"Total Knee Arthroplasty in the Context of Severe and Morbid Obesity in Adults"

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Abstract: Medical treatment for knee osteoarthritis proves insufficient in a considerable number of patients, who thus require surgical intervention, with arthroplasty being one of the most common procedures. The rate of knee replacement is consequently higher in the obese population. Obese patients who undergo knee arthroplasty face a larger number of associated comorbidities than do non-obese individuals, and this greater comorbidity can lead to more postoperative complications and worse outcomes. Given that obesity defined according to BMI would cover a large proportion of the population (a quarter of adults have a BMI > 30 kg/m^2 in some western societies) attention has focused on which sub-groups might present the greatest problems. It appears that morbidly obese patients (BMI > 40 kg/m^2) are most at risk of complications. Some authors suggest the need to study more precise methods for component alignment in these patients. The use of an intramedullary guide made surgical intervention easier and was associated with a significantly shorter tourniquet time. Although the studies refer greater surgical difficulties on the basis of their BMI, the difficulty of surgery will ultimately depend on the morphology of the knee. The factors associated with a worse postoperative WOMAC score in severely and morbidly obese patients were the number of comorbidities, infrapatellar anthropometric index below percentile 75, greater intraoperative difficulty and the number of postoperative complications. When starting from a comparable preoperative status, severely and morbidly obese patients show a similar improvement than other patients.

Keywords: Morbid obesity, Obesity, Total knee arthroplasty.

1. DEFINITION OF OBESITY

In the past, weight was the sole measure used for classifying patients as obese [1]. However, the World Health Organization (WHO) has established a classification, accepted by all scientific groups, based on the relationship between weight and height [2] (Table **1**). Body mass index (BMI) is given by the individual's weight divided by the square of their height, and on this basis the WHO classification includes four categories. Several recent papers establish groups for a BMI over 40 kg/m^2, although these are not officially recognized by the WHO. The term 'super morbid obese' is used for a BMI up to 50 kg/m^2, and 'super mega morbid obese' for a BMI over 60 kg/m^2.

Table 1. Classification of Obesity According to the World Health Organization (WHO)

BMI	Category
25-29,99 kg/m^2	Overweight. Class 0
30-34,99 kg/m^2	Obesity. Class I
35-39.99 kg/m^2	Severe obesity Class II
>40 kg/m^2	Morbid obesity. Class III

2. INCIDENCE OF OBESITY IN THE POPULATION

Data published in 2003 by the International Association for the Study of Obesity (IASO) showed that in Spain 13.9% of adult men and 15.1% of women were obese (BMI > 30kg/m^2) [3]. In Catalonia, the ENCAT study published in 2007 used BMI to compare the incidence of overweight and obesity in the population [4]. The data showed that the proportion of obese men had increased from 9.9% in 1992-3 to 16.6% in 2002-03, whereas the rate for women remained stable over the same period of time (15.0% in 1992-3 and 15.2% in 2002-03). Data for other European countries show that in England, in 2007, 23.6% of men and 24.4% of women were obese, whereas the corresponding figures for France were 16.1% and 17.6% respectively (data for 2006), and for Germany 20.5% and 21% (data from 2003) [3]. In Canada the proportion of the population who are obese has risen from 14% in the 1980s to 23% in 2007 (men 22.9%; women 23.2%). Data from 2003-4 for the US show that 31.1% of adult men and 33.2% of women were obese (BMI > 30 kg/m^2) [3].

3. RELATIONSHIP BETWEEN OBESITY AND KNEE OSTEOARTHRITIS

Several reports have demonstrated the relationship between obesity and the development of degenerative disease in the knee [5-7].

3.1. Risk of Osteoarthritis in Obese Patients

Obese patients have an estimated risk of between 9-13% of developing osteoarthritis (OA) of the knee for each additional kilo of body mass. With each 5 kg of weight gain, their risk of developing osteoarthritis increases by 35% [6].

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According to the US National Health and Nutrition Examination Survey, adults with a BMI over 30 kg/m^2 are four times more likely to present radiographic signs of knee osteoarthritis than adults with BMI below this figure [7].

