

Erectile Dysfunction in Men with Psoriatic Arthritis: A Population-based Cohort Study

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Running Title: Erectile Dysfunction in PsA

Abstract

Objective: To define the incidence of erectile dysfunction (ED) in a population-based cohort of men with psoriatic arthritis (PsA).

Methods: Data pertaining to demographics, ED, and potential confounding diagnosis were extracted from a comprehensive medical record system for a population-based cohort of men with PsA and an age-matched male comparator cohort. Cumulative incidence of ED adjusted for competing risk of death was compared between the two cohorts.

Results: There were 128 age-matched pairs of men with PsA and without PsA in the described cohorts. At baseline there was a 7% prevalence of ED in men with PsA prior to diagnosis compared to a 3% prevalence of ED in the comparator cohort ($p=0.16$). After PsA diagnosis / index date, diagnosis with PsA was associated with an increased risk of ED (age-adjusted HR 1.45, 95%CI: 0.79-2.68), but this association did not reach statistical significance. This was based on 24 cases of ED in the men with PsA and 18 cases within the comparator cohort. No confounding factors or ED treatment strategies differed significantly between men with PsA and ED and comparators with ED.

Conclusion: Men with PsA may have an increased risk of ED, which was detected, but likely underpowered in this study. Whether this difference is secondary to higher prevalence of traditional risk factors of ED in men with PsA compared to general population will require further study.

Introduction

Psoriatic arthritis (PsA) is a systemic inflammatory disease which, in addition to chronic inflammatory joint and enthesal symptoms, confers an increased risk of comorbidities, including both cardiovascular disease (1-8) and sexual dysfunction (9-12). PsA is associated with increased mortality, with cardiovascular disease representing the leading cause of death (13). Cardiovascular events and symptoms are more common in patients with PsA compared to the general population (1, 14). Although the majority of cardiovascular risk has been attributed to traditional cardiovascular risk factors, whether PsA disease activity plays a role is controversial – with some studies showing a role for inflammation (1, 14-16), while others do not (17). This is complicated by the increased prevalence of cardiovascular risk factors in patients with PsA (reviewed in (18)).

Sexual and erectile dysfunction (ED) are common in the general population, and are associated with increased cardiovascular risk. Specifically, sexual dysfunction is a broad term that encompasses many forms of sexual conditions, including areas of desire, arousal, orgasm and pain during sexual intercourse (19). These can include ED, low sexual desire, vagismus, dyspareunia, inability to orgasm, marital difficulties and psychogenic aversion to sexual activity. Sexual dysfunction can apply to either male or female patients, and can be the result of a variety of medical or psychologic states (20). The heterogeneity of sexual dysfunction makes it a difficult area to study, especially when trying to relate to epidemiologic risk. ED, in contrast, is a specific diagnosis that reflects the decreased ability of a man to have and maintain an erection adequate for his desired sexual activity (21, 22). Other definitions including biologic parameters, such as penile blood flow via doppler ultrasound have been described, but are rarely used in clinical practice (23-26). ED is a more specific diagnosis, but can still be secondary to both medical and psychogenic causes. From a vascular perspective, ED can be secondary to atherosclerotic disease, which limits blood flow to the penile vasculature and prevents adequate

erection (27-29). Neurologically, if there is compromise at any level of the nervous system leading to the innervation of the penis, this can also result in ED (30, 31). From a psychological perspective, if a patient is experiencing stress, depression, marital complications or other psychological states, he may not experience an erection upon initiating sexual activity, but will still experience nocturnal erections, which are generally unaffected by psychological state (32).

Vascular ED has even been labelled as a “harbinger of cardiovascular disease,” generally occurring 2-5 years before cardiovascular events or symptoms (33, 34). Given this close association between cardiovascular disease and vascular ED, men with PsA might have an increased rate of ED, potentially occurring earlier or more commonly than in the general population. Moreover, PsA patients have a higher risk of psychiatric comorbidities such as anxiety, depression; and the psychological impact of psoriasis and PsA may be associated with sexual dysfunction (35). Previous studies have shown that PsA (9, 10, 12) and psoriatic disease activity (36-38) are both risk factors for ED in men with psoriasis, a population known to have an increased risk of sexual dysfunction. However, unlike sexual dysfunction, and despite this implied association, the incidence of ED in men with PsA has not been previously analyzed in a population-based cohort and has been minimally analyzed by other methods (39). By defining the incidence of ED in men with PsA, we can begin to explore the relationship between vascular ED and cardiovascular risk within this population of men with a heightened risk of cardiovascular morbidity and mortality.

