Chapter 6
Osteoarthritis and Gender-Specific Joint Replacement

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Abstract Osteoarthritis is a debilitating joint disease which primarily affects women for reasons that remain unclear. There are many treatment options available to address the pain and loss of function in osteoarthritis, ranging from noninvasive physical therapy to total joint replacement. Most of the treatments are gender neutral, but recently knee implants have been marketed to women as gender specific. This chapter reviews the most recent literature on these topics.

The literature suggests that gender-neutral knee and hip implants used for total joint replacements are equally beneficial in both men and women. Gender-specific knee implants have not shown any increased benefit in short-term studies, and it remains to be seen how they will compare to gender-neutral knee implants in the long term. There are no gender-specific hip implants on the market, and there is not a clear consensus about whether the production of a gender-specific hip is necessary.

Keywords Osteoarthritis • Joint replacement • Total knee replacement • Total knee arthroplasty • Total hip replacement • Total hip arthroplasty • Gender • Women

Abbreviations

AAOS	American Academy of Orthopaedic Surgeons
ACR	American College of Rheumatology
HRT	Hormone Replacement Therapy

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NSAIDs	Nonsteroidal Anti-Inflammatory Drugs
OA	Osteoarthritis
OP	Osteoporosis
THR	Total Hip Replacement
TKR	Total Knee Replacement

Introduction

Osteoarthritis (OA) is a degenerative joint disease caused by a combination of genetic, mechanical, and inflammatory factors that are not well understood. Most patients present with cartilage destruction, narrowed joint space, and osteophyte formation, which result in pain and loss of function (Fig. 6.1a, b) [1]. OA is the most prevalent joint disorder [2] and leading cause of disability in the USA [3]. The cost of treatment and loss of function makes OA a huge financial burden to individuals and society [4].

Epidemiologic studies consistently show that women have an increased risk over men for developing knee and hip OA, the two most common forms of the disease [5, 6]. To make matters worse, women with OA generally express higher levels of pain than men with OA, even when compared with men who have the same radiographic severity of OA [7–9]. The pain of OA not only limits physical function but has psychological impact as well; women with OA report lower satisfaction in life than women without OA [10].

With such widespread impact, it is important for women to understand current risk factors and prevention for development of OA, updated recommendations for management of OA, and whether women should be receiving different or supplementary treatment to achieve the most optimum outcomes.

In this chapter, we will explore:

- Some of the potential reasons why women are at greater risk for developing OA, with specific attention paid to knee OA and hip OA
- Treatments prior to total joint replacement for knee and hip OA
  - Treatments specific to women
- Total joint replacement as an option for treating knee and hip OA
  - Do women and men have similar outcomes with standard total joint replacement?
  - Are gender-specific replacements necessary?

Women and Osteoarthritis

Loss of cartilage is an important risk factor for developing osteoarthritis (OA) [1]. Women are at an especially high risk because they generally lose cartilage in the knee at a faster rate than men [11]. The influence of estrogen on cartilage loss and OA development as estrogen levels change during menopause has been investigated

