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Abstract

Total joint arthroplasty (TJA) is an effective treatment for end stage osteoarthritis (OA), which aims to alleviate pain and improve function and mobility. Despite the remarkable success of TJA, complications can arise, leading to unplanned hospital readmission, implant failure, morbidity and mortality. Recently, there has been a growing interest in analysing sex-based differences in diseases and response to medical interventions. This review summaries evidence pertaining to the widening gap between men and women regarding the utilisation and outcome of TJA surgery. Interactions between sex and patient-reported outcome, implant failure and medical complication are complex and often demonstrates conflicting results. Significantly, there is a global consensus that men are at a higher risk of developing prosthetic joint infection (PJI) following joint arthroplasty. Guided by the literature, there is a clear need for standardised methods of collecting, analysing and reporting sex-specific data to improve outcomes for both men and women who undergo TJA.

Main Text

Introduction

Published data has made it increasingly clear that males and females differ in the vulnerability to diseases, injuries and response to medical interventions. Within musculoskeletal health, women have a higher prevalence of osteoarthritis (OA), spinal disorders and certain soft tissue tumours(1, 2); the incidence of anterior cruciate ligament (ACL) injury is significantly higher in women compared to men(3); and differences in the efficacy of analgesics to treat conditions such as arthritis has been previously described(4). It is noteworthy that females remain underrepresented in clinical trials and animal models of disease, and in addition, studies are often limited by the fact that results are not analysed or reported separately by sex(5). As a result, the knowledge pertaining to the effect of female physiology, biology and responses to medical interventions is less well known when compared to males(5).

Total joint arthroplasty (TJA) is considered the gold standard treatment for OA, a leading cause of disability(6), and offers to improve patients' mobility, independence and quality of life (QoL)(7). In Australia alone, 66,346 and 50,784 total knee and total hip arthroplasties (TKA, THA) were performed in 2019 respectively(8). By 2030, the incidence of TKA and THA is forecasted to increase by 276% and 208% respectively, at a total cost to the Australian healthcare system of $AUD5.32 billion(9). Due to an aging population and

growing obesity rates, this upward trend is expected to continue in in both Australia and worldwide(7, 8).

This narrative review highlights the importance of investigating sex in TJA research and identifies reported differences between men and women in the utilisation of surgery, patient reported outcomes, implant survival, medical complications and infection following hip and knee arthroplasty. Bringing awareness to the themes and issues in the TJA literature, we intend to lay the foundation for future research to further investigate the implications of sex differences for diagnosis and treatment of complications, and by doing so help clinicians to facilitate equitable delivery of medical information and treatment resources to patients.

Why is Sex-Specific Analysis and Reporting Important in Research?

The terms ‘sex’ and ‘gender’ are controversial in research and often inappropriately conflated in scientific literature and public media. In accordance to the Institute of Medicine(10), this review defines ‘sex’ as a biological classification generally as male or female according to their reproductive organs and function assigned at birth and ‘gender’ pertains to the socially constructed roles and behaviours which render an individual’s self-presentation as male, female, woman, man or gender diverse. While both biological (sex) and social/cultural (gender) differences are important, this review focuses on how patients’ sex can impact health, disease and treatment outcome.

Accounting sex as a key biological factor in research is crucial to promoting reproducibility through rigor and transparency and yet, only a decade ago, 70% of the orthopaedic literature failed to conduct sex-specific analysis and reporting(11). The historical underrepresentation of females in human clinical trials and animal models of disease has generated incomplete data relating to the aetiology, presentation and treatment of diseases which have been traditionally examined in the context of the male sex(11). As a result, treatment guidelines are

generated with a substantial male bias, which has important consequences. This was highlighted in 2005 when 80% of drugs withdrawn from the USA market were due to adverse reactions affecting women that weren't captured during initial trials(2).