Signs of knee osteoarthritis in radiographic studies, in association with clinical symptoms of knee osteoarthritis in obese elderly men and women appeared a mean of 37 years earlier than in their non-obese. The association of overweight and knee osteoarthritis is stronger in women than in men. Fifty per cent of middle-aged obese healthy women with unilateral radiographically demonstrated knee OA developed osteoarthritis in the contralateral knee within two years, a 5-fold higher incidence than non-obese women in the same age range [5, 7].

Obesity is also related to the progression of osteoarthritis. More severe forms of radiological osteoarthritis are found in patients with already established osteoarthritis who gain weight [8].

It has not been clearly established how excess weight causes the degeneration of joint cartilage. As in cardiovascular disease and diabetes, the risk of developing knee osteoarthritis increases with BMI, but there does not seem to be a relationship with the patient's morphotype – as there is between central or truncal obesity and the diseases mentioned [9, 10].

3.2. Theories of the Relationship Between Obesity and Osteoarthritis

The degeneration may occur through various mechanisms. Biomechanical, imaging, histological and analytical studies have shown that cartilage volume loss in obese patients is greater and occurs more quickly than in the non-obese population, and that the higher the degree of obesity, the faster and more profound the deterioration [11].

3.2.1. Biomechanics and Knee Osteoarthritis

From the biomechanical perspective, obesity causes a repeated application of axial forces on the surface of the joint, damaging the articular cartilage and leading to subchondral bone sclerosis. Magnetic resonance imaging (MRI) studies show that the main effects of the increase in BMI are the appearance of defects in the joint cartilage and an increase in the size of the tibia due to the formation of osteophytes [12].

The presence of glycosaminoglycans (GAG) in joint cartilage increases when there are compressive forces, in response to the damage caused. When the GAG content is studied as a measure of chondrocyte activity and of the progress of osteoarthritis in the knee, there is a significant correlation between increased glycosaminoglycan levels and patients' BMI [13].

In the weight-bearing joints, such as the knee, the axial load is the cause of deterioration, especially in knees presenting major varus malalignment, in which the excess load on the internal compartment alters chondrocyte biosynthesis. In joints that do not support axial load, for example the hands, this mechanism is not involved [14].

MR imaging studies have shown that the increase in fat mass reduces volume and increases cartilage defects, while an increase in fat-free mass (total body weight without fat or muscle mass) increases knee cartilage volume [14]. This suggests that there may be other reasons for the development of knee osteoarthritis in addition to biomechanical causes.

Other authors suggest that excess fat may lead to an irregular growth of joint cartilage and may inhibit cartilage repair mechanisms [15-17].

3.2.2. Hormonal Influence on the Development of Knee Osteoarthritis

Several studies have linked the obesity gene (ob) and the hormone it produces, leptin, with the deterioration of joint cartilage [15- 20]. Both experimental and clinical trials have shown significant levels of this hormone in chondrocytes of obese patients developing osteoarthritis, whereas it is virtually nonexistent in chondrocytes from patients who did not develop OA. Leptin is synthesized in osteoblasts and chondrocytes as well as in adipocytes [15]. Receptors for this hormone have been found in joint cartilage. Systemic variations in leptin levels regulate the proliferation of the chondrocytes and the anabolic function, producing osteophyte formation during osteoarthritis [17].

Studies by various authors have found that leptin levels in joint cartilage increase in line with the patient's BMI [16, 19] and significant levels of this hormone have been found in the osteophytes and the chondrocytes of the joint cartilage of people with OA, whereas in healthy subjects chondrocytes that produce leptin are few [15].

Further evidence of the role of leptin in the development of osteoarthritis is the prevalence of knee osteoarthritis in women [17]. As women have more body fat, the production of this hormone is higher in women than in men and its level in blood is also higher. This is also the case in pre-pubertal females, so high levels of leptin in the blood may influence the development of cartilage and predispose to degenerative changes in adulthood. Weight reduction in obese patients suffering from osteoarthritis decreases in blood leptin levels, correlating with improved symptoms [16].

A relationship has been found between reduction in knee cartilage volume with blood leptin levels in obese female adults. In focal defects of the cartilage this relationship was not found, indicating that these defects may be related more to non-hormonal factors [18].

Leptin contributes to the abnormal functioning of osteoblasts in osteoarthritic knees, causing the proliferation of various cytokines that damage the cartilage [21].

