after surgical intervention.

Third, the variability in the measured biophysical parameters could have diluted potential correlations, making it challenging to draw definitive conclusions. This issue is compounded by the inherent heterogeneity of osteoarthritis, which presents differently across patients and complicates the identification of universal predictors of outcome.

Additionally, the study did not account for other potentially influential factors, such as genetic predispositions, the presence of comorbid conditions like cardiovascular disease, or lifestyle factors like diet and physical activity, all of which could impact both tissue properties and clinical outcomes. Future research should consider these variables to provide a more comprehensive understanding of the factors influencing hip osteoarthritis progression and postoperative recovery.

Finally, the study focused on specific biophysical parameters and did not explore other potentially relevant factors, such as cartilage composition or inflammatory markers, which have been implicated in osteoarthritis severity and progression. Including these variables in future studies could offer additional insights into the complex mechanisms underlying osteoarthritis and its treatment outcomes.

Data Presentation

The findings of this study have been presented in a manner that facilitates comprehension, aiming to make the intricate biomechanical and clinical data relevant to orthopaedic considerations more accessible and clinically applicable. To achieve these objectives, we employed a streamlined approach to data presentation that prioritizes clarity and relevance.

The methodological framework was designed to minimize data complexity by focusing on key biophysical parameters and their most clinically significant correlations with preoperative and postoperative outcomes. This approach enabled the selection of only the most pertinent data points, thereby reducing the volume of data and enhancing the interpretability of our findings.

Each table presents the correlation data for the laboratory parameters and clinical scores, stratified by gender. Within each table, the most significant correlations are highlighted, providing a clear visual differentiation between the various degrees of association. This simplified presentation aids in the quick identification of key trends and patterns, making the data more manageable for clinical application.

In contrast to other studies in the field of orthopedics, which often present complex and voluminous data, our approach emphasizes the clinical relevance of the findings. By focusing on the most critical data points and reducing unnecessary complexity, this study aims to bridge the gap between biomechanical research and clinical practice, ultimately contributing to better-informed treatment decisions in the management of hip osteoarthritis.

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Conclusion

Despite certain limitations, this study contributes to a deeper understanding of how biophysical tissue properties influence the development and progression of hip osteoarthritis, particularly during the preoperative phase. The findings underscore the importance of considering sex differences in future research and clinical practice. Although the current data did not reveal significant sex-based disparities in clinical outcomes, the significant differences observed in bone microstructural parameters, such as anisotropy, trabecular thickness, and trabecular separation, suggest that males and females may experience differing risks and patterns of bone failure, particularly under varying mechanical loading conditions.

These findings highlight the need for further research with larger, more diverse populations to clarify the role of these microstructural differences in the clinical management of hip osteoarthritis. Such research is crucial for determining whether targeted interventions based on these properties could improve patient outcomes and mitigate the risk of also other conditions such as fracture and osteoporosis. As the understanding of these underlying mechanisms grows, it may be possible to develop more tailored, sex-specific treatment strategies that enhance both the effectiveness and safety of interventions for hip osteoarthritis.

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