The specific diagnostic nature of ED (encompassed by ICD-10 codes), its close association with cardiovascular risk, as well as the clear link between vascular ED and cardiovascular risk suggested that ascertaining the incidence of ED, with a focus on vascular etiologies, may help to further delineate cardiovascular risk in PsA and inform risk estimates for cardiovascular risk in men with PsA. Given the association of cardiovascular and psychiatric diseases with ED, and previous studies suggesting an association between ED and psoriatic

disease, we aimed to define the incidence of ED in a population-based cohort of men with PsA in relation to age-matched male comparators.

Materials and Methods

Study Populations. The Rochester Epidemiology project (40) was used to identify PsA and comparator cohorts, who were composed of residents of Olmsted County (Minnesota, USA) aged 18 years or older, as previously published (41). The incident PsA cohort included men diagnosed with PsA (according to the Classification of Psoriatic Arthritis (CASPAR) Criteria (42)) in Olmsted County between January 1st, 1970 and December 31st, 2008. A comparator cohort of men of similar age without PsA was established to match the PsA cohort. Longitudinal follow-up was completed until death, migration from Olmsted county or December 31, 2018. Patients who denied use of their medical records for research purposes were excluded per Minnesota law. However, no patients were excluded for this reason in our study, as noted in Figure 1. This study was approved by the Institutional Review boards at the Mayo Clinic (17-002943) and the Olmsted Medical Center (024-OMC-17).

Data abstraction. Relevant data was abstracted from the medical record and used in conjunction with previously extracted data (1, 41). New data collection included information about ED diagnosis (date of diagnosis, type of ED), risk factors for ED (alcohol concerns, hypogonadism, thyroid disease, Peyronie disease, penile or spinal trauma, systemic neurologic disease, radical prostatectomy or pelvic radiation), treatments for ED (phosphodiesterase 5 / PDE5 inhibitors, testosterone, penile self-injection, penile vacuum device use or surgical penile device placement), and common underlying medications (anti-hypertensives, anti-depressants, anti-androgens) that might predispose to ED. Specifically, ED diagnoses was extracted after identifying relevant ICD-9 and ICD-10 codes. KMW then reviewed the medical records and ensured that the diagnosis was present and made by a physician or mid-level provider. The

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medical specialty (urology, internal medicine, family medicine, etc.) of the provider was also recorded. The diagnosis was made in all cases per usual clinical decision-making employed at the institutions. No formal ED diagnostic criteria were required. In the cases where the clinician formally considered and described in the medical record psychologic components that could be primarily responsible for or contributing to the ED (32), “possible psychogenic ED” was noted. This data was recorded in the secure Research Electronic Data Capture (REDCap) system without personally identifying information.

Statistical Methods. Descriptive statistics (quantity, percentage, mean, standard deviation, etc.) were used to summarize the data. For continuous numeric data, characteristics of the cohorts were compared by Kruskal Wallis testing for statistical significance. For categorical groups, Chi-square testing was used to determine statistically significant differences.

Cumulative incidence of ED in each of the cohorts was estimated adjusting for competing risk of death (43), which accounts for those who died before experiencing ED without censoring, and thus avoids overestimating the incidence of ED in surviving members of the cohort. Subjects who were diagnosed with ED before their respective diagnosis date / index date were excluded from the cumulative incidence analysis. Analyses were performed using SAS version 9.4 (SAS Institute) and R 3.6.2 (R foundation for statistical computing).

Results

There were 128 matched pairs of male PsA patients and age-matched male comparators with similar ages (PsA mean 42.3, standard deviation (SD) 13.1; comparator mean 42.4, SD 13.1, $p=0.97$). There was no difference in the baseline ED prevalence with 7% of the men with PsA (9/128) and 3% of the comparators (4/128, $p=0.16$) having an ED diagnosis preceding their PsA diagnosis / index date (Figure 1). The mean follow-up was 18.8 years (SD 10.5) in the PsA cohort and 19.1 years (SD 9.4) in the comparator cohort.