4. TREATMENT OF KNEE OSTEOARTHRITIS IN THE OBESE PATIENT

4.1. Weight Loss

According to the Framingham study [5] women who reduce their BMI by two units reduce the likelihood of developing OA by over 50%. Exercise combined with a dietary programme designed to produce weight loss can improve the functionality and symptomatology of obese patients with gonarthrosis [5-7, 22-25]. Messier [23] found that a 5% reduction in a patient's weight over an eighteen-month period led to an 18% improvement in the patient's functionality. When weight loss was linked to an exercise programme, function improved by 24% and was

accompanied by a significant improvement in mobility. In terms of functional outcomes, measured by means of the Western Ontario and McMasters Universities Osteoarthritis Index (WOMAC), research has shown that in overweight women with knee pain due to osteoarthritis a 7 kg weight reduction over a period of six months led to a significant change in WOMAC ratings for pain (46% reduction) and function (38% improvement) [26]. A population-based case control study carried out in England by Coggon [27] concluded that if all overweight or obese people reduced their weight by 5 kg or until their BMI was within the normal recommended range, 24% of surgical interventions for knee osteoarthritis might be avoided.

4.2. Total Knee Arthroplasty

Medical treatment for knee osteoarthritis proves insufficient in a considerable number of patients. Among surgical interventions, arthroplasty is one of the most common procedures. The rate of knee replacement is higher in the obese population. As noted above, the proportion of obese individuals in Canada has risen from 14% twenty-five years ago to 23% in 2007 [28]. Concomitantly, the number of knee and hip replacements performed rose by 87% over the ten years from 1993/4 to 2003/2004. If normal weight patients are used as a baseline with respect to the need for intervention in the form of arthroplasty (RR 1.00), it can be seen that as BMI increases so does the likelihood of the need for joint replacement. In patients with class III (morbid) obesity the risk is more than 30 times higher. In the UK a study known as the 'Million Women Study' prospectively followed a cohort of 1.3 million women aged 50–64 years recruited between 1996 and 2001, in order to ascertain the risk of requiring a hip or knee replacement on the basis of BMI [29]. The authors report a RR of 69% in middle-aged women with a BMI $\geq$ 25 kg/m^2. Furthermore, analysis of the relative risk of requiring surgical intervention according to the different categories of obesity in these women showed that the risk rose exponentially with increasing BMI. Another study in the UK examined the age at which patients with gonarthrosis undergo surgery in relation to their BMI at the time of the operation [30], and found a statistically significant relationship between BMI and age at the time of surgery ($p<0.001$): morbidly obese patients underwent surgery 13 years earlier than normal weight individuals. In a study of the BMI of patients undergoing hip and knee replacement surgery over the period 1990-2005 in a specialist clinic in North Carolina (US), Fehring [31] found that 10.5% of surgical patients in 1990 were morbidly obese, 8.3% in 1995, 10.3% in 2000 and 17.1% in 2005.

5. THE OBESE PATIENT AND TOTAL KNEE ARTHROPLASTY

Given the anatomical difficulties related to the airway, pharmacokinetic changes, and the risk of cardiorespiratory complications, regional anaesthesia has certain advantages over general anaesthesia in these patients [32]. It requires only minimal manipulation of the airway, avoids the need for anaesthetic drugs that induce cardiopulmonary depression, reduces postoperative nausea and vomiting, and enables better control of postoperative pain. This means that lower doses of postoperative opiates are required, something which is of vital importance in these patients, who are at greater risk of postoperative respiratory complications. However, peripheral nerve blocking techniques are more difficult to perform than in the general population [32], and the rate of failed blocks increases in line with BMI. In the event of a failed nerve block, general anaesthesia is often required, with the risks that this implies. Performing neuroaxial blocks also presents certain technical challenges, since it is more difficult to locate anatomical reference points and more puncture attempts are required to achieve the block. Compared to the general population, obese patients require lower doses of local anaesthesia to achieve the same degree of epidural or intradural block, and they are more likely to present cephalic migration of the local anaesthetic. In the case of intradural anaesthesia this can be explained by the fact that these patients have a smaller volume of cerebrospinal fluid. Given the anatomical difficulties associated with obese patients the use of ultrasound to guide the techniques of local or regional anaesthesia is recommended, since this increases the rate of successful peripheral blocks.

