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The influence of obesity on developing osteoarthritis and the recovery after knee joint replacement – a review

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Abstract

Obesity is a chronic disease accompanied by inflammation. It is becoming more and more prevalent all around the world and so are its consequences. Osteoarthritis (OA) is a degenerative disease of the joints. The range of its risk factors is broad, but the most common is obesity. OA can be treated in a surgical and non-surgical way. The surgical method - knee replacement is the most effective way of treating OA, but unfortunately it does not solve the problem. Obesity takes a part not only in development of OA but is also involved in developing

postoperative complications and impairing the recovery in general. The influence of obesity is determined not only by the weight and increased mechanical forces affecting the organism, but also on a molecular level by the hormonal activity of the substances produced by white adipose tissue. Condition of the patient should be optimised before the surgery in order to minimize the risk of complications and increase the chances for fast and effective recovery. Obese patients after the surgery need proper nutrition and care focused on their needs, which often is a challenge to the healthcare providers. After the surgery those patients cannot be sent back to the condition that made them sick. Reduction of weight is suggested to prevent the development of postoperative complications and OA. Prehabilitation seems to improve the immediate postoperative results. Starting regular training a few weeks after the surgery seems to positively affect the process of recovery.

Material and methods

We searched PubMed and Google Scholar using the words “obesity”, “osteoarthritis”, “knee arthroplasty”, “post-operative surgery” and “healing”.

Keywords: osteoarthritis, knee joint, obesity, healing, recovery

1. Introduction

According to the World Health Organization (WHO) malnutrition is a deficiency, excess or imbalance in an individual's consumption of energy or nutrients. Within the term 3 groups of conditions can be distinguished. The first one is undernutrition and refers to low-weight-for-height (wasting), low height-for-age (stunting) and low weight-for-age (underweight). The second group applies to micronutrient-related malnutrition such as micronutrient deficiency or micronutrient excess. The third one concerns overweight, obesity and non-communicable diseases related to diet, such as stroke, diabetes, certain types of cancer [1].

Relationship between a person's height and weight can be described using Body Mass Index (BMI), which is defined as an individual's weight in kilograms divided by the square of their height in meters. The result of that equation can be assigned to one of three categories. For

adults the results between 18.5 kg/m2 and 24.9 kg/m2 are classified by WHO as normal weight-for-height, while results lower and higher than that are recognized as underweight and overweight respectively. Results over 30.0 kg/m2 are classified as obesity [2].

Full recovery is a crucial element of every successful surgery. According to many research papers, the sooner the patient starts walking, eating and drinking on his own, the better [3]. There are many factors affecting the recovery and the healing itself, and malnutrition is among them [4]. What makes this particular factor important is its modifiability giving some possibility of influencing the process of wound healing and hence the recovery.

The purpose of this paper is to describe the impact of obesity on the joints and on the recovery after surgery, especially after total knee joint replacement.

2. Relationship between obesity and knee osteoarthritis

Osteoarthritis (OA) is a chronic condition of joints leading to their destruction. First, the articular cartilage is gradually damaged, then the subchondral bone and surrounding structures are destroyed [5]. It is a common disease in the general population, resulting in progressive disability [6]. Its incidence increased in recent years, making OA one of the most prevalent orthopaedic conditions [7, 8].

The range of risk factors is broad and according to different studies includes unmodifiable factors such as injury in the past, ethnicity - OA is more prevalent in Black people, gender – more incidents reported in women, but also modifiable factors such as obesity [9,10.

In terms of signs and symptoms the most common are pain and movement limitations during physical activity, which become permanent in more advanced stages of the disease [11].

There are surgical and non-surgical methods of treating OA. Knee replacement is a surgical method of treating knee OA. It is a procedure in which the patient's knee is replaced with an implant adequate to the specific problems of that patient [12]. It improves the health-related quality of life (HRQL) measured with standardised questionnaires such as EQ5D [13,14].

The non-surgical methods include education, exercise, reduction of weight, use of paracetamol, anti-inflammatory drugs and corticosteroids. They are recommended as the first line of treatment; however knee replacement is the most effective way of treating knee OA [15].