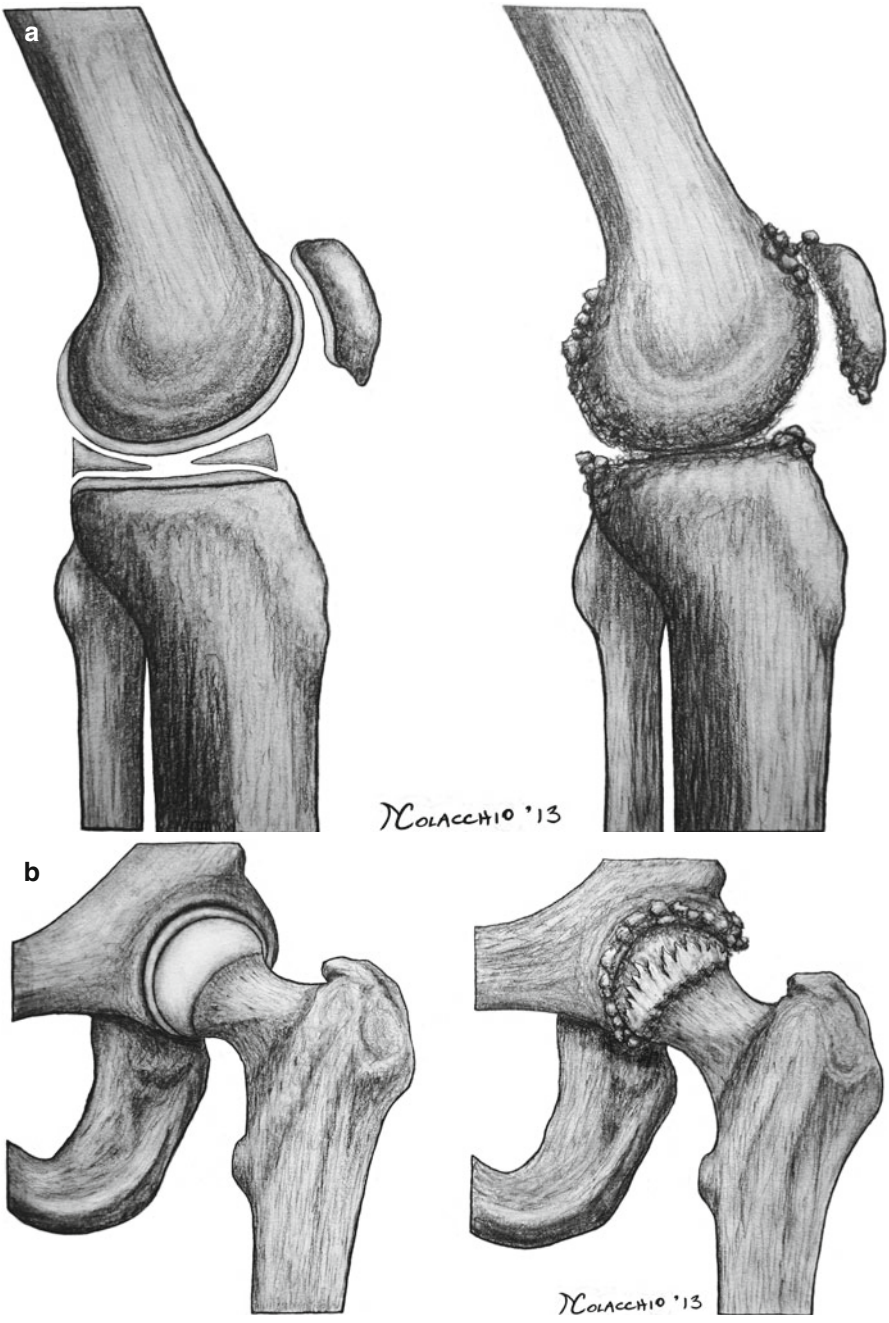

Fig. 6.1 (**a**, **b**) Pathogenesis of knee (**a**) and hip (**b**) OA

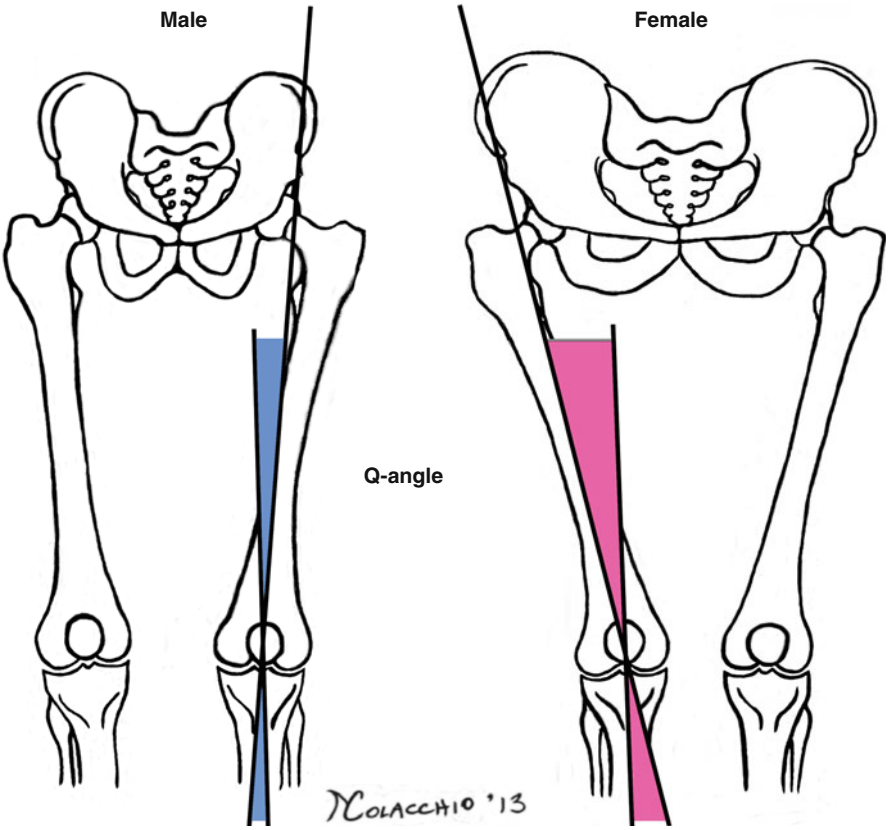

Fig. 6.2 Q angle. Draw a line from the anterior superior iliac spine of the hip to the patella, then another line from the patella to the tibial tuberosity. The Q angle is measured in between these *two lines*

[12]. Despite two decades of research, the impact of estrogen levels on OA is inconclusive and the mechanism by which estrogen physiologically affects cartilage remains elusive [13]. Interestingly, genetic variations in genes for estrogen receptors have been associated with either higher or lower rates of OA, implying that the estrogen hormone does play some role in OA [14, 15]. Much of the research on estrogen and OA has focused on hormone replacement therapy (HRT), which will be discussed in detail in the treatment section; however, results of HRT on OA are similarly equivocal.

There are many anatomic differences between men and women in the knee and hip joints. Joint malalignment has been shown to negatively affect the progression of OA [16, 17], and therefore, different anatomic factors in women could potentially predispose women to higher levels of OA than men. Women generally have wider hips [18] and a larger Q angle than men (Fig. 6.2) [19, 20]. Women also have a thinner patella [21], and differences in the development of knee cartilage from an early age have been noted, which could account for the decreased knee cartilage thickness that is seen in adult women [22]. Women are predisposed to a

higher rate of anterior cruciate ligament injuries [23, 24], which has been associated with knee OA later in life [25, 26].

Obesity is a risk factor for development of OA for men and women [27], impacting joints mechanically and hormonally. The knee absorbs between two and five times the normal body weight of an individual, so the increased body weight in obesity is hypothesized to add significant mechanical pressure to the knee with each step taken [27]. However, the increased mechanical strain can only explain part of the increase of OA with obesity, because there is also an association between obesity and increased risk of hand OA [28–30]. Interestingly, obesity is not associated with an increase in hip OA [30, 31]. One possible hormonal explanation for the correlation between obesity and OA is that the increased adipose (fat) tissue releases certain chemical signals, which could systemically affect the joints of the body. One chemical hypothesized to be involved is called leptin, which is released by adipose cells [28]. Women generally have a higher percentage of body fat than men [32], so this could be part of the explanation for why women have a higher prevalence of OA. In fact, one recent study found that obese women having higher leptin levels were associated with an increased chance of developing knee OA [33]. Indeed, weight loss is a recommended treatment for OA for both men and women (see treatment section).

The prevalence of osteoporosis (OP) (disease of decreased bone density) is much higher in women [34], and there have been links between OP and OA, although the exact relationship is uncertain. According to a recent report by the National Institutes of Health Osteoporosis and Related Bone Diseases National Resource Center [35], patients with OA may be less likely to develop OP. However, other studies have found contradictory results, arguing that OP is not looked for often enough in patients with OA [36, 37]. The exact relationship remains undefined at this point, and future research will help us determine whether OA and OP are risk factors for each other and how best to optimize prevention and treatment for these two similar but very different disease processes.