Obese patients present a reduced immune response. This is because obesity is associated with insulin resistance and hyperglycaemia, which reduce leukocyte function. This situation may even arise in obese patients who are not diagnosed with diabetes. At all events, their pharmacokinetic status is altered due to changes in renal clearance, in liver metabolism and in the distribution volume. Obesity also involves an increased adipose tissue mass, which affects any medication with lipophilic properties. Likewise, hydrophilic drugs may be affected by the increase in organic mass, in free fat mass and in blood volume that characterize obesity. These changes affect both intravenous anaesthesia and antibiotics. Indeed, the usual dose of prophylactic antibiotics may be insufficient in these patients, who by their very nature already present a higher incidence of postoperative infection. It is therefore advisable to tailor the dosage to the individual patient and to monitor the antibiotic dose in the event of infections that require prolonged treatment with intravenous antibiotics [33].

5.1. Associated Comorbidities in the Obese Patient

Obese patients who undergo knee arthroplasty face a larger number of associated comorbidities than non-obese individuals, and this greater comorbidity can lead to more postoperative complications and worse outcomes. In one study of patients undergoing knee arthroplasty Miric [34] found a significantly higher rate of associated comorbidities among obese patients, with a prior medical history ($p<0.0001$), a history of cardiac problems ($p<0.02$) and diabetes mellitus ($p<0.006$) all being more common in obese individuals. A more detailed analysis revealed that the greatest difference was observed among patients in obesity class II (BMI > 35 kg/m^2). In another study of comorbidities, Namba [35] reviewed 1813 hip and knee replacement operations carried out in eleven hospitals in the US, and found that the group of patients with a BMI above 35 kg/m^2 spent longer in hospital and had a higher rate of infections. Although severely and morbidly obese patients had a significantly higher rate of diabetes most of the patients who suffered an infection were not diabetic. In 2010 Nuñez [36] studied a population of morbidly obese patients who had undergone total knee arthroplasty, comparing them with a

between 2001 and 2002, Namba [35] drew attention to the high rate of infection following arthroplasty in patients with a BMI > 35 kg/m^2. In this series 23% of patients (422/1813) had a BMI > 35 kg/m^2, and their risk of infection (odds ratio) was 6.7-fold higher. These figures are in line with the previously mentioned results of Winiarsky [37] in a group of morbidly obese patients. Namba [35] attributed the greater risk of infection to the difficulty of exposing the surgical field, the longer duration of surgery, the poor vascularization of fatty tissue and the reduced immune response found in obese individuals. The rate of diabetes mellitus in the severely and morbidly obese patients in this series was significantly high, although only one of the six cases of infection occurred in a diabetic patient. Even in the absence of diabetes, obesity is associated with insulin resistance and hyperglycaemia, conditions which contribute to poor leukocyte function. The syndrome characterized by truncal obesity, a sedentary lifestyle and insulin resistance is known as 'metabolic syndrome' or 'X syndrome'.

Various studies have examined large series of TKA in the search for risk factors for infection and other complications, and several regression analyses have shown that obesity, specifically a BMI over 40 kg/m^2, is associated with a greater risk of infection. In a retrospective study conducted by Patel [42] in 2007 of the factors that predisposed toward implant infection in 1226 arthroplasties, obesity was the only independent factor associated with the risk of infection. In a 2008 study of 1509 knee replacement operations, Chesney [43] found that diabetes and a BMI > 40 kg/m^2 were associated with higher rates of implant infection. Also in 2008 Pulido [44] carried out a prospective study of 9245 patients who underwent total hip or total knee replacement in order to examine the factors associated with joint infection. The results of the multivariate logistic regression analysis showed that morbid obesity, among other factors, predisposed towards this infection (OR 3.23; p<0.001). In 2009 Bordini [45] studied 9735 knee prostheses implanted in 8892 patients between 2000 and 2005 recorded on a database in the Italian region of Emilia-Romagna. Of the 9735 implants, 186 required early revision, 58 due to sepsis. Regression analyses revealed no relationship between BMI and the presence of complications or early implant failure, nor with the presence of implant infection or the length of hospital stay. The study included 172 morbidly obese patients (BMI > 40 kg/m^2). Also in 2009 Jämsen [46] analysed 2647 consecutive knee arthroplasties performed in Finland and found that prosthetic joint infection was related with complex surgery, associated comorbidity and obesity. In the same year a study by Dowsey [47] of 1214 TKA carried out in Australia found that the factors associated with prosthetic infection were morbid obesity (OR 8.96) and diabetes (OR 6.87). The cases of infection in diabetic patients were associated with obesity. Finally, Malinzak [48], also in 2009, published a retrospective review of 8494 hip and knee arthroplasties and found that a BMI above 50 kg/m^2 increased the risk of suffering a deep infection by an odds ratio of 21.3 (p<0.0001).

5.4. Clinical and Functional Outcomes of Total Knee Arthroplasty in Obese Patients

The literature regarding functional outcomes in obese patients undergoing arthroplasty has produced disparate findings [37, 38, 49-54]. Given that some studies compare obese and non-obese individuals without discriminating between the various BMI categories it is necessary to examine each series individually in order to determine whether the data are actually comparable. Furthermore, the results vary depending on the type of obese population studied and the type of study. Specifically, those series with a greater number of morbidly obese patients report worse clinical and functional outcomes in comparison to non-obese patients. For example, Winiarsky ([37] found significantly worse (p<0.00005) outcomes after TKA in morbidly obese patients compared to the other categories of patients. In two studies published in 2004, Foran [52, 53] compared TKA outcomes in a population of obese and non-obese patients. In the first study [52] the authors analysed 78 TKA performed in obese patients over a seven-year period and found that this group had worse functional outcomes (measured according to the Knee Society score) than non-obese controls. The worst outcomes of all were found in the subgroup of morbidly obese patients. It should be noted that in this series the obese and non-obese patients had a similar preoperative clinical and functional status, with no significant differences in Knee Society objective and functional scores. However, the non-obese patients showed significantly better postoperative objective scores, and there was also a significant difference in the mean change in objective knee score. In the second study [53] the authors conducted a 15-year follow-up of 30 non-cemented knee implants in matched case and control groups with no preoperative differences in functional status. At the end of follow-up the non-obese patients had a better Knee Society objective score (89 *vs.* 81 in obese patients). Stickles [49] in 2001 and Rajgopal [54] in 2007 analysed outcomes in obese patients undergoing total joint arthroplasty according to scores on the WOMAC. Both studies considered not only absolute outcomes but also the postoperative change in score. Stickles [49] found an inverse relationship between BMI and WOMAC scores at one-year follow-up, although there were no significant differences between pre- and postoperative scores; preoperative WOMAC scores were lower with higher BMI, and postoperative outcomes were also worse with higher BMI. These results were corroborated by Rajgopal [54] in a Canadian study that divided patients into morbidly obese (n=69) and non-morbidly obese (n=481). Although the morbidly obese patients had lower postoperative WOMAC scores, their changes in score were comparable to those of the non-morbidly obese patients.

Two studies by Núñez, in 2007 [55] and 2009 [56], analysed the factors associated with worse functional outcomes following total knee arthroplasty. Follow-up over three and seven years showed that WOMAC scores, especially on the pain scale, were worse among severely obese patients (BMI > 35 kg/m^2) than in with non-obese individuals. WOMAC scores were also worse in patients who presented postoperative complications. The factors associated with a worse postoperative WOMAC score in severely and morbidly obese patients were the number of comorbidities, infrapatellar anthropometric index below percentile 75, greater intraoperative difficulty and the number of postoperative complications. Postoperative pain at one year was associated with an infrapatellar anthropometric index below percentile 75, greater surgical difficulty and a

Fig. (6). Use of a slotted-base leg positioner to assist the surgical procedure.

Fig. (7). The knee as it appears when using the slotted-base leg positioner. The device enables different degrees of flexion and extension to be achieved.

Fig. (8). Frontal radiograph of an implant with tibial rod.

(slotted-base leg positioner; see Figs. **6** and **7**). In these patients we also use implant models that ensure minimal constriction – either posterior stabilized implants or, in the event of instability or extreme axial deviation, rotating hinge prostheses. In order to prolong the survival of the tibial implant we use short tibial rods (45-50 mm) which increase the area of contact and reduce the load of the bone under the tibial plate (Fig. **8**); more recently, we have introduced trabecular metal tibial components that provide early anchoring of the tibial implant to the bone (Figs. **9** and **10**).

Fig. (9). The moment of implanting a trabecular metal tibial component.

Fig. (10). Radiograph of a knee implant with a trabecular metal tibial component.

CONFLICT OF INTERESTS

None declared.

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