Obesity is a serious condition that goes far beyond its visual aspect among others, due to hormonal activity of the adipose tissue [16, 17]. Its consequences can be found in every system of the body, and it is recognized as one of the major risk factors of knee OA. Misra et

al. conducted a study among 1653 individuals with no radiographic signs of OA at the baseline. After 60 months the patients were examined during a follow-up visit and new radiographs were assessed. The researchers found in their study increased risk of OA in obese patients regardless of gender. Analogical situation was found in sarcopenic obese patients although the results were not statistically significant in men [18]. Another study states that overweight or obese individuals have 2.96 times the risk of OA in comparison to patients with normal BMI (95% CI 2.56-3.43) [19]. According to Niu et al. regardless of knee alignment, the risk of developing knee OA seems to increase with the increase of BMI [20]. The above studies unanimously suggest that weight is a critical factor affecting the development of knee OA and general condition of the knee joints.

What is interesting is that weight may not be the only obesity-related factor important in the pathogenesis of OA, as non-weigh bearing joints are also affected in obese patients. Patients with hand OA showed direct correlation between leptin serum levels and the intensity of chronic pain, however not with the severity of the process judged by the radiographic symptoms [21, 22, 23]. In extremely obese patients leptin signalling is disrupted. This induces changes in the subchondral bone with no alterations in systemic inflammatory cytokine levels or incidence of OA [24,25]. Studies conducted on mice found that leptin-deficient (ob/ob) mice experienced altered bone microarchitecture and reduced bone mass, which resulted in changes in biomechanical properties of the bones, potentially affecting the healing of bone fractures [26, 27, 28, 29]. Leptin affects bone formation, acting through the central nervous system or peripherally, it can inhibit [29] or enhance [30] it, respectively. In humans, combination of leptin-resistance and overweight results in poor bone health outcomes [31]. Further studies are needed to determine the role of leptin in the development of OA.

Another product of adipose tissue associated with the development of OA is a protein called adiponectin. Its circulating levels are low in morbidly obese patients and tend to increase with weight loss and thiazolidinediones treatment, making the individual more sensitive to insulin [32, 33]. Laurberg et al. observed in their study that levels of adiponectin in plasma and serum of the patients with OA was significantly higher than in healthy controls [34]. In another study an association between OA biomarkers, local synovial inflammation and serum levels of adiponectin was found [35, 36].

Resisting is a protein which in humans is mostly produced by macrophages [37]. Its levels in serum increases with the increase of adipose tissue, as it is connected with the inflammation [38]. Further studies are needed to understand the role of resisting, and many

other adipokines, in the development of OA, as its pro-inflammatory effect and association with obesity suggest that it might be involved in the process.

Post-operative wound healing

Regardless of the mechanism of injury, three phases of wound healing can be recognized - the inflammatory, the proliferative and the remodelling phase. The first one happens right after the formation of the wound. Inflammatory mediators increase local blood flow by vasodilation which result in the influx of neutrophils and macrophages. The phagocytic leucocytes perform a significant function in digestion of the bacteria and autolysis of the tissue. The proliferative phase is when the wound defect is filled with collagen, granulation tissue and extracellular matrix, and the new blood vessels are formed. When the wound is closed remodelling can take place. Collagen fibres reorganise and the wound is devascularized returning to its basic blood supply [39].

In general, two mechanisms of wound healing can be recognized – primary and secondary healing. Majority of surgical wounds heal through the primary healing [39]. Regardless of the type of healing, the main objective is the same – effective healing with no complications.

There are many local and systemic factors affecting the process of wound healing. Local factors include oxygenation, infection or presence of a foreign body. Systematic factors are a broad group of elements such as age, gender, stress, ischaemia, level of sex hormones, diseases (diabetes, fibrosis, jaundice, etc.), obesity, nutrition, drugs, alcoholism, smoking [40]. Many of those factors are linked and tend to interact with each other mutually intensifying their negative impact on wound healing.

Nutrition is long known to be important in the process of wound healing [41]. Lack of specific elements or malnutrition in general can deeply impair the healing after surgery [41]. Protein is especially important, as its deficiency can negatively affect formation of capillaries, synthesis of collagen and proliferation of fibroblasts, which are all important in the process of wound healing [41].