Treatments Prior to Total Joint Replacement for Knee and Hip OA

Osteoarthritis (OA) is a progressive, degenerative disease with a wide range of treatment options for patients at different stages of disease ranging from non-pharmacologic methods to total joint replacement. This section will cover treatments that are generally used before resorting to knee or hip implant. These non-replacement treatments for knee and hip OA are generally the same and will be presented as such except where noted. The core treatments for knee and hip OA do not vary between men and women, but some alternative therapeutic methods studied in women will be presented as well at the end of this section.

The American Academy of Orthopaedic Surgeons (AAOS) has put out a set of guidelines for treatment of knee OA [38]. In its guidelines, the AAOS recommends, suggests, provides the option, or remains inconclusive—for or against treatments—based on the level of evidence in the literature and based on the balance of benefit versus harm for a particular treatment.

The non-pharmacologic therapeutic methods recommended by the AAOS are participation in self-management programs, strength training, low-impact aerobic fitness, neuromuscular education, and physical activity in accordance with national guidelines. The AAOS suggests weight loss for patients with symptomatic OA and a body mass index ≥25. The American College of Rheumatology (ACR) additionally suggests psychosocial intervention, Tai Chi, walking aids as needed, and thermal agents plus manual therapy with exercise supervised by a physical therapist [39]. The AAOS, however, found inconclusive evidence on the use of manual therapy. There was also inconclusive evidence on the use of valgus force-directing knee braces and physical agents like nerve stimulation or electromagnetic therapy. The AAOS recommends *against* the use of glucosamine and chondroitin as well as the use of acupuncture. The AAOS suggests *against* using a lateral wedge insole for symptomatic medial compartment knee OA.

In terms of pharmacological interventions, the AAOS recommends Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) or Tramadol for pain relief. This recommendation includes both non-selective NSAIDs and selective NSAIDS (cyclo-oxygenase-2 inhibitors). The evidence was inconclusive on the use of acetaminophen (new FDA maximum of 3 grams/day), opioids, or pain patches, based on a lack of relevant studies in the literature. The ACR, however, strongly recommends the use of opioid analgesics for those patients with pain refractory to standard pharmacological treatments and who are not willing or able to undergo total joint replacement [39].

The AAOS guidelines also review procedural treatments for knee OA that are less invasive than surgery. Based on a lack of evidence, the guidelines are inconclusive on the use of corticosteroid intra-articular injection, growth factor injection, or platelet rich plasma injection. There is a strong recommendation *against* the use of hyaluronic acid (viscosupplementation) intra-articular injection based on lack of clear evidence showing benefit. The AAOS also suggests *against* the use of needle lavage based on lack of benefit to patients.

There are also a number of surgical approaches, prior to total replacement, that can be used to treat knee OA, often in patients with specific conditions. For patients with medial compartment knee OA, the AAOS gives the option for a valgus producing proximal tibial osteotomy based on limited evidence. For patients with knee OA and a torn meniscus, the AAOS remains inconclusive on arthroscopic partial meniscectomy. In patients with a primary diagnosis of knee OA, the AAOS makes a strong recommendation *against* arthroscopy with lavage and/or debridement based on lacking beneficial evidence and risks from surgery. Also, despite a lack of reliable evidence in the literature, the AAOS workgroup came to a consensus recommendation based on expert opinion that the use of a free-floating interpositional device in patients with medial compartment knee OA is *not* recommended.

There are some treatments for OA specific to women as well, but these are not the primary treatments used in general for knee or hip OA. The most well-known treatment that has been used in the past but has now fallen out of favor is hormone replacement therapy (HRT). There may be a slight reduction in risk of OA [40] with the use of HRT, but the risks of cancer, cardiovascular disease, venous thromboembolism, and gallbladder disease, among other conditions, significantly outweigh the benefits [41]. And some studies on HRT have also shown no benefit of HRT on OA

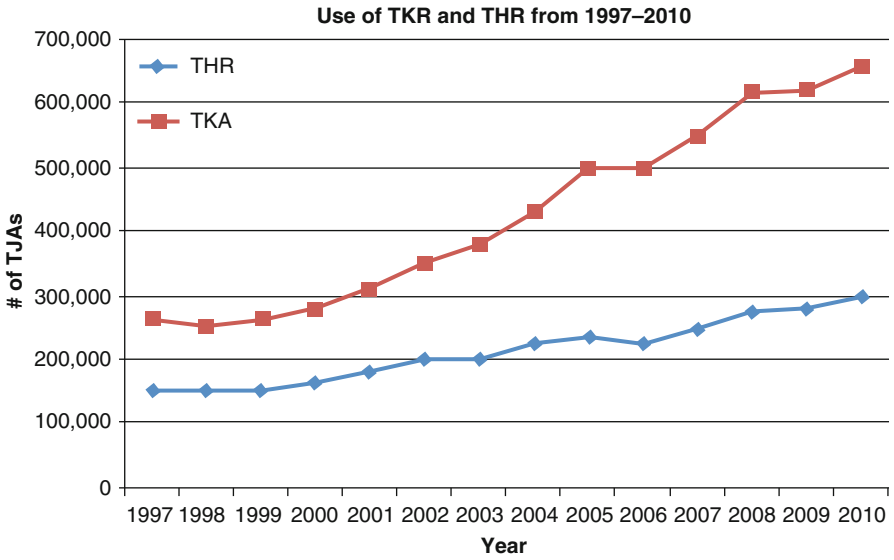

Fig. 6.3 The number of total knee and total hip replacements per year from 1997 to 2010 (Source: Healthcare cost and utilization project (HCUP), Nationwide inpatient sample (NIS) [4])

or have even suggested a deleterious effect of HRT on OA [40, 42]. For young athletic women, treatment with topical NSAIDs as a first-line treatment has been suggested to avoid the gastrointestinal and cardiovascular risks of oral NSAIDs [43]. Finally, there has been research indicating a beneficial effect on overall knee OA outcome with the incorporation of balancing exercises as a compliment to a standard strength-training regime [44].

Total Joint Replacement

Introduction

Total joint replacement is a last resort for patients who have failed nonoperative treatments for osteoarthritis (OA). The total joint replacement procedure has become commonplace in the USA; over 900,000 total knee and hip arthroplasties were performed last year [4], a number that is predicted to rise to 3.8 million in the year 2030 (Fig. 6.3) [45]. The vast majority of patients receive marked functional improvement, and the rate of feared complication is remarkably low [46–48]. Total joint replacement is generally performed on middle-aged to elderly patients, with about 90 % of procedures being done in people aged 45–84 [4].

