

Review Article

Diabetes and Osteoarthritis Disability: An Important Underrepresented Topic in the Related Literature

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Received: December 15, 2015; Accepted: February 26, 2016; Published: April 01, 2016

Abstract

Diabetes prevalence, increasing rapidly among older populations, has several orthopedic consequences. This brief specifically examines whether adults with type 2 diabetes are at increased risk for developing osteoarthritis, and if so, whether this adversely impacts health outcomes, in general, and hip arthroplasty surgery outcomes, in particular. The possibility that osteoarthritis is a contributing factor to diabetes type 2 is also discussed. To examine these issues, relevant literature located in key databases and published over the last 5 years using key words: *hip arthroplasty outcomes, diabetes and osteoarthritis, diabetes and falls injuries*, among others, were sought and carefully examined. These data revealed: 1) There is a possible increased risk of developing osteoarthritis, as well as more complications and delayed healing after surgery among cases with type 2 diabetes compared to non diabetic cases. 2) Osteoarthritis may be a possible risk factor for diabetes 2. These observations suggest further exploration of the linkages between diabetes type 2 and osteoarthritis may be highly valuable in efforts to promote healthy aging and reduce health costs attributable to diabetes type 2 and osteoarthritis among the elderly.

Keywords: Diabetes; Hip joint, Osteoarthritis; Surgical outcomes; Type 1 and Type 2

Background

Diabetes, a leading cause of comorbidity in the United States and around the world, can lead to many complications, including, but not limited to blood vessel damage, including blood vessels that supply the heart and brain [1]. Other well-established complications include eye problems, kidney disease, and neuropathy or nerve damage [2]. Less well documented are musculoskeletal impairments, an increased fracture and falls risk, possible increased rates of osteoarthritis, and adverse health outcomes after surgery to repair a fracture or replace a diseased joint, along with impaired bone health and gait [3,4]. Indeed, in our view, diabetes, a frequent co-occurring disease in people with osteoarthritis [5,6], is often overlooked as a highly significant risk factor for osteoarthritis, and consequently for its impact on the person with this condition, as well as on any surgery that is undertaken to treat this disabling health condition. This is disappointing in light of a fair number of early studies describing an association between diabetes and osteoarthritis, and recent findings that show the immense negative impact of diabetes on life quality, and other data that reveal osteoarthritis is often as disabling and painful as far as life quality goes, as the impact of hypertension. In fact, although Stürmer et al. [7] hypothesized that type 2 diabetes might be a potentially important systemic risk factor for knee and hip osteoarthritis, approximately 15 years ago, it seems little has been done to embed this message in public health education programs and others designed to maximize type 2 diabetes outcomes.

In light of the increasing numbers of people anticipated to acquire type 2 diabetes in the next few decades, along with an increasingly older population, prone to painful disabling osteoarthritis, this

brief specifically aims to highlight what is currently known about the possible linkage between diabetes and osteoarthritis, the most common chronic disease disabler of older adults. To this end, this brief details some recent literature dealing with evidence linking diabetes and osteoarthritis in general, and the suffering that accompanies this. Information on the impact of diabetes on outcomes of surgery for hip joint osteoarthritis was also sought to examine if function after this form of surgery is likely to be more compromised than not in the case of a patient with type 2 diabetes based on studies of the outcomes of knee joint surgery for osteoarthritis among type 2 diabetes sufferers [8]. The goal was to identify selected facts that might have future implications for reducing the extent of the disability suffered by older adults with type 2 diabetes.

To attain the goal of the brief, a systematic search using key data bases including, Academic Search Complete, PubMed, Scopus, and Web of Science was implemented. Key terms used were: *Diabetes and osteoarthritis, hip arthroplasty outcomes and diabetes, falls and diabetes, bone and diabetes, and motor dysfunction in diabetes*. Only full length English language clinical reports and empirical papers published in the last five years were deemed acceptable for this narrative review, the method adopted for organizing these data, given the scarcity of publications on this topic, as well as their immense heterogeneity.

Results

Employing the term: *diabetes and osteoarthritis* there were 305 articles listed in Academic Search Complete, 469 in PubMed and 461 in Scopus. Employing the term: *hip arthroplasty outcomes and diabetes*, there were 15 listing on PubMed, 10 of which focused on

Table 1: Case control and cohort studies conducted over the last two decades showing osteoarthritis, diabetes linkages.

