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Nicotine Dependence and Incident Hip Replacement Surgery in Individuals with Type 2 Diabetes Mellitus, TRINET-X, 2021

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Abstract

The purpose of this research is to examine the association between nicotine dependence (yes, no) and hip replacement (yes, no) among people with type 2 diabetes mellitus (T2DM). Data were obtained through the TRINET-X data depository of 18 years or older patients with T2DM and nicotine dependence history. Then, the incidence of hip replacement surgery was determined. Propensity score matching (PSM) was used to determine the risk of hip replacement surgery. After PSM, the risk ratio of hip replacement surgery among people with T2DM was 1.45 (95% confidence interval: 1.45, 1.57; $p < 0.0001$) for those who had nicotine dependence versus those who did not. Nicotine dependence among people with T2DM was identified as a risk factor for future hip replacement need. Patients who have nicotine dependence should be cautioned about this potential risk.

Keywords
- hip replacement
- type 2 diabetes mellitus
- nicotine dependence

Hip replacement surgery has been steadily increasing worldwide with a reported 30% increase between 2007 and 2017.[1] The 2010 prevalence of total hip arthroplasties (total hip replacements) in the United States was 0.83% (2.5 million people, 1.4 million women and 1.1 million men).[2] The quarterly incidence for that year was 101,500.[3] Associated trends over the previous decade are an increase in the number of people receiving total hip arthroplasty procedures, an increase in the number of successes with the prostheses, and an increase in the number of people living longer with the prostheses.[2] If these trends continue, by 2030, an estimated 4 million people will have total hip replacement prostheses.[2] Total hip arthroplasty is a complex, effective surgery that provides pain relief and improved function[4]; however, it is associated with an increased long-term mortality and morbidity compared with matched controls.[5] Additionally, the financial burdens on the health care system and individual are staggering.

The significant risk factor for hip replacement surgery is arthritis.[2] And, it is quite common for osteoarthritis (OA) and osteoporosis to be comorbidities in older adults.[6] It was reported that 74% of females with OA of the hip had osteopenic or osteoporotic signs of increased bone turnover.[7] Unfortunately, prevention of OA or its treatment with medication has limitations and may increase the demand for joint replacement.[2]

Smoking has deleterious effects throughout the body. However, the relationship between smoking and bone

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mineral density is complex and inconclusive.[8] In one study, the relationship between smoking and bone mineral density became non-significant in adjusted analyses.[9] Similarly, body mass index (BMI), a risk factor for OA which leads to total hip arthroplasty, was not related to smoking.[10] However, other researchers have noted smoking is associated with decreased bone mass at the trochanter site in men but not women.[11] And other researchers determined that smokers had reduced bone mass compared with nonsmokers at all bone sites, especially at the hip where the bone mass was one-third standard deviation less than never smokers.[12] Some researchers indicated smoking increased the risk of total hip replacement for women, but decreased the risk of total hip replacement for men.[8] And, on the contrary, a group of researchers indicated male and female smokers were 40 and 30%, respectively, less likely to have total hip replacement, controlling for age, BMI, socioeconomics, and exercise[13] with a potential mechanism of nicotine having a beneficial effect on chrondrocyte function.[14]

The relationship between hip/knee replacement surgery and type 2 diabetes mellitus (T2DM) was examined in a systematic review. Of the included studies, three showed no association of hip/knee replacement with T2DM; one showed a reduction in risk for persons with T2DM and one showed an increased risk.[15] In a study using data from the Pittsburgh, Pennsylvania, the site of the Osteoporotic Fractures in Men study, men with T2DM had a higher total hip bone mineral density than men without DM.[16] Similarly, in secondary data analysis of National Health and Nutrition Examination Survey data of adults, ages 50 years or older, researchers did not find a significant association between T2DM and OA.[17] And, in a meta-analysis pooling 295,100 participants, T2DM was not an independent risk factor for OA; nevertheless, 16 of the 31 studies examined showed a positive association between OA and T2DM.[18]

To the authors' knowledge, the association of hip replacement surgery among people with T2DM comparing those with nicotine dependence and those without has not been examined. As the risk of hip replacement surgeries has been on the rise, it is important to determine burdens and examine risk factors among vulnerable groups for potential, targeted interventions.

