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ORIGINAL RESEARCH

PEYRONIE'S DISEASE

Increased Risk of Incident Disease in Men with Peyronie's Disease: Analysis of U.S. Claims Data

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ABSTRACT

Background: The subsequent health risks associated with Peyronie's disease (PD) are unknown.

Aim: This cohort study assesses the risk of developing auto-immune conditions and common chronic health conditions after a diagnosis of PD. We hypothesize that an increase in auto-immune disease will be evident in men with PD, as has been suggested in smaller studies.

Methods: We determined the longitudinal incidence of 13 auto-immune diseases and 25 common chronic conditions in a cohort from the Truven Health Analytics (Ann Arbor, Michigan, USA) database from 2007−2013. The cohort included men with 1 of 3 exposures in 2007: (1) men with PD, (2) men with erectile dysfunction (ED) but not PD, and (3) men without PD or ED, matched on age and follow-up duration.

Outcomes: To assess incidence, we utilized a Cox regression model adjusting for age, smoking, obesity, health care visits per year, urology visits per year, and years of follow-up.

Results: We included 8,728 men with PD; 204,147 men with ED; and 87,280 controls. Men with PD had an increased risk of developing benign prostatic hyperplasia (hazard ratio [HR] 1.21, 95% CI 1.16−1.27), prostatitis (HR 1.21, 95% CI 1.12−1.31), and lower urinary tract symptoms (HR 1.10, 95% CI 1.05−1.16) when compared to both men with ED and age-matched controls without ED or PD even when controlling for the number of urology visits per year. Compared to controls, men with PD also had an increased risk of developing keloids. No significant risk for any auto-immune disease was observed.

Clinical Implications: Clinicians should have heightened awareness for these relevant co-morbidities when treating men with PD.

Strengths & Limitations: Utilizing a claims database provides one of the largest cohorts of men with PD ever published but claims databases lack some individual patient data such as risk factors and demographic information relevant to PD, including: penile injury, history of urologic procedures, and other lifestyle factors.

Conclusion: Men with PD had a higher risk of benign prostatic hyperplasia, lower urinary tract symptoms, prostatitis, and keloids after a diagnosis of PD, but no increased risk of auto-immune conditions. These findings suggest a common etiology for these conditions that may manifest itself in diseases at different times in men's life cycle. **Pastuszak AW, Rodriguez KM, Solomon ZJ, et al. Increased Risk of Incident Disease in Men with Peyronie's Disease: Analysis of U.S. Claims Data. J Sex Med 2018;15:894−901.**

Key Words: Peyronie's Disease; Auto-Immune Disease; Prostatic Hyperplasia; Benign; Prostatitis; Cardiovascular Diseases; Insurance Claim Reporting

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INTRODUCTION

Peyronie's disease (PD) is a progressive condition resulting in fibrous plaque formation within the tunica albuginea of the penis, in some cases leading to penile deformity (shortening, narrowing, and/or curvature), pain with intercourse, and considerable distress.[1] The incidence of PD is estimated to be 22.4−25.6 per 100,000 men and most commonly presents in the 5th decade of life.[2,3] Although PD most commonly presents

in older men, it can affect boys and men from adolescence into late adulthood.[4–7] Given the pathogenesis of PD, there is particular interest in the association between PD and other sclerotic conditions (eg, auto-immune diseases).

Superficial fibrosing disorders related to PD include Dupuytren disease (DD), a fibro-proliferative disorder resulting in palmar fibrosis, and Ledderhose disease (LD), which results in fibrosis of the plantar fascia. Both DD and LD, like PD, show strong genetic links, and recent genome association studies have identified several risk-conferring polymorphisms for the former 2 diseases.[8–10] A 2010 study by Rhoden et al[11] compared men with PD to age-matched controls with similar rates of smoking and alcohol consumption demonstrating that DD was more frequent among men with PD compared to controls ($P < .001$) and that PD was not associated with serum androgen levels. A 2015 study by Ventimiglia et al[12] investigated the relationship between PD and prevalent co-morbidities; of 1,140 men presenting consecutively to a urology clinic, 13% (n = 148) were diagnosed with PD. Men with PD had higher rates of DD, hypertension, diabetes, and smoking compared to men without PD (all $P < .02$). In multiple studies of men with PD, the estimates of concurrence of PD and DD range from 3–22%.[13–16]

