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Tobacco use as a risk factor for reoperation in patients with stress urinary incontinence: a multi-institutional electronic medical record database analysis

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Abstract

Introduction and hypothesis—Recurrence rates of stress urinary incontinence after surgery are reported to be between 8 to 15%. Both surgical technique and non-surgical risk factors have been shown to affect post-operative outcomes. Tobacco use is a possible risk factor that may increase the surgical failure rate, however, there are currently conflicting reports in the literature regarding the affect of tobacco use on surgical outcomes. Our objective is to evaluate the effect of tobacco use on the risk of repeat surgery for stress urinary incontinence (SUI).

Methods—We performed a retrospective cohort analysis using a de-identified clinical database from a large multi-institution electronic health records data web application EPM:Explore™ (Explorys Inc, Cleveland, Ohio) to identify women with and without a history of tobacco use who underwent reoperation for stress urinary incontinence within 2 years of the first surgery. We then evaluated previously described risk factors for reoperation: diabetes mellitus (DM), pelvic organ prolapse (POP), anti-muscarinic (AM) use at initial surgery, obesity, and advanced age on rate of reoperation and the impact of tobacco use on these risk factors.

Results—Tobacco use was associated with an increased rate of a second surgery for SUI (OR=1.43, $p < 0.001$), as was anti-muscarinic use (OR = 1.68, $p < 0.001$), DM (OR = 1.21, $p = 0.005$), age >50 years (OR= 1.16, $p = 0.040$), and BMI > 30 kg/m² (OR = 2.97 $p < 0.001$). The odds of a second surgery for SUI in patients who used tobacco and anti-muscarinic medications or had pelvic organ prolapse were lower when compared to non-users. The odds of a second surgery for SUI were higher in patients who used tobacco and had asthma when compared to non-users who had asthma.

Conclusions—Tobacco increases the overall risk of second surgery for SUI, however, in patients with specific risk factors, tobacco use is associated with a decrease risk of reoperation.

Keywords

Stress urinary incontinence; Tobacco use; Risk factors

Introduction

Stress urinary incontinence (SUI) is defined as involuntary leakage of urine with increased abdominal pressure, such as with exertion, coughing, and laughing [1]. It is estimated to affect 4% to 35% of women in the US and can lead to significant functional impairment and decreased quality of life [2]. Approximately 200,000 procedures annually are performed in the United States alone for urinary incontinence, with one-third performed for SUI [3]. Recurrence rates for SUI after surgery have been reported between 8 to 15% [4–6]. While choice of surgical technique significantly influences treatment outcomes, non-surgical risk factors are also associated with treatment failures and reoperation. These risk factors include: advancing age, increasing stage of pelvic organ prolapse (POP), diabetes mellitus (DM), obesity, and anti-muscarinic (AM) use at the time of the initial surgery [3,6–11].

Cigarette smoking is a commonly cited risk factor for adverse surgical outcomes such as increased healing time, myocardial infarction, venous thromboembolism, and decreased quality of life after incontinence surgery [8]. The impact of cigarette smoking specifically on the failure rates of primary surgery for SUI remains unclear. A positive association between current tobacco use and stress incontinence has been reported by several investigators and Erata found that a history of tobacco use was found to be a risk factor for having corrective surgery for SUI [7,8,12]. In contrast, Daneshgari reported a possible protective effect within 1 year of the initial surgery [3]. Other investigators have suggested that smokers were more likely to manifest symptoms of detrusor overactivity rather than stress urinary incontinence [13,14].

Given that surgical failure rates increase with each subsequent procedure [15], a better understanding of tobacco's impact on surgical outcomes could potentially lead to reduced failure rates of initial incontinence procedures.