The standard procedure for total joint replacement is a relatively simple concept. For the knee, shave the arthritic areas of the distal femur (thigh) bone and tibia (shin) bone and replace them with metal, ceramic, or plastic implants (Fig. 6.4a, b).

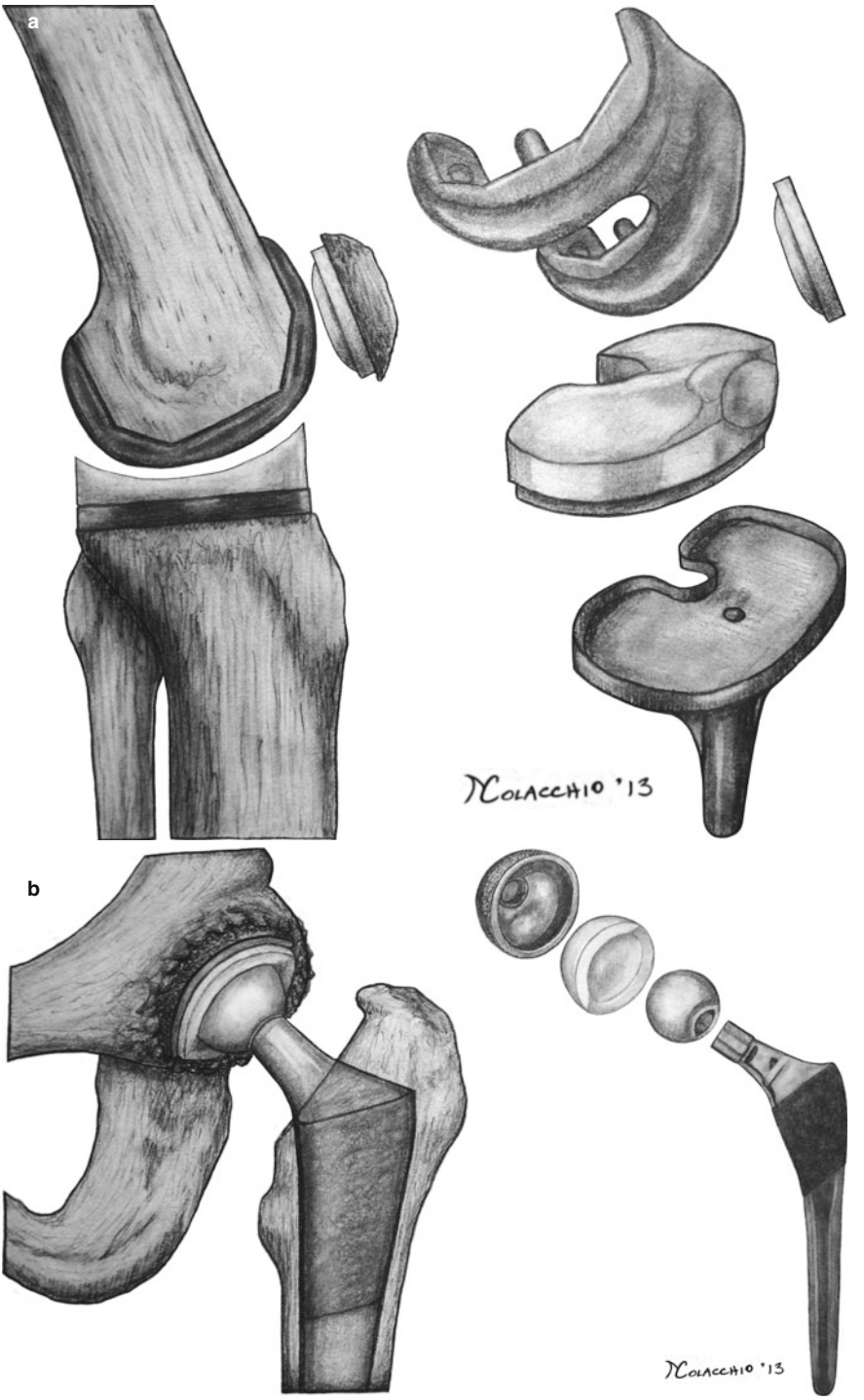

Fig. 6.4 (**a**, **b**) Total knee replacement (**a**). Total hip replacement (**b**)

For the hip, shave the arthritic areas of the proximal femur bone and the acetabulum (hip socket) and replace them with metal, ceramic, or plastic parts. Two of the most important factors for successful joint replacement are alignment and fit of the implanted parts. Certainly much of the success is attributed to the skill of the orthopedic surgeon, but it is also imperative that the proper size and make of the implant fit well with the natural anatomy of the joint of the specific patient. There are many companies making implants of various sizes to fit people with knees and hips of different dimensions, but these implants are generally designed based on average knee and hip dimensions without regard to gender differences.

Evidence-based studies have shown that there are anatomic differences between the male and female knee and hip joints, which could impact total joint replacement. Women have a wider pelvis [18], more bowing of the femoral shaft [49], and a larger Q angle than men (Fig. 6.2) [19, 20]. Within the knee joint, women generally have smaller femoral and tibial condylar heights, narrower transepicondylar widths, a narrower femur, and smaller patella [50]. The rotation of the femur on the tibia is also slightly different in the female than the male knee [51]. Within the hip joint, women generally have a smaller acetabulum, a shorter femoral head, and increased anteversion (femoral neck leans forward causing internal rotation of the knee and foot) [52]. Whether these anatomic differences lead to different outcomes with a generic knee or hip implant or whether they warrant gender-specific knee or hip implants is the subject of the upcoming sections.

For over 6 years, implant companies have been manufacturing knee implants specifically designed for the female anatomy. Unlike the pharmaceutical industry, in which medications must go through a long process before approval by the Food and Drug Administration, small changes in implant design can be brought to the market sooner. With the proven anatomic differences between men and women, implant companies are making and marketing more expensive women-specific implants, which may or may not lead to better outcomes. The women-specific knee implants are generally smaller, narrower, and have a deeper trochlear groove than their generic counterparts, to match the female anatomy.

