

The relationship between overactive bladder and prostate cancer: A scoping reviewAsher Khan¹; R. Trafford Crump, PhD²; Kevin V. Carlson, MD²; Richard J. Baverstock, MD²¹Department of Science, University of Calgary, Calgary, AB, Canada; ²Department of Surgery, University of Calgary, Calgary, AB, Canada

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Abstract

Introduction: The relationship between prostate cancer (PCa) and overactive bladder (OAB) is poorly understood. PCa and OAB are frequently diagnosed in elderly populations, so it could be expected that both conditions would be observed in older patients. Whether PCa and OAB occur independently with age, or the presence of PCa leads to the onset of OAB/lower urinary tract symptoms (LUTS) has not been explored. This review aimed to investigate whether men newly diagnosed with prostate cancer (PCa) are more likely to have overactive bladder (OAB) compared to the general population, and if the various treatment modalities for PCa are likely to impact the incidence or exacerbation of OAB.

Methods: The University of Calgary's databases for Medline and PubMed were searched for relevant publications. No restrictions were placed on the study design reported. Any publications reporting OAB and a PCa diagnosis and/or observation relating to PCa diagnosis and rates of OAB/LUTS in an adult population were included for full review.

Results: Of the studies examining the relationship between PCa and LUTS, results varied, but frequently indicated an inverse association between PCa and LUTS in which patients newly diagnosed with prostate cancer were more unlikely to have LUTS compared to the general population. Following treatment, brachytherapy resulted in a higher prevalence of OAB symptoms compared to surgical treatment and external beam radiation therapy.

Conclusions: Diverse evidence was found regarding the relationship between the prevalence of pre-treatment OAB and PCa diagnosis. However, limited evidence, as well as uncertainty regarding pre-treatment symptoms and their impact on post-treatment outcomes, restricts potential conclusions.

Introduction

Prostate cancer (PCa) is the second most common cancer, and fifth leading cause of cancer-related deaths in men worldwide. Estimates suggest approximately 1.3 million new cases and 359,000 associated deaths globally in 2018.¹ Advanced age is a primary risk factor for PCa, with men 65 years old and over accounting for roughly 75% of observed cases; men under 40 are rarely diagnosed.² Family history, race and environmental conditions are additional factors in the overall development of the disease.³

As defined by the International Continence Society, idiopathic overactive bladder (OAB) involves storage-related LUTS including urgency, with or without urgency incontinence, usually accompanied by frequency and nocturia in the absence of other pathologies that could lead to similar symptoms.⁴ A substantial body of research has established that OAB can result in worse patient-reported outcomes, including less frequent socialization, reduced daily activities,⁵ and increased anxiety and depression.⁶ Prevalence of OAB is difficult to establish due to differences in survey methods and definitions.⁷ However, it is estimated that OAB occurs in 6.5% - 11.8%⁸ of the adult population in developed countries.⁹ Prevalence of OAB and its symptom severity also appears to increase with age.^{7,9}

Some men who experience lower urinary tract symptoms (LUTS) and OAB-related symptoms express fear that their symptoms may be associated with PCa.¹⁰ It is common that these symptoms motivate a consultation and diagnostic tests to rule out cancer.¹¹ Since PCa and OAB are frequently diagnosed in elderly populations,^{3,9} it is expected that both conditions would be observed in patients. Furthermore, an argument could be made linking the two conditions anatomically. The prostate gland merges with the bladder neck, which plays a significant role in the internal sphincteric mechanism vital to micturition.¹² One might suggest that in some cases the development of a tumor in the base of the prostate could cause obstruction to the urethra, affecting overall functionality of the bladder neck and ultimately resulting in higher prevalence of OAB in those with PCa.

Relatedly, treating PCa could result in injury to the bladder neck, leading to an incidence of OAB or exacerbation of existing urinary symptoms. Standard treatment options for men diagnosed with localized PCa include radical prostatectomy (RP), brachytherapy (BT), and external beam radiation therapy (ERBT).¹³ These treatments may result in changes to bladder neck morphology and physiology, or direct injury to the bladder in the case of radiation. Consequently, a potential side effect of treatment is LUTS which can include symptoms

associated with OAB¹⁴ as well as urinary incontinence.^{15,16} In this paper, we did not specifically focus on stress urinary incontinence because it is commonly reported and studied after prostatectomy.

