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GENDER ASYMMETRY IN LARGE JOINT ARTHROPLASTY: A SYSTEMATIC REVIEW OF EPIDEMIOLOGICAL, BIOMECHANICAL, AND METABOLIC DETERMINANTS

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ABSTRACT
This review presents a systematic analysis of a persistent clinical and epidemiological phenomenon characterized by the predominance of males among patients undergoing total hip arthroplasty and females among those undergoing total knee arthroplasty. Based on retrospective data from national registries of Australia, the United Kingdom, Sweden, the United States, and South Korea spanning the period from 2010 to 2024, this pattern is demonstrated to be reproducible across diverse populations, with the greatest disproportion observed in Asian cohorts, reaching 78% females in knee arthroplasty, and the smallest in the American registry at 66%. Key pathophysiological mechanisms are examined, including morpho-biomechanical differences (Q-angle and gait biomechanics), metabolic dimorphism mediated by adipokinetic activity of visceral adipose tissue, and hormonal suppression of chondrogenesis in the postmenopausal period. A clinically significant finding of this work is the demonstration that male sex serves as an independent predictor of revision due to periprosthetic joint infection, with hazard ratios of 1.60 for hip and 2.06 for knee arthroplasty, necessitating the implementation of sex-specific antibiotic prophylaxis protocols. The proposed conceptual model, integrating biomechanical, metabolic, and behavioral factors, provides a rationale for a differentiated approach to preoperative preparation: weight reduction and anti-osteoporotic therapy for females, and screening for methicillin-resistant *Staphylococcus aureus* colonization and glycemic control for males. Future research should focus on polymorphisms of estrogen receptor genes ESR1 and ESR2, which may enable prediction of individual osteoarthritis risk long before clinical manifestation.

KEYWORDS: total hip arthroplasty, total knee arthroplasty, osteoarthritis, gender epidemiology, periprosthetic joint infection, adipokines

INTRODUCTION

The history of large joint arthroplasty spans slightly more than five decades; however, it is during the last two decades that these procedures have transformed from exceptional interventions into the most frequently performed elective surgical procedures worldwide. From the first attempt at femoral head replacement undertaken by Gluck in 1891 using ivory implants and cement, to the introduction of the Charnley design with cemented fixation in the 1960s, more than 70 years elapsed [1]. Nevertheless, these operations became routine—that is, accessible to broad segments of the population and performed in tens of thousands annually—only in the 1980s–1990s, a development driven by the introduction of porous cementless implants, advances in highly cross-linked polyethylene, and standardization of surgical approaches [2, 3].

Today, according to data from the Organisation for Economic Co-operation and Development, the average annual incidence of primary total hip arthroplasty in developed countries ranges from 130 to 170 procedures per 100,000 population, while that of total knee arthroplasty ranges from 140 to 200 per 100,000 [4]. The total economic burden of arthroplasty in the United States alone exceeds 15 billion dollars annually, elevating the study of risk factors and outcomes to a priority in public health research [2, 5]. Against this background, one statistical finding remains invariant regardless of geographic location: sex disproportion, and moreover, this disproportion exhibits a directional vector—hip in males, knee in females [6, 7].

The aim of this review is not merely to document this phenomenon but to systematically analyze its constituent components: mechanical, hormonal, metabolic, and behavioral, with the ultimate goal of proposing clinically applicable algorithms for complication prevention that account for patient sex.

Epidemiological Overview: Evolution of Data Across Time and Geography

While early studies from the 1990s frequently attributed the predominance of females in arthroplasty to their greater life expectancy, contemporary registries have refined these conclusions. Analysis of age-stratified cohorts demonstrates that even after adjustment for demographic structure, the peak incidence of knee osteoarthritis in females is shifted leftward by 5–7 years, and the relative risk of primary knee arthroplasty for females aged 60–70 years is 1.8 compared with 1.0 for males of the same age [6, 8].