Another factor involved in the wound healing is the way the wound is treated. It is an important part of post-operative recovery. In order to early recognize healing complications, it is crucial to regularly review the wound, cleanse and dress it [42]. There is no such thing as two wounds being the same, which is why every wound should be treated individually. Proper care is a key to successful and rapid healing. The general rule is that wounds should be maintained

as clean as possible to minimize the risk of infection. If there is a suspicion of infection, an antibiotic covering most probable causative organisms should be administered [42]. Factors such as excessive exudate or devitalised tissue may delay wound healing, which is why the wound should be cleansed if those occur. Nevertheless, excessive cleansing is also a factor potentially delaying the healing, as it is a kind of interference with the wound [42]. Another important issue is dressings, which optimally should keep a moist environment for the wound, simultaneously being a strong barrier against potentially harmful external factors [42].

Impact of obesity on recovery

Post-operative recovery is a complex process of returning to normal functioning and fitness. It includes healing of the wound but also proper care and rehabilitation. It is well known that obesity has a negative impact on an individual's health, as it is a risk factor of many diseases such as type 2 diabetes, coronary heart disease, stroke, dyslipidemia, hypertension or even cancer. Obese patients are prone to wound healing complications such as dehiscence, infection, formation of seroma, hematoma or ulcers [43]. Although precise mechanisms are not identified, that can be due to ischaemia and reduced perfusion occurring in subcutaneous adipose tissue. In obese patients the tension on the edges of the surgical wound is increased which often leads to dehiscence of the wound. The tension causes an increase in the pressure exerted on the tissue, hence reduced microperfusion and therefore reduced influx of oxygen [43, 44].

It was also reported that obese patients more often experience complications such as implant failure [45]. Individuals with BMI > 40 kg/m2 appear to have worse mobility of the joints at the baseline, which may worsen after the surgery due to several reasons [45]. According to Lai et al. the higher the BMI, the greater the risk of misalignment after the surgery [46]. They also found that the higher the patient's BMI, the greater the decrease in functional scores, which may affect the individual's satisfaction post-surgery [46].

Obesity generates many perioperative difficulties. The most basic one is the impact of concomitant diseases, especially of the heart and lungs on the general condition of the patient, management of anaesthesia and its consequences [47]. Risk of difficult intubation is increased in obese patients. There is also a greater risk of obese patients being admitted to intensive care unit after the surgery [47]. Perioperative thromboembolic events are more popular among obese patients, than among patients with normal BMI, too [48].

Additionally adipose tissue was found to produce a large variety of adipokines which are bioactive substances affecting the inflammatory response and immune system [49, 50, 51].

Obesity is accompanied by chronic low-grade inflammation which may be contributing to the development of post-surgery complications as it negatively modulates the response to surgery [51]. Among substances produced by white adipose tissue, a cytokine-like hormone - leptin is worth mentioning. The greater the BMI and amount of white adipose tissue, the greater the level of leptin [52]. In general, its role is to regulate the food intake and consumption of energy. It induces anorexigenic factors and suppresses orexigenic neuropeptides [53]. Leptin receptor is widely expressed in peripheral tissues, which is why leptin is regarded as a pleiotropic hormone regulating processes such as lipid homeostasis, thermogenesis, inflammation, insulin secretion, reproductive functions or angiogenesis [54, 55].

According to Maniar et al. impact of obesity on recovery after total knee arthroplasty (TKA) is dependent on the class of obesity [56]. They found in their study that class I obese experience similar, both early and late, functional recovery as the non-obese. Class II has as good early functional recovery as the non-obese, however when it comes to late functional recovery they may have lower results. Class III has lower functional results and lesser flexion of the knee postoperatively, yet that can be called an improvement compared to their preoperative condition [56].

Another important factor is the impact of obesity on post-operative care. According to Gaulton et al. obese patients are a group with increased risk of developing dependence during the first 2 years after joint surgery [57]. This applies especially to morbidly obese patients, as they have increased risk of many post-operative complications [57]. Care facilities may not be prepared to meet the needs of obese patients, as some additional supplies and equipment may be required [43]. Patients undergoing knee arthroplasty usually have a higher BMI and tend to be less active, which results in decreased range of motion and difficult rehabilitation [58].