In 1993, the National Institutes of Health (NIH) Revitilisation Act mandated appropriate inclusion of women in clinical trials(11). Almost 30 years have elapsed and sex-specific reporting and analysis remains inadequate(5). The common practice of adjusting results by sex means the average combined male and female data can mask existing variances, and therefore clinically relevant differences related to the efficacy of medical devices may be obscured(2). In order to examine these differences, investigators should: (i) consider sex when formulating research questions and hypothesis testing, (ii) appropriately enrol a sufficient number of males and females within the sample cohort, (iii) analyse and report data separately for males and females and (iv) consider the influence of sex when interpreting and generalising research findings(12). As opposed to a one-size-fits-all approach, highlighting differences between men and women in medical research provides clinicians with an enhanced understanding of disease mechanisms, thereby facilitating shared decision-making and empowering patients to exercise control over their healthcare journey.

Sex, Gender and the Utilisation of TJA

The treatment of OA has become a global healthcare challenge. Not only do women have a higher overall prevalence of OA(13), but they also experience worse symptoms and disability compared to man despite sharing similar radiographic severity(13, 14). While the mechanisms remain unclear, declining levels of oestrogen, as seen in postmenopausal women, has been associated with reduced adult cartilage health(6). In addition, women presenting for TJA tend to be at a more advanced stage of their disease trajectory(15), while also being older and more obese, both of which are known risk factors for OA(6). Despite the greater need for joint arthroplasty in women, both utilisation and willingness to undergo TJA surgery is less for women than men (16-18). In this regard, a pronounced gender bias has

been reported when it comes to the clinical decision making of elective surgery. A prior study indicates that in clinical practice, a physician and orthopaedic surgeon is less likely to refer a knee arthroplasty to a female patient compared to a male(18). Possible explanations for this finding include, gender norms that are reflected in healthcare in which clinicians have been reported to not take women's pain seriously and assign symptoms to psychological rather than physical causes(19) and the stereotype that women don't receive the same benefit from joint arthroplasty when compared to men. In addition, women are typically the primary family caregiver which might partially explain why women are more likely to accept persistent functional decline and delay in treatment(20). This indicates that women are potentially at a more advanced stage in their disease trajectory when presenting for TJA than males, which is important since those with more severe OA preoperatively report worse postoperative outcomes(21). Moreover, linking the anatomical sex-differences of the hip and knee to normal limb/joint kinematics and function has led to the development and use of sex-specific implant designs which to date have failed to demonstrate superiority in functional, pain or implant survival outcomes(22).

Sex in TJA and Postoperative Outcomes

Patient-reported Outcomes

Women show a greater risk of moderate to severe postoperative pain at two and five years after TKA(23). Possible mechanisms that might contribute to this difference are found in studies that report women are more sensitive to painful stimuli and are more likely to report high levels of distress and pain symptoms as opposed to men(24). However, in a sex-specific analysis, Nandi et al(24) found that by six weeks postoperatively, differences in reported pain between men and women were no longer evident. Importantly, due to the underrepresentation of females in clinical research, the influence of sex on anaesthetic and pain medication

remains scant and unclear(25). Nevertheless, evidence suggests numerous physiological and pharmacological differences between male and females which might impact the safety and effectiveness of certain pain medication and therefore contribute to the observed differences in postoperative pain(25). Aside from pain, postoperative quality of life and functional status can also be indicated by clinical rating scores and self-reported questionnaires(26). For both six months and two years following knee surgery, women report to have greater improvements in Oxford Knee Score, Knee Society Score and Short Form-36 Health Survey (SF-36), however men report higher overall clinical scores as well as better knee flexion(27). This suggests women achieve greater improvements of function than men following TKA, but do not attain the same final level of function. For hips, Singh and Lewallen(28) found that female sex was associated with significantly higher dependence on walking aids and activity limitation at two- and five-years postoperatively. It has been postulated that increased severity of postoperative pain in women could potentially interfere with their functional recovery.