The most representative absolute data are presented in the 2024 annual report of the Australian Orthopaedic Association National Joint Replacement Registry (AOANJRR), which covers the period from September 1, 1999, to December 31, 2023 [9]. This registry has accumulated data on 721,122 primary total knee arthroplasties performed for osteoarthritis. The absolute figures compellingly demonstrate gender asymmetry: 400,150 procedures were performed in females and 320,972 in males. In the structure of hip arthroplasty, according to the same registry, the sex distribution approaches parity: 24,535 (51%) females and 23,577 (49%) males. Similar patterns are reported in the National Joint Registry for England and Wales, where females constitute 73% of knee arthroplasty patients and 53% of hip arthroplasty patients [10]. In the Swedish Hip Arthroplasty Register, the proportion of females among knee arthroplasty patients reaches 74%, while for hip arthroplasty it is 54% [11]. The American Kaiser Permanente registry demonstrates the smallest disproportion: 66% females among knee arthroplasty patients and 49% among hip arthroplasty patients [12]. The most pronounced asymmetry is observed in Asian populations: according to the Korean Health Insurance Review and Assessment Service registry, females constitute 78% of all knee arthroplasty patients and 47% of hip arthroplasty patients [13]. Trends over the past 15 years indicate a modest but steady increase in the proportion of females in both groups (an average of +2–3 percentage points), attributed to increased life expectancy and the rising prevalence of obesity [6, 8, 14].

Table 1 presents absolute figures for the Australian registry and percentage distributions for other registries, stratified by two temporal intervals.

Table 1. Sex distribution of patients undergoing primary total hip and knee arthroplasty according to national registries

Registry (Country)	Period	THA (female / male)	TKA (female / male)
Australia (AOANJRR)	2024	24,535 / 23,577	400,150 / 320,972
Australia (AOANJRR)	2010–2014	48% / 52%	67% / 33%
Australia (AOANJRR)	2020–2024	51% / 49%	69% / 31%
Sweden (SHAR)	2010–2014	52% / 48%	72% / 28%
Sweden (SHAR)	2020–2024	54% / 46%	74% / 26%
England and Wales (NJR)	2010–2014	51% / 49%	70% / 30%
England and Wales (NJR)	2020–2024	53% / 47%	73% / 27%
USA (Kaiser Permanente)	2010–2014	46% / 54%	64% / 36%
USA (Kaiser Permanente)	2020–2024	49% / 51%	66% / 34%
South Korea (KHIRA)	2010–2014	43% / 57%	75% / 25%
South Korea (KHIRA)	2020–2024	47% / 53%	78% / 22%

Note: Absolute figures for the Australian registry represent the entire observation period (1999–2023); for other registries, percentage distributions are age-adjusted; THA — total hip arthroplasty, TKA — total knee arthroplasty.

The data presented in Table 1 compellingly demonstrate that the knee joint is a predominantly female localization, requiring arthroplasty 2–2.5 times more frequently than in males, whereas the hip joint exhibits sex parity with a tendency toward slight female predominance in older age groups. This contrast necessitates investigation of biological mechanisms extending beyond simple demographic differences.

Biomechanical Analysis: Anatomical Determinants of Lesion Localization

The biomechanical model of lower extremity joint loading represents a fundamental cause of gender asymmetry [15]. Analysis of gait kinematics reveals a statistically significantly higher valgus moment at the knee joint during the stance phase in females [16]. This phenomenon is attributable to the magnitude of the Q-angle—the angle between the line of action of the quadriceps muscle and the patellar ligament. Owing to the wider pelvis in females, the femur assumes a more oblique orientation in the sagittal and frontal planes, resulting in a mean Q-angle of 15–17 degrees in females compared with 10–12 degrees in males [17–19]. Each additional degree of Q-angle increases the lateral tractional component at the joint space, leading to chronic microstress of the articular cartilage of the medial tibial plateau, hyperpression of the lateral fascia, and disruption of patellofemoral congruity [20, 21]. Furthermore, studies demonstrate that reduced hip abductor strength correlates with increased Q-angle, creating a vicious cycle: weakness of the pelvic girdle muscles leads to contralateral pelvic drop during gait, which increases the moment arm of the ground reaction force and, consequently, the adduction moment at the knee joint [22, 23].