Authors	Sample Studied	Key Finding
Bottie et al. [38]	Hip and knee replacement patients rates of return to the theatre	Diabetes was associated with higher odds of requiring these additional index procedures
Fadhil et al. [12]	65 type 2 diabetes patients	Type 2 diabetes predicted the development of severe knee OA independent of age and other known risk factors for OA
King et al. [39]	450,000 patients with diabetes type 2	Rates of OA progression were higher in the diabetic patients when compared to control individuals
Martinez-Huedo et al. [40]	Reviewed 122,926 cases undergoing total hip arthroplasty	Immediate outcomes were worse in diabetes cases
Mednick et al. [32]	27130 primary total hip arthroplasty cases	Diabetes increased risk for readmission
Miksch et al. [16]	Examined 3,546 type 2 diabetes cases	Patients with diabetes and OA had low quality of life scores for pain and impairment
Nuesch et al. [17]	1163 OA patients over age 35	Patients with comorbid diabetes had increased mortality rates
Paxton et al. [33]	41,750 knee OA cases were followed from 2001-2008	Diabetes was a strong predictor of the risk for failure after knee joint arthroplasty
Rahman et al. [41]	577,601 randomly selected individuals	Younger adults and older women with OA have increased risks of developing diabetes compared to age-sex matched non-OA controls
Rajamaki et al. [19]	134 cases OA after hip/knee replacement	25% [934/1340] had diabetes, 19 had prior preexisting diabetes
		Those with previous type 2 diagnoses had pain in operated joint for up to 2 years after surgery
Ray et al. [53]	Examined 100 diabetic cases	27% had knee osteoarthritis, 17% had hand osteoarthritis
Schett et al. [10]	927 men and women followed 20yr	Rates of surgery were elevated in diabetes
		Type 2 diabetes independently predicts onset of severe OA, when controlling for age and BMI
Sturmer et al. [7]	809 knee or hip OA cases awaiting surgery	Bilateral cases often also had type 2 diabetes
Schairer et al. [52]	1415 hip arthroplasty cases	Unplanned hospital readmissions were associated with diabetes
Wang et al. [11]	2000 residents over 45 yrs in Mongolia	Prevalence of osteoarthritis was affected by diabetes

hip joint replacement, rather than knee, shoulder, ankle, or other forms of joint replacement, and 67 in total in Scopus. Key themes that emerged are discussed below.

Evidence linking diabetes and osteoarthritis

In terms of a possible cause effect relationship between diabetes and osteoarthritis, several studies and a recent review by Louati et al. [5] and by King et al. [9] affirm diabetes is a possible risk factor for osteoarthritis or for heightening osteoarthritis disability. Schett et al. [10] too, found that type 2 diabetes was a significant predictor of the need for joint surgery due to osteoarthritis, and that this association was more profound relative to the duration of the condition. Moreover, this group found more severe clinical symptoms of osteoarthritis existed in cases examined over 20 years in those patients with type 2 diabetes, when compared to those with no diabetic condition (Table 1). Wang et al. [11] also noted that the prevalence of osteoarthritis in middle-aged Mongolian and senior residents was affected negatively by diabetes, as did Fadhil et al. [12] who also noted type 2 diabetes not only predicted the presence of knee osteoarthritis in a group ages 40-50 years of age, but the development of severe knee osteoarthritis independent of age and other known risk factors for the condition.

Diabetes and osteoarthritis progression

Several studies have examined the impact of type 2 diabetes on osteoarthritis outcomes [9]. In their related study, Eymard et al. [13] concluded diabetes is an independent risk factor for progression of osteoarthritis of the knee joint. Diabetes type 2 also appeared associated with increased hand pain in a population based study of cases with hand osteoarthritis [14], and among a variety of comorbid health conditions, Zullig et al. [15] who examined patient reported outcomes in veterans with hip and knee osteoarthritis were worse in this subgroup even when adjusting for demographic and clinical

factors. The presence of diabetes and other comorbidities was associated with pain, depressive symptoms, fatigue and insomnia, as well as more limited functioning.

Miksch et al. [16] concluded that the impact of osteoarthritis in those with type 2 diabetes was higher than the impact of hypertension, and patients assessed for quality of life who had both diabetes and osteoarthritis were said to have remarkably lower scores than other subgroups on all the Medical Outcome Study Short form subscales examined. The impact of self-reported diabetes on increasing mortality rates of adults over age 35 with either hip or knee osteoarthritis has been observed in a population based cohort study [17].