Materials and methods

In January of 2014, we performed a retrospective cohort analysis using a de-identified clinical database from a large multi-institution electronic health records data web application EPM:Explore™ (Explorys Inc., Cleveland, OH, USA) to identify women with and without a history of tobacco use, who underwent a second SUI surgery within 2 years of the first surgery. The Explorys platform is in compliance with the Health Insurance Portability and Accountability Act of 1996 (HIPPA) and incorporates clinical data from electronic health records and other health information such as billing and scheduling [15]. Nineteen unique hospital systems participate in the database, including our institution (Appendix 1). Because not all involved healthcare systems utilize the same medical record systems, data involving diagnoses, procedures, and findings are standardized using the Systematized Nomenclature for Medicine – Clinical Terms, SNOMED-CT [16]. Pharmacologic data, of the specific drug and pharmaceutical class, are standardized using SNOMED and RxNorm. At the time of this

study, Explorys contained inpatient and outpatient data of 38.5 million unique patients. Each patient had a clinical record covering an average span of 1642 days, with a range of 1 day to 5475 days. The duration 2 years (730 days) from the initial surgery, was chosen to capture the maximum number of patients undergoing a reoperation within the same hospital system, and limit the number of patient attrition in the data set.

We identified 109,140 women with stress urinary incontinence. We then identified 15,360 women (14.1%) who underwent their first surgery for stress urinary incontinence between January, 1999- and January, 2014 using the following SNOMED-CT terms: “urinary incontinence/sling operation”, “repair of stress incontinence by suprapubic sling”, “repair of stress incontinence”, “bladder neck operation for female stress incontinence”, “laparoscopic repair of urinary stress incontinence using sling”, “insertion of transobturator tape for female urinary incontinence”, “urethrocytopexy by levator muscle sling”, “fixed suspension procedure of bladder neck”, “introduction of tension free vaginal tape”, “urethropexy”, “Marshall Marchetti Krantz retropubic suspension of urethra”, and. “retropubic urethral suspension”. We then identified those women who underwent a second surgery within 730 days of the initial procedure using these same clinical terms.

Tobacco users were identified by using the following inclusion SNOMED-CT terms: “diagnosis: tobacco dependence syndrome”, “finding: tobacco user”, “social history: uses (tobacco)”; and exclusion terms: “finding: non-smoker”. Non-users were identified with the following inclusion terms: “diagnosis: tobacco dependence syndrome (NOT)”, “finding: tobacco user (NOT)”, “social history: uses (tobacco) (NOT)”; and exclusion terms: “diagnosis: tobacco dependence syndrome”, “finding: tobacco user”, “social history: uses (tobacco)”. Patients with unknown tobacco use history were excluded using the term “social history: unknown (tobacco): (NOT)”. This created four distinct groups of tobacco users and non-users with or without a second SUI surgery. All population counts were rounded to the nearest 10. EPM:Explore™ application does not report population sizes less than 10 in compliance with HIPPA, to prevent patient identification.

To analyze the association between smoking history and risk of a second incontinence surgery and account for possible confounders, we used multiple logistic regression analyses in R [17]. The level of statistical significance was set to 0.05. The focal predictor variable in our model was tobacco use. The control variables included pelvic organ prolapse, diabetes mellitus, BMI > 30 kg/m², asthma, anti-muscarinic use and age. These were chosen because they have been previously described as likely risk factors for primary surgical failure [3, 6–11]. We included asthma to evaluate the effect of chronic cough instead of COPD to avoid confounding the effect of tobacco use given that the majority of chronic smokers develop a measurable decrease in lung function [18]. Additionally, we used separate multiple logistic regression models in the subset of individuals who used tobacco and in the subset of individuals who did not in order to assess whether the magnitude or direction of effect of each control variable differed between the two subgroups. Statistical significance of difference in effect was determined via a full model including main effects and interactions with tobacco.

This study had an Institutional Review Board (IRB) review waiver at our institution because it included only de-identified population data.