Few studies have examined the association between PD and auto-immune conditions. In 1997, Schiavino et al[17] assessed 66 patients with PD and 20 age-matched controls, and found that 76% of patients with PD had 1 or more abnormal immunologic tests compared to only 10% of controls ($P < .0001$). In their 2015 study of co-morbidities among 148 men with PD, Ventimiglia et al[12] also found that auto-immune diseases were more prevalent among men with PD compared to controls ($P < .01$). Notably, psoriasis, psoriatic arthritis, and rheumatoid arthritis were more common in men with PD (all $P < .03$). There was no association between PD and auto-immune thyroiditis, systemic lupus erythematosus, systemic sclerosis, granulomatosis with polyangiitis, or vitiligo.[12] While the literature suggests a relationship between PD and auto-immune diseases, these studies have been limited by small sample sizes and cross-sectional study designs, limiting the impact of the findings. Further, rarely have studies examined the association between PD and other chronic disease outside of auto-immune diseases.

Given existing data suggesting an association between PD and co-morbidity, this longitudinal cohort study examines the relationship between PD and the risk of adverse health outcomes following the diagnosis of PD. Using data from a commercial insurance claims database to provide a large sample size, we compare the incidence of co-morbid conditions in men with a diagnosis of PD, men with a diagnosis of erectile dysfunction (ED) (a related urologic condition commonly seen by urologists), and age- and follow-up–matched control men while using a Cox regression model to control for age, smoking, obesity, physician visits per year, urology visits per year, and years of follow-up. We hypothesize that an increase in auto-immune disease will be evident in men with PD, as has been suggested in smaller studies.

METHODS

Patients

We analyzed data contained in the Truven Health Analytics MarketScan Commercial Claims and Encounters database, which provides de-identified data from adjudicated and paid claims filed for the care of privately insured individuals with employment-based insurance. We accessed all available inpatient and outpatient claims data between 2007 and 2013. While the number of individuals represented within the database varies over time, the more recent MarketScan data contain more than 30 million covered lives. As MarketScan contains de-identified national data, institutional review board approval was not required.

This study focuses on a cohort of men with 1 of 3 exposures: PD, ED (a related urologic condition commonly seen by urologists), and men without PD or ED who were matched to PD patients on age and frequency of follow-up visits (true controls).

To be eligible for inclusion, subjects had to be men, at least 18 years of age, and enrolled in an insurance plan covered by the database for at least 1 year prior to and 1 year after the index date (the first date of a diagnostic code for PD or ED). We excluded men whose claims indicated the diagnosis of another relevant co-morbidity before the index date or within 1 year after the index date to avoid prevalent disease. Relevant co-morbidities were those included in the outcome analysis (see below).

Men with PD were identified by the presence of a PD diagnostic code (*International Statistical Classification of Diseases, 10th Revision, Clinical Modification* [ICD-9-CM] code 607.85). Men with ED were identified by the presence of an *ICD-9-CM* 607.84 diagnostic code. Lastly, we compiled a control group of age- and follow-up–matched men, obtaining a 10:1 control-to-PD ratio based on date of enrollment.

For each man in the cohort, the number of all outpatient visits and urology-specific outpatient visits after the index date was ascertained based on the presence of claims with *Current Procedural Terminology* codes indicating new and follow-up office visits, consultations, or preventative medicine encounters.

Outcome Ascertainment

For the PD and ED groups, we investigated subsequent diagnoses after the index date, while for the control group, we utilized the age matching as a surrogate for an index date.

Diagnosis of the following co-morbid conditions after the index date was assessed using the parenthetical ICD-9-CM codes: hypertension (401), hyperlipidemia (272.0–272.4), diabetes (250), renal disease (580–588), chronic pulmonary disease (490–496), liver disease (570–573), depression (296.2, 296.3, 298.0, 300.4, 309.1, 311), peripheral vascular disease (440–443), cerebrovascular disease (430–438), ischemic heart disease (410–414), other heart disease (420–429), liver fibrosis (571.5), pancreatic cancer (157), lung fibrosis (516.3), benign