The relationship between PCa and OAB is poorly understood and under-studied. The purpose of this study is to examine the literature regarding the relationship between these two conditions. By doing so, we aim to answer the following two research questions: 1) Are men diagnosed with PCa more likely to be diagnosed with OAB compared to the general population; and, 2) are the various treatments for PCa likely to impact the incidence and/or exacerbation of OAB?

Methods

Study design

A scoping review was conducted of the peer-reviewed literature on 1) the prevalence of OAB in men diagnosed with PCa prior to treatment, and 2) the incidence/exacerbation of OAB in men after treatment for PCa. The primary purpose of this review was to determine whether an anatomical link between OAB and PCa has been made in peer-reviewed literature. Additionally, we aimed to undertake an analysis of the prevalence and/or incidence rates of OAB in men with PCa and compare those rates with what has been reported in the general population.

The aim of this study was to analyze knowledge gaps in the relationship between PCa and OAB. We had a sense that there was little published on the topic; therefore, we conducted a scoping review as opposed to a formal systematic review. Consequently, the review protocol was not registered with PROSPERO. However, in order to transparently report the methods and allow readers to assess the strengths and limitations of this scoping review, we followed the PRISMA Guideline checklist.

Search strategy

An initial search was conducted in June 2018 that was restricted to prostate cancer and OAB. Very few publications were retrieved in this initial search. Therefore, a second search was conducted in July 2018 expanding the search terms to include both OAB and LUTS. We were specifically interested in symptoms of urgency, urge incontinence, frequency, or nocturia that may be indicative of OAB, but reported as part of a broader evaluation of LUTS. We included reports of any study design (e.g., review, observational, etc.) limited to those published in English after 2004. This cut-off date was chosen because it is approximately when OAB became a formally defined urologic condition. Resulting publications were further restricted to surgical and radiation treatment due to the level of reporting in the literature and the commonality of these specific treatment methods. The search was updated in November 2018; two search strategies were used to address both research questions respectively.

Search terms

Both researchers used a PICOS approach to search the literature. Boolean logic was used with MeSH headings or the search terms. Full details are provided in Table 1. Broad search terms and inclusion criteria were applied to identify any publications reporting patients with PCa and OAB-related symptoms. The full search strategy is presented in Appendix 1.

Search engines

The University of Calgary's databases for Medline and PubMed were searched. References from relevant publications resulting from our search were also reviewed and potentially applicable studies were retrieved. Conference proceedings, publications that may be in-press, and materials published in the grey literature were not considered.

Study identification

The search results were screened for eligibility by a review of the publication's title and abstract. Two researchers (AK, RTC) performed the initial screen. In the case of a dispute, a third researcher (RJB or KVC) was consulted. At this stage, publications were included for full review if they reported an OAB and PCa diagnosis in the adult population. Publications were excluded if: 1) they did not report OAB/LUTS pre-PCa treatment, 2) LUTS reported post-treatment were not symptoms associated with OAB, 3) the publications compared two different methods of the same treatment (i.e. open vs robotic radical prostatectomy), or 4) the publications were not available in full text.

Data extraction

Those publications that met the inclusion criteria were reviewed in-full with the intent of extracting any information related to: 1) the anatomical link between the prostate and OAB, 2) observations relating PCa diagnosis and rates of OAB/LUTS, or 3) observations of the treatment of PCa resulting in OAB/OAB-related symptoms.

We summarized the study design, participants, interventions, comparisons, and results from those publications of interest. No attempt was made to assess the risk of bias of individual studies.

Results

We executed two different searches to address the respective research questions. The results from these searches are provided in sub-sections below.

Research question 1: Are men diagnosed with PCa more likely to have LUTS/OAB-related symptoms?

The search related to this question resulted in 245 publications that were screened for eligibility. Of those, 53 were read in-full, from which 11 were ultimately included in our review. The remainder had not explicitly measured or indicated the prevalence of OAB/LUTS at PCa

diagnosis/positive biopsy. A complete flow diagram of the study selection is provided in Figure 1. Amongst the included publications, 10 were prospective studies and 1 was a retrospective study.

Details for the 11 publications included in the review are provided in Table 2. All studies examined LUTS as an outcome measurement, however, they did not differentiate between voiding and storage symptoms. These studies used four different questionnaires to measure LUTS. Each of these studies reported PCa-related factors, including: prostate specific antigen (PSA) levels and tumor stage. Of the studies examining the relationship between PCa and LUTS, results varied but tended to indicate an inverse association between PCa and LUTS.