Survivorship Free of TJA Revision

Along with pain relief, an increasing number of patients seek TJA to maintain an active lifestyle, regain the ability to participate in various sporting activities and maintain general health(29). Despite the remarkable success of the procedure, some implants will fail which can require additional surgeries and burden the healthcare system(30). The impact of sex on TJA revision rates from aseptic causes varies in the literature. An earlier systematic review found that men experiences an increased the risk of aseptic revision(30). Age has been suggested as a driver of aseptic failure in men because they tend to present for TJA at a younger age(30) and reported to be more active than women(31). In this regard, the elevated muscular strength from physical activity among men could result in increased torsional forces on femoral components which might influence aseptic loosening, but this was examined in

rheumatoid patients rather than osteoarthritic patients(32). Some implants have been shown to perform worse in women than men such as the metal-on-metal (MoM) hip implants where a large UK registry-based study reported poorer implant survivorship in women (33). However, controversy remains over MoM hip replacements with concerns involving metallosis and adverse reactions which increase the risk of aseptic and seems to be more prevalent in female patients(34, 35). Interestingly, another systematic review and meta-analysis found geographic variability with regards to sex and implant failure(36). In this study, males in Europe had an increased risk of THA revision, whereas males in the US had a decreased risk. The causes for this are unclear but the authors suggest it could partially be due to varying criteria for revision between the two regions(36-38).

Considering implant dislocation, Kim et al concluded that females were 2.5 times more likely to dislocate their hip implant compared to males(39). However, the substantial underrepresentation of females in the sample (n=464) as compared to males (n=804) gives rise to a potential source of bias which can lead to a systematic over- or under-estimation of dislocation rates across sex groups. In contrast, a study done in Australia(40) reported no significant effect of sex on dislocation outcomes. However, not only was a sex-specific analysis and reporting absent from the methodology, but the true dislocation rate remains unknown. The study's variable of interest was dislocation resulting in revision surgery and therefore fails to account for patients who incur a dislocation but are unable or unwilling to undergo a revision surgery.

Medical complications

While the impact of sex on medical complications has been widely published in literature pertaining to vascular surgery(41), this is not the case for TJA. In addition to the paucity of sex-specific analysis and reporting, the absence of a standardised grading system for postoperative TJA complications can lead to confusion and hamper accurate interpretation of surgical outcomes(42). For instance, Basques et al(43) investigated 6,123,637 TKA and THA

patients and concluded that women had increased overall adverse events, however, this was primarily due to a higher frequency of urinary tract infections (UTI). In the same study, men had increased rates of infection, cardiac arrest, myocardial infarction, pneumonia and mortality. This is important since infection and cardiovascular event are leading reasons for 30-day readmission following TJA(44) and also because cardiac arrest and pneumonia are frequently occurring complications among those who die following THA(45). Other findings include, women showing higher rates of deep vein thrombosis, pulmonary embolism and blood transfusions(46, 47).

Notably, most studies that focus on the influence of sex on medical complications are (i) conducted in the US, (ii) have extracted data from the same registry, the American College of Surgeons National Surgical Quality Improvement Program, and (iii) are conducted within overlapping years(43, 45, 47). While it is possible for authors to perform different or more complex analyses with the same dataset, looking into sample groups from other global locations, such as Australia, could add meaningful information due to factors such as geographic variability.

Surgical Site Infection

‘‘Postoperative infection after total hip replacement is the saddest of all complications”. - Sir John Charnley at the Hip Society, 1982(48).

Surgical site infections (SSI) can be superficial, deep incisional, organ/space or implant infections and are known to inflict deep physical, mental and economic suffering(49). While evidence of sex differences for other complications seem to be inconsistent, it is increasingly clear that males are at a substantially higher risk of developing infections after TJA

surgery(50). This phenomenon might be explained by the varying influence of sex-specific hormones on immune response, in that oestrogen increases antibody production while testosterone decreases antibody production(51). Not to mention, men have significantly longer operative time for TJA surgery and prolonged operative time is associated with increased risk of joint infection(52). A Norwegian study reported that males are 2.4 times more likely to have a revision for joint infection when compared to females (95% CI 1.8-3.1 P<0.001)(53) and at the 2013 International Consensus Meeting on Prosthetic Joint Infections (PJI), experts agreed that male sex increased the risk for surgical site infections (SSI) and in particular PJI following TJA(50). Along with the devastating impact on patients' physical and mental health, there are substantial economic costs associated with PJI. Joint infection is the leading cause of implant failure in the United States(54), while in Australia, revision surgeries due to infection has increased 72% from 2006-2012 to 2013-2018(8).