Knee

Introduction

Osteoarthritis (OA) pain refractory to nonoperative treatments is an indication for total knee replacement [53], and women have higher rates of OA than men [5, 6]. Women undergo more total knee replacements than men [4]. However, it has been shown that the proportion of women who need a knee replacement and actually get one is significantly lower than the proportion of men who need a knee replacement and receive one [54, 55]. Women also generally have worse pain, poorer function [56], and worse quadriceps (front thigh) muscle strength [55] prior to knee replacement. According to the literature, highest postoperative success after TKR can be best predicted by better preoperative knee function scores and quadriceps muscle strength [46]. Therefore, it is important for both the doctor and female patient to recognize that women generally wait longer to have a TKR than men and that it may be advantageous to undergo TKR earlier in the disease process.

Outcomes with Generic Total Knee Replacement (TKR)

While the male and female knee anatomy does have differences, are they clinically significant when comparing outcomes after total knee replacement with *generic* knee implants? To summarize a growing body of evidence-based, peer-reviewed literature, the answer to this question is no; there is no significant difference between the outcomes in women and men with generic knee implants. Women achieve similar functional improvement in a range of different physical tests, equal pain and flexion improvement, and in some cases achieve greater improvement than men with generic knee implants [50, 57–61]. Although there was one study that showed poorer patellofemoral function in women versus men with standard TKR [62] and another study suggesting that African-American women show poorer recovery than other groups [63], most studies report no significant functional difference and outcome, and a recent study showed that women recover faster than men after generic TKR [64]. Overall, the literature suggests that gender does not impact clinical outcome after standard TKR.

Outcomes with Gender-Specific TKR

Despite no significant difference in the outcome after TKR between men and women with generic implants, many women have opted to receive gender-specific knee implants (Fig. 6.5). Much like the data on generic TKRs, there is no significant effect on clinical outcome in women using gender-specific TKRs instead of generic TKRs; major evidence-based studies have shown similar radiologic outcome, range of motion, and functional scores [50, 65–68]. Interestingly, a recent study in which patients underwent a bilateral TKA receiving one gender-specific knee and one generic knee noted similar results. Patients preferred the generic and gender-specific knees at the same rates [67].

Final Remarks

The data is essentially unequivocal in finding no advantage for gender-specific knee implants and no difference in clinical outcome in women with standard generic knee implants. It is worth noting, however, that studies on gender-specific knee implants are early results due to their recent introduction. Knee implants are expected to last 20–30 years, so it is unknown whether these gender-specific knee implants will last longer or shorter in women than conventional total knee replacements.

Hip

Generic and Gender-Specific Total Hip Replacement (THR)

To date, there are no gender-specific hip replacements on the market. However, there are custom hips to fit the anatomy of individual patients in certain situations.

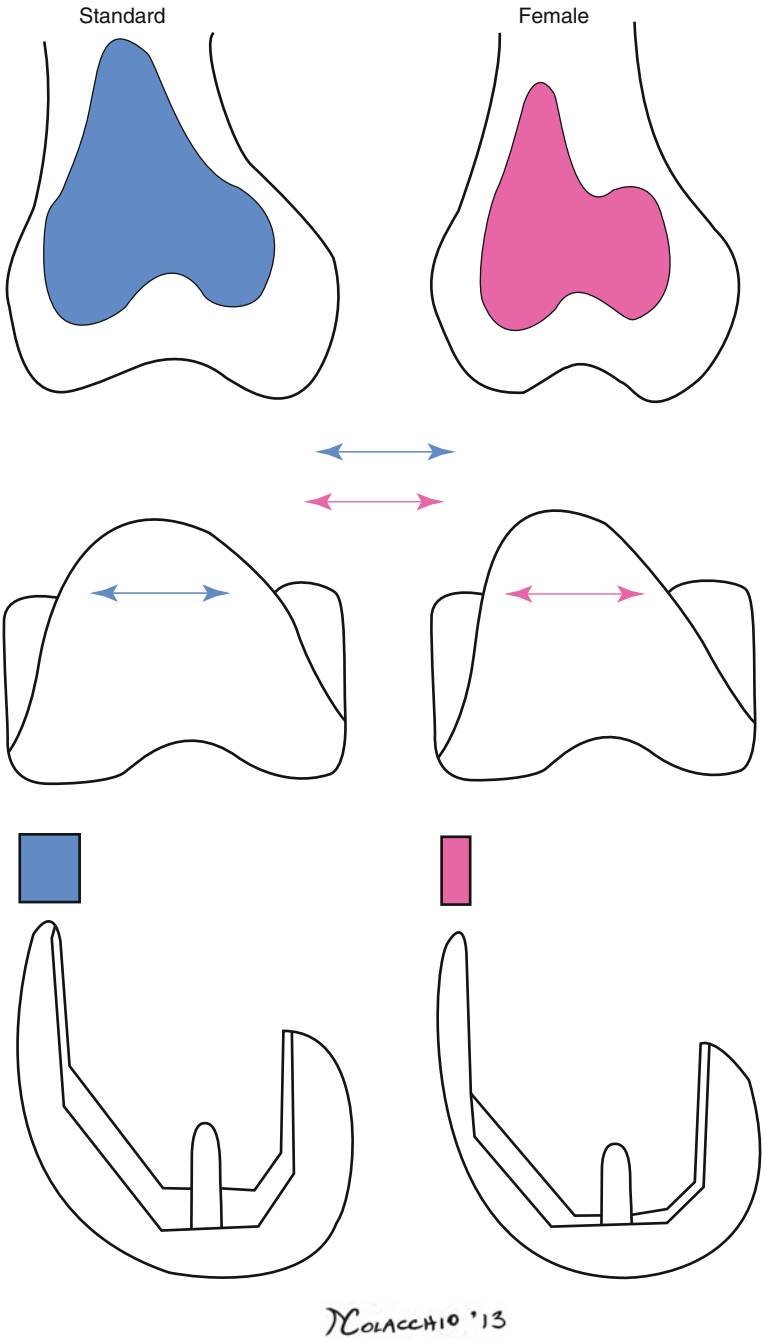

Fig. 6.5 Example of a gender-specific knee implant (Zimmer)

Research has primarily focused on determining whether the anatomical differences suggest a need for gender-specific THR and whether the current standard hip implants work as well in women as they do in men.