Theory for Hip Replacement Needs among People with T2DM

The theory used for this study was the Krieger eco-social epidemiological theory.[19] In the theory, there is a health–-disease/condition continuum in which a person embodies multiple factors including those which are biological, behavioral, and physical/environmental. A person's health–-disease/condition continuum is also influenced by systematic domains such as class, gender, race/ethnicity, and the ability of the person to have agency over his/her/their health. An individual also embodies the societal and eco-social factors including household, area/group, region, nation, and world.[19] The theory describes the health–disease continuum as occurring across the lifespan with an interaction of exposure, susceptibility, and resistance to disease. In the theory, social and economic hardship, exposure to hazardous materials/conditions; social trauma/abuse; inadequate health care; and targeting marketing of harmful substances (tobacco, alcohol, and licit/illicit drugs) are paths to the embodiment of disease.[19] As the theory for health–disease/conditions continuum is complex, not all variables can be considered in every study. However, if possible, certain factors should be included. These factors involve social factors (sex, race, age, marital status, etc.) and environmental factors (household income/poverty level, educational level, smoking, drinking, and other negative environmental exposures).

Purpose

The purpose of this research is to examine the association between nicotine dependence (yes, no) and incident hip replacement surgery (yes, no) among people with T2DM.

Methods

Study Design

The study had a cross-sectional secondary data analysis design.

Data Source

TriNetX (Cambridge, MA) Research network system provided the publicly available data for the research. TriNetX researchers collect data from a network of facilities and provide access to de-identified electronic health/medical record (EHR) data for researchers. The data are presented in a cloud-based system with the ability to directly perform observational research. A Western Institutional Review Board acknowledgment is in place for TriNetX to present data in outputs of frequencies, summaries, and analyses.[20] Data collection is ongoing and current.[20] The health care facilities engaging with TriNetX include facilities that provide inpatient, outpatient, and specialty care services across the United States.[20]

Measures

In this study, the data were limited to United States patients, ages 18 years or older, who had a T2DM diagnosis based upon the International Classification of Diseases, Tenth Revision, Clinical Modification codes from E08 to E13. Data used in this study were those available from system inception to March 17, 2021. The outcome variable was the risk of hip replacement surgery (codes, 0SR90JZ, 0SRB0JZ, 0SR90JA, 0SRB0JA, 0SR90J9, 0SRB0J9, 0SRR0JZ, and 0SRS0JA). The key predictor variable was the diagnosis of nicotine dependence coded with F17. Other variables of interest included in the study were sex, race, socioeconomic status (SES, Z55–Z65 codes), BMI (Z68 codes); hypertension (I10–I16 codes), and chronic obstructive pulmonary disease (COPD, J44 codes).

Statistical Analysis

Sample characteristics were described with frequency analyses. Propensity score matching (PSM) was used for logistic

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regression analyses of the risk of total hip replacement among people with T2DM with nicotine dependence versus people with T2DM who did not have nicotine dependence. The TriNetX system includes longitudinal data so that an outcome event (hip replacement surgery in this case) can be identified to occur after other criteria have been met. The system uses PSM to imitate randomization to provide analyses that may be interpreted as risk. The PSM balances the cohorts to distribute variables known and unknown between groups. The TriNetX software analytics was used for the data analysis. It consists of a Java 1.8.0_171, R 3.44 platform (R core Team, Vienna, Austria) and Python 3.6.5 platform.[21] A priori significance was set with an α value at less than 0.05.

Results

The sample characteristics before and after PSM are presented in ►**Table 1**. The sample was matched on age, sex, race, hypertension, COPD, BMI, and SES. After PSM, there were 1,302,414 participants; 651,207 participants with nicotine dependence and 651,207 without nicotine dependence. The sample mean age was 60.3 years. There were 585,081 (44.9%) women, and 841,988 Whites (64.6%) in the sample. There were 929,394 (71.4%) individuals reporting hypertension.

Before PSM, the risk ratio of hip replacement surgery among people with T2DM was 1.09 (95% confidence interval [CI]: 1.04, 1.16; $p = 0.0069$) for participants with nicotine dependence as compared with those without nicotine dependence. It increased to 1.45 (95% CI: 1.45, 1.57; $p < 0.0001$) after PSM.

