Chapter 4

Predictors of Pain and Function Following Total Joint Replacement

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Additional information is available at the end of the chapter

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1. Introduction

Osteoarthritis (OA) is one of the most disabling diseases in developed countries and is responsible for significant disability in over 43 million people worldwide, 27 million of whom are 60 years of age or older [1]. Age is the strongest predictor of the development and progression of osteoarthritis, as such the number of people suffering with OA is expected to continue to increase over the coming years due to the ageing population [2]. Other predictors associated with OA include; gender, obesity, physical inactivity, smoking, excess alcohol and injuries [2].

Total joint replacement is the treatment of choice (among suitably 'fit' candidates) for end-stage OA [3]. It is a high-cost and high-volume procedure, which dominates surgical waiting lists and this is expected to become critical with the rapidly ageing population [4]. The number of hip and knee replacement being performed each year has risen markedly over the past decade in most OECD countries [2]. On average, the rate of hip replacement has increased by over 25% and the rate of knee replacement has nearly doubled. While joint replacement surgery is mainly carried out in people aged 60 and over, the rate of surgery is also increasing in younger people due to the increasing prevalence of obesity, advances in surgery and greater patient demand.

Many studies have confirmed the beneficial impact of TJR on pain, disability and quality of life [5, 6]. However, surgery is not without risk. In the immediate post-operative period, there is a small but important risk of severe complications [7-9] and in the longer term there is the risk of prosthesis failure, primarily through loosening, resulting in the need for complex revision surgery [10]. While the majority can expect improvements in pain and function in the intermediate period, there is a minority who remain dissatisfied after TJR and this is despite procedurally excellent outcomes. There are a number of risk factors for continuing

pain and disability after surgery and given the increasing demand for TJR, understanding more about the determinants of good and bad outcomes has become an imperative.

This chapter provides an overview of baseline patient characteristics and predictors associated with pain and function following total joint replacement.

2. Incidence

The incidence of dissatisfaction or suboptimal outcome following total joint replacement varies in the literature. Quantifying the influence of a single patient factor on the functional and quality of life outcomes in joint replacement is a complex process. Variations in reporting may in part be due to the range of instruments used to measure patient centred outcomes and the lack of consensus and consistency amongst health professionals in how these tools are used [11-14]. Furthermore, to understand the complexities of what contributes to a suboptimal outcome, large data sets with samples representative of the total study population and extensive follow-up are essential, however this is a labour intensive and challenging process.

In 1998 our institution established a joint replacement registry to respond to this issue and to contribute to our understanding of what constitutes and predicts a good versus poor outcome following TJR. The St Vincent's Total Joint Replacement Registry (SVHM JRR) currently contains over 8000 procedures undertaken in over 7000 consecutive patients, and grows by approximately 800 procedures each year. Data include patient demographics, diagnoses, and type of surgery, prostheses, co-morbidities and peri-operative interventions, and an extensive range of outcomes including death, re-hospitalisation and complications. The registry includes marginalised and disadvantaged groups and is characterised by i) cultural and linguistic diversity (15% from a non-English speaking background representing over 20 languages); ii) 15% rural representation; and iii) socio-economic diversity (20% are ranked as living in the most "disadvantaged" socio-economic areas (Australian Bureau of Statistics [15]). Since 2006, we have obtained near complete (> 99%) 12 month follow-up of our cohort. Pain and functional outcomes as well as quality of life (QoL) are measured using validated surveys including; the Harris Hip Score [13, 16], the International Knee Society Score[17, 18] and Short Form Health Survey[12, 13, 19].

From our registry and that of the literature, dissatisfaction (variously measured) is as high as 50% among patients undergoing total joint replacement [20-25]. The level of dissatisfaction amongst recipients of hip and knee replacement is considerably different with a much higher rate of satisfaction reported amongst patients undergoing hip than knee replacement.

2.1. Pain

Chronic pain is a major global health care problem reported in 1 in 5 adults. The major causes of non-cancer chronic pain are; arthritis (40%) and surgery or injury (25%). For many, chronic pain substantially impairs daily physical activities, social activities and ability to enjoy life [26]. It carries a major economic burden with estimated costs running into billions in

many OECD countries; US$635 billion in America [27], EUR$32 billion in Sweden [28] and AU$34 billion in Australia [29].

Chronic disabling pain is the primary indicator for recommending TJR in those with radiographic evidence of arthritis. For those that present with early disease, conservative treatment modalities including physical and pharmacological therapies are the first line of treatment [30, 31] however arthritis is a progressive disease and non-surgical modalities can effectively delay but not negate the need for eventual surgical intervention. Surgical interventions such as arthroscopy, bone marrow stimulation or osteotomy, may be recommended in carefully selected patients, however TJR remains the most effective and cost effective intervention for relieving pain and restoring function in suitably fit patients [32, 33]

Total joint replacement is a major surgical procedure that requires multidisciplinary input prior to and after surgery to ensure the best possible outcome. Recovery from surgery is optimized with the inclusion of rehabilitation programs which are tailored to restore mobility and independence [34]. Time to recovery can vary following TJR and most patients will report substantial gains between 3 to 6 months after surgery. Patients undergoing THR report faster recovery in terms of both pain and function, with significant improvements occurring within the first 3 months of surgery [35]. In comparison patients undergoing TKR are more likely to report improvement between 3 to 6 months [36, 37]. Overall a continuing pattern of improvement can be observed up to 12 months following surgery [5, 38].

While on average a majority of patients report an improvement in pain following total joint replacement [39, 40] for a substantial number of individuals the level of improvement is suboptimal or does not meet expectation at 12 months or more after surgery. In total knee replacement ongoing pain has been reported in as many as 53% of patients and for hip replacement the incidence is as high as 38% (Table 1).

The causes of ongoing pain following TJR are not clearly understood. Recent literature reports a high prevalence of features of pain sensitisation in knee OA patients. Wylde et al (2011) identified 70% of patients as having various somatosensory abnormalities in a study of 117 knee OA patients [44]. Hochman et al (2011) reported neuropathic symptoms in 28% of older adults with chronic symptomatic knee OA [52]. Ohtori et al (2012) reported similar findings with neuropathic symptoms in as many as 20.6% of patients with radiographically confirmed knee OA [53]. These mechanisms of pain are not necessarily addressed by undergoing joint replacement.