Diabetes and arthroplasty outcomes

Several studies have examined outcomes such as death rates, functional outcomes and complications, as well as revision rates following knee or hip joint replacement or arthroplasty surgery for disabling end stage osteoarthritis [8,9]. In the systematic review by Wang et al. [11], patients with type 2 diabetes or 12.2 percent of cases had increased risks of deep infection, deep vein thrombosis, aseptic loosening, periprosthetic fractures, and a poorer overall functional score than non diabetic cases. Tsang et al. [18] who conducted a systematic review and meta-analysis of cohort studies found the prevalence of type 2 diabetes increased the risk of infection after hip joint replacement surgery. In addition, Rajmaki et al. [19] found diabetes to be associated with the presence of persistent pain after hip and knee replacement surgery, even if the diabetic patients' baseline pre operative pain scores were lower than those with no diabetes as a whole. This, the authors conjectured was possibly attributed to their chronic systemic inflammatory state, and/or possible state of neuropathy.

Impact of type 2 diabetes on joint structures

The term joint structures refers to the elements that comprise the joints affected by osteoarthritis, namely, the articular cartilage lining the joint and its structural backbone comprised of collagen and proteoglycan molecules, the synovial membrane lining the joint capsule, the subjacent bones forming the joint, and the ligaments providing stability to the joint. In terms of impacting one or more of these structures, a study by Laiguillon et al. [20] revealed that osteoarthritic cartilage extracted from cases with type 2 diabetes tends to show a heightened responsiveness to inflammation induced by the inflammatory agent Interleukin (IL-1B) –that could increase the extent to which the patient experiences pain and joint destruction processes. Ribeiro et al. [21] found that the metabolic process known as autophagy, which is defective in osteoarthritis is a possible mechanism whereby diabetes impairs articular cartilage integrity. Other data imply that alterations in lipid metabolism, including changes in the level of adipokines associated with obesity can produce inflammatory joint changes that might be destructive to a joint, as well as hyperglycemia that can alter cartilage metabolism negatively in people with diabetes [22]. Although it is not known with any certainty if diabetes is predictive of osteoarthritic joint changes in the area of the knee joint and others, Onur et al. [23] found type 2 diabetes associated with degeneration of the lateral and medial femoral condyles of the knees, along with altered articular cartilage at the medial condyles, and cysts within the articular cartilage and at the junction between the articular cartilage and subchondral bone in a rat model of the disease.

Umpierrez et al. [24] who examined incubated rat articular cartilage showed collagen content decreased to 49% in mildly diabetic rats and 16% in severely diabetic rats, suggesting a possible effect of diabetes on collagen, a key component of articular cartilage. Based on results of an animal study in the rat, Rosa et al. [25] concluded that the exposure of human chondrocytes to high glucose, favors degenerative chondrocyte changes that may promote articular cartilage degradation, and ultimately, the development and/or progression of osteoarthritis.

Berenbaum [26] has drawn attention to the fact that hyperglycemia can induce an inflammatory state, and that an inflammatory state might predispose cartilage to damage that leads to osteoarthritis due to its systemic effect. Hyperglycemia could also have a negative impact on chondrocyte function and viability according to this author. The author also noted that other joint structures that could be affected by type 2 diabetes are nerves, muscles, and ligaments that may reduce joint protection mechanisms, thus fostering the risk of further joint destruction. This claim is supported by research by Atayde et al. [27] who found the joint ligaments, synovia, and cartilage were compromised in the presence of diabetes due to abnormal collagen production, which predisposed to weakening the cartilage matrix and joint function [26] (Figure 1 and Box 1).

Athanasiciou et al. [28] found cartilage extracted from patients with diabetes to be significantly softer and more permeable than cartilage from control subjects, suggesting the tissue is less able to bear stresses. Another factor often not mentioned in the related literature is the impact of diabetes on activities in general, as well as exercise, in particular, which can have deleterious effects locally on