During the follow-up period, 24 of 119 men with PsA were diagnosed with ED after their PsA diagnosis (20 year cumulative incidence 19%; 95% CI: 13-29%). In the comparator cohort, 18 of 124 men were diagnosed with ED after their index date (20 year cumulative incidence 13%; 95% CI: 8-21%). As shown in **Figure 2**, the cumulative incidence of ED in PsA was higher than the cumulative incidence in comparators, with an increasing divide between the men with PsA and the comparators with time. However, the 45% increased risk of ED in men with PsA compared to men without PsA did not reach statistical significance (age-adjusted hazard ratio: 1.45, 95% CI: 0.79-2.68). Of note, the specialty of the diagnosing clinicians was varied in both groups and included urologists, internal medicine and family medicine clinicians. There was no statistically significant difference in the specialty of the clinicians that diagnosed ED between the two groups ($p=0.55$).

The men who developed ED in the PsA and comparator cohorts were further analyzed to determine if there were any clear confounding factors. As shown in **Table 1**, the potential confounding conditions, including psychological factors, medication use, relevant trauma, cancer therapies and other pre-disposing diagnoses were compared between the two groups. In addition, BMI was not statistically different between the two groups ($p=0.49$). There were no significant differences in investigated confounding factors between the cohorts which may have been due to the small number of affected individuals.

Additionally, the initial treatment strategies (started within the first year after ED diagnosis) were similar between the two cohorts. As shown in **Table 1**, phosphodiesterase inhibitors were highly used in both cohorts, being prescribed within the first year after diagnosis in 67% of men with PsA and ED, and 83% of comparator men with ED ($p=0.22$). Testosterone replacement, penile self-injection and vacuum device were not used within the first year after ED diagnosis in this study.

Discussion

In this study, PsA was associated with a trend toward an increased risk of ED. There were no clear confounding factors observed in patients with ED.

This is the first population-based study to directly investigate the incidence of ED in men with PsA. Previous studies found an increased risk of ED in patients with psoriasis who also had PsA (9, 10, 12). The findings of this study are consistent with previous studies, although the increased risk in this study did not reach statistical significance due to the low numbers of ED cases (24 and 18 cases in the PsA and comparator cohorts, respectively). Of note, the incidence of ED in this study was relatively low within the comparator cohort. However, this was consistent with prior reports of ED incidence and prevalence in men residing in Olmsted County of equivalent age (44, 45).

When considering the implications of ED diagnosis in men with PsA, there are several obvious areas of consideration. First, it has been previously shown that psoriasis has been linked to psychological sequelae that cause sexual dysfunction (46, 47). This is particularly prominent in men who are affected with genital psoriasis lesions (46). However, even in men without psoriasis, anxiety, depression and marital complications can lead to ED (32). Although we did not directly assess the predominance of psychologic comorbidities in this study, we did find that clinicians were considering psychogenic ED in both men with PsA and male comparators (Table 1) at similar rates. There was also similar anti-depressant use in both groups. Although these measures are only proxies of underlying psychological disorders, they do indicate that a large percentage of the ED seen in men with PsA is not fully accounted for by psychologic pathologies. The underlying psychologic impacts of PsA and their implications for sexual dysfunction are an underexplored area that could greatly increase quality of life for men with PsA. Considering sexual comorbidities in men with PsA is important both for future

research directions and for the care of individuals with PsA. It will be important for clinicians to initiate these conversations, as early recognized ED may help to highlight underlying psychological needs.

A secondary area in which diagnosis of ED may have important implications is in the area of cardiovascular morbidity and mortality. Given the common underlying pathology involving atherosclerotic lesions, lipid deposition and arterial insufficiency, vascular erectile dysfunction is physiologically linked to cardiovascular disease (33, 34). In the general population, the implications of ED on future cardiovascular health have been clear – ED generally precedes cardiovascular events and symptoms (33, 34). However, in men with PsA, the implication of ED is less clear. With current knowledge, the prevailing assumption would be that ED also signals increased risk in men with PsA, and should prompt consideration of cardiovascular risk – however at the current time, this remains an assumption. Future work to detail the link between ED and cardiovascular health in men with PsA, with consideration of their baseline heightened cardiovascular risk will help to guide more directed intervention and hopefully inform treatment of a major cause of morbidity and mortality in PsA.