Possible remedies

In order to create optimal conditions for wound healing and therefore for the recovery the nutritional needs of the patient should be fulfilled. On a cellular level there are large numbers of cell types involved in the process and therefore the wound's nutritional needs are complex. Nutrition support including substances such as proteins, polyunsaturated fatty acids, carbohydrates, vitamin C, A and E, magnesium, zinc, iron and copper would benefit wound healing [59].

In terms of OA Felson et al. suggested in their study that decreasing an individual's weight of 5kg decreases the risk of developing OA by about 50% [60]. This suggests that weight

loss may be an effective tool in prevention of development of OA. It may also be the most basic way of preventing post-operative complications of knee arthroplasty since elimination of OA is in fact elimination of the most common indication for the procedure. Not to mention the other benefits of weight loss, as obesity and related with it chronic inflammation affects many systems of the organism.

Furthermore, de Mello et al. found in their study that weight loss can cause improvement in many of the changes in immune function caused by obesity [61]. Weight loss decreases the production of pro-inflammatory factors and promotes the synthesis of anti-inflammatory cytokines produced by the subcutaneous adipose [62]. Levels of leptin and CRP are also reduced [62].

Hsu et al. conducted a study in which they divided a group of patients who underwent total knee arthroplasty into an exercise group and control group. The exercise group was subjected to 24 weeks of circuit training, starting 3 months after TKA. For the group they found the improvement in the active range of motion, step velocity and stride length compared to the control group. Greater improvement in pain and total scores, as well as in general health and social function was noted for the exercise group [63]. The study suggests benefits for patients undergoing circuit training, however further investigation is needed.

Matassi et al. stated in their study that the most important factor affecting the final flexion after TKA is the preoperative range of motion (ROM) [64]. In their study they evenly divided 122 patients with gonarthrosis into 2 groups – treatment and control. The treatment group was subjected to 6 weeks of exercise program prior to TKA. The study found improved motion of the knee in the treatment group before TKA and faster achievement of 90º of knee flexion after the surgery [64]. However, no prolonged effect was observed between 6 weeks and 1 year after the surgery [64]. The study suggests that prehabilitation improves the immediate postoperative recovery after TKA.

Calatayud et al. carried out similar research. The objective of their study was to determine the effect of a preoperative high-intensity resistance training on patients undergoing TKA [65]. The study had 44 participants, mostly women, the assessment was made 8 weeks before the surgery, after 8 weeks of training, 1 month after the surgery and 3 months after the surgery [65]. The researchers concluded that pre-operative high intensity resistance training improves the strength of muscles and range of motion, while reducing the pain, what results in faster recovery after TKA [65].

However further studies are needed to determine the importance of prehabilitation in the process of recovery and kind of exercises bringing the best results, especially in combination with obesity.

Conclusion

Obesity is becoming more and more prevalent and so are its consequences. It affects the joints, especially the knee, not only in a mechanical way, but also through the hormonal activity of the substances produced by the adipose tissue and their impact on the signalling pathways of the organism. Obesity is a serious problem since as a major risk factor of osteoarthritis it leads to a situation in which the joint must be replaced in order to treat the patient. Yet when the joint is replaced, the same obesity that led to the surgery impairs the healing process, resulting in complications and dissatisfaction of the patients, which is why the problem of obesity and proper nutrition should be addressed at early stages of treatment and prevention. Understanding how obesity affects the degeneration of the joints, and the healing process is crucial to successful intervention and elimination of its consequences. Various studies suggested that the severity of the post-operative complications is positively correlated with the weight of the patient. Pre-operative weight loss seems to be a potentially successful way to prevent the complications and improve the process of healing, yet further study is needed. Physical activity a few weeks before and after the surgery also possibly improves the recovery of the patient, but more research is needed in order to fully understand the dependence between the type of exercise, optimal time, intensity and recovery. It seems that prevention of obesity is the best way to prevent secondary diseases.