Recent trials of the use of second-generation antiepileptic drugs (AED's), which are commonly used to treat neuropathic pain however, report mixed results in TJR studies. Both Gabapentin and Pregalbin use are associated with a reduction in post-operative opioid consumption following knee replacement [54, 55]. A randomized controlled trial comparing pre-operative Pregalbin to placebo has also reported a significant reduction in neuropathic pain at 6 months post TKR [54]. In contrast, Gabapentin had no effect on post-operative opioid consumption or pain scores at 6 months following total hip replacement [56]. While pre-operative Pregalbin has shown to reduce post-operative opioid consumption following THR, the longer term effects on post surgery pain have not been reported.

Overall higher rates of persistent pain are reported after knee replacement as compared to hip replacement (Table 1). Features of pain sensitisation and neuropathic type symptoms are also predominately reported in knee OA patients. This may explain the differences in response to AED's between hip and knee replacement recipients and is an indication that the underlying mechanisms of persistent pain following surgery differ according to the surgical site.

Author	Cohort	Follow-up	Pain Measure	Incidence of Ongoing Pain
Liu et al 2012 [41]	TJR = 1030	Minimum 1 year 32% response rate	McGill Pain Questionnaire [42]	Persistent pain THR = 38.0% TKR = 53.0%
Dowsey et al 2012 [40]	TKR = 478	99.4% at 1 year 93.5% at 2 years	IKSS [43] pain	Moderate to severe pain 29.5% at 12 months 30.6% at 2 years
Wylde et al 2011 [44]	THR = 909 TKR = 860	3 to 4 years 73.0% hip and knee	WOMAC [45] pain	Persistent pain THR = 27.0% TKR = 44.0%
Singh & Lewallen 2010 [46]	THR = 9,154 (2yrs) 6,243 (5yrs)	62.3% at 2 years 52.7 at 5 years	Mayo [47] Hip Score	Moderate to severe pain 8.1% at 2 years 10.6% at 5 years
Czurda et al 2010 [5, 48]	TKR = 411	18 to 42 months 80.3%	WOMAC [45] pain	Knee pain 13.9%
Wylde et al 2009 [49]	THR = 1,534 TKR = 857	5 to 8 years 72.5% hip 71.5% knee	Oxford [50] pain	Moderate to severe pain THR = 13.0% TKR = 26.0%
Baker et al 2007 [51]	TKR = 9417	87.4% at 1 year	Oxford [50] pain	Persistent pain 19.8% at 1 year

(IKSS – International Knee Society Score, WOMAC – Western Ontario and McMaster Universities Arthritis Index)

Table 1. Incidence of self reported pain > 12 months following TJR

2.2. Function

While arthritis accounts for 40% of non-cancer chronic pain it is the leading cause of disability in most developed countries. [57-59]. For many sufferers of arthritis even the most basic daily activities such as dressing, walking and stair climbing are substantially restricted. Pain and deformity associated with the progression of arthritis are the main contributors to impeding function and activity. As such joint replacement surgery that results in amelioration of pain and correction of deformity should lead to improved function and activity participation. However poor function and difficulty with daily activities have been reported up to 51% of TJR recipients, (Table 2).

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A decrease in activity participation outside those required for basic daily functioning has also been noted in a proportion of patients who have undergone TJR. Wylde et.al interviewed 56 hip and 60 knee replacement patients about their leisure activities [60]. They reported that THR patients participated in 209 leisure activities but rated 82% of these activities as difficult to perform prior to surgery and TKR patients participated in 171 leisure activities 86% of which were rated as difficult to perform prior to surgery due to joint problems. At 1 year post surgery THR patients still rated 25% of leisure activities as difficult to perform and TKR patients rate 32% of leisure activities difficult to perform. In a larger study Groen et.al measured adherence to an activity regimen recommended to maintain health in patients who underwent total knee replacement and found that 42% of patients were not active enough to maintain their health and fitness [61].

Author	Cohort	Follow-up	Functional Measure	Incidence of Functional Impairment
Dowsey et al 2012 [40]	TKR = 478	99.4% at 1 year 93.5% at 2 years	IKSS [43] function	Poor function 48.9% at 12 months 50.7% at 2 years
Wylde et al 2009 [49]	THR = 1,534 TKR = 857	5 to 8 years 72.5% hip 71.5% knee	Oxford [50] function	Extreme difficulty with individual activities THR = 5% to 17% TKR = 7% to 24%
Franklin et al 2008 [175]	TKJR = 17270	46.6% at 1 year	SF12 PCS [12] function	Function score worse than baseline = 19.0%
Lubbeke et al 2007 [62]	THR = 435	4 to 6 years 80.2%	HHS [16] function	Fair or poor function 9.0%
Nilsdotter et al 2003 [25]	THR = 211	26 to 65 months 94%	OARSI Criteria [63]	No improvement in function = 8.7%
Singh & Lewallen 2010 [64]	THR = 9,154 (2yrs) 6,243 (5yrs)	62.3% at 2 years 52.7% at 5 years	Mayo [47] Hip Score	Moderate to severe activity limitation 30% at 2 years 35% at 5 years
Singh et al (2010) [126]	TKR = 10,957 (2 yrs) 7,404 (5yrs)	65.0% at 2 years 57.0% at 5 years	IKSS [43] function	Moderate to severe activity limitation 20.7% at 2 years 27.1% at 5 years

(SF-12 PCS – Short Form 12 Physical Component Summary, HHS – Harris Hip Score, OARSI – Osteoarthritis Research Society International

Table 2. Incidence of self reported functional impairment > 12 months following TJR

As function and activity levels depends on all other joints and systems, not just the joint being replaced, improvements may not be achieved as a result of joint replacement alone in patients who have multiple joint arthropathy or systemic health issues. Functional outcomes also seem to be dependent on the site of joint replacement (Table 2). Consistent with pain outcomes, a higher proportion of patients undergoing TKR report poor function or difficulty with activities than do patients undergoing THR. Demographic and patient characteristics are of predictive value in determining barriers to functional gain and activity participation following TJR recipients.

3. Predictors of pain and function

Intuitively, those who present with the "worst" symptoms might be those who should be prioritized for TJR. However, the literature reports a mismatch between patient reported symptom severity and response to surgery and it is becoming clearer that TJR outcomes are influenced by a multitude of factors. Recent work has identified a number of baseline risk factors for continuing pain and disability after TJR and these can be stratified into those which are modifiable and non-modifiable. Non-modifiable risk factors include; age, gender, socio-economic status, aetiology and culture and ethnicity. Modifiable risk factors include; psychological state, co-morbidities, obesity, baseline symptom severity and patient expectation.

Importantly, our work to date has demonstrated that a majority of baseline patient characteristics (obesity, mental health, co-morbidities, radiographic OA severity, baseline pain and function) associated with sub-optimal outcome following TJR are those that could be "modified" with appropriate intervention [8, 39, 40, 65]; hence there is opportunity to alter patient outcomes. Appreciating the nature of patient pre-operative risk factors and the impact of different outcomes is critical for improving response rates to surgery.