This study has several strengths and limitations inherent to its design. First, this was the first population-based cohort to investigate the incidence of ED in men with PsA. Given the retrospective population-based design, and comprehensive record system, this study was able to account for all men diagnosed with ED by a physician, and able to be considered in the context of a comprehensive medical record. However, it was limited in its ability to detect subclinical ED or undiagnosed ED. This study focused on ED, a more specific diagnosis than previous studies that have investigated overall sexual dysfunction, which may be confounded by sexual aversion secondary to genital psoriatic disease and joint pain (11, 46). Another limitation is that this study is not able to account for diagnostic delays, which are common in both ED and PsA. In both cases, for a retrospective study to detect a case, the patient must experience the

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symptoms significantly enough to prompt the patient to seek medical attention. In the case of PsA, some men might have a higher tolerance of pain, or subscribe to a culture that is less likely to present with pain as a chief complaint. This means that patients will present at various stages of psoriatic disease, with some presenting with mild early disease and other presenting with more severe disease at diagnosis. Studies, including a recent meta-analysis, have shown that approximately 10-15% of patients with psoriasis actually have symptoms and meet diagnostic criteria for PsA, despite not being previously diagnosed (48, 49). Another study found that, in 2000, the time from initial symptom onset to diagnosis of PsA was approximately 53 months, but this lag in diagnosis has decreased to approximately 3-4 months in 2011 (50). Given this range in time to diagnosis, our cohort, which was initially diagnosed between 1970 and 2008, may be particularly heterogeneous at their functional status and disease severity at time of diagnosis. Similarly, some men may seek treatment early for mild erectile dysfunction, while others may never seek treatment due to a variety of reasons, including being sexually inactive or having medical conditions that make sexual activity unsafe (45). Future studies could circumvent this complication by utilizing a prospective design with more quantitative testing. In addition, we examined some of the known confounders of ED, and the primary treatment strategies. However, we did not examine other baseline traditional risk factors for ED such as smoking, obesity, metabolic syndrome or depression, which are higher in PsA compared to general population. Other limitations include the retrospective nature of the current study with all the respective limitations, and that the Olmsted County population is predominantly Caucasian, which may limit generalizability to more diverse populations.

This study showed an increased incidence of ED in men with PsA in relation to a comparator cohort, which did not reach statistical significance. Future studies, in larger population-based areas could further inform this observation and confirm if ED is more prevalent in men with PsA. In addition, future studies could determine if the risk of ED in PsA is driven by

traditional cardiovascular risk factors, as in the general population, or driven by psoriatic inflammation. In addition, it has been shown that psoriatic disease activity is associated with increased risk of sexual dysfunction in men with psoriasis (14-16), so it is possible that a PsA cohort with well controlled disease activity might have a lower rate of ED. The potential effect of intensification of PsA treatment with better disease control on ED could also be informed by future studies. ED has been used as a marker of men with subclinical cardiovascular disease in the general population, guiding cardiovascular intervention. It is currently unclear whether this is true for men with PsA. Future studies, which may be able to ascertain the incidence of ED in larger, perhaps country-based, populations of PsA could help to more clearly define both the risk of ED, and its association with cardiovascular risk and perhaps, predictive ability. The prospective use of erectile dysfunction screening, including penile tumescence studies, use of the IIEF questionnaires and ultrasound-based diagnostics of atherosclerosis could all help to further determine if there is a predictive value of early ED pathogenesis to the development of heart disease. Collaborations between experts in rheumatology and andrology / urology could optimize these studies in order to best inform both fields. Given the relevance of ED to cardiovascular disease, more studies on ED risk could inform both the management of sexual dysfunction and cardiovascular risk in men with PsA. In addition, clinicians caring for patients with PsA should be aware of the possibility that men with PsA may be at higher risk of ED, and should screen their patients accordingly to increase quality of life, and perhaps, eventually, to help ascertain future cardiovascular risk.