Author's contribution

Conceptualization, KP, HP, KM, KK, MP, MK, PK, UK, KK; methodology KP, HP, KM, KK, MP, MK, PK, UK, KK; software KP, HP, KM, KK, MP, MK, PK, UK, KK; check KP, HP, KM, KK, MP, MK, PK, UK, KK; formal analysis KP, HP, KM, KK, MP, MK, PK, UK, KK; investigation KP, HP, KM, KK, MP, MK, PK, UK, KK; resources KP, HP, KM, KK, MP, MK, PK, UK, KK; data curation KP, HP, KM, KK, MP, MK, PK, UK, KK; writing – rough preparation KP, HP, KM, KK, MP, MK, PK, UK, KK; writing – review and editing KP, HP, KM, KK, MP, MK, PK, UK, KK; visualization KP, HP, KM, KK, MP, MK, PK, UK, KK;

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References

1. Fact sheets - malnutrition. World Health Organization. Accessed March 17, 2024. https://www.who.int/news-room/fact-sheets/detail/malnutrition.
2. A healthy lifestyle - who recommendations. World Health Organization. Accessed March 17, 2024. https://www.who.int/europe/news-room/fact-sheets/item/a-healthy-lifestyle---who-recommendations.
3. Cornett E, Kaye A, Urman R, et al. Enhanced recovery pathways in orthopedic surgery. *Journal of Anaesthesiology Clinical Pharmacology*. 2019;35(5):35. doi:10.4103/joacp.joacp_35_18
4. Ghaly P, Iliopoulos J, Ahmad M. The role of nutrition in wound healing: An overview.

British Journal of Nursing. 2021;30(5). doi:10.12968/bjon.2021.30.5.s38

5. Hunter DJ, Bierma-Zeinstra S. Osteoarthritis. *The Lancet*. 2019;393(10182):1745-1759. doi:10.1016/s0140-6736(19)30417-9

6. Pereira DC, Ramos E, Branco J. Osteoarthritis. *Acta MéDica Portuguesa*. 2014;28(1):99-106. doi:10.20344/amp.5477

7. Safiri S, Kolahi A, Hoy D, et al. Global, regional and national burden of osteoarthritis 1990-2017: a systematic analysis of the Global Burden of Disease Study 2017. *Annals of the Rheumatic Diseases*. 2020;79(6):819-828. doi:10.1136/annrheumdis-2019-216515

8. Xia B, Chen D, Zhang J, Hu S, Jin H, Tong P. Osteoarthritis Pathogenesis: A review of Molecular mechanisms. *Calcified Tissue International*. 2014;95(6):495-505. doi:10.1007/s00223-014-9917-9

9. Giorgino R, Albano D, Fusco S, Peretti GM, Mangiavini L, Messina C. Knee osteoarthritis: Epidemiology, pathogenesis, and Mesenchymal Stem Cells: What else is new? an update. *International Journal of Molecular Sciences*. 2023;24(7):6405. doi:10.3390/ijms24076405

10. Palazzo C, Nguyen C, Lefèvre-Colau MM, Rannou F, Poiraudeau S. Risk factors and burden of osteoarthritis. *Annals of Physical and Rehabilitation Medicine*. 2016;59(3):134-138. doi:10.1016/j.rehab.2016.01.006

11. 3. Michael JW-P, Schlüter-Brust KU, Eysel P. The epidemiology, etiology, diagnosis, and treatment of osteoarthritis of the knee. Deutsches Arzteblatt international. March 2010. Accessed March 21, 2024. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2841860/.

12. Katz JN, Arant KR, Loeser RF. Diagnosis and treatment of hip and knee osteoarthritis. *JAMA*. 2021;325(6):568. doi:10.1001/jama.2020.22171

13. Jenkins PJ, Clement ND, Hamilton DF, Gaston P, Patton JT, Howie CR. Predicting the cost-effectiveness of total hip and knee replacement. *The Bone & Joint Journal*. 2013;95-B(1):115-121. doi:10.1302/0301-620x.95b1.29835

14. Räsänen P, Paavolainen P, Sintonen H, et al. Effectiveness of hip or knee replacement surgery in terms of quality-adjusted life years and costs. *Acta Orthopaedica*. 2007;78(1):108-115. doi:10.1080/17453670610013501

15. Kan H, Chan PK, Chiu KY, et al. Non-surgical treatment of knee osteoarthritis. *Hong Kong Medical Journal*. Published online March 28, 2019. doi:10.12809/hkmj187600

16. Xie C, Chen Q. Adipokines: new therapeutic target for osteoarthritis? *Current Rheumatology Reports*. 2019;21(12). doi:10.1007/s11926-019-0868-z