3.1. Patient demographics

3.1.1. Age

As age is the strongest predictor of the development and progression of osteoarthritis the ageing population has no doubt contributed to the world wide increase in TJR numbers. However, TJR in younger patients is also on the rise particularly for knee replacement [66], and this is likely due in part to the rising incidence of obesity in patients presenting for surgery [8, 39]. The median age at presentation for joint replacement demonstrates a downward trend over the past 10 years at our institution (Figure 1)

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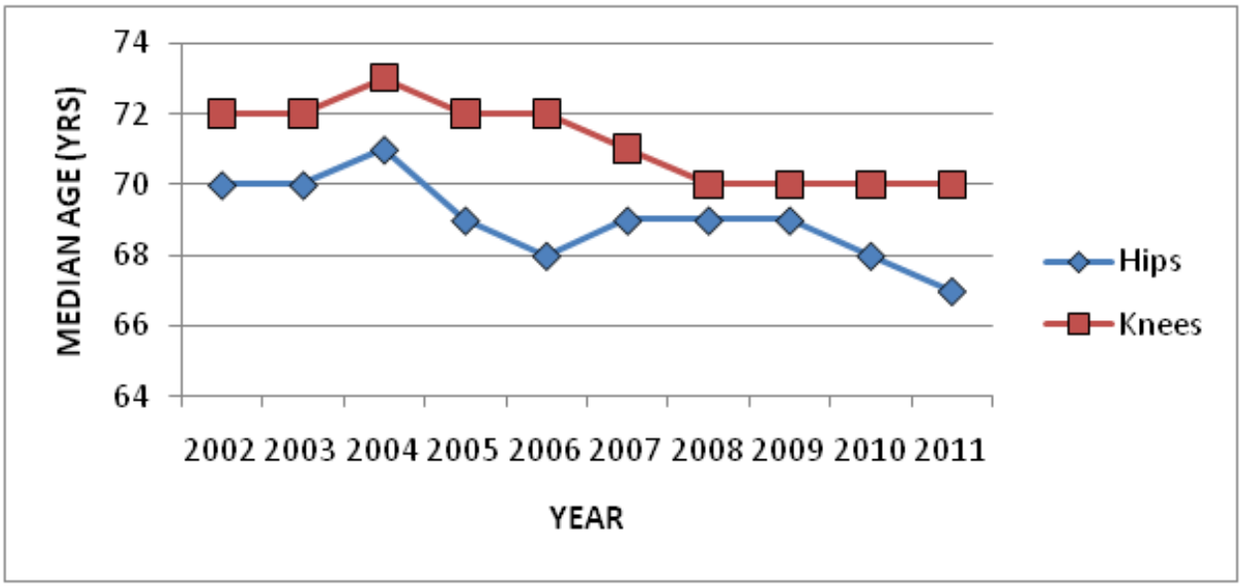

Figure 1. Median age at presentation for primary elective TJR (SVHM JRR)

Total joint replacement in the elderly carries a higher risk of peri-operative complication, requires a longer recovery time and is associated with a significant mortality rate in the longer term [67, 68]. However advancing age is not a barrier to pain and functional improvements after TJR surgery [67, 68] and excellent pain relief has been reported in individuals in their 80's and 90's [69-71]. While advancing age is associated with poorer function and activity levels following TJR [40] higher satisfaction with activity levels have been reported in those older than 70 years when compared to their younger counterparts [72].

3.1.2. Gender

Worldwide more females than males undergo joint replacement each year, with the greatest difference being for knee replacement. Various National Joint Replacement Registries report the ratio of females to males undergoing knee replacement as high as 2:1 and this concurs with gender patterns at our institution (Figure 2), [73-76]. Despite these figures inequities in referral patterns and reluctance in women to undergo joint replacement, resulting in late presentation have been reported [77, 78]. A gender bias in physician referral for knee replacement was identified in one study, with family physicians twice as likely and orthopaedic surgeons 22 times more likely to recommend knee replacement to male patients [79]. However it has also been identified that women delay seeking joint replacement until a later point in their functional decline [77].

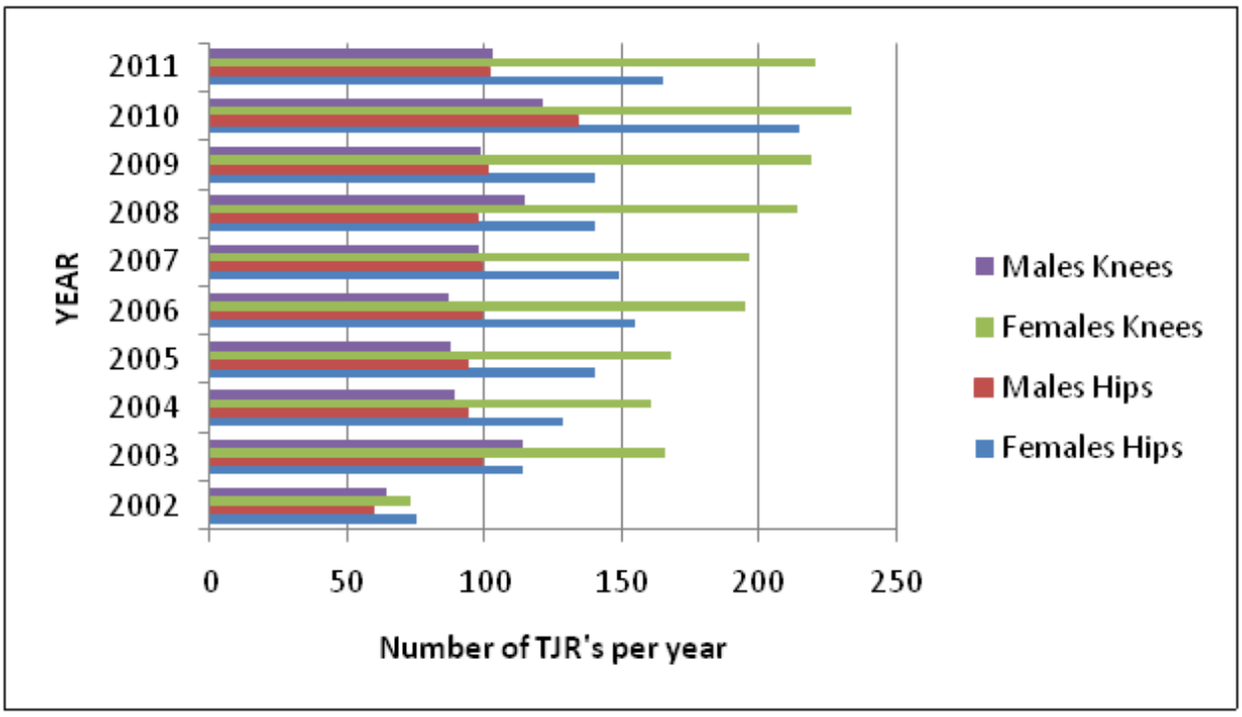

Figure 2. Gender breakdowns at presentation for primary elective TJR (SVHM JRR)