LUTS

Three studies observed that the absence of LUTS was related to a greater risk of successive PCa diagnoses.^{18,20,21} Two studies reported a positive association between increasing severity of LUTS and a PCa diagnosis.^{16,25} However, one of these studies observed that the relationship was confined only to localized disease.¹⁶ This suggests that urinary symptoms were not caused by the tumor itself, but led to the diagnosis of early stage PCa. Four studies observed no significant association between LUTS and PCa.^{17,19,22,24}

LUTS and PSA

Three studies utilized both LUTS severity and PSA levels to evaluate the relationship between LUTS and PCa. The results from these studies were mixed. One study observed that more severe LUTS and elevated PSA did not indicate higher risk of PCa.¹⁹ One study observed that the absence of voiding symptoms in men with elevated PSA was an independent risk factor for PCa detection.²³ One study observed that men with elevated PSA and LUTS were more likely to be diagnosed with benign disease than PCa.¹⁶

Research question 2: Are treatments for PCa likely to lead to greater/lesser incidence of OAB?

The search related to this question resulted in 259 publications that were screened for eligibility. Of those, 78 were read in-full, from which 18 were ultimately included in our review. Those excluded had either utilized a treatment method other than surgical, radiation therapy or brachytherapy; focused on symptoms following PCa treatment that were not specifically symptoms associated with OAB; or compared outcomes of two different approaches of the same procedure/treatment. A complete flow diagram of the study selection is provided in Figure 2. Amongst the included publications, 10 were prospective studies and 8 were retrospective studies.

Details for the 18 publications included in the review are provided in Table 3. All studies examined OAB symptoms, urge incontinence, urgency, frequency, nocturia, and/or storage symptoms as an outcome measure. A variety of measurements were used across studies, including: clinical assessments;²⁶ urodynamic examination;⁴⁰ study-specific

questionnaires;^{27,28,30,43} and a variety of validated questionnaires, including the IPSS,^{29,32,33,39,41} DAN-PSS,³¹ EORTC,^{32,36,42} ICS questionnaire,³² S-IPSS,³⁴ OABSS,³⁴ N-QOL,³⁵ AUASI,³⁷ and the Bristol-LUTS questionnaire.³⁸

Radical prostatectomy

Eleven studies examined the incidence, exacerbation or resolution of OAB-related symptoms following RP. Both robot-assisted RP and open RP were included for analysis.

Incidence of de novo OAB-related symptoms following radical prostatectomy

Three studies specified the incidence of OAB-related symptoms in initially asymptomatic patients following RP.^{26,27,38} One study reported de-novo OAB incidence after RP (19%) along with specific OAB-related symptoms.²⁶ One study observed an incidence rate of 25% for frequency,²⁷ and another study demonstrated an incidence rate of 36% for nocturia.³⁸

Prevalence of specific OAB-related symptoms following radical prostatectomy

Three studies evaluated the prevalence of urge incontinence following RP, which ranged from 3.2% to 27.3%.^{28,31,40} One study observed the prevalence of frequency symptoms following RP of 8.5%.³¹ Two studies observed the prevalence of urgency symptoms following RP ranging from 15% to 27%.^{31,43} Three studies observed the prevalence of nocturia symptoms following RP ranging from 9% to 49%.^{31,35,43}

Prevalence of general OAB/storage symptoms following radical prostatectomy

Three studies examined the prevalence of OAB/storage symptoms, or its burden, following RP.^{32,37,41} A prevalence rate of 11% was observed,³² and in one study 39% of participants reported an increase in symptom burden.⁴¹

Brachytherapy

In total, 6 studies were found that examined the incidence, exacerbation, or resolution of OAB-related symptoms following BT.

Prevalence of OAB/storage symptoms following brachytherapy

Four studies examined the prevalence of OAB/storage symptoms, burden, or exacerbation following BT.^{32,33,34,37} Prevalence rates ranged from 30% to 79%^{32,33} and a higher burden of storage symptoms was observed among those patients undergoing BT compared to EBRT or RP ($p < .001$).³⁷

Prevalence of specific OAB-related symptoms following brachytherapy

Two studies examined the prevalence of urge incontinence following BT.^{29,34} One study observed a prevalence rate of 72%.²⁹ An elevated OAB storage symptom score was reported in

one study.³⁴ One study examined urgency and nocturia symptoms following BT using the IPSS.³⁹ No studies examined the prevalence of frequency symptoms.

External beam radiation therapy

In total, 6 studies were found that examined the incidence, exacerbation or resolution of OAB-related symptoms following EBRT.