17. Wang TT, He C. Pro-inflammatory cytokines: The link between obesity and osteoarthritis. *Cytokine & Growth Factor Reviews*. 2018;44:38-50. doi:10.1016/j.cytogfr.2018.10.002

18. Misra D, Fielding RA, Felson DT, et al. Risk of knee osteoarthritis with obesity, sarcopenic obesity, and sarcopenia. *Arthritis & Rheumatology*. 2019;71(2):232-237. doi:10.1002/art.40692

19. Blagojevic M, Jinks C, Jeffery A, Jordan KP. Risk factors for onset of osteoarthritis of the knee in older adults: a systematic review and meta-analysis. *Osteoarthritis and Cartilage*. 2010;18(1):24-33. doi:10.1016/j.joca.2009.08.010

20. Niu J, Zhang Y, Torner JC, et al. Is obesity a risk factor for progressive radiographic knee osteoarthritis? *Arthritis Care & Research*. 2009;61(3):329-335. doi:10.1002/art.24337

21. Yusuf E, Nelissen RGHH, Ioan-Facsinay A, et al. Association between weight or body mass index and hand osteoarthritis: a systematic review. *Annals of the Rheumatic Diseases*. 2009;69(4):761-765. doi:10.1136/ard.2008.106930

22. Massengale M, Lü B, Pan JJ, Katz JN, Solomon DH. Adipokine hormones and hand osteoarthritis: radiographic severity and pain. *PLOS ONE*. 2012;7(10):e47860. doi:10.1371/journal.pone.0047860

23. Yusuf E, Ioan-Facsinay A, Bijsterbosch J, et al. Association between leptin, adiponectin and resistin and long-term progression of hand osteoarthritis. *Annals of the Rheumatic Diseases*. 2011;70(7):1282-1284. doi:10.1136/ard.2010.146282

24. Griffin TM, Huebner JL, Kraus VB, Guilak F. Extreme obesity due to impaired leptin signaling in mice does not cause knee osteoarthritis. *Arthritis & Rheumatism*. 2009;60(10):2935-2944. doi:10.1002/art.24854

25. Upadhyay J, Farr OM, Mantzoros CS. The role of leptin in regulating bone metabolism. *Metabolism*. 2015;64(1):105-113. doi:10.1016/j.metabol.2014.10.021

26. McGee-Lawrence ME, Wenger K, Misra S, et al. Whole-Body vibration mimics the metabolic effects of exercise in male leptin Receptor–Deficient mice. *Endocrinology*. 2017;158(5):1160-1171. doi:10.1210/en.2016-1250

27. Reimer RA, LaMothe JM, Zernicke RF. Leptin deficiency and its effects on tibial and vertebral bone mechanical properties in mature genetically lean and obese JCR:LA-Corpulent rats. *Journal of Obesity*. 2012;2012:1-7. doi:10.1155/2012/650193

28. Liu P, Cai M. Leptin influences healing in the Sprague Dawley rat fracture model. *Medical Science Monitor*. 2017;23:258-265. doi:10.12659/msm.899259

29. Iwaniec UT, Turner RT. Influence of body weight on bone mass, architecture and turnover. *Journal of Endocrinology*. 2016;230(3):R115-R130. doi:10.1530/joe-16-0089

30. Steppan CM, Crawford DT, Chidsey-Frink KL, Ke HZ, Swick AG. Leptin is a potent stimulator of bone growth in ob/ob mice. *Regulatory Peptides*. 2000;92(1-3):73-78. doi:10.1016/s0167-0115(00)00152-x

31. Dimitri P, Jacques R, Paggiosi M, et al. Leptin may play a role in bone microstructural alterations in obese children. *The Journal of Clinical Endocrinology & Metabolism*. 2015;100(2):594-602. doi:10.1210/jc.2014-3199

32. Kadowaki T, Yamauchi T. Adiponectin and adiponectin receptors. *Endocrine Reviews*. 2005;26(3):439-451. doi:10.1210/er.2005-0005

33. Maeda N, Takahashi M, Funahashi T, et al. PPARΓ ligands increase expression and plasma concentrations of adiponectin, an Adipose-Derived protein. *Diabetes*. 2001;50(9):2094-2099. doi:10.2337/diabetes.50.9.2094