Females generally present with worse self-reported pain and functional impairment compared to males at the time hip and knee replacement [80-83], as such females do not tend to achieve the same level of physical function after surgery as males [84, 85]. However when taking into account baseline pain and function, women generally demonstrate greater improvements in pain and function scores after surgery than men [84-86]. Faster recoveries in terms of pain and function have also been reported in females undergoing total knee replacement when compared to males [87]. Despite this a significantly higher odds of poor function at 12 months (OR 1.81; 95% CI 1.08-3.03) and 2 years (OR 2.06; 95% CI 1.20 – 3.53) post knee replacement have been reported by women undergoing TKJR [40]. Impairment with specific activities such as stair climbing, despite achieving greater improvements in knee flexion, have also been reported in females compared to males [86]. These data suggest women may benefit from tailored rehabilitation programs following joint replacement surgery.

3.1.3. Socio-economic status

Differences among nations in their socio-economic fabric, ethnic composition, health care systems and cultural expectations, may confound studies examining the importance of socioeconomic status as a predictor of outcome following TJR. Variations in classifications of socio-economic status also require that caution should be exercised in making direct comparisons between studies. To date studies have largely focused on socio-economic status in patients undergoing total hip replacement, with most data derived from cohorts in Western countries.

A large UK study by Jenkins et.al (2009) reported significant differences in SF-36 physical improvement between the least and most "deprived groups" 18 months post THR [88]. A study based in Scotland by Clement et.al (2011) reported similar findings. In a cohort of 1312 patients who underwent primary THR a significant improvement in Oxford scores across all socioeconomic categories was noted, however social deprivation predicted a poorer functional outcome [89]. In a smaller study based in the US, Allen-Butler et.al (2011) conducted a secondary analysis of a prospective randomised study originally comparing 2 different hip stems. They also concluded that individual socioeconomic parameters such as education level, household income, as well as being African American were associated with lower Harris Hips Scores up to 2 years post THR [90]. Finally a German based study by Schafer et.al (2010) also concluded that socioeconomic parameters independently predicted response to THR as measured using the WOMAC [91]. An increased risk for "non-response" to surgery at 6 months was demonstrated in widowed patients, those who lived alone, those on a disability pension and those who had a shorter duration of school education.

Only one study reported outcomes according to socioeconomic status in patients undergoing total knee replacement. In a multicentre study conducted in several countries (USA, UK, AU, Canada) socio-economic status did not appear to affect the outcome of knee replacement [92]. Socioeconomic data were derived from a pre-operative questionnaire regarding education, income, working status and living arrangements, to allow for direct comparison between countries. Despite reporting a correlation between lower income and worse pre-operative pain and function, there were no differences in post-operative pain and function at 24 months.

Despite variations in definitions and study designs, patient reported outcomes following THR are consistently poorer for disadvantaged groups. In contrast there is a dearth of literature on TKR with only one study that reported no differences in patient reported outcomes. Poorer outcomes in socioeconomically disadvantaged groups may occur as a result underutilization of health services [93] and this has important implications in relation to preparing disadvantaged patients for joint replacement surgery.

3.1.4. Culture and ethnicity

Racial and ethnic TJR utilization disparities exist and are likely due to a lower willingness to undergo surgery amongst ethnic minorities rather than lower disease prevalence [78, 94, 95]. Poor health literacy, financial constraints, cultural influences and concerns about possible outcomes are amongst reported reasons for a lower willingness to undergo surgery and delayed presentation [96-100]. As such self-reported baseline pain and function are worse amongst ethnic minorities presenting for total joint replacement surgery [100-103].

Substantial improvements in pain and function have been reported following primary total joint replacement irrespective of race and ethnicity however ethnic minorities do report worse outcomes following both hip and knee replacement surgery. Lavernia et al (2011) studied patient reported outcomes in a large cohort of hip and knee replacements (739 hips and 1010 knees) and found that ethnic minorities had worse pain, function and well-being scores 2 years after surgery compared to Whites and worse outcomes was

most pronounced for African Americans [103]. Kamath et al (2010) reported similar findings for African-Americans undergoing TKJR [100]. In an Australian study of 237 TKR's, 41 were non-English speaking patients, Dowsey et al (2009) reported poorer International Knee Society pain and function scores at 12 months after surgery in those who required Interpreters compared to their English speaking counterparts[104]. A Swedish study analysed 1216 patients' pre and 1 year after THR, comparing those who were born inside and outside the country. Krupic et al (2012) reported lower self care and activity scores and more pain amongst those born abroad [102].

Promoting greater dialogue with health care providers and understanding the health literacy needs of ethnic minorities may help to address willingness to undergo joint replacement surgery and lead to better patient reported outcomes [105, 106].

3.2. Patient characteristics

3.2.1. Aetiology

Osteoarthritis is the principle diagnosis for a majority of total joint replacements performed each year [73-76]. In Australia it accounted for 88% of primary elective total hip replacement and 97% of primary elective knee replacement in 2010 [73]. The remaining diagnoses for elective THR included avascular necrosis (3.7%), dysplasia (1.3%) and rheumatoid arthritis (1.3%) and for TKR; rheumatoid arthritis (1.7%), inflammatory arthritis (0.5%) and necrosis (0.4%) [73].

Despite the worldwide increase in TJR numbers in recent years, the rate of joint replacement surgery in patients with rheumatoid arthritis has remained relatively stable and for some countries a decrease in numbers has been noted [107-110]. Contemporary treatment of rheumatoid arthritis now includes disease modifying medications or biologics, anti-tumour necrosis factor drugs and corticosteroids are proving to be more effective in the management of this immune disease when taken in combination as opposed to mono-therapy [111]. Despite advances in conservative management of rheumatoid arthritis, joint replacement remains a viable treatment option for those with significant joint pain and stiffness although joint destruction, osteoporosis and severe deformity make surgery technically challenging in this group [110]. Nevertheless rheumatoid patients demonstrate substantial improvements in pain, function and quality of life following TJR [112-115]. Although functional outcomes after surgery are inferior, rheumatoid patients report equivalent pain relief from TJR when compared to OA patients[110].