Importantly, comorbidities such as obesity and blood transfusions, have also been cited as risk factors for PJI development(49). However, despite higher infection rates in men, the literature suggests that female TJA patients present with significantly higher rates of obesity, morbid obesity and postoperative transfusions rates than male TJA patients(46, 55). In addition, evidence has associated diabetes mellitus (DM) with increased risk of joint infection, and worse QoL after TKA, with females experiencing poorer outcomes compared to males(56). This highlights the complex interactions among covariates that could potentially lead to infection. Moreover, in a meta-analysis investigating TJA infection rates, Chen et al(57) noted that "gender-specific effect estimates were rarely concluded", implying that there is a need for increased methodological rigor and sex-specific analysis to improve the quality of evidence to draw conclusions.

Summing Up: The Need for Further Research

Investigating differences between men and women is a pressing issue in orthopaedics, a field in which substantial sex differences are demonstrated in the prevalence of osteoarthritis,

utilisation of arthroplasty and baseline pain and function of patients presenting for TJA. In addition, the interaction between sex and postoperative outcomes of TJA is complex. Women report more severe postoperative pain and reduced overall functional ability compared to men. The risk of an adverse event is greater for women, but this is mainly due to the higher frequency of UTIs in this group, whereas men show higher rates of cardiac events and mortality following surgery. Evidence regarding sex and risk of aseptic revisions, is inconsistent. Nevertheless, there is a global consensus that men have a significantly higher risk for developing joint infection following TJA. PJI is a major cause for revision surgery worldwide and a significant burden for both patients and surgeons. To the best of our knowledge there is a paucity of literature that investigates the characteristics of joint infection between men and women or sex differences in PJI treatment outcomes. Given the growing evidence that men and women often experience disparate outcomes following TJA, there is a clear need for standardised methods of collecting, analysing and reporting sex specific information to improve outcomes for both men and women who undergo TJA.

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Authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Author Contribution Statement

All authors contributed to the conception, design of the study, and interpretation of the data. AC and CS were responsible for data and literature acquisition. AC wrote the first draft. All authors contributed to revising the manuscript for critically important intellectual content, read, and approved the submitted version.

References

1. Tosi LL, Boyan BD, Boskey AL. Does sex matter in musculoskeletal health?: The influence of sex and gender on musculoskeletal health. JBJS. 2005 Jul 1;87(7):1631-47..
2. Novicoff WM, Saleh KJ. Examining sex and gender disparities in total joint arthroplasty. Clinical Orthopaedics and Related Research®. 2011 Jul 1;469(7):1824-8.
3. Wolf JM, Cannada L, Van Heest AE, O'Connor MI, Ladd AL. Male and female differences in musculoskeletal disease. JAAOS-Journal of the American Academy of Orthopaedic Surgeons. 2015 Jun 1;23(6):339-47.
4. Craft RM. Sex differences in opioid analgesia:"from mouse to man". The Clinical journal of pain. 2003 May 1;19(3):175-86.
5. Wizeman TM. Sex-specific reporting of scientific research: a workshop summary. National Academies Press; 2012 Jan 27.
6. Litwic A, Edwards MH, Dennison EM, Cooper C. Epidemiology and burden of osteoarthritis. British medical bulletin. 2013 Mar 1;105(1):185-99.
7. Culliford D, Maskell J, Judge A, Cooper C, Prieto-Alhambra D, Arden NK, COASt Study Group. Future projections of total hip and knee arthroplasty in the UK: results from the UK Clinical Practice Research Datalink. Osteoarthritis and cartilage. 2015 Apr 1;23(4):594-600.
8. Australian Orthopaedic Association National Joint Replacement Registry (AOANJRR). Hip, Knee & Shoulder Arthroplasty: 2019 Annual Report. Adelaide: AOA. 2019.

9. Ackerman IN, Bohensky MA, Zomer E, Tacey M, Gorelik A, Brand CA, De Steiger R. The projected burden of primary total knee and hip replacement for osteoarthritis in Australia to the year 2030. BMC musculoskeletal disorders. 2019 Dec 1;20(1):90.