34. Laurberg TB, Frystyk J, Ellingsen T, et al. Plasma Adiponectin in Patients with Active, Early, and Chronic Rheumatoid Arthritis Who Are Steroid- and Disease-Modifying Antirheumatic Drug-Naive Compared with Patients with Osteoarthritis and Controls. *The Journal of Rheumatology*. 2009;36(9):1885-1891. doi:10.3899/jrheum.080907

35. Koskinen A, Juslin S, Nieminen R, Moilanen T, Vuolteenaho K, Moilanen E. Adiponectin associates with markers of cartilage degradation in osteoarthritis and induces production of proinflammatory and catabolic factors through mitogen-activated protein kinase pathways. *Arthritis Research & Therapy*. 2011;13(6):R184. doi:10.1186/ar3512

36. De Boer TN, Van Spil WE, Huisman A, et al. Serum adipokines in osteoarthritis;

comparison with controls and relationship with local parameters of synovial inflammation and cartilage damage. *Osteoarthritis and Cartilage*. 2012;20(8):846-853. doi:10.1016/j.joca.2012.05.002

37. Patel L, Buckels AC, Kinghorn I, et al. Resistin is expressed in human macrophages and directly regulated by PPARγ activators. *Biochemical and Biophysical Research Communications*. 2003;300(2):472-476. doi:10.1016/s0006-291x(02)02841-3

38. Degawa-Yamauchi M, Bovenkerk JE, Juliar BE, et al. Serum resistin (FIZZ3) protein is increased in obese humans. *The Journal of Clinical Endocrinology & Metabolism*. 2003;88(11):5452-5455. doi:10.1210/jc.2002-021808

39. Velnar T, Bailey TA, Smrkolj V. The Wound Healing Process: An overview of the cellular and molecular mechanisms. *Journal of International Medical Research*. 2009;37(5):1528-1542. doi:10.1177/147323000903700531

40. Guo S, DiPietro LA. Factors affecting wound healing. *Journal of Dental Research*. 2010;89(3):219-229. doi:10.1177/0022034509359125

41. Arnold MA, Barbul A. Nutrition and wound healing. *Plastic and Reconstructive Surgery*. 2006;117(SUPPLEMENT):42S-58S. doi:10.1097/01.prs.0000225432.17501.6c

42. Yao K, Bae L, Yew WP. Post-operative wound management. *Australian Family Physician*. 2013;42(12). https://www.racgp.org.au/afp/2013/december/post-operative-wound-management/

43. Wilson JA, Clark JJ. Obesity: impediment to postsurgical wound healing. *Advances in Skin & Wound Care*. 2004;17(8):426-432. doi:10.1097/00129334-200410000-00013

44. Anaya DA, Dellinger EP. The obese surgical patient: a susceptible host for infection. *Surgical Infections*. 2006;7(5):473-480. doi:10.1089/sur.2006.7.473

45. Campi S, Papalia GF, Esposito C, et al. Unicompartmental Knee Replacement in Obese Patients: A Systematic Review and Meta-Analysis. *Journal of Clinical Medicine*. 2021;10(16):3594. doi:10.3390/jcm10163594

46. Lai Y, Cao J, Li ZX, Feng W, Xu H, Zhou Z. Effect of body mass index on postoperative mechanical alignment and long-term outcomes after total knee arthroplasty: a retrospective cohort study of 671 knees. *Annals of Translational Medicine*. 2022;10(15):829. doi:10.21037/atm-22-3212

47. Domi R, Laho H. Anesthetic challenges in the obese patient. *Journal of Anesthesia*. 2012;26(5):758-765. doi:10.1007/s00540-012-1408-4

48. Samama C, Gafsou B, Jeandel T, et al. Prévention de la maladie thromboembolique veineuse postopératoire. Actualisation 2011. Texte court. *Annales Francaises D Anesthesie Et De Reanimation*. 2011;30(12):947-951. doi:10.1016/j.annfar.2011.10.008

49. Juge-Aubry CE, Henrichot E, Meier CA. Adipose tissue: a regulator of inflammation. *Best Practice & Research Clinical Endocrinology & Metabolism*. 2005;19(4):547-566. doi:10.1016/j.beem.2005.07.009

50. Calabro P, Yeh ET. Obesity, inflammation, and vascular disease: the role of the adipose tissue as an endocrine organ. *Subcell Biochem*. 2007;42:63-91.