Aside from rheumatoid arthritis total hip replacement in young adults is generally reserved for those with developmental dysplasia (DDH) and slipped upper femoral epiphysis (SUFE). Anatomical abnormalities including acetabular or femoral deformity, leg length discrepancy and the age at which joint replacement is performed can contribute to higher failure rates observed in these patient compared to patients with osteoarthritis [73, 116, 117]. Setting aside the higher likelihood of revision surgery for patients who have hip replacement for DDH or SUFE in the longer term, post-operative outcome scores for these patients are comparable to patients with OA in the short term. No significant differences in Oxford

hips scores at 6 months have been observed in THR patients with either DDH or SUFE when compared OA patients [118, 119]. Excellent functional outcomes have also been reported in patients with DDH under the age of 30 years with an average Harris Hips score of 90.6 at 9 [3-14] years follow-up [117]. Similar Harris Hip Scores (average 93) have been reported in THR for SUFE at 15 years follow-up [120].

3.2.2. Co-morbidities

Individual comorbidities such as diabetes, cardiovascular and respiratory disease are commonly reported in patients undergoing TJR and many patients carry multiple comorbidities [7, 8, 39, 40, 121]. When reported as a composite, self-reported functional outcomes are poorer in patients with multiple comorbidities for both hip and knee replacement. Lingard et al (2004) reported an association with higher comorbidity and poorer SF-36 physical function scores at 1 year after knee replacement [122] and Gandhi et al (2010) reported similar findings at 3 [1–8] years [123]. In total hip replacement Young et al (2008) reported better functional outcomes following hip replacement in those had no comorbid disease [124].

Deyo-Charlson comorbidity index, a validated clinical comorbidity index [125] is an independent predictor of functional outcome in TJR. Singh & Lewallen (2010) studied activity limitation and dependence on walking aids in both hip and knee replacement patients 2 and 5 years after surgery. Deyo-Charlson comorbidity index independently predicted a greater reliance on walking aids at 2 and 5 years after both total hip and knee replacement and higher odds of moderate to severe activity limitation at 2 years after knee replacement [64, 126]. We have reported similar findings in patients undergoing TKR using an Age-Adjusted Charlson Comorbidity Index [127], demonstrating higher odds of reporting poor function at 2 years in those with a higher comorbidity index [40].

Very little is known about the effect of individual comorbidities on patient reported outcomes in TJR. A recent study of 677 consecutive primary knee and 547 consecutive primary hip replacements, demonstrated an association between metabolic syndrome risk factor and 1 year WOMAC scores [128]. Metabolic syndrome risk factors were self-reported and defined as body mass index >30kg/m^2, hypercholesterolemia, hypertension and diabetes. While increasing number of metabolic risk factors were associated with higher (worse) WOMAC scores, individual risk factors were found to better predict outcome. Obesity predicted higher WOMAC scores in both total hip and total knee replacement and hypertension also predicted higher WOMAC scores in total hip replacement only.

3.2.3. Obesity

Obesity features prominently in the patho-physiological mechanisms underpinning OA especially end-stage OA requiring TJR [129]. Obesity affects 1 in 4 members of the community, but our data indicate a 2-3 fold over-representation of obesity in patients presenting for TJR (Figure 3). The economic impact of obesity-related OA in Australia was estimated to be $221.3 million in 2005 [130]. While the real costs of treating obese patients with TJR remain unknown, we have demonstrated higher episode of care costs for TKR in the first 12 months

(+$1,821[95% CI $245, $3,398]; p=0.024) in a comparative cohort of 520 patients [131]. The cost of THR is also estimated to be higher for obese ($523) and morbidly obese patients, ($1,432) patients [132]. In addition to the increasing overrepresentation of obese patients presenting for TJR (Figure 3) our data demonstrates that the severity of obesity is also increasing over time (Figure 4), as such developing strategies to reduce the burden of obesity-related joint disease should be an imperative [133].

Weight loss in obese patients awaiting TJR is a problem because the symptoms of disabling arthritis may limit an individual's ability to exercise. Patients often identify this as the reason for the inability to lose weight, and believe that joint replacement would be critical for weight loss. However, numerous studies have confirmed that undergoing total joint replacement does not result in clinically significant weight loss and as many as one-third of patients gain weight at 12 months after surgery [8, 39, 134-140]. It has also been demonstrated that weight gain continues to increase over time after joint replacement [141].

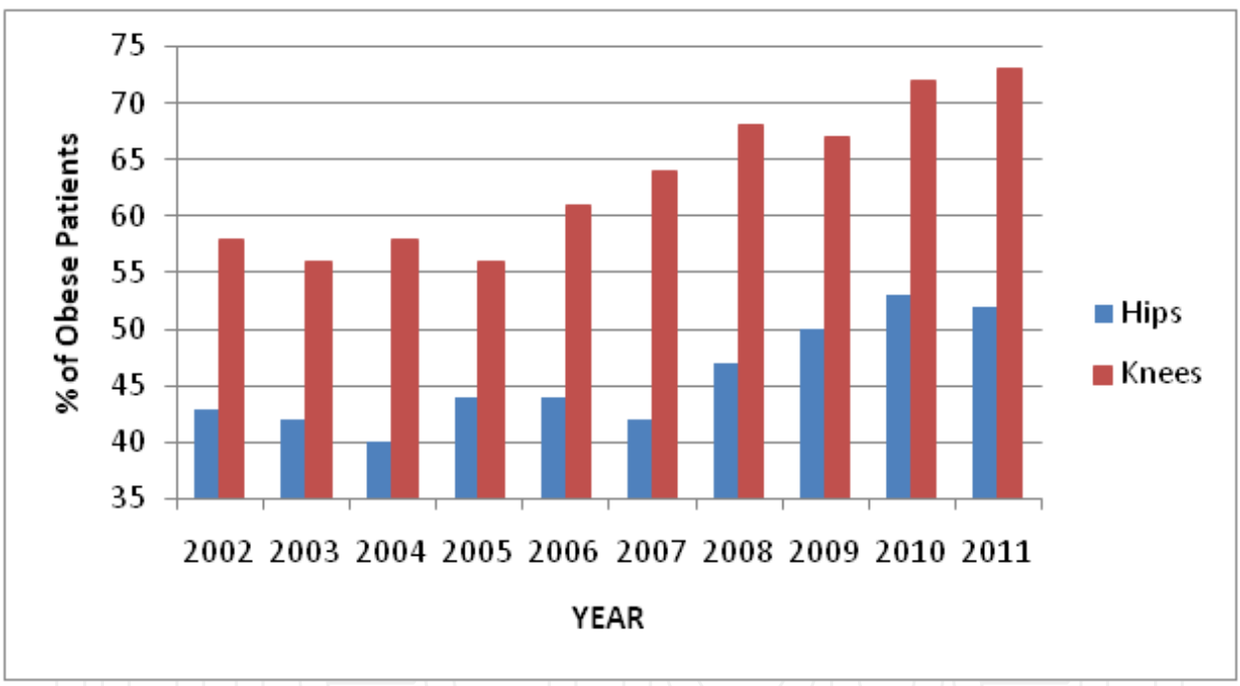

Figure 3. Obesity rates in OA patients at presentation for primary elective TJR (SVHM JRR)

Data from our registry demonstrates that both the number of obese patients presenting for joint replacement (Figure 3) and the average BMI of patients is increasing over time, particularly in the past 5 years. Of note there are higher rates of obesity and a more rapid rise in average BMI demonstrated amongst recipients of knee replacement compared to recipients of hip replacement, with females undergoing knee replacement recording the highest BMI average.