In males, by contrast, hip joint biomechanics are subject to higher peak compressive loads in the superolateral quadrant of the acetabulum, associated with greater muscle mass and, consequently, more powerful adductor and abductor muscles generating a high pressure gradient on the cartilage even at normal body weight [24]. Additionally, insufficient femoral neck anteversion is significantly more common in males, generating a

pathological rotational moment during gait that accelerates wear of the anterior acetabular rim [15, 25]. A 2022 systematic review demonstrated that anthropometric differences between sexes (distal femoral aspect ratio, anterior condylar height, condylar width) are so substantial that standard implants achieve adequate fit in less than one-quarter of cases, confirming the necessity of considering sex in implant selection [26, 27]. Thus, from a biomechanical perspective, the knee joint in females operates in a mode of chronic shear overload, whereas the hip joint in males operates in a mode of chronic compressive overload—two fundamentally distinct pathophysiologies converging on the same endpoint: terminal osteoarthritis [28].

Obesity and Metabolic Syndrome: The Role of Adipokines in Cartilage Degeneration

Addressing knee osteoarthritis necessitates consideration of the metabolic phenotype. The association between body mass index and the risk of knee osteoarthritis is among the strongest in epidemiology, with an estimated odds ratio of 2.8 for females with a body mass index exceeding 30 compared with normoweight individuals [29, 30]. However, this association has long transcended the purely mechanical wear paradigm and is now conceptualized within the framework of systemic inflammation induced by visceral adipose tissue [31]. The concept of metabolic osteoarthritis was formulated in the 2010s, with dysregulation of adipokines playing a pivotal role [32]. Adipose tissue represents not a passive storage depot but an active endocrine organ producing more than 50 biologically active molecules. The principal adipokines implicated in cartilage degeneration include leptin, adiponectin, and tumor necrosis factor-alpha [33]. Serum leptin concentration correlates with body mass in females; leptin stimulates the production of matrix metalloproteinases by chondrocytes and upregulates inducible nitric oxide synthase expression, leading to chondrocyte apoptosis [33–35]. Adiponectin normally exerts anti-inflammatory effects; however, in obesity, upregulation of its receptors in synovial tissue develops, converting its effect to pro-inflammatory and elevating interleukin-6 levels [36]. Tumor necrosis factor-alpha, produced by macrophages infiltrating adipose tissue, suppresses type II collagen and proteoglycan synthesis while concurrently activating the NF-κB signaling pathway, establishing a state of chronic aseptic inflammation within the joint [31, 32].

The percentage of visceral fat in total body composition is higher in females than in males with equivalent body mass index. Moreover, estrogens modulate leptin receptor expression; with the onset of menopause, leptin resistance increases, leading to compensatory hyperadipokinemia [37, 38]. Miller and colleagues demonstrated that in females, unlike males, weight loss is accompanied by a significant reduction in leptin levels, confirming the existence of sex-specific features of adipokine metabolism [39]. In an experimental model of systemic endotoxemia in rats, chronic elevation of lipopolysaccharide was found to induce adipocyte hypertrophy and increased leptin concentration in females but not males, accompanied by histological signs of temporomandibular joint osteoarthritis [40]. These data confirm the existence of sex differences in susceptibility to metabolically mediated joint degeneration.

Thus, in postmenopausal females, a vicious pathogenetic cycle is established, schematically represented in Figure 1. The decline in estrogen levels triggers redistribution of adipose tissue to the visceral compartment, accompanied by leptin hyperproduction by adipocytes and infiltration of adipose tissue by macrophages with secretion of tumor necrosis factor-alpha. These adipokines, in turn, suppress type II collagen synthesis by chondrocytes and induce matrix metalloproteinases MMP-1 and MMP-13, leading to degradation of the extracellular cartilage matrix and progression of knee osteoarthritis, ultimately determining the increased requirement for arthroplasty in females.