References

1. Ernste FC, Sanchez-Menendez M, Wilton KM, Crowson CS, Matteson EL, Maradit Kremers H. Cardiovascular risk profile at the onset of psoriatic arthritis: A population-based cohort study. *Arthritis Care Res (Hoboken)* 2015;67:1015-21.
2. Jamnitski A, Symmons D, Peters MJ, Sattar N, McInnes I, Nurmohamed MT. Cardiovascular comorbidities in patients with psoriatic arthritis: A systematic review. *Ann Rheum Dis* 2013;72:211-6.
3. Kondratiouk S, Udaltsova N, Klatsky AL. Associations of psoriatic arthritis and cardiovascular conditions in a large population. *The Permanente Journal* 2008;12:4.
4. Li L, Hagberg KW, Peng M, Shah K, Paris M, Jick S. Rates of cardiovascular disease and major adverse cardiovascular events in patients with psoriatic arthritis compared to patients without psoriatic arthritis. *Journal of Clinical Rheumatology* 2015;21:405.
5. Polachek A, Touma Z, Anderson M, Eder L. Risk of cardiovascular morbidity in patients with psoriatic arthritis: A meta-analysis of observational studies. *Arthritis Care Res (Hoboken)* 2017;69:67-74.
6. Popescu C, Pintilie AM, Bojinca V, Balanescu A, Ionescu R. Cardiovascular risk in psoriatic arthritis - a cross-sectional study. *Maedica (Buchar)* 2014;9:19-24.
7. Sinnathurai P, Buchbinder R, Hill C, Lassere M, March L. Comorbidity in psoriatic arthritis and rheumatoid arthritis. *Intern Med J* 2018;48:1360-8.
8. Tam LS, Tomlinson B, Chu TT, Li M, Leung YY, Kwok LW, et al. Cardiovascular risk profile of patients with psoriatic arthritis compared to controls--the role of inflammation. *Rheumatology (Oxford)* 2008;47:718-23.
9. Molina-Leyva A, Salvador-Rodriguez L, Martinez-Lopez A, Ruiz-Carrascosa JC, Arias-Santiago S. Association between psoriasis and sexual and erectile dysfunction in epidemiologic studies: A systematic review. *JAMA Dermatol* 2019;155:98-106.
10. Chen YJ, Chen CC, Lin MW, Chen TJ, Li CY, Hwang CY, et al. Increased risk of sexual dysfunction in male patients with psoriasis: A nationwide population-based follow-up study. *J Sex Med* 2013;10:1212-8.
11. Gupta MA, Gupta AK. Psoriasis and sex: A study of moderately to severely affected patients. *Int J Dermatol* 1997;36:259-62.
12. Sampogna F, Gisondi P, Tabolli S, Abeni D. Impairment of sexual life in patients with psoriasis. *Dermatology* 2007;214:144-50.
13. Gladman D. Mortality in psoriatic arthritis. *Clinical & Experimental Rheumatology* 2008;26:S62.
14. Gladman DD, Ang M, Su L, Tom BD, Schentag CT, Farewell VT. Cardiovascular morbidity in psoriatic arthritis. *Ann Rheum Dis* 2009;68:1131-5.
15. Gonzalez-Gay MA, Gonzalez-Juanatey C, Martin J, editors. *Rheumatoid arthritis: A disease associated with accelerated atherogenesis. Seminars in arthritis and rheumatism; 2005. Elsevier.*
16. Egeberg A, Skov L, Hansen PR, Gislason GH, Wu JJ, Thyssen JP, et al. Duration of psoriatic arthritis as a risk factor for myocardial infarction. *Rheumatol Adv Pract* 2018;2:rky011.
17. Cooksey R, Brophy S, Kennedy J, Gutierrez FF, Pickles T, Davies R, et al. Cardiovascular risk factors predicting cardiac events are different in patients with rheumatoid arthritis, psoriatic arthritis, and psoriasis. *Semin Arthritis Rheum* 2018;48:367-73.
18. Liew JW, Ramiro S, Gensler LS. Cardiovascular morbidity and mortality in ankylosing spondylitis and psoriatic arthritis. *Best Pract Res Clin Rheumatol* 2018;32:369-89.
19. Calmasini FB, Klee N, Webb RC, Priviero F. Impact of immune system activation and vascular impairment on male and female sexual dysfunction. *Sex Med Rev* 2019;7:604-13.