As mentioned earlier, clear anatomical differences in the female hip have been demonstrated; a smaller acetabulum, a shorter femoral head, increased anteversion, and a larger Q angle could impact the outcome of total hip replacement. There is also data that suggests as women age, their bone structure changes more than men [52], which implies that women may benefit from a different hip implant because this is a surgery generally performed on older patients [4]. Like the findings in TKR, women have higher pain and lower functional ability prior to THR [69]. The AAOS has recommended, based on female anatomy, female aging, biomechanics, and the female burden of osteoporosis, the production of a hip implant for women with a femoral stem that has a smaller metaphysis and shorter base neck [52].

Despite anatomic and biomechanical indications for gender-specific THR, the studies on outcomes between women and men with standard THR generally suggest no need for the use of gender-specific THR. A major review of the THR literature by the Clinical Orthopaedics and Related Research journal concluded that standard THR systems, which already have the capability to adjust for slight anatomic differences, have not led to different outcomes between men and women [50]. They do *not* see the benefit of developing and using gender-specific total hip implants if the standard hip implants are sufficient.

There have been some peer-reviewed studies in isolation that could suggest a need for gender-specific hip implants or at least some revision of the current hip implant protocol for women. Women have been shown to be at higher risk than men for peri-prosthetic fracture after THR [70], abnormal gait 1 year after THR [71], and for increased pain, NSAID use, and narcotic use 2–5 years after THR [72]. In addition, a low bone muscle density (as seen in osteoporosis) has been shown to lead to slower femoral stem osseointegration and poorer initial stability in women [73].

Final Remarks

There are currently no hip replacements designed specifically for women, and the evidence is still unclear as to whether a gender-specific hip is necessary. Anatomic differences suggest a potential use for them, but if current THRs are sufficient, then maybe it is not necessary for manufacturers to create a “fix” to a problem that does not exist. Women should generally feel very comfortable receiving a standard hip replacement.

Conclusion

Osteoarthritis is a very prevalent and debilitating disease that affects women more than men, although the exact reasons for this predilection remain unclear. There are

many treatments for osteoarthritis that should be exhausted before opting for surgery. Total joint replacement is a safe and effective procedure to relieve knee and hip pain and improves functionality resulting from osteoarthritis. Results in women have been on par with the results observed in men using both gender-neutral and gender-specific joint implants, and thus, it does not seem necessary for women to seek more costly and less proven gender-specific implants.

References

1. Bijlsma JW, Berenbaum F, Lafeber FP. Osteoarthritis: an update with relevance for clinical practice. Lancet. 2011;377(9783):2115–26.
2. Lawrence RC, Felson DT, Helmick CG, et al. Estimates of the prevalence of arthritis and other rheumatic conditions in the united states. Part II. Arthritis Rheum. 2008;58(1):26–35.
3. Brault MW, Hootman J, Helmick CG, Theis KA, Armour BS. Prevalence and most common causes of disability among adults. MMWR Morb Mortal Wkly Rep. 2009;58(16):421.
4. Healthcare cost and utilization project (HCUP), Nationwide inpatient sample (NIS). Agency for healthcare research and quality: Rockville. http://hcupnet.ahrq.gov/2009. Accessed Dec 2012.
5. O'Connor MI, Hooten EG. Breakout session: gender disparities in knee osteoarthritis and TKA. Clin Orthop Relat Res. 2011;469(7):1883–5.
6. Srikanth VK, Fryer JL, Zhai G, Winzenberg TM, Hosmer D, Jones G. A meta-analysis of sex differences prevalence, incidence and severity of osteoarthritis. Osteoarthritis Cartilage. 2005; 13(9):769–81.
7. Cho H, Chang C, Yoo J, Kim S, Kim T. Gender differences in the correlation between symptom and radiographic severity in patients with knee osteoarthritis. Clin Orthop Relat Res. 2010;468(7):1749–58.
8. Keefe FJ, Lefebvre JC, Egert JR, Affleck G, Sullivan MJ, Caldwell DS. The relationship of gender to pain, pain behavior, and disability in osteoarthritis patients: the role of catastrophizing. Pain. 2000;87(3):325–34.
9. Tosi LL, Boyan BDP, Boskey ALP. Does sex matter in musculoskeletal health? The influence of sex and gender on musculoskeletal health. J Bone Joint Surg Am. 2005;87-A(7):1631–47.
10. Tak SH, Laffrey SC. Life satisfaction and its correlates in older women with osteoarthritis. Orthop Nurs. 2003;22(3):182–9.
11. Hanna FS, Teichtahl AJ, Wluka AE, et al. Women have increased rates of cartilage loss and progression of cartilage defects at the knee than men: a gender study of adults without clinical knee osteoarthritis. Menopause. 2009;16(4):666–70.
12. Tsai CL, Liu TK. Osteoarthritis in women: its relationship to estrogen and current trends. Life Sci. 1992;50(23):1737–44.
13. Stevens-Lapsley JE, Kohrt WM. Osteoarthritis in women: effects of estrogen, obesity and physical activity. Womens Health (Lond Engl). 2010;6(4):601–15.
14. Lian K, Lui L, Zmuda JM, et al. Estrogen receptor alpha genotype is associated with a reduced prevalence of radiographic hip osteoarthritis in elderly Caucasian women. Osteoarthritis Cartilage. 2007;15(8):972–8.
15. Fytili P, Giannatou E, Papanikolaou V, et al. Association of repeat polymorphisms in the estrogen receptors alpha, beta, and androgen receptor genes with knee osteoarthritis. Clin Genet. 2005;68(3):268–77.
16. Sharma L, Song J, Felson DT, Cahue S, Shamiyeh E, Dunlop DD. The role of knee alignment in disease progression and functional decline in knee osteoarthritis. JAMA. 2001;286(2):188–95.
17. Felson DT. Clinical practice. Osteoarthritis of the knee. N Engl J Med. 2006;354(8):841–8.
18. Moore K, Dalley A, Agur A. Clinically oriented anatomy. 6th ed. Baltimore: Lippincott Williams & Wilkins; 2010. p. 331.