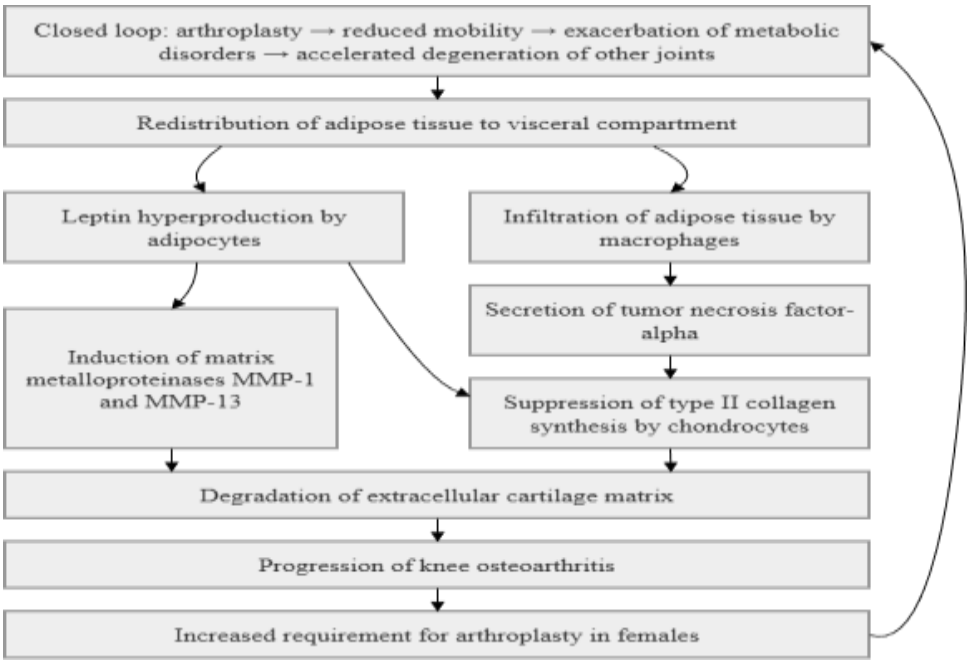

Figure 1. Pathogenetic cycle of metabolic osteoarthritis in postmenopausal females

Hormonal Status: Estrogen Deficiency as a Catalyst of Degeneration

The hormonal component of gender asymmetry is traditionally associated with the postmenopausal period in females [41]. Estrogens exert pronounced chondroprotective effects mediated through nuclear receptors ERα and ERβ expressed on the surface of chondrocytes [42]. The estrogen-receptor complex stimulates fibroblast growth factor-2 and transforming growth factor-β, which support extracellular matrix synthesis [43]. The abrupt decline in 17β-estradiol levels following menopause leads to reduced chondrocyte activity, decreased hyaluronic acid production by synoviocytes, and increased cartilage susceptibility to oxidative stress due to reduced glutathione peroxidase activity [41, 44]. A 2025 systematic review demonstrated that in ovariectomy animal models, significantly more pronounced histological cartilage degeneration is observed compared with control groups, and hormone replacement therapy exerts a protective, though not always statistically significant, effect [45]. In males, estrogen levels decline linearly throughout life and are largely bound by sex hormone-binding globulin; therefore, no cascading hormonal impact on joints occurs [46]. This explains why the structure of hip osteoarthritis in males is dominated not by primary degenerative but by vascular-necrotic and post-traumatic variants, including a history of Legg-Calvé-Perthes disease, femoral neck fractures, and avascular necrosis secondary to alcoholism or glucocorticoid use [15, 47].

Sociocultural and Behavioral Patterns of Healthcare-Seeking

Beyond biological mechanisms, psychosocial factors influence healthcare-seeking statistics [48]. Clinical observations and qualitative research data using the Western Ontario and McMaster Universities Osteoarthritis Index questionnaire indicate that males tend to minimize pain intensity and delay consultation with an orthopedist until conservative modalities (intra-articular hyaluronic acid injections, physical therapy) are no longer effective [49]. This results in a higher Kellgren-Lawrence grade (III–IV) at the time of surgical intervention and a greater likelihood of requiring hip arthroplasty specifically, where pain syndrome manifests early during gait due to radiation to the groin and knee [6, 49]. Females, conversely, demonstrate higher healthcare-seeking adherence; paradoxically, this does not reduce but rather increases the absolute number of surgeries, as knee osteoarthritis is diagnosed earlier and more frequently, and over time, even with treatment, progresses to an operable stage [8, 50]. An additional factor is the role-stress hypothesis: females aged 55–70 years who care for grandchildren and manage active household duties experience higher cumulative daily knee joint loading, including stair climbing and carrying heavy items, which further exacerbates the mechanical component of degeneration [51].