20. Lotti F, Maggi M. Sexual dysfunction and male infertility. *Nature Reviews Urology* 2018;15:287-307.
21. Mitidieri E, Cirino G, d'Emmanuele di Villa Bianca R, Sorrentino R. Pharmacology and perspectives in erectile dysfunction in man. *Pharmacology & therapeutics* 2020;208:107493.
22. Yafi FA, Jenkins L, Albersen M, Corona G, Isidori AM, Goldfarb S, et al. Erectile dysfunction. *Nat Rev Dis Primers* 2016;2:16003.
23. Caretta N, De Rocco Ponce M, Minicuci N, Palego P, Valente U, Garolla A, et al. Penile doppler ultrasound predicts cardiovascular events in men with erectile dysfunction. *Andrology* 2019;7:82-7.
24. Ioakeimidis N, Vlachopoulos C, Rokkas K, Kratiras Z, Angelis A, Samentzas A, et al. Dynamic penile peak systolic velocity predicts major adverse cardiovascular events in hypertensive patients with erectile dysfunction. *J Hypertens* 2016;34:860-8.
25. Chung E. Contemporary and novel imaging studies for the evaluation of erectile dysfunction. *Med Sci (Basel)* 2019;7.
26. Zou Z, Lin H, Zhang Y, Wang R. The role of nocturnal penile tumescence and rigidity (nptr) monitoring in the diagnosis of psychogenic erectile dysfunction: A review. *Sex Med Rev* 2019;7:442-54.
27. Montorsi P, Ravagnani PM, Galli S, Rotatori F, Briganti A, Salonia A, et al. Common grounds for erectile dysfunction and coronary artery disease. *Curr Opin Urol* 2004;14:361-5.
28. Montorsi P, Ravagnani PM, Galli S, Rotatori F, Briganti A, Salonia A, et al. The artery size hypothesis: A macrovascular link between erectile dysfunction and coronary artery disease. *Am J Cardiol* 2005;96:19M-23M.
29. Kapur V, Schwarz ER. The relationship between erectile dysfunction and cardiovascular disease. Part i: Pathophysiology and mechanisms. *Rev Cardiovasc Med* 2007;8:214-9.
30. Shridharani AN, Brant WO. The treatment of erectile dysfunction in patients with neurogenic disease. *Translational Andrology and Urology* 2016;5:88-101.
31. Del Popolo G, Cito G, Gemma L, Natali A. Neurogenic sexual dysfunction treatment: A systematic review. *Eur Urol Focus* 2020;6:868-76.
32. Bodie JA, Beeman WW, Monga M. Psychogenic erectile dysfunction. *The International Journal of Psychiatry in Medicine* 2003;33:273-93.
33. Montorsi P, Ravagnani PM, Galli S, Rotatori F, Veglia F, Briganti A, et al. Association between erectile dysfunction and coronary artery disease. Role of coronary clinical presentation and extent of coronary vessels involvement: The cobra trial. *European heart journal* 2006;27:2632-9.
34. Baumhäkel M, Böhm M. Erectile dysfunction correlates with left ventricular function and precedes cardiovascular events in cardiovascular high-risk patients. *International journal of clinical practice* 2007;61:361-6.
35. Zhao SS, Miller N, Harrison N, Duffield SJ, Dey M, Goodson NJ. Systematic review of mental health comorbidities in psoriatic arthritis. *Clinical Rheumatology* 2020;39:217-25.
36. El-Mawla A, Hashim AA, Zidan A-S. Assessment of the effect of psoriasis on male sexual function. *Human Andrology* 2018;8:69-75.
37. Tasliyurt T, Bilir Y, Sahin S, Seckin HY, Kaya SU, Sivgin H, et al. Erectile dysfunction in patients with psoriasis: Potential impact of the metabolic syndrome. *Eur Rev Med Pharmacol Sci* 2014;18:581-6.
38. Bardazzi F, Odorici G, Ferrara F, Magnano M, Balestri R, Patrizi A. Sex and the pasi: Patients affected by a mild form of psoriasis are more predisposed to have a more severe form of erectile dysfunction. *J Eur Acad Dermatol Venereol* 2016;30:1342-8.
39. Perez-Garcia LF, Te Winkel B, Carrizales JP, Bramer W, Vorstenbosch S, van Puijenbroek E, et al. Sexual function and reproduction can be impaired in men with rheumatic diseases: A systematic review. *Semin Arthritis Rheum* 2020.