Results

A total of 15,360 women underwent their first surgery for SUI, of these, 3,780 were tobacco users and 11,580 were non-users. Of these patients, 1,240 women underwent a second surgery for SUI within 2 years, including, 420 tobacco users and 820 non-users (Table 1). The reoperation rate in our cohort was 8.0% for all patients. In tobacco users, 12.5% required a second surgery and 7.6% of non-users required a second surgery [odds ratio OR 1.63, $p < 0.001$].

Table 1 shows the odds ratios, p-values and 95% confidence interval (CI) for our regression model based on the full study population. After controlling for other risk factors, we found BMI > 30 kg/m², age > 50 years, anti-muscarinic use and diabetic status to be significantly associated with odds of second SUI surgery, while POP and asthma were not. BMI > 30 kg/m² had the greatest associated risk of a second surgery for SUI. Women with a BMI > 30 kg/m² had odds of second SUI surgery 2.97 times greater (95% CI [2.47, 3.56], $p < 0.001$) than women with a BMI > 30 kg/m². Women 50 years of age or older were 16% more likely (95% CI [1.01, 1.34], $p = 0.033$) than women 49 years or younger to undergo a second surgery. An increased risk of reoperation was also seen in women using anti-muscarinic medications for urgency symptoms at the time of the initial surgery, with 68% greater odds (95% CI [1.63, 2.21], $p < 0.001$) in those using anti-muscarinic medications compared to those who were not on these medications. Women with diabetes mellitus at the time of first surgery had 21% greater odds of second SUI surgery (95% CI [1.06, 1.39], $p = 0.005$) compared to non-diabetics. In the full study population, asthma and POP were not found to be significantly associated with odds of second SUI surgery, with odds ratio for asthma at 1.05 (95% CI [0.92, 1.19], $p = 0.49$) and for POP at 1.03 (95% CI [0.91, 1.16], $p = 0.64$). Table 2 shows the regression analyses stratified by tobacco use. Figure 1 shows the odds ratio estimates and 95% confidence intervals for second surgery stratified by tobacco use and interaction p-values, showing the statistical evidence for a difference in odds ratios between tobacco users and non-users. After controlling for other risk factors, BMI > 30 kg/m², age > 50 years, and diabetic status did not significantly differ in their respective odds ratios across the strata ($p = 0.228$, $p = 0.185$ and $p = 0.125$, respectively), while POP, asthma and anti-muscarinic use did. Patients with POP who did not use tobacco (versus patients without POP and who did not use tobacco) showed a tendency toward increased odds of undergoing a second SUI surgery [OR=1.13 (95% CI [0.98, 1.31]), $p = 0.096$]. In contrast, we see a tendency toward decreased odds of second surgery in tobacco users with POP [OR=0.86 (95% CI [0.70, 1.06]), $p = 0.157$]. While neither of these marginal odds ratios was statistically significant, the difference in risk associated with POP between tobacco users and non-users was significant ($p = 0.024$).

Asthma was significantly associated with increased odds of second surgery in smokers [OR=1.26, 95% CI [1.01, 1.57], $p = 0.04$], but no association was found in non-smokers [OR=0.96, 95% CI [0.81, 1.13], $p = 0.584$] (Table 2). The difference in these odds ratios was statistically significant ($p = 0.049$).

The risk of a second surgery due to anti-muscarinic use at the time of the first surgery was decreased in tobacco users [OR=1.32, 95% CI [1.05, 1.65], $p=0.016$] compared to non-users [OR = 1.84, 95% CI [1.57, 2.15], $p<0.001$] (Table 2). This difference in odds ratios for anti-muscarinic use between tobacco users and non-users was also statistically significant ($p = 0.016$) (Fig. 1).

Discussion

Non-surgical factors, such as BMI, age, and co-morbid conditions such as diabetes and co-existing detrusor over activity, have been shown to adversely affect outcomes of SUI surgery [3, 7–11, 19–21]. Tobacco use, and smoking in particular, is a well described cause of adverse surgical outcomes, however, the evaluation of tobacco use on surgical management of SUI has yielded inconsistent results, particularly on the risk of undergoing a second surgery. This may reflect to the fact that previous studies were not sufficiently powered to specifically evaluate the effect of tobacco use on treatment failure.