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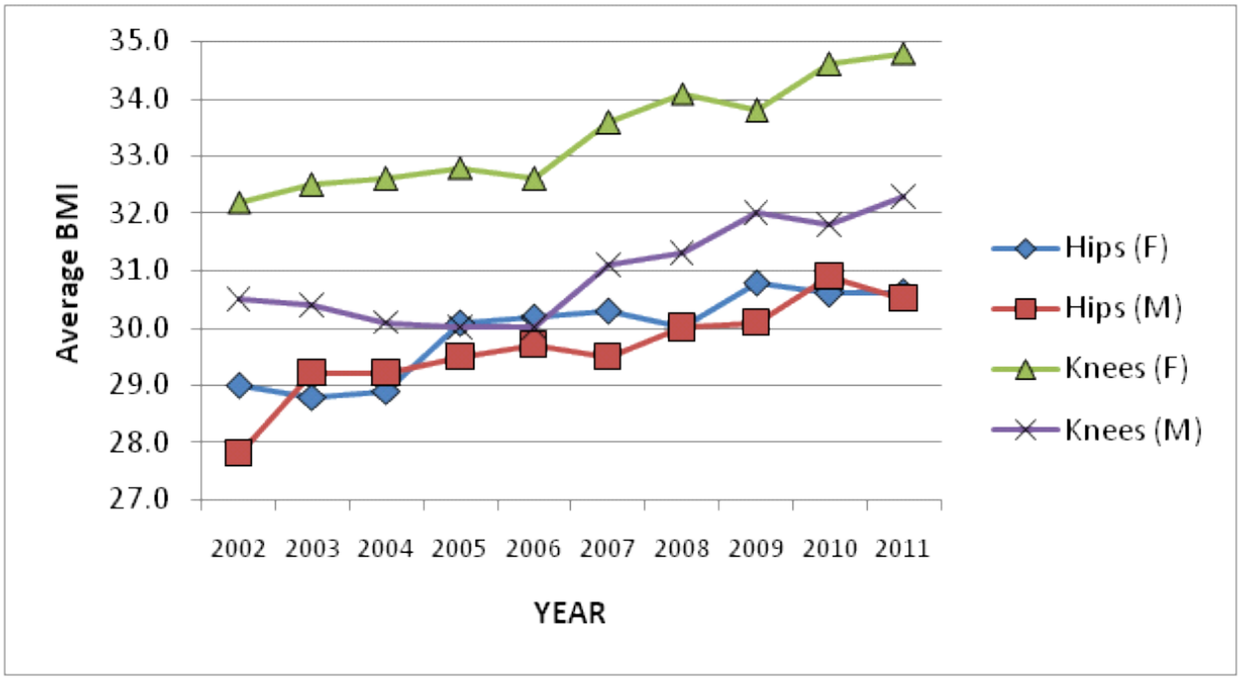

Figure 4. Mean BMI of OA patients at presentation for primary elective TJR (SVHM JRR)

Although widely reported there remains disagreement in the literature as to the impact of obesity on patient reported outcomes following TJR. Numerous reviews confirm that obese patients report substantial improvements in pain and function following joint replacement surgery [142-145]. However when limited to level 1 studies [146], the evidence does suggests that obese and particularly morbidly obese patients may not achieve the same level of functional improvement after TJR when compared to non-obese patients in both the short and longer term.

3.2.3.1. Outcomes for primary THR

Obesity and advancing BMI have been shown to have a negative impact on pain and more so function after primary elective total hip replacement in both the short and longer term. Functional gains and activity levels after THR remain poorer for obese when compared to non-obese individuals. Obese groups also report worse pain and higher usage of pain medication after THR. A review of level 1 large cohort studies is presented.

Moran et al (2005) compared functional and QoL outcomes using the Harris Hip Score (HHS) and Short-Form-36 (SF-36) in 800 patients undergoing total hip replacement, pre surgery (100% follow-up) and at 6 (97% follow-up) and 18 months (86% follow-up) [147]. BMI was found to be a significant predictor of poorer function at both 6 and 18 months. The authors concluded that the difference between obese and non-obese scores were small and therefore not clinically significant, however this was based on comparing post-operative scores only and the change in scores between groups was not provided.

Gandhi et al (2010) investigated the influence of self-reported metabolic syndrome risk factors defined as obesity, hypertension, hypercholesterolemia and diabetes on patient function in a consecutive cohort of 547 primary hip replacements [128]. As measured using the WOMAC obesity was associated with higher odds (2.4; 95% CI 1.4 – 4.2) of less functional improvement at 12 months after surgery.

Dowsey et al (2010) compared pain, function (HHS) and quality of life (SF-12) in a consecutive cohort of 471 primary THR's with 98.5% follow-up. Function and physical health scores were worse at baseline and 12 months after surgery for obese and morbidly obese patients. Baseline mental health scores were also worse in obese and morbidly obese patients, however were comparable at 12 months with obese patients demonstrating a significantly greater improvement in scores compared to non-obese patients [39].

Lubbeke et.al (2007) reported significantly poorer functional outcomes in obese patients (n=182), who underwent primary THR compared to non-obese patients (n=635), at 5 years follow-up, as measured using the Harris Hip Score [148]. Eighty-one percent of hips in the non obese group and 70% in the obese group had a good to excellent results according to their HHS. When broken down by gender it was obese females who demonstrated significantly poorer outcomes compared to non-obese females with very little differences in outcomes demonstrated between obese and non obese males.

Singh & Lewallen (2010) measured activity limitation and dependence on walking aids in 5,707 patients at 2 years and 3,289 patients at 5 years after primary total hip replacement [64]. Predictors of moderate to severe activity limitation (defined as limitation in 3 or more activities), included BMI > 30kg/m^2 at both time intervals. Obese (BMI > 30kg/m^2) patients had higher odds of complete dependence on a walking aid at 2 years and severely obese (BMI >35kg/m^2) had a higher odds of complete dependence on a waking aid at 5 years.