Incidence of de novo OAB-related symptoms following external beam radiation therapy

Two studies examined the incidence of OAB-related symptoms in initially asymptomatic patients following EBRT.^{27,38} One study observed an incidence rate of 54% for frequency symptoms following treatment.²⁷ Another study observed an incidence of 48% for nocturia symptoms following treatment.³⁸

Prevalence of OAB/storage symptoms following external beam radiation therapy

One study examined storage symptom burden following EBRT. A lower burden of storage symptoms for those patients who underwent EBRT was observed compared to those who underwent BT ($P < .001$).³⁷

Prevalence of specific OAB-related symptoms following external beam radiation therapy

Three studies examined the prevalence of urge incontinence following EBRT.^{28,36,42} Prevalence rates of 23% to 36% were observed at 15-years post-treatment.^{28,36} Two studies examined urgency symptoms following EBRT and both reported an elevated risk of symptoms.^{30,42}

Discussion

Recognizing the role of the prostate in urinary control motivated us to investigate the possible relationship between OAB and PCa. The prostate merges with the bladder neck, which contributes to the autonomic internal sphincter mechanism that plays a role in both continence and micturition.¹² We questioned whether the presence of a prostate tumor in some cases may contribute to OAB symptoms by obstructing the outlet, and subsequently putting pressure on the bladder neck. However, the results from this scoping review suggest that no such anatomical relationship between OAB and PCa exists and that the association is more clinical. A similar clinical association has been observed between benign prostatic hyperplasia (BPH) – the benign enlargement of the prostate – and PCa. Weight et al. conducted a cohort study of 1,922 men and concluded that any association between BPH and successive PCa was likely due to an increased diagnostic intensity stemming from greater patient-physician interactions.⁴⁶ Up to 73% of men experiencing LUTS visit their physicians expressing fear and seeking reassurance that their symptoms are not associated with PCa.⁵¹ Hence, patients visiting their physicians with LUTS may undergo more PSA testing and subsequently be diagnosed with PCa.¹⁰

The results from this study raises a counter argument to the anatomical relationship. With localized PCa, the tumor would not likely impact the urethra or bladder neck unless it had advanced into local tissue.⁴⁴ Moreover, since 70% of tumors originate in the peripheral zone of the prostate,⁴⁵ an observable relationship between localized disease and subsequent OAB is unlikely.

However, the lack of strong clinical studies into the association of OAB and PCa should be underscored. Because of this, we had to expand our original search from OAB to include a broader array of symptoms - LUTS. While LUTS are closely associated with OAB, this was not quite what we were originally aiming for. More rigorous studies, powered to detect statistically significant changes in OAB, as a result of PCa treatment are needed.

Whether treatments for PCa result in the de novo incidence of OAB-related symptoms, the exacerbation of symptoms, or the resolution of symptoms remains an area of uncertainty. There is a biological rationale for hypothesizing that some PCa treatments can alleviate symptoms in the short term. RP can surgically remove an enlarged prostate that had previously been causing urinary symptoms. This may cause short-term relief of these symptoms. However, anastomosis of the bladder neck to the urethra, and possible bladder neck contracture, may lead to long-term OAB-related symptoms.

Radiation therapy of PCa can reduce OAB-related symptoms by avoiding complications associated with surgical intervention. However, ischemia and fibrosis caused by BT can create an obstructive outlet and/or detrusor instability, subsequently leading to post-treatment OAB symptoms. The results from this study suggest an advantage of surgical treatment over radiation therapy for PCa in terms of post-treatment symptom prevalence, however, the limited evidence collected restricts any conclusions that can be drawn from the obtained data. We also acknowledge that both surgical and radiotherapy techniques and technology have changed over time so this review, encompassing 2004 to 2018, may or may not have captured these changes based on heterogeneity of the timeframe in which patients were treated.

There are limitations of this scoping review that should be noted. First, we restricted our search to English publications published in a peer-reviewed journal. We did this for two reasons. Initially it was because we did not have the ability to accurately translate publications in other languages. Additionally, we wanted the assurance of scientific credibility that comes with peer-review. However, based on an informal review of search results without these restrictions, we do not believe we have missed any substantial publications that would have substantially changed our observations. Furthermore, a formal systematic review was not conducted due to the lack of literature found. A scoping review was more inclusive of the diversity of the already scarce literature on the association between these two conditions. The implemented search strategy resulted in a very low number of studies, both in examining the prevalence of OAB in PCa patients and OAB symptoms in PCa treatment. This significantly limited conclusions that could be drawn. The absence of studies looking specifically at OAB prevalence in PCa patients

required an expansion of search criteria to analyze LUTS as opposed to OAB specifically. Although symptoms associated with OAB fall under LUTS, it does not give a definitive relationship between the two conditions in consideration for the review.