We used a large, de-identified, multi-hospital medical record database to determine whether tobacco increases the risk of patients undergoing a second surgery for stress urinary incontinence. In addition to tobacco use we also analyzed commonly acknowledged risk factors for recurrent SUI, including: BMI > 30 kg/m², age > 50 years, anti-muscarinic use, pelvic organ prolapse and diabetes mellitus and whether tobacco use affects these variables. We chose to include all surgical techniques used for stress urinary incontinence rather than only focusing our analysis on mid-urethral slings, because data collection began with the year 1999, and non-sling procedures were still frequently performed in the late 1990s and early 2000s.

In our model, tobacco use was positively associated with an increased risk of undergoing a second surgery for stress urinary incontinence when controlling for other variables. Previous studies which evaluated tobacco use and risk of reoperation showed contrasting results, either showing a protective effect of smoking or no statistically significant relationship between smoking and reoperation rates [3, 7, 22, 23]. The difference between our findings and those of previous studies may be the result of our significantly larger sample size, allowing us greater power to detect the previously unrecognized effect of tobacco on surgical outcomes.

Consistent with previously published results, BMI greater than 30 kg/m², anti-muscarinic use at the time of the first surgery, diabetes mellitus, and age greater than 50 years were all associated with an increased risk of a second surgery. In the stratified regression model, asthma was associated with a significant increase in risk of reoperation in patients who used tobacco compared to non-users. This may be due to worse cough in asthmatics who are tobacco users compared to non-users and possible compounding of cough symptoms due to presence of emphysema leading to recurrence or persistence of SUI symptoms.

As the majority of chronic smokers will develop some component, of COPD, one possible mechanism by which tobacco use may increase the rate of reoperation is an increase in intra-vesicular pressure due to chronic cough being more prevalent in users compared to non-

users [24]. Bump et al demonstrated that smokers tended to develop SUI at an earlier age despite stronger urethral sphincter tone and lower risk profile compared to non-smokers and attributed this to more violent coughing in smokers [13]. Additionally, there is association between chronic smoking and decreased muscle mass and increased muscle fatigability due to chronic hypoxemia which may contribute to pelvic floor dysfunction leading to both a predisposition to developing SUI as well as postoperative persistence or recurrence of symptoms [25–26].

Interestingly, in the stratified model, all variables, with the exception of asthma, were associated with a decreased risk of reoperation in users compared to non-users. However, only the interactions between tobacco use and asthma, anti-muscarinic medication use and pelvic organ prolapse were statistically significant. Patients who were prescribed anti-muscarinic medications prior to their first surgery and used tobacco had a lower risk of a second surgery compared to patients who were taking anti-muscarinic medications but did not use tobacco. In patients who used tobacco, POP tended to be protective against the risk of a second surgery, whereas in non-users the risk tended to be increased in the presence of POP.

These findings may explain the “protective” effect of tobacco use described in other studies [3,23]. The reduction in risk may also be attributable to the fact that patients with a history of tobacco use may actually be less likely to undergo surgery due to increased baseline medical co-morbidities, associated with increased risk of adverse surgical outcomes including acute myocardial infarction, obesity and diabetes mellitus. These patients may be more likely to opt for less-invasive treatments.

In interpreting the results, several limitations of this study must be considered, one of these being the retrospective design relying on electronic medical record data of tobacco use history. Tobacco use is based on patient self-reporting and provider documentation into the electronic medical record which is utilized by the EPM:Explore™ platform. While this allows for the identification of current users it does not provide specific information regarding the amount of tobacco consumed or chronicity of use. Several studies have shown population data based of self-reported tobacco habits tends to be lower actual use, possibly leading to an exclusion bias in our dataset [27–28].