Singh & Lewallen (2010) also examined pain as measured by the Mayo Hip Score and the use of pain medications at 2 and 5 years following primary total hip replacement in the same cohort of patients [46]. The odds of reporting ongoing moderate to severe pain at 2 years after surgery were higher in those with a BMI 35-39.9kg/m^2 (OR 1.8; 95% CI 1.2 – 2.4) and BMI > 40kg/m^2 (1.7; 95% CI 1.0 – 2.9) compared to those with a BMI < 25kg/m^2. At 5 years the odds of reporting ongoing moderate to severe pain was higher for all weight groups compared to the baseline group; BMI 25 – 29.9kg/m^2, (OR 1.5; 95% CI 1.1 – 2.1); BMI 30-34.9kg/m^2, (OR 1.8; 95% CI 1.2 – 2.6); BMI 35-39.9kg/m^2, (OR 1.9; 95% CI 1.2 – 3.1); and BMI > 40kg/m^2, (OR 3.1 95% CI 1.7 – 5.7). BMI 35-39kg/m^2 was also a predictor of non-steroidal anti-inflammatory use at 2 years and BMI 30-34.9kg/m^2 predicted use of opioid medication at 5 years after THR.

3.2.3.2. Outcomes for primary TKR

Obesity and advancing BMI have been shown to have a negative impact on function after primary elective total knee replacement in both the short and longer term. Functional gains and activity levels after TKR are poorer for obese when compared to non-obese individuals.

Obese groups however do report comparable pain outcomes compared to non-obese patients after surgery. A review of level 1 large cohort studies is presented.

Gandhi et al (2010) investigated the influence of self-reported metabolic syndrome risk factors defined as obesity, hypertension, hypercholesterolemia and diabetes on patient function in a consecutive cohort of 677 primary knee replacements with 83% follow-up [128]. As measured using the WOMAC, obesity (BMI > 30kg/m^2) was associated with higher odds (3.6; 95% CI 0.02 – 7.2) of less functional improvement at 12 months after surgery.

Rajgopal et al (2008) compared functional outcomes between morbidly obese (BMI > 40kg/m^2) and non-morbidly obese (BMI < 40kg/m^2) patients 12 months after total knee replacement in a series of 550 patients; of which 69 patients were classified as morbidly obese [149]. BMI ≥ 40 predicted 12 month WOMAC scores (coefficient −5.188, 95% CI −9.771 −0.606), however no differences in the change in WOMAC or SF-12 scores were demonstrated when comparing morbidly obese to non-morbidly obese patients.

We also measured improvement in pain, function and quality of life from baseline to 12 months following elective primary knee replacement in consecutive series of 529 patients with 98% follow-up [8]. The change in IKSS function scores were 10 points lower for both obese (BMI > 30kg/m^2) and morbidly obese (BMI > 40kg/m2) patients compared to non-obese (BMI <30kg/m^2), (p=0.002). No significant difference in IKSS pain scores was noted between the 3 groups at baseline or 12 months and there was no significant difference in SF-12 scores between the 3 groups at baseline or 12 months.

Singh et al (2010) measured activity limitation in 4,701 patients at 2 years and 2,395 patients at 5 years after primary knee replacement [126]. Predictors of moderate to severe activity limitation (defined as limitation in 3 or more activities), included all BMI groups > 30 compared to BMI < 25kg/m^2 at 2 years after surgery; BMI 30-34.9kg/m^2, (OR 1.5; 95% CI 1.0 – 2.0); BMI 35-39.9kg/m^2, (OR 1.8; 95% CI 1.3 – 2.7); and BMI > 40kg/m^2, (OR 3.0 95% CI 2.0 – 4.5). Higher BMI also predicted moderate to severe activity limitation at 5 years; BMI 35-39.9kg/m^2, (OR 2.1; 95% CI 1.4 – 3.3); and BMI > 40kg/m^2, (OR 3.9 95% CI, 2.3 – 6.5).

Sing et al (2011) also examined whether BMI was associated with pain as measured using the IKSS after primary knee replacement at 2 and 5 years after surgery [150]. Patients were classified into BMI groups as above for comparison. In contrast to their study on activity limitation, there was no association demonstrated between BMI and ongoing moderate to severe pain at either 2 or 5 years after TKR.

Our findings mirror that of Singh et al (2010 & 2011). We reported pain and function outcomes in a cohort of 478 consecutive primary elective total knee replacements at 1 and 2 years post surgery with 99% and 94% follow-up respectively [40]. Each incremental increase in BMI significantly increased the odds of poor function as measured using the IKSS at 12 months (OR 1.07, 95% CI 1.03 – 1.12) and at 2 years (OR 1.09, 95% CI 1.05 – 1.14). However we found no association between advancing BMI and ongoing moderate to severe pain at either time point.

3.2.4. Psychosocial state

Psychological distress leading to patient dissatisfaction after TJR is an important cause for TJR failure. Pre-operative psychological distress is associated with excessive analgesic intake and higher rates of hospital readmission and long term mortality [151]. Our research has also drawn a link between poorer pre-operative mental health and weight gain after TJR [39]. Published results from the SVHM TJR cohort and that of others have i) identified a high rate (30-60%) of self-reported psychological distress in TJR patients [152-154] and ii) determined that pre-operative psychological distress is an independent risk factor for poorer post-operative outcomes after surgery [8, 65]. A number of recent comprehensive literature reviews have found pre-operative psychological distress to be an independent predictor of pain and function after TKR in a majority of published studies [155, 156].

Psychological co-morbidities and traits reported in TJR patients include; anxiety, depression, neuroticism, catastrophising and poor self-esteem. These individual traits and poorer pre-operative mental health scores in general are associated with poorer function and/or greater pain after TJR in the short and longer term.

In general pre-operative psychological distress is associated with poorer pain and worst function 1 year after total joint replacement. We have reported an association between lower SF-12 MCS scores and risk for ongoing moderate to severe pain and poor function at 12 months and 2 years following TKR. Lingard et al (2004) also reported an association between lower SF-36 MCS scores and worse WOMAC pains scores at 1 and 2 years after TKR [122]. An analysis of pre-operative and one-year post-operative data in 6,158 patients from the Swedish Hip Arthroplasty Register, also demonstrated that anxiety/depression measured on the EQ-5D [157] was a strong predictor of pain after THR [158].