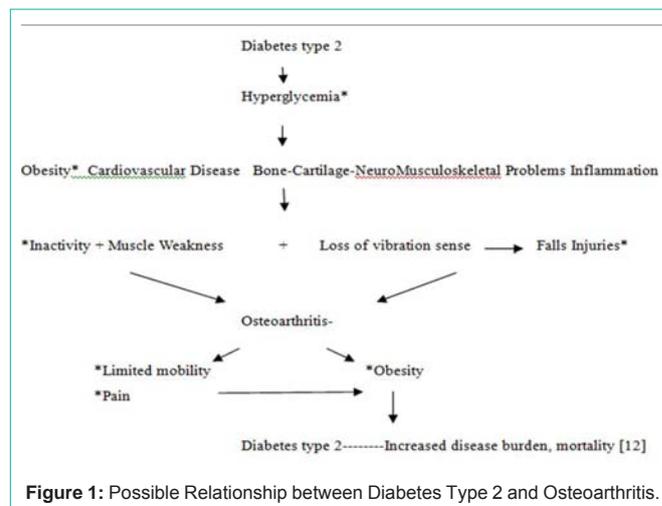


Figure 1: Possible Relationship between Diabetes Type 2 and Osteoarthritis.

- Metabolic problems [10, 45]
- Bone quality and possible healing deficits [12,42,44]
- Cardiovascular complications [44]
- Cartilage structural abnormalities [10,44,48]
- Falls [26]
- Gait abnormalities [4]
- Hypertension
- Inflammation [5,50]
- Lipid abnormalities [50]
- Musculoskeletal changes [49]
- Physical inactivity [21]
- Obesity [5]
- Pain
- Poor healing or delayed healing after trauma or surgery [19,46,47,51]
- Neurological problems [25]
- Vision impairments

Box 1: Diabetes and associated health sequelae that could impact osteoarthritis disease progression.

a joint, as well increase the risk for obesity and challenges to weight control efforts [6]. Poor bone healing can also be attributable in part to excess inactivity, and accompanying bone changes observed in people with type 2 diabetes [12].

Discussion

The possible linkage between osteoarthritis and diabetes has been quite well discussed, although opposing views of the nature of this linkage prevail. This brief examined the question of whether there a link between diabetes type 2 and osteoarthritis that is of sufficient magnitude to impact one or both of these ubiquitous diseases adversely, and if so, to derive implications for the prevention of excess disability in both these conditions. Employing several data sources likely to house up to date research findings and others on this topic, and in accord with Louati et al. [5] and King et al. [9] who carried out recent comprehensive narrative reviews of research on diabetes type

2 and osteoarthritis disability, a small more up to date scan of studies reported in Table 1 supports a possible clinical link between these two prevalent health conditions, even though not all studies reported by Louati found an association, and Eymard et al. [13] reported no such definitive association, as did Kirkman et al. [29].

This linkage, which could perhaps arise per chance [7,9], is however, supported more often than not in the current literature by basic research findings, as well as an array of clinical findings, and hence it appears reasonable to suggest it is important to continue to examine whether diabetes type 2 is as an independent risk factor for osteoarthritis, given the high prevalence of this irreversible health condition globally, and the tendency for those with diabetes type 2 to be more severely impaired than those with no diabetes [9]. This argument is also supported by an extensive survey conducted between 1988-2003 where it was observed that a total of 65, 769 cases with diabetes type 2 underwent either total hip or total knee arthroplasty surgery for severe disabling osteoarthritis [30], and seven studies showing an independent linkage between diabetes type 2 and osteoarthritis when adjusted for body mass index [5]. The reported prevalence of type 2 diabetes cases in some of these studies may also be underestimates, because diabetes type 2 may not only be underdiagnosed in the larger population, but also within the osteoarthritis population as observed by Rajaki et al. [19]. Diabetes also clearly impacts rates of early revision after knee replacements adversely [31], its presence affects readmission rates after total hip arthroplasty surgery negatively [32], as well as postoperative complications after total knee, elbow, and shoulder arthroplasty, respectively [33-35]. In addition to increasing the risk of post-operative infection rates [18,36,37], Yang et al. [37] found the prevalence of type 2 diabetes among patients needing a total knee replacement of 12.2%, which they stated exceeded a projected global estimate of 8.4% in a recent study. Louati et al. [5] also found a high mean frequency of osteoarthritis of 29.5% among 5,788 cases with type 2 diabetes based on a review and meta-analysis of 299 publications. The risk of osteoarthritis was also found to be greater in the diabetic than the non-diabetic population, and conversely, the risk of diabetes type 2 was found to be greater in the osteoarthritic population than the non-osteoarthritic population.