Another limitation of the retrospective design is that procedure coding in the electronic medical record using SNOMED-CT terms could either be broad or specific, e.g “urinary incontinence/sling operation” or “introduction of tension free vaginal tape”. While both may be used to code for a tension-free vaginal tape (TVT), the former term may also be used to code for a non-TVT procedure, such as a fascial sling. A recent Cochrane review showed that currently performed procedures demonstrate comparable efficacy, however, the inability to include the type of procedure in the regression analysis is a possible confounding factor [29]. The EPM:Explore™ platform also cannot be reliably used to distinguish between stages of pelvic organ prolapse. This may account for why POP was not a statistically significant risk factor for reoperation in contrast to previous observations that advanced stage (stage III and IV) is associated with recurrent surgery [3,22]. The major strength of this study is the large cohort of patients included, in particular patients who were tobacco

users and underwent a second procedure for SUI. Our results are also applicable to the general population because they represent patients across all regions of the United States. Our findings suggest that there is a correlation between tobacco use and an increased risk of undergoing a second surgery for stress incontinence, further research into the pathophysiology of SUI due to tobacco exposure is required in order to better understand how it impacts surgical outcomes.

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Appendix 1: institutions participating in Explore platform

1. Cleveland Clinic Foundation: Cleveland, OH
2. Adventist Health System: Altamonte Springs, FL
3. University Hospitals: Cleveland, OH
4. MetroHealth Medical Center: Cleveland, OH
5. OhioHealth: Columbus, OH
6. Meritus Health: Hagerstown, MD
7. Centura Health: Englewood, CO
8. MedStar Health, Baltimore, MD-Washington, D.C.
9. Legacy Health: Portland, OR
10. St. Joseph Health: Irvine, CA
11. Catholic Health Partners: Cincinnati, OH

12. Trinity Health: Livonia, MI
13. Catholic Health East: Newtown Square, PA
14. Lancaster General Health: Lancaster, PA
15. UnityPoint Health: Des Moines, IA
16. Akron General Health System: Akron, OH
17. Summa Health System: Akron, OH
18. Baylor Scott and White: Dallas, TX; Temple, TX
19. Trinity Mother Frances Hospitals and Clinics: Tyler, TX
20. The Queen's Medical Center: Honolulu, HI

Fig. 1. Odds ratio estimates and 95 % confidence intervals for second surgery stratified by tobacco use. The p values located above each risk factor are interaction p values

Table 1

Multiple logistic regression results for population

	Estimated OR	95 % CI	<i>p</i> value
Tob.	1.43	1.26–1.62	<0.001
BMI>30 kg/m ²	2.97	2.47–3.56	<0.001
POP	1.03	0.91–1.16	0.641
DM	1.21	1.06–1.39	0.005
AM	1.68	1.48–1.90	<0.001
Age 50	1.16	1.01–1.34	0.033
Asthma	1.05	0.92–1.19	0.488

OR odds ratio, *CI* confidence interval, *BMI* body mass index

Table 2

Multiple logistic regression results stratified by tobacco use

	Estimated OR	95 % CI	<i>p</i> value
Tobacco users			
BMI>30 kg/m ²	2.53	1.82–3.50	<0.001
POP	0.86	0.70–1.06	0.157
DM	1.03	0.80–1.32	0.823
AM	1.32	1.05–1.65	0.016
Age 50	1.04	0.83–1.29	0.731
Asthma	1.26	1.01–1.57	0.040
Nonusers			
BMI>30 kg/m ²	3.22	2.58–4.02	<0.001
POP	1.13	0.98–1.31	0.096
DM	1.30	1.10–1.53	0.002
AM	1.84	1.57–2.15	<0.001
Age 50	1.26	1.05–1.51	0.013
Asthma	0.96	0.81–1.13	0.584