Discussion

Statement of Principal Finding

The main finding of this study was that the risk of hip replacement surgery among participants with T2DM who were identified as having nicotine dependence was high. It was significantly higher than participants with T2DM who did not have nicotine dependence recorded (risk ratio: 1.45; 95% CI: 1.45, 1.57; $p < 0.0001$). This result is important as it indicates a greater health care burden among people with T2DM who also have nicotine dependence.

The most common route to nicotine dependence is the use of tobacco products. The most common methods used for tobacco delivery are to smoke it (for example, cigarette, e-cigarette, cigar, pipe, etc.) or to use smokeless delivery systems. The use of tobacco products increases the risk of osteoporosis/OA, major risk factors for hip replacement surgery. In a study of hip fractures in older women, self-rated health and smoking was three times as likely to be related to hip fracture in women reporting intermediate self-related health.[22] Higher hazard ratios (HR) for osteoporotic hip fractures were found in current smokers (HR, 1.21) than non-smokers in a 10-year study of 1,033 women.[23] Also, in a meta-analysis of 59,232 men and women, current smoking was associated with a significantly increased risk of hip fracture (risk ratio, 1.84) compared with non-smokers.[24] Hernigou and Schuind concluded that smokers have an increased risk for fracture, and smoking cessation is significant in reducing this risk.[25] In terms of individuals with T2DM, the research results on the effects of T2DM on bone mineral density are mixed. A recent systematic review and meta-

Table 1 Sample characteristics and risk ratio of hip replacement among people with diabetes and nicotine dependence

Risk ratio	Before propensity matching			After propensity matching		
	Nicotine use, $n = 672{,}854$	No use, $n = 3{,}767{,}536$	*p*-Value	Nicotine use $n = 651{,}207$	No use, $n = 651{,}207$	*p*-Value
	1.09 (95% CI: 1.04, 1.16)	**Reference**	**0.0069**	**1.45 (95% CI: 1.34, 1.57)**	**Reference**	**< 0.0001**
Incident hip replacements (*n*)	264	15,588		1,517	1,048	
Age, y, mean ± SD	60.2 ± 13.6	65.5 ± 15.7	< 0.0001	60.3 ± 13.7	60.3 ± 14.1	0.1974
Female	44.9% (302,157	51.3% (1,931,248)	< 0.0001	45,2% (294,160)	44.7% (290,921)	< 0.0001
Male	55.1% (370,567)	48.7% (1,822,775)	< 0.0001	54.8% (356,917)	55.3% (360,155)	< 0.0001
White	64.9% (436,738)	63.0% (2,372,290)	< 0.0001	64.9% (422,591)	64.4% (419,397)	< 0.0001
Black	22.9% (153,762)	16.7% (630,673)	< 0.0001	22.6% (146,948)	23.0% (149,867)	< 0.0001
Race unknown	10.5% (70,650)	16.9% (635,839)	< 0.0001	10.8% (70,014)	10.8% (70,258)	0.4904
Hypertension	72.0% (484,431)	57.69% (2,170,745)	< 0.0001	71.2% (463,747)	71.5% (465,647)	0.0002
COPD	21.3% (143,010)	4.9% (186,016)	< 0.0001	19.0% (123,569)	18.8% (122,532)	< 0.0001
BMI	19.0% (127,661)	9.1% (341,485)	< 0.0001	17.8% (115,961)	18.8% (122,532)	< 0.0001
SES[a]	4.3% (28,894)	1.0% (34,566)	< 0.0001	3.5% (22,537)	3.7% (23,952)	< 0.0001

Abbreviations: BMI, body mass index in kg/meter^2; CI, confidence interval; COPD, chronic obstructive pulmonary disease; SD, standard deviation; SES, socioeconomic status.

[a]This variable included persons potential health hazards related to socioeconomic and psychosocial circumstances.

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analysis revealed no relationship between T2DM and low bone density.[26] However, findings in a systematic review and meta-analysis were that T2DM was significantly more likely to be associated with the development or presence of OA.[27] Eller-Vainicher et al reported that individuals with T2DM have an increased risk of bone fragility fractures compared with individuals without T2DM.[28] One mechanism may be that hyperglycemia contributes to joint vulnerability through the formation of advanced glycation end-products in the cartilage, causing the joint to be more susceptible to routine stress.[29] The additional burden of smoking within individuals with T2DM was shown to increase the risk of hip replacement surgery in this study.