Gender Asymmetry in Surgical Outcomes: Periprosthetic Joint Infection and Other Complications

Following the decision for surgical intervention, gender differences persist—they transform into differences in the frequency of postoperative complications [52]. Table 2 summarizes the principal pathogenetic mechanisms explaining outcome differences between sexes.

Table 2. Pathogenetic mechanisms and clinical manifestations of gender differences in arthroplasty outcomes

Pathogenetic Level	Males	Females	References
Periprosthetic infection risk	Elevated (HR 1.60 for THA, 2.06 for TKA)	Reduced	[53, 54]
Infection risk mechanisms	More alkaline skin pH (5.5–6.0), high *S. aureus* colonization, testosterone-mediated immunosuppression	More acidic skin pH (4.5–5.0), estrogen-mediated immunostimulation	[53, 55]
90-day complications	Higher risk of cardiac events, pneumonia, AKI	Higher risk of UTI, DVT, wound complications, readmission	[52, 56]
5-year outcomes	Lower revision and dislocation risk	Higher revision (1.8% vs 1.4%), periprosthetic fracture (1.2% vs 0.7%), dislocation (1.8% vs 1.2%) rates	[56]
Long-term function	Better functional outcomes (60% of studies)	Approximately 50% of studies show worse outcomes	[57]

The most clinically significant parameter demonstrating male predominance is the risk of chronic periprosthetic joint infection [53]. A multinational registry study encompassing 4.8 million primary arthroplasties from nine registries (Australia, Belgium, Canada, Catalonia, Germany, Italy, New Zealand, Norway, United Kingdom) yielded the following adjusted hazard ratios for males compared with females: for total hip arthroplasty—1.60 (95% CI 1.42–1.80); for total knee arthroplasty—2.06 (95% CI 1.90–2.46) [53]. These results persisted throughout the 10-year observation period and after adjustment for age, body mass index, ASA class, fixation type, and implant type [54]. The elevated infection risk in males is attributed to skin microbiome characteristics: more alkaline pH (5.5–6.0 versus 4.5–5.0 in females), higher density of sebaceous and apocrine glands, creating a favorable environment for *Staphylococcus aureus* colonization [55]. Additionally, testosterone-mediated

suppression of Th1 responses reduces the efficacy of neutrophil phagocytosis in the implant zone [53, 55]. Comorbidity burden also contributes: males have a statistically significantly higher prevalence of untreated type 2 diabetes mellitus, smoking, and vasculopathies, impairing postoperative wound oxygenation [52, 56].
However, data on other complications are less consistent. A study using the PearlDiver database (780,745 patients, 2010–2022) following matching for age and Elixhauser comorbidity index demonstrated that females had a higher risk of any adverse events within 90 days (odds ratio 1.36), serious complications (odds ratio 1.76), and readmissions (odds ratio 1.25) [56]. Females more frequently exhibited surgical site infection, deep vein thrombosis, urinary tract infection, and wound dehiscence, whereas males more frequently exhibited cardiac events, pneumonia, and acute kidney injury [56]. At 5 years, females had higher rates of revision (1.8% vs 1.4%), periprosthetic fracture (1.2% vs 0.7%), and dislocation (1.8% vs 1.2%) [56]. A 2025 scoping review reported that in 60% of studies following hip arthroplasty and 51% following knee arthroplasty, males demonstrated superior long-term functional outcomes, which may be attributable to both biological and socioeconomic factors [57].
Collectively, these data indicate the necessity of a differentiated approach to preoperative preparation and postoperative management of patients of different sexes, accounting for both differences in complication spectrum and long-term outcomes.