10. Pardue ML, Wizemann TM, editors. Exploring the biological contributions to human health: does sex matter?. National Academies Press; 2001 Aug 2.

11. Hettrich CM, Hammoud S, LaMont LE, Arendt EA, Hannafin JA. Sex-specific analysis of data in high-impact orthopaedic journals: how are we doing?. Clinical Orthopaedics and Related Research®. 2015 Dec 1;473(12):3700-4.

12. Food and Drug Administration. Evaluation of sex-specific data in medical device clinical studies-Guidance for industry and food and drug administration staff. Rockville, Maryland, United States Food and Drug Administration (FDA). 2014 Aug 22.

13. Vos T, Barber RM, Bell B, Bertozzi-Villa A, Biryukov S, Bolliger I, Charlson F, Davis A, Degenhardt L, Dicker D, Duan L. Global, regional, and national incidence, prevalence, and years lived with disability for 301 acute and chronic diseases and injuries in 188 countries, 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. The Lancet. 2015 Aug 22;386(9995):743-800.

14. 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 and cartilage. 2005 Sep 1;13(9):769-81.

15. Parsley BS, Bertolusso R, Harrington M, Brekke A, Noble PC. Influence of gender on age of treatment with TKA and functional outcome. Clinical Orthopaedics and Related Research®. 2010 Jul 1;468(7):1759-64.

16. Hawker GA, Wright JG, Coyte PC, Williams JI, Harvey B, Glazier R, Badley EM. Differences between men and women in the rate of use of hip and knee arthroplasty. New England Journal of Medicine. 2000 Apr 6;342(14):1016-22.

17. Jüni P, Low N, Reichenbach S, Villiger PM, Williams S, Dieppe PA. Gender inequity in the provision of care for hip disease: population-based cross-sectional study. Osteoarthritis and cartilage. 2010 May 1;18(5):640-5.

18. Borkhoff CM, Hawker GA, Kreder HJ, Glazier RH, Mahomed NN, Wright JG. The effect of patients' sex on physicians' recommendations for total knee arthroplasty. Cmaj. 2008 Mar 11;178(6):681-7.

19. Samulowitz A, Gremyr I, Eriksson E, Hensing G. "Brave men" and "emotional women": A theory-guided literature review on gender bias in health care and gendered norms towards patients with chronic pain. Pain Research and Management. 2018 Feb 25;2018.

20. Karlson EW, Daltroy LH, Liang MH, Eaton HE, Katz JN. Gender differences in patient preferences may underlie differential utilization of elective surgery. The American journal of medicine. 1997 Jun 1;102(6):524-30.

21. Fortin PR, Clarke AE, Joseph L, Liang MH, Tanzer M, Ferland D, Phillips C, Partridge AJ, Belisle P, Fossel AH, Mahomed N. Outcomes of total hip and knee replacement: preoperative functional status predicts outcomes at six months after surgery. Arthritis & Rheumatism: Official Journal of the American College of Rheumatology. 1999 Aug;42(8):1722-8.

22. Xie X, Lin L, Zhu B, Lu Y, Lin Z, Li Q. Will gender-specific total knee arthroplasty be a better choice for women? A systematic review and meta-analysis. European Journal of Orthopaedic Surgery & Traumatology. 2014 Dec 1;24(8):1341-9.

23. Singh JA, Gabriel S, Lewallen D. The impact of gender, age, and preoperative pain severity on pain after TKA. Clinical orthopaedics and related research. 2008 Nov 1;466(11):2717-23.

24. Nandi M, Schreiber KL, Martel MO, Cornelius M, Campbell CM, Haythornthwaite JA, Smith MT, Wright J, Aglio LS, Strichartz G, Edwards RR. Sex differences in negative affect and postoperative pain in patients undergoing total knee arthroplasty. Biology of sex differences. 2019 Dec 1;10(1):23.

25. Campesi I, Fois M, Franconi F. Sex and gender aspects in anesthetics and pain medication. InSex and Gender Differences in Pharmacology 2013 (pp. 265-278). Springer, Berlin, Heidelberg.