Strengths and Limitations

This research has several strengths. It is a large, national project using current data. It was possible to match groups to provide similar characteristics among the participants. There was a large sample size for both groups. It was possible to use the data to create the outcome variable to follow diagnoses of T2DM and the presence or absence of nicotine dependence.

However, there were some limitations. Other, unknown variables could be confounding the results. Also, nicotine dependence may not have been recorded in the electronic health history, leading to a misclassification bias, or patients may have answered that they did not have nicotine dependence when, in fact, they did (social desirability bias). In both of these cases, the results would have tended toward the null. The opinion as to when a person should undergo hip-replacement surgery varies widely. Comorbidities (in addition to T2DM) enter into the decision process as to when surgery is advised and may have influenced the results. As a result of such comorbid confounders, nicotine use may not be causative due to the other factors that may coexist with smoking and nicotine use. Nevertheless, the association strongly indicates nicotine dependence in persons with T2DM is a potential risk factor for future hip replacement surgery.

Implications for Policy, Practice, and Research

In this study, the mean age in the sample was 60 years, an age at which patients are not usually on Medicare and may have limited access to health care due to financial constraints. Nevertheless, many patients that have T2DM are seen frequently for the maintenance of glucose regulation and preventive care. Typically, physical activity is evaluated on yearly visits for patients with T2DM. Implementation of an EHR program that flags patients with T2DM and nicotine dependence could be used to alert practitioners to consider earlier/more frequent assessments for hip fractures and screening for fall risks. Bone mineral density (BMD) testing could be indicted for women earlier if T2DM and nicotine dependence are present. Although BMD is not indicated for men until a fracture occurs, health care providers may be prompted to evaluate men with T2DM and nicotine dependence for BMD levels to rule out osteopenia.

It is important for health care providers to communicate tobacco cessation messages to their patients who use tobacco, not only for health reasons but also as life and health insurance premiums may be increased if their members are identified as using nicotine, or help could be provided to encourage the members' providers to a whole health approach. That is, to create a system in which providers are alerted to members that need help with tobacco cessation, lowering their risks of T2DM and evaluating them for fracture risk as a secondary prevention measure at the yearly health maintenance visit.

Policies are currently in place that address tobacco cessation in health care. To further reduce the risk of fractures, targeted education on lifestyle changes to minimize complications of T2DM could be added to patients with T2DM that use tobacco while promoting tobacco cessation. Since BMD is not a routine screen for men, insurance companies can authorize this screening method for men prior to the average age of fracture. At that point, interventions to prevent ongoing bone loss can be instituted.

Future researchers should investigate additional risk factors that contribute to osteopenia. Diet, weight-bearing activity, hormonal status, and vitamin D levels should be evaluated in men, as well as women, to determine the added risk to the diagnosis and subsequent outcome. Additional studies are needed for methods to successfully aggregate risk factors in EHR and flag patients' charts accordingly. Identifying patients at risk will provide insight into common factors that inform interventions and lifestyle modifications. Understanding the population and demographic factors of patients at risk will provide insight into creating programs and education. Additional funding is needed to support the expansion of such programs, public service announcements to not initiate combustible or smokeless tobacco use, and similar educational efforts that could save thousands of lives and thousands of hours of quality life.

Conclusion

Individuals with T2DM and nicotine dependence are at an increased risk for hip replacement surgery. Health care providers need to make their patients with T2DM aware that tobacco product use can result in poor glycemic control due to insulin resistance. In caring for people with T2DM, nicotine dependence cessation is pertinent to lower diabetic complications, which potentially includes the need for hip replacement surgery. Health care providers should be encouraged to assess all patients with T2DM for tobacco use and provide or refer for evidence-based tobacco cessation pharmacotherapy combined with counseling.

Note

Authors have followed the guidelines of the International Committee of Medical Journal Editors in which they have substantial contributions to (1) conception and design, or acquisition of data or analysis and interpretation of data; (2) drafting the article or revising it critically for important intellectual content; and (3) final approval of the version to be published.

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Data Availability

The data used to support the findings of this study are held by TRINET-X, https://trinetx.com.[30]

Ethical Statement

The West Virginia University provided the acknowledgment of this study as meeting the characteristics of a non-human subject research study.

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Conflict of Interest

None declared.

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