40. St Sauver JL, Grossardt BR, Leibson CL, Yawn BP, Melton LJ, 3rd, Rocca WA. Generalizability of epidemiological findings and public health decisions: An illustration from the rochester epidemiology project. *Mayo Clin Proc* 2012;87:151-60.
41. Wilton KM, Crowson CS, Matteson EL. Malignancy incidence in patients with psoriatic arthritis: A comparison cohort-based incidence study. *Clin Rheumatol* 2016;35:2603-7.
42. Taylor W, Gladman D, Helliwell P, Marchesoni A, Mease P, Mielants H, et al. Classification criteria for psoriatic arthritis: Development of new criteria from a large international study. *Arthritis Rheum* 2006;54:2665-73.
43. Gooley TA, Leisenring W, Crowley J, Storer BE. Estimation of failure probabilities in the presence of competing risks: New representations of old estimators. *Stat Med* 1999;18:695-706.
44. Inman BA, Sauver JLS, Jacobson DJ, McGree ME, Nehra A, Lieber MM, et al., editors. A population-based, longitudinal study of erectile dysfunction and future coronary artery disease. *Mayo Clinic Proceedings*; 2009. Elsevier.
45. Gades NM, Jacobson DJ, McGree ME, St Sauver JL, Lieber MM, Nehra A, et al. Longitudinal evaluation of sexual function in a male cohort: The olmsted county study of urinary symptoms and health status among men. *J Sex Med* 2009;6:2455-66.
46. Molina-Leyva A, Almodovar-Real A, Carrascosa JC, Molina-Leyva I, Naranjo-Sintes R, Jimenez-Moleon JJ. Distribution pattern of psoriasis, anxiety and depression as possible causes of sexual dysfunction in patients with moderate to severe psoriasis. *An Bras Dermatol* 2015;90:338-45.
47. Molina-Leyva A, Molina-Leyva I, Almodovar-Real A, Ruiz-Carrascosa JC, Naranjo-Sintes R, Jimenez-Moleon JJ. Prevalence and associated factors of erectile dysfunction in patients with moderate to severe psoriasis and healthy population: A comparative study considering physical and psychological factors. *Arch Sex Behav* 2016;45:2047-55.
48. Villani AP, Rouzaud M, Sevrain M, Barnette T, Paul C, Richard MA, et al. Prevalence of undiagnosed psoriatic arthritis among psoriasis patients: Systematic review and meta-analysis. *J Am Acad Dermatol* 2015;73:242-8.
49. Coates LC, Savage L, Waxman R, Moverley AR, Worthington S, Helliwell PS. Comparison of screening questionnaires to identify psoriatic arthritis in a primary-care population: A cross-sectional study. *Br J Dermatol* 2016;175:542-8.
50. Sørensen J, Hetland ML. Diagnostic delay in patients with rheumatoid arthritis, psoriatic arthritis and ankylosing spondylitis: Results from the danish nationwide danbio registry. *Ann Rheum Dis* 2015;74:e12.

Figure Legends

Figure 1 : Study Design and Exclusions. The number of initial men with psoriatic arthritis (left column), and male comparators (right column) are shown. There were no exclusions in this study due to lack of consent. A total of 13 study subjects were excluded for having a diagnosis of ED before their diagnosis or index date.

Figure 2 : Cumulative Incidence of Erectile Dysfunction (ED) in Men with Psoriatic Arthritis (PsA). The cumulative incidence of erectile dysfunction was assessed over time after initial psoriatic arthritis diagnosis or respective index date in the comparator cohort. The incidence of ED was adjusted for competing risk of death, and those who developed ED before the index date were excluded. Analysis was done with adjustment for age. There were 18 cases of ED in the comparator cohort and 24 in the PsA cohort (HR 1.45, 95% CI 0.79-2.68). HR: hazards ratio; CI: confidence interval

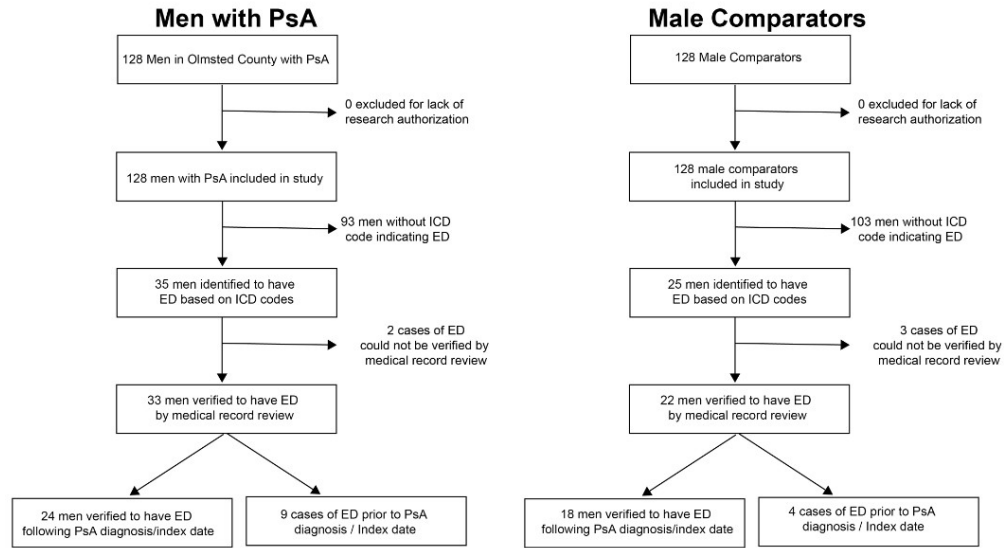


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Table 1 Potential Diagnostic Confounders and Initial Treatment Strategies in Men with Psoriatic Arthritis (PsA) and Erectile Dysfunction (ED)