19. Grelsamer RP, Dubey A, Weinstein CH. Men and women have similar Q angles: a clinical and trigonometric evaluation. J Bone Joint Surg Br. 2005;87(11):1498–501.
20. Woodland LH, Francis RS. Parameters and comparisons of the quadriceps angle of college-aged men and women in the supine and standing positions. Am J Sports Med. 1992;20(2):208–11.
21. Chmell M, McManus J, Scott R. Thickness of the patella in men and women with osteoarthritis. Knee. 1995;2(4):239–41.
22. Jones G, Glisson M, Hynes K, Cicuttini F. Sex and site differences in cartilage development: a possible explanation for variations in knee osteoarthritis in later life. Arthritis Rheum. 2000; 43(11):2543–9.
23. Prodromos CC, Han Y, Rogowski J, Joyce B, Shi K. A meta-analysis of the incidence of anterior cruciate ligament tears as a function of gender, sport, and a knee injury-reduction regimen. Arthroscopy. 2007;23(12):1320–1325.e6.
24. Arendt E, Dick R. Knee injury patterns among men and women in collegiate basketball and soccer. NCAA data and review of literature. Am J Sports Med. 1995;23(6):694–701.
25. Vairo GL, McBrier NM, Miller SJ, Buckley WE. Premature knee osteoarthritis after anterior cruciate ligament reconstruction dependent on autograft. J Sport Rehabil. 2010;19(1): 86–97.
26. Hootman JM, Dick R, Agel J. Epidemiology of collegiate injuries for 15 sports: summary and recommendations for injury prevention initiatives. J Athl Train. 2007;42(2):311–9.
27. Sridhar MS, Jarrett CD, Xerogeanes JW, Labib SA. Obesity and symptomatic osteoarthritis of the knee. J Bone Joint Surg Br. 2012;94(4):433–40.
28. Teichtahl AJ, Wluka AE, Proietto J, Cicuttini FM. Obesity and the female sex, risk factors for knee osteoarthritis that may be attributable to systemic or local leptin biosynthesis and its cellular effects. Med Hypotheses. 2005;65(2):312–5.
29. Cicuttini FM, Baker JR, Spector TD. The association of obesity with osteoarthritis of the hand and knee in women: a twin study. J Rheumatol. 1996;23(7):1221–6.
30. Grotle M, Hagen KB, Natvig B, Dahl FA, Kvien TK. Obesity and osteoarthritis in knee, hip and/or hand: an epidemiological study in the general population with 10 years follow-up. BMC Musculoskelet Disord. 2008;9:132-2474-9-132.
31. Reijman M, Pols HA, Bergink AP, et al. Body mass index associated with onset and progression of osteoarthritis of the knee but not of the hip: the Rotterdam study. Ann Rheum Dis. 2007; 66(2):158–62.
32. Jackson AS, et al. The effect of sex, age and race on estimating percentage body fat from body mass index: the heritage family study. Int J Obes Relat Metab Disord. 2002;26(6):789–96.
33. Karvonen-Gutierrez CA, Sowers MR, Heeringa SG. Sex dimorphism in the association of cardiometabolic characteristics and osteophytes-defined radiographic knee osteoarthritis among obese and non-obese adults: NHANES III. Osteoarthritis Cartilage. 2012;20(7): 614–21.
34. International osteoporosis foundation (IOF): Who's at risk? http://www.iofbonehealth.org/whos-risk. Accessed March 2013.
35. National Institutes of Health Osteoporosis and Related Bone Diseases National Resource Center Osteoporosis and arthritis: two common but different conditions. 2012.
36. Labuda A, Papaioannou A, Pritchard J, Kennedy C, DeBeer J, Adachi JD. Prevalence of osteoporosis in osteoarthritic patients undergoing total hip or total knee arthroplasty. Arch Phys Med Rehabil. 2008;89(12):2373–4.
37. Makinen TJ, Alm JJ, Laine H, Svedstrom E, Aro HT. The incidence of osteopenia and osteoporosis in women with hip osteoarthritis scheduled for cementless total joint replacement. Bone. 2007;40(4):1041–7.
38. Clinical Practice Guideline Work Group. American Academy of Orthopaedic Surgeons (AAOS). Rosemont, IL 60018: American Academy of Orthopaedic Surgeons Clinical Practice Guideline on the Treatment of Osteoarthritis of the Knee 2013.
39. Hochberg MC, Altman RD, April KT, et al. American college of rheumatology 2012 recommendations for the use of nonpharmacologic and pharmacologic therapies in osteoarthritis of the hand, hip, and knee. Arthritis Care Res (Hoboken). 2012;64(4):455–74.