Conclusions

We found mixed evidence regarding the relationship between OAB and PCa. There is uncertainty in the current literature regarding LUTS prevalence in PCa patients as results have varied. The nature of the results, as well as conclusions from authors, indicate that an inverse relationship is likely. Following treatment, BT appeared to result in a higher prevalence of OAB symptoms compared to surgical treatment and ERBT. However, limited evidence as well as existing uncertainty regarding pre-treatment symptoms and their impact on post-treatment symptoms restricts conclusions that can be made. This review highlights the need for further research in comparing these treatment modalities, which can provide insight for physicians in making treatment decisions with patients based on the presence or absence of pre-treatment symptoms.

DRAFT

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Figures and Tables

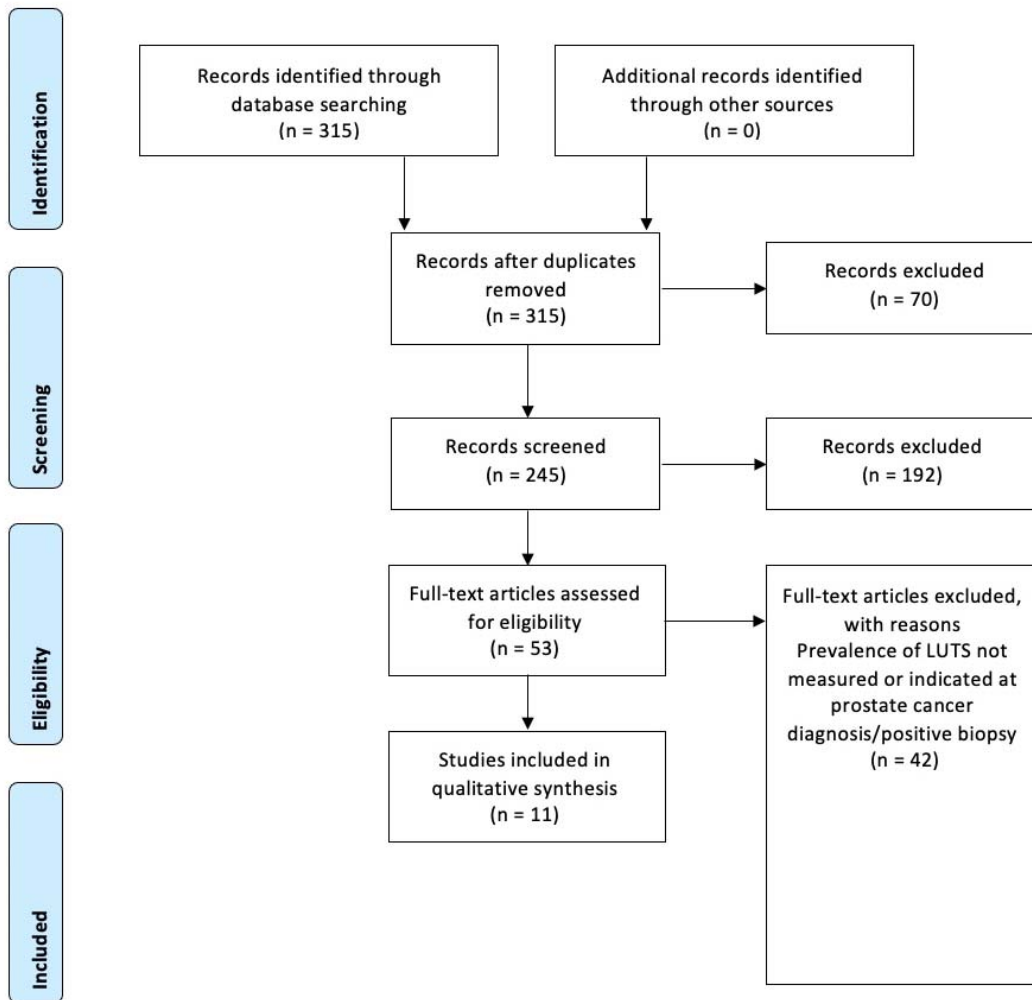
Fig. 1. Flowchart of study selection (prevalence of lower urinary tract symptoms [LUTS] in prostate cancer patients).