26. Lingard EA, Katz JN, Wright RJ, Wright EA, Sledge CB, Kinemax Outcomes Group. Validity and Responsiveness of the Knee Society Clinical Rating System in Comparisonwith the SF-36 and WOMAC. JBJS. 2001 Dec 1;83(12):1856-64.

27. Lim JB, Chi CH, Lo LE, Lo WT, Chia SL, Yeo SJ, Chin PL, Tay KJ, Lo NN. Gender difference in outcome after total knee replacement. Journal of Orthopaedic Surgery. 2015 Aug;23(2):194-7.

28. Singh JA, Lewallen D. Age, gender, obesity, and depression are associated with patient-related pain and function outcome after revision total hip arthroplasty. Clinical rheumatology. 2009 Dec 1;28(12):1419.

29. Swanson EA, Schmalzried TP, Dorey FJ. Activity recommendations after total hip and knee arthroplasty: a survey of the American Association for Hip and Knee Surgeons. The Journal of arthroplasty. 2009 Sep 1;24(6):120-6.

30. Prokopetz JJ, Losina E, Bliss RL, Wright J, Baron JA, Katz JN. Risk factors for revision of primary total hip arthroplasty: a systematic review. BMC musculoskeletal disorders. 2012 Dec 1;13(1):251.

31. Azevedo MR, Araújo CL, Reichert FF, Siqueira FV, da Silva MC, Hallal PC. Gender differences in leisure-time physical activity. International journal of public health. 2007 Feb 1;52(1):8.

32. Lehtimäki MY, Kautiainen H, Lehto MU, Hämäläinen MM. Charnley low-friction arthroplasty in rheumatoid patients: a survival study up to 20 years. The Journal of arthroplasty. 1999 Sep 1;14(6):657-61.

33. Smith AJ, Dieppe P, Vernon K, Porter M, Blom AW. Failure rates of stemmed metal-on-metal hip replacements: analysis of data from the National Joint Registry of England and Wales. The Lancet. 2012 Mar 31;379(9822):1199-204.

34. Bayley N, Khan H, Grosso P, Hupel T, Stevens D, Snider M, Schemitsch E, Kuzyk P. What are the predictors and prevalence of pseudotumor and elevated metal ions after large-diameter metal-on-metal THA?. Clinical Orthopaedics and Related Research®. 2015 Feb 1;473(2):477-84.

35. Silverman EJ, Ashley B, Sheth NP. Metal-on-metal total hip arthroplasty: is there still a role in 2016?. Current reviews in musculoskeletal medicine. 2016 Mar 1;9(1):93-6.

36. Towle KM, Monnot AD. An assessment of gender-specific risk of implant revision after primary total hip arthroplasty: a systematic review and meta-analysis. The Journal of Arthroplasty. 2016 Dec 1;31(12):2941-8.

37. Inacio MC, Ake CF, Paxton EW, Khatod M, Wang C, Gross TP, Kaczmarek RG, Marinac-Dabic D, Sedrakyan A. Sex and risk of hip implant failure: assessing total hip arthroplasty outcomes in the United States. JAMA internal medicine. 2013 Mar 25;173(6):435-41.

38. Howard JL, Kremers HM, Loechler YA, Schleck CD, Harmsen WS, Berry DJ, Cabanela ME, Hanssen AD, Pagnano MW, Trousdale RT, Lewallen DG. Comparative survival of uncemented acetabular components following primary total hip arthroplasty. JBJS. 2011 Sep 7;93(17):1597-604.

39. Kim YH, Choi Y, Kim JS. Influence of patient-, design-, and surgery-related factors on rate of dislocation after primary cementless total hip arthroplasty. The Journal of arthroplasty. 2009 Dec 1;24(8):1258-63.

40. Conroy JL, Whitehouse SL, Graves SE, Pratt NL, Ryan P, Crawford RW. Risk factors for revision for early dislocation in total hip arthroplasty. The Journal of arthroplasty. 2008 Sep 1;23(6):867-72.

41. Arnaoutakis GJ, Schneider EB, Arnaoutakis DJ, Black III JH, Lum YW, Perler BA, Freischlag JA, Abularrage CJ. Influence of gender on outcomes after thoracic endovascular aneurysm repair. Journal of Vascular Surgery. 2014 Jan 1;59(1):45-51.