40. Dennison EM, Arden NK, Kellingray S, Croft P, Coggon D, Cooper C. Hormone replacement therapy, other reproductive variables and symptomatic hip osteoarthritis in elderly white women: a case–control study. Br J Rheumatol. 1998;37(11):1198–202.
41. Marjoribanks J, Farquhar C, Roberts H, Lethaby A. Long term hormone therapy for perimenopausal and postmenopausal women. Cochrane Database Syst Rev. 2012;7, CD004143.
42. Von Muhlen D, Morton D, Von Muhlen CA, Barrett-Connor E. Postmenopausal estrogen and increased risk of clinical osteoarthritis at the hip, hand, and knee in older women. J Womens Health Gend Based Med. 2002;11(6):511–8.
43. Altman RD, Fowler PJ. Pharmacologic treatment of knee osteoarthritis in athletic women. Phys Sportsmed. 2011;39(3):39–44.
44. Silva A, Serrao PR, Driusso P, Mattiello SM. The effects of therapeutic exercise on the balance of women with knee osteoarthritis: a systematic review. Rev Bras Fisioter. 2012;16(1):1–9.
45. Kurtz S, Ong K, Lau E, Mowat F, Halpern M. Projections of primary and revision hip and knee arthroplasty in the united states from 2005 to 2030. J Bone Joint Surg Am. 2007;89(4):780–5.
46. Lingard EA, Katz JN, Wright EA, Sledge CB, Kinemax Outcomes Group. Predicting the outcome of total knee arthroplasty. J Bone Joint Surg Am. 2004;86-A(10):2179–86.
47. Januel JM, Chen G, Ruffieux C, et al. Symptomatic in-hospital deep vein thrombosis and pulmonary embolism following hip and knee arthroplasty among patients receiving recommended prophylaxis: a systematic review. JAMA. 2012;307(3):294–303.
48. Vissers MM, Bussmann JB, Verhaar JA, Arends LR, Furlan AD, Reijman M. Recovery of physical functioning after total hip arthroplasty: systematic review and meta-analysis of the literature. Phys Ther. 2011;91(5):615–29.
49. Lu ZH, Yu JK, Chen LX, Gong X, Wang YJ, Leung KK. Computed tomographic measurement of gender differences in bowing of the sagittal femoral shaft in persons older than 50 years. J Arthroplasty. 2012;27(6):1216–20.
50. Johnson AJ, Costa CR, Mont MA. Do we need gender-specific total joint arthroplasty? Clin Orthop Relat Res. 2011;469(7):1852–8.
51. Poilvache PL, Insall JN, Scuderi GR, Font-Rodriguez DE. Rotational landmarks and sizing of the distal femur in total knee arthroplasty. Clin Orthop Relat Res. 1996;331(331):35–46.
52. Glassman A, Lachiewicz P, Tanzer M. Hip and knee reconstruction. In: Orthopaedic knowledge update. 4th ed. Rosemont: American Academy of Orthopaedic Surgeons; 2011.
53. Mahomed NN, Barrett J, Katz JN, Baron JA, Wright J, Losina E. Epidemiology of total knee replacement in the United States Medicare population. J Bone Joint Surg Am. 2005;87(6):1222–8.
54. Hawker GA, Wright JG, Coyte PC, et al. Differences between men and women in the rate of use of hip and knee arthroplasty. N Engl J Med. 2000;342(14):1016–22.
55. Petterson SC, Raisis L, Bodenstab A, Snyder-Mackler. Disease-specific gender differences among total knee arthroplasty candidates. J Bone Joint Surg Am. 2007;89–A(11):2327–33.
56. Tonelli SM, Rakel BA, Cooper NA, Angstom WL, Sluka KA. Women with knee osteoarthritis have more pain and poorer function than men, but similar physical activity prior to total knee replacement. Biol Sex Differ. 2011;2:12.
57. O'Connor MI. Implant survival, knee function, and pain relief after TKA: Are there differences between men and women? Clin Orthop Relat Res. 2011;469(7):1846–51.
58. Lin J, Yang B, Weng XS, Jin J, Zhao Q, Qiu GX. Effect of osteoarthritis patients' gender on rehabilitation after total knee arthroplasty. Chin Med Sci J. 2009;24(2):102–6.
59. Pun SY, Ries MD. Effect of gender and preoperative diagnosis on results of revision total knee arthroplasty. Clin Orthop Relat Res. 2008;466(11):2701–5.
60. Ritter MA, Wing JT, Berend ME, Davis KE, Meding JB. The clinical effect of gender on outcome of total knee arthroplasty. J Arthroplasty. 2008;23(3):331–6.
61. Lustig S, Barba N, Magnussen RA, Servien E, Demey G, Neyret P. The effect of gender on outcome of unicompartmental knee arthroplasty. Knee. 2012;19(3):176–9.
62. Sensi L, Buzzi R, Giron F, De Luca L, Aglietti P. Patellofemoral function after total knee arthroplasty: gender-related differences. J Arthroplasty. 2011;26(8):1475–80.

63. Kamath AF, Horneff JG, Gaffney V, Israelite CL, Nelson CL. Ethnic and gender differences in the functional disparities after primary total knee arthroplasty. Clin Orthop Relat Res. 2010;468(12):3355–61.
64. Liebs T, Herzberg W, Roth-Kroeger A, Rüther W, Hassenpflug J. Women recover faster than men after standard knee arthroplasty. Clin Orthop Relat Res. 2011;469(10):2855–65.
65. Kim Y, Choi Y, Kim J. Comparison of a standard and a gender-specific posterior cruciate-substituting high-flexion knee prosthesis: a prospective, randomized, short-term outcome study. J Bone Joint Surg Am. 2010;92(10):1911–20.
66. Tanavalee A, Rojpornpradit T, Khumrak S, Ngarmukos S. The early results of gender-specific total knee arthroplasty in Thai patients. Knee. 2011;18(6):483–7.
67. Song EK, Jung WB, Yoon TR, Park KS, Seo HY, Seon JK. Comparison of outcomes after bilateral simultaneous total knee arthroplasty using gender-specific and unisex knees. J Arthroplasty. 2012;27(2):226–31.
68. Kim YH, Choi Y, Kim JS. Comparison of standard and gender-specific posterior-cruciate-retaining high-flexion total knee replacements: a prospective, randomised study. J Bone Joint Surg Br. 2010;92(5):639–45.
69. Holtzman J, Saleh K, Kane R. Gender differences in functional status and pain in a Medicare population undergoing elective total hip arthroplasty. Med Care. 2002;40(6):461–70.
70. Singh JA, Jensen MR, Harmsen SW, Lewallen DG. Are gender, comorbidity, and obesity risk factors for postoperative periprosthetic fractures after primary total hip arthroplasty? J Arthroplasty. 2013;28(1):126–31.
71. Perron M, Malouin F, Moffet H, McFadyen BJ. Three-dimensional gait analysis in women with a total hip arthroplasty. Clin Biomech (Bristol, Avon). 2000;15(7):504–15.
72. Singh JA, Lewallen D. Age, gender, obesity, and depression are associated with patient-related pain and function outcome after revision total hip arthroplasty. Clin Rheumatol. 2009;28(12):1419–30.
73. Aro HT, Alm JJ, Moritz N, Makinen TJ, Lankinen P. Low BMD affects initial stability and delays stem osseointegration in cementless total hip arthroplasty in women: a 2-year RSA study of 39 patients. Acta Orthop. 2012;83(2):107–14.