	PsA (n=24)	Non-PsA (n=18)	p-value
<u>Specialty of Diagnosing Clinician</u>			0.55
Urology	7 (29%)	3 (17%)	
Internal Medicine	8 (33%)	9 (50%)	
Family Medicine	8 (33%)	6 (33%)	
Other Subspecialist	1 (4%)	0 (0%)	
<u>Potential Confounders</u>			
BMI (kg/m ²), mean (SD)	30.3 (4.9)	28.9 (2.2)	0.49
Possible Psychogenic ED	3 (13%)	4 (22%)	0.40
Alcohol Concerns	7 (29%)	5 (28%)	0.92
Anti-Hypertensive Use	11 (46%)	8 (44%)	0.93
Anti-Depressant Use	5 (21%)	3 (17%)	0.73
Anti-Androgen Use	0 (0%)	0 (0%)	-
Hypogonadism Diagnosis	0 (0%)	0 (0%)	-
Thyroid Disease Diagnosis	0 (0%)	0 (0%)	-
Peyronie Disease	1 (4%)	1 (6%)	0.83
Penile Trauma	0 (0%)	1 (6%)	0.24
Spinal Cord Trauma	0 (0%)	0 (0%)	-
Neurological Disease	0 (0%)	1 (6%)	0.24
Radical Prostatectomy	2 (8%)	0 (0%)	0.21
Radiation Therapy	0 (0%)	0 (0%)	-
<u>Treatments in First Year</u>			
Phosphodiesterase 5 Inhibitor	16 (67%)	15 (83%)	0.22
Testosterone Replacement	0 (0%)	0 (0%)	-
Penile Self-Injection	0 (0%)	0 (0%)	-
Penile Vacuum Device	0 (0%)	0 (0%)	-
Penile Device Placement	1 (4%)	0 (0%)	0.38

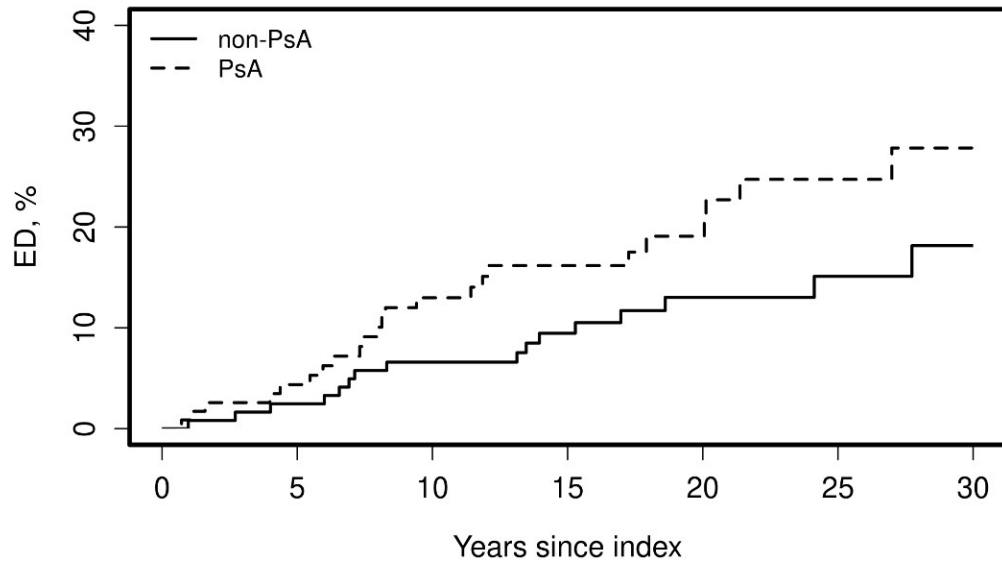


Figure 2 : Cumulative Incidence of Erectile Dysfunction (ED) in Men with Psoriatic Arthritis (PsA). The cumulative incidence of erectile dysfunction was assessed over time after initial psoriatic arthritis diagnosis or respective index date in the comparator cohort. The incidence of ED was adjusted for competing risk of death, and those who developed ED before the index date were excluded. Analysis was done with adjustment for age. There were 18 cases of ED in the comparator cohort and 24 in the PsA cohort (HR 1.45, 95% CI 0.79-2.68). HR: hazards ratio; CI: confidence interval

275x155mm (96 x 96 DPI)