Thus, even if the linkage between these two chronic health conditions is not confirmed, in the context of primary care, as depicted in Figure 1, and the aforementioned literature, compelling evidence that diabetes is associated with many health outcomes known to increase the risk of poor joint and bone health prevails (Box 1). This further includes a significantly greater negative impact on outcomes experienced by adults with osteoarthritis, such as fatigue [15], and findings that people with type 2 diabetes undergoing joint replacement surgery for their osteoarthritis suffer more than those having the individual disease alone, or other combinations of age-associated chronic health conditions [13,19]. Osteoarthritis may also be a less well recognized risk factor for type 2 diabetes due to its adverse impact on mobility and body weight [26].

However, when comparing the numbers of articles on linkages of diabetes to obesity, and cardiovascular health outcomes, the importance of the impact of type 2 diabetes on the risk of incurring osteoarthritis and excess disability, and those discussing how osteoarthritis can increase the risk for type 2 diabetes, is significantly

underrepresented in our view, given the immense global burden of osteoarthritis in its own right, and evidence diabetes type 1 and 2 may heighten the risk for incurring osteoarthritis, as well as for accelerating its rate of progression and/or severity, and risk of poor joint replacement surgical outcomes. As outlined above, and summarized in Box 1, reasons for this are multiple, including vascular, metabolic, and sensorimotor impacts of type 2 diabetes on general health, as well as joint physiology, and each correlate may impact the disease independently, as well as collectively, and suggests predictive models to minimize diabetes as well as osteoarthritis disability would be important to conduct in the future. More research to examine how osteoarthritis, in turn, can arguably impact risk of diabetes type 2, or exacerbate its symptoms, by virtue of its negative impact on mobility, and weight status is also recommended given the widespread prevalence of this age associated disease.

In sum, as stated by Yan and Li [42], the observed linkage between diabetes and osteoarthritis, although not universal [43], appears deserving of future study in efforts to minimize the prevalence of osteoarthritis, as well as its disabling outcomes, as well as efforts to reduce the poor health outcomes associated with type 2 diabetes such as physical activity challenges and pain, among others. In addition to examining the presence of both these health conditions routinely in the primary care setting, sufficient data supports the view that those with either pre-diabetes, or a type 1 or 2 diabetes diagnosis should receive routine education about the importance of weight control and physical activity. In addition, those with a definitive diagnosis should receive information on how to optimize their bone and joint health specifically, and why. Placing emphasis on the importance of regular physical activity that is carefully and insightfully applied, and avoidance of trauma is highly recommended. In addition, those osteoarthritis cases undergoing surgery should be screened especially carefully as far as their diabetes status goes, and appropriate education about their increased risk for complications after joint replacement surgery should be forthcoming when surgeons seek informed consent [37]. Meticulous peri-operative care [19], and enriched rehabilitation periods and pre-operative strategies should be forthcoming to offset complications in the event a diabetes diagnosis is evidenced. Conversely, adults diagnosed as having osteoarthritis of one or more joints should be specifically appraised of the need to maintain healthful body weights and to avoid weight gain and a sedentary lifestyle that can lead to the onset of diabetes type 2. As outlined by King et al. [9] more basic attention to understanding the link between type 2 diabetes and osteoarthritis and its implications for reducing the magnitude of the burden of both these health conditions is warranted, especially more efforts to examine how diabetes type 2 and type 1 diabetes and osteoarthritis are differentially or uniquely linked, and how each correlate in Box 1 contributes to the risk of an excess disease burden. Findings that the presence of osteoarthritis may diminish efforts to control diabetes using medication implies this fact should be taken into account in treating the diabetic as recommended by Wami et al. [54]. Other research reveals that pioglitazone an antidiabetic medication may be helpful in reducing the severity of osteoarthritis [55]. In addition, Al-Jaralle et al. [56] found patients with diabetes type 2 and knee osteoarthritis who were on insulin therapy had less radiographic osteophytes compared to those patients not on insulin. However, other medication approaches

such as the use of DPP-4 inhibitors used to control glucose levels may induce joint symptoms [57]. Osteoarthritis, which is negatively affected by diabetes [58], can in turn, significantly reduce the life quality of people with type 2 diabetes [59], hence future efforts to examine these linkages and biological outcomes, such as adverse arthroplasty outcomes [60], will undoubtedly not only improve the lives of many, but will enable efforts to use shrinking health resources advantageously and optimally.

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