Conceptual Model and Personalized Approach

Based on the data presented, a conceptual model integrating all examined pathogenetic links may be proposed. This model is illustrated in Figure 2. Initial sex differences are realized through three principal channels. The first channel is biomechanical: in females, a wide pelvis determines increased Q-angle and valgus knee stress, whereas in males, a powerful muscular corset generates peak compression of the acetabulum. The second channel is hormonal-metabolic: in females, menopausal estrogen deficiency combines with increased visceral adipose tissue, leptin and tumor necrosis factor-alpha hyperproduction, leading to chondrocyte apoptosis; in males, weak estrogen protection and androgen effects on vascular tone predispose to osteonecrosis. The third channel is behavioral: females seek care earlier, and knee osteoarthritis is more frequently detected, whereas males present late, and advanced hip osteoarthritis is diagnosed.
These channels converge into two clinical phenotypes—knee involvement in females and hip involvement in males—each accompanied by a characteristic spectrum of surgical risks: females have a relatively low risk of infectious revisions, whereas males have a high risk (hazard ratio 1.60–2.06). This necessitates personalized management strategies: for females—weight correction, anti-osteoporotic therapy, and early functional rehabilitation; for males—screening for methicillin-resistant *Staphylococcus aureus* carriage, glycemic control, and extended antibiotic prophylaxis.

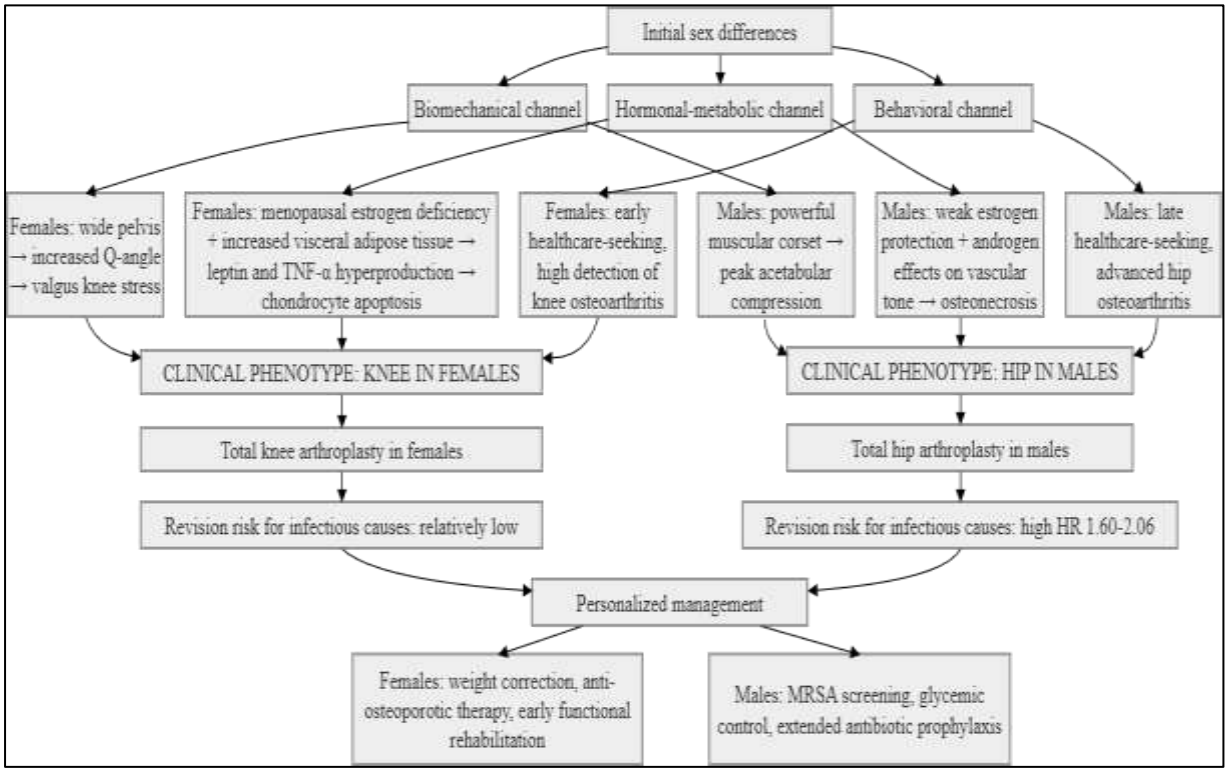

Figure 2. Conceptual model of gender asymmetry formation in arthroplasty and its clinical consequences

DISCUSSION

The present systematic review consolidates current evidence demonstrating a robust and reproducible pattern of gender asymmetry in large joint arthroplasty, characterized by a marked predominance of females in total knee

arthroplasty and a near-parity distribution in total hip arthroplasty with a slight female predominance in older age groups. The consistency of this pattern across geographically and ethnically diverse populations—from the Australian registry (69% females in TKA) to the Korean registry (78% females in TKA)—strongly suggests that the phenomenon is not an artifact of healthcare system variation but rather reflects fundamental biological and biomechanical differences between sexes [6, 9, 13].