42. Clavien PA, Barkun J, De Oliveira ML, Vauthey JN, Dindo D, Schulick RD, De Santibañes E, Pekolj J, Slankamenac K, Bassi C, Graf R. The Clavien-Dindo classification of surgical complications: five-year experience. Annals of surgery. 2009 Aug 1;250(2):187-96.

43. Basques BA, Bell JA, Sershon RA, Della Valle CJ. The influence of patient gender on morbidity following total hip or total knee arthroplasty. The Journal of arthroplasty. 2018 Feb 1;33(2):345-9.

44. Avram V, Petruccelli D, Winemaker M, de Beer J. Total joint arthroplasty readmission rates and reasons for 30-day hospital readmission. The Journal of arthroplasty. 2014 Mar 1;29(3):465-8.

45. Belmont Jr PJ, Goodman GP, Hamilton W, Waterman BR, Bader JO, Schoenfeld AJ. Morbidity and mortality in the thirty-day period following total hip arthroplasty: risk factors and incidence. The Journal of arthroplasty. 2014 Oct 1;29(10):2025-30.

46. Basques BA, Bell JA, Fillingham YA, Khan JM, Della Valle CJ. Gender differences for hip and knee arthroplasty: complications and healthcare utilization. The Journal of arthroplasty. 2019 Aug 1;34(8):1593-7.

47. Robinson J, Shin JI, Dowdell JE, Moucha CS, Chen DD. Impact of gender on 30-day complications after primary total joint arthroplasty. The Journal of Arthroplasty. 2017 Aug 1;32(8):2370-4.

48. Charnley J. The future of total hip replacement. The hip. 1982 Jan 1:198-210.

49. Tande AJ, Patel R. Prosthetic joint infection. Clinical microbiology reviews. 2014 Apr 1;27(2):302-45.

50. Aggarwal VK, Tischler EH, Lautenbach C, Williams Jr GR, Abboud JA, Altena M, Bradbury T, Calhoun J, Dennis D, Del Gaizo DJ, Font-Vizcarra L. Proceedings of the International Consensus Meeting on Periprosthetic Joint Infection: Mitigation and education. InInternational Consensus Meeting on Periprosthetic Joint Infection 2013.

51. Bouman A, Heineman MJ, Faas MM. Sex hormones and the immune response in humans. Human reproduction update. 2005 Jul 1;11(4):411-23.

52. Duchman KR, Pugely AJ, Martin CT, Gao Y, Bedard NA, Callaghan JJ. Operative time affects short-term complications in total joint arthroplasty. The Journal of arthroplasty. 2017 Apr 1;32(4):1285-91.

53. Dale H, Skråmm I, Løwer HL, Eriksen HM, Espehaug B, Furnes O, Skjeldestad FE, Havelin LI, Engesæter LB. Infection after primary hip arthroplasty: a comparison of 3 Norwegian health registers. Acta orthopaedica. 2011 Dec 1;82(6):646-54.

54. Parvizi J, Shohat N, Gehrke T. Prevention of periprosthetic joint infection: new guidelines. The bone & joint journal. 2017 Apr;99(4_Supple_B):3-10.

55. Whitlock KG, Piponov HI, Shah SH, Wang OJ, Gonzalez MHJTJoA. Gender role in total knee arthroplasty: a retrospective analysis of perioperative outcomes in US patients. 2016;31(12):2736-40.

56. Tew M, Dowsey MM, Choong A, Choong PF, Clarke P. Co-Morbidities and Sex Differences in Long-Term Quality-of-Life Outcomes among Patients with and without Diabetes after Total Knee Replacement: Five-Year Data from Registry Study. Journal of Clinical Medicine. 2020 Jan;9(1):19.

57. Chen J, Cui Y, Li X, Miao X, Wen Z, Xue Y, Tian J. Risk factors for deep infection after total knee arthroplasty: a meta-analysis. Archives of orthopaedic and trauma surgery. 2013 May 1;133(5):675-87.