Anxiety is a psychological and physiological state characterized by somatic, emotional, cognitive, and behavioural components [159]. Anxiety can occur as a result of transient negative stimuli such as in a threatening situation and this is referred to as state anxiety. In contrast trait anxiety is referred to as a general tendency to experience anxiety [160]. In patients undergoing total hip replacement trait anxiety has shown to correlate with impaired health related quality of life 3 to 6 months after surgery [161, 162]. In contrast state anxiety had no effect on outcome suggesting pre-existing anxiety disorder rather than anxiety induced by fear of surgery predicts poorer outcomes form joint replacement.

Pre-existing depression has been shown to predict greater pain and poorer function in patients undergoing total knee replacement at 1 year and it has also been demonstrated that worse outcomes persist at 5 years [20, 163]. However this finding is not consistent, with some studies suggesting that there is no association between depression measured prior to surgery and pain and function outcomes following TJR. Of note Riddles et al (2010) measured the association between a range of psychological comorbidities including depression, anxiety and panic disorders, self efficacy and fear of movement and found that only pain catastrophising predicted poorer pain outcomes after total knee replacement [164],

Pain catastrophising has been described as a tendency to magnify or exaggerate the threat value or seriousness of pain sensations [165]. Pre-operative pain catastrophising is a predic-

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tor of worse post-surgical pain following TKR in the short (6 weeks and 6 months) term, but does not correlate with function [164, 166]. The correlation between catastrophising and poorer post-operative pain has also been shown to persist at 24 months following TKR [167]. To date the link between pain catastrophising and post operative pain after TJR seems to be unique to knee replacement, with no evidence of pain catastrophising in total hip replacement patients.

Neuroticism is a personality trait described as an enduring tendency to experience negative emotional states [168]. There is a dearth of literature examining the association between neuroticism and TJR, however one study on total hip replacement did report that neuroticism was amongst a number of psychological traits that predicted poorer quality of life outcomes at 6 months after surgery [162].

3.3. Baseline symptom severity

Total joint replacement is most often performed for the management of "end-stage' arthritis characterised by retractable pain, loss of function and deformity [30]. According to the NIH statements for both hip and knee replacement, candidates for elective TJR should have radiographic evidence of joint damage, moderate-to-severe persistent pain that is not adequately relieved by an extended course of nonsurgical management, and clinically significant functional limitation resulting in diminished quality of life [32, 33]. However there is discordance between radiographic changes and patient reported symptom severity at presentation for surgery, with some people receiving joint replacement reporting severe preoperative symptoms of pain and disability and mild radiographic changes [80, 83].

3.3.1. Baseline clinical symptoms

Baseline symptom severity is a predictor of outcome for both total hip and knee replacement. Several studies have concluded that those with worse pain and poor function at the time of surgery also report comparatively worse pain and function after surgery, suggesting that surgery could be prioritized based on clinical symptom severity [169].

In a multicentre study involving more than 200 hip and knee replacements Fortin et al (1999] reported that lower preoperative physical function scores predicted worse WOMAC pain and function at 6 months compared to those with higher baseline function scores [170]. Fortin et al (2002) continued to follow the cohort up at 2 years post surgery and confirmed that their initial findings at 6 months persisted [169], concluding that undergoing surgery earlier in the course of functional decline may be associated with better outcome.

In a larger study involving 860 recipients of primary TKR from 3 different countries, Lingard et al (2004) reported that worse baseline WOMAC pain scores were a strong determinant of worse pain at 1 and 2 years after surgery. Pre-operative WOMAC function was also the strongest predictor of worse function at both 1 and 2 years after surgery [122].

3.3.2. Baseline radiographic characteristics

In contrast to clinical symptoms emerging literature suggests that those with the worst radiographic OA symptoms report better outcomes after total joint replacement.

We recently evaluated the association between pre-operative radiographic changes and outcomes after primary total knee replacement for osteoarthritis. We reported that pain relief was unsatisfactory in about 30% and functional improvement suboptimal in about 50% of patients [40]. In this study radiographic OA severity was measured using a modified version of the Kellgren-Lawrence Classification system [80]. We noted that radiographic OA severity was an independent predictor of pain and function at 12 months following TKR. Patients with evidence of mild radiographic OA changes were 5 times more likely (OR 5.39, 95% CI 1.23 – 15.69) to report moderate to severe pain at 12 months post TKR than those with severe radiographic changes.

Merle-Vincent et al (2011) examined predictors of satisfaction in 299 patients undergoing primary TKR and reported an association between radiographic OA severity and outcome 2 years after surgery [171]. Those with severe pre-operative joint space narrowing were nearly 4 times more likely to report satisfaction with surgery at 2 years compared to those with mild to moderate narrowing, (OR 3.9, 95% CI 1.1 – 14.3).

Valdes et al (2012) examined predictors of chronic pain using the WOMAC in 860 patients who had undergone TKR and 928 patients who had undergone THR with an average of 3.2 years follow-up [172]. They reported an OR 1.56 (95% CI 1.04 – 2.36) of ongoing pain in TKR patients with a Kellgren-Lawrence grade <3 and in THR patients with minimal joint space narrowing (>2mm width).

Cushnaghan et al (2007) reported on long term (approximately 8 years) functional outcomes following THR in a series of 282 patients matched with 295 community controls [173]. Radiographic OA severity defined as Croft grade 5 OA[174] was a predictor of greater functional improvement in cases as measured using the SF-36 physical function scores (19.4, 95% CI 7.7 – 31.2), when compared to cases with Croft grade < 3.

These findings suggest an inverse relationship between baseline radiographic OA and outcome up to 8 years following total joint replacement. More severe radiographic changes predict worse pain and to a lesser degree suboptimal function after surgery, providing important implications for timing of joint replacement.

4. Conclusion

Total joint replacement is the most effective and cost effective treatment for end-stage osteoarthritis. Most patients derive substantial benefits from joint replacement surgery; however those that don't are subject to chronic pain and disability and a higher risk for revision surgery. The causes of poor outcomes of surgery are multifactorial but almost certainly patient selection is a key determinant. While those who present with the "worst" symptoms might

be those who should be prioritized for TJR, the literature reports a mismatch between patient reported symptom severity and response to surgery. Although many risk factors are recognised, their individual or combined contributions to the *absolute risk* of suboptimal outcome after TJR remains poorly quantified. Importantly a majority of baseline patient characteristics (obesity, mental health, co-morbidities, radiographic OA severity, baseline pain and function) associated with sub-optimal outcome following TJR are those that could be "modified" with appropriate intervention. However baseline risk factors tend to remain unidentified or identified and managed at the point of surgery, which is too late. Hence there remains a need for exploring early interventions where there is opportunity to alter patient outcomes.

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