The biomechanical argument appears compelling: the wider female pelvis and consequent increased Q-angle create a chronic valgus stress at the knee joint, predisposing to medial compartment overload and accelerated cartilage wear [17, 19]. In males, by contrast, greater muscle mass and higher peak compressive forces at the hip, combined with a higher prevalence of femoral neck retroversion and post-traumatic changes, shift the degenerative burden to the acetabulum [15, 24]. However, biomechanics alone cannot fully explain the observed asymmetry. The near-parity in hip arthroplasty distribution, despite males having greater mechanical exposure, suggests that hormonal and metabolic factors play a permissive or protective role depending on sex and joint location.

The metabolic phenotype emerges as a crucial mediator, particularly for knee osteoarthritis in females. The concept of metabolic osteoarthritis, driven by adipokine dysregulation from visceral adipose tissue, provides a mechanistic link between obesity and cartilage degeneration that transcends purely mechanical explanations [31, 32]. Leptin, adiponectin, and tumor necrosis factor-alpha exert direct catabolic effects on chondrocytes, inducing matrix metalloproteinase expression and suppressing type II collagen synthesis [33, 35]. The menopausal transition, with its abrupt estrogen decline and concomitant increase in visceral adiposity, creates a state of metabolic dysregulation that disproportionately affects females and explains the accelerated progression of knee osteoarthritis in this population [41, 45]. This is consistent with the epidemiological observation that the peak incidence of TKA in females is shifted leftward by 5–7 years relative to males [8].

Clinically, the most actionable finding of this review is the elevated risk of periprosthetic joint infection in males, with adjusted hazard ratios of 1.60 for hip and 2.06 for knee arthroplasty [53]. As summarized in Table 2, the mechanisms underlying this disparity include sex-specific differences in skin microbiome, testosterone-mediated immunosuppression, and higher rates of smoking and diabetes [55, 56]. These findings have direct implications for perioperative management: routine screening for methicillin-resistant *S. aureus* colonization, optimization of glycemic control, and extended antibiotic prophylaxis should be considered standard practice in male patients undergoing arthroplasty. Conversely, in females, the focus should be on weight reduction, anti-osteoporotic therapy, and early functional rehabilitation to mitigate the higher rates of periprosthetic fractures and revisions observed at 5 years [56, 57].

The conceptual model proposed in Figure 2 integrates biomechanical, metabolic, and behavioral channels, illustrating how initial sex differences converge into distinct clinical phenotypes and surgical risk profiles. This model provides a framework for personalized perioperative protocols and highlights the need for multidisciplinary preoperative assessment involving endocrinologists, nutritionists, and rehabilitation specialists.

CONCLUSION

Gender asymmetry in large joint arthroplasty represents a complex systemic phenomenon that cannot be attributed solely to random epidemiological fluctuations. This review has demonstrated that biomechanical parameters (Q-angle and compressive load characteristics), endocrine status (menopausal estrogen deficiency and adipokine dysregulation), and obesity epidemiology create a constellation of conditions predisposing to predominant knee involvement in females. Conversely, for males, the principal determinants remain mechanical overload and vascular pathology of the hip joint, accounting for their more frequent inclusion in the candidate cohort for hip arthroplasty with an inherently higher risk of infectious complications. The transition to personalized medicine in orthopedics implies not merely sex-based implant size selection but the establishment of fundamentally different perioperative protocols for males and females. Future research should focus on genetic markers of susceptibility to joint degeneration, particularly polymorphisms of estrogen receptor genes ESR1 and ESR2, and their interaction with metabolic profiles, enabling prediction of individual arthroplasty risk long before clinical symptom onset.

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