51. Wozniak SE, Gee LL, Wachtel MS, Frezza EE. Adipose tissue: the new endocrine organ? A review article. *Digestive Diseases and Sciences*. 2008;54(9):1847-1856. doi:10.1007/s10620-008-0585-3

52. Gualillo O, Eiras S, Lago F, Diéguez C, Casanueva FF. Elevated serum leptin concentrations induced by experimental acute inflammation. *Life Sciences*. 2000;67(20):2433-2441. doi:10.1016/s0024-3205(00)00827-4

53. Ahima RS, Prabakaran D, Mantzoros CS, et al. Role of leptin in the neuroendocrine response to fasting. *Nature*. 1996;382(6588):250-252. doi:10.1038/382250a0

54. Sierra-Honigmann MR, Nath AK, Murakami C, et al. Biological action of leptin as an angiogenic factor. *Science*. 1998;281(5383):1683-1686. doi:10.1126/science.281.5383.1683

55. Collins S, Kuhn CM, Petro A, Swick AG, Chrunyk BA, Surwit RS. Role of leptin in fat regulation. *Nature*. 1996;380(6576):677. doi:10.1038/380677a0

56. Maniar RN, Maniar PR, Singhi T, Gangaraju B. WHO class of obesity influences functional Recovery Post-TKA. *Clinics in Orthopedic Surgery*. 2018;10(1):26. doi:10.4055/cios.2018.10.1.26

57. Gaulton TG, Fleisher LA, Neuman MD. The association between obesity and disability in survivors of joint surgery: analysis of the health and retirement study. *British Journal of Anaesthesia*. 2018;120(1):109-116. doi:10.1016/j.bja.2017.11.011

58. Jahić D, Omerovic D, Tanović AT, Džanković F, Tirić–Čampara M. The effect of Prehabilitation on postoperative outcome in patients following primary total knee arthroplasty. *Medicinski Arhiv*. 2018;72(6):439. doi:10.5455/medarh.2018.72.439-443

59. Guo S, DiPietro LA. Factors affecting wound healing. *Journal of Dental Research*. 2010;89(3):219-229. doi:10.1177/0022034509359125

60. Felson DT, Zhang Y, Anthony JM, Naimark A, Anderson JJ. Weight loss reduces the risk for symptomatic knee osteoarthritis in women. *Annals of Internal Medicine*. 1992;116(7):535-539. doi:10.7326/0003-4819-116-7-535

61. De Mello VD, Kolehmainen M, Schwab U, et al. Effect of weight loss on cytokine messenger RNA expression in peripheral blood mononuclear cells of obese subjects with the metabolic syndrome. *Metabolism*. 2008;57(2):192-199. doi:10.1016/j.metabol.2007.08.024

62. Moschen AR, Molnar C, Geiger S, et al. Anti-inflammatory effects of excessive weight loss: potent suppression of adipose interleukin 6 and tumour necrosis factor expression. *Gut*. 2010;59(9):1259-1264. doi:10.1136/gut.2010.214577

63. Hsu W, Shen WJ, Lin ZR, Chang SH, Hsu RWW. Circuit training enhances function in patients undergoing total knee arthroplasty: a retrospective cohort study. *Journal of Orthopaedic Surgery and Research*. 2017;12(1). doi:10.1186/s13018-017-0654-4

64. Matassi F, Duerinckx J, Vandenneucker H, Bellemans J. Range of motion after total knee arthroplasty: the effect of a preoperative home exercise program. *Knee Surgery, Sports Traumatology, Arthroscopy*. 2012;22(3):703-709. doi:10.1007/s00167-012-2349-z

65. Calatayud J, Casaña J, Ezzatvar Y, Jakobsen MD, Sundstrup E, Andersen LL. High-intensity preoperative training improves physical and functional recovery in the early post-operative periods after total knee arthroplasty: a randomized controlled trial. *Knee Surgery, Sports Traumatology, Arthroscopy*. 2016;25(9):2864-2872. doi:10.1007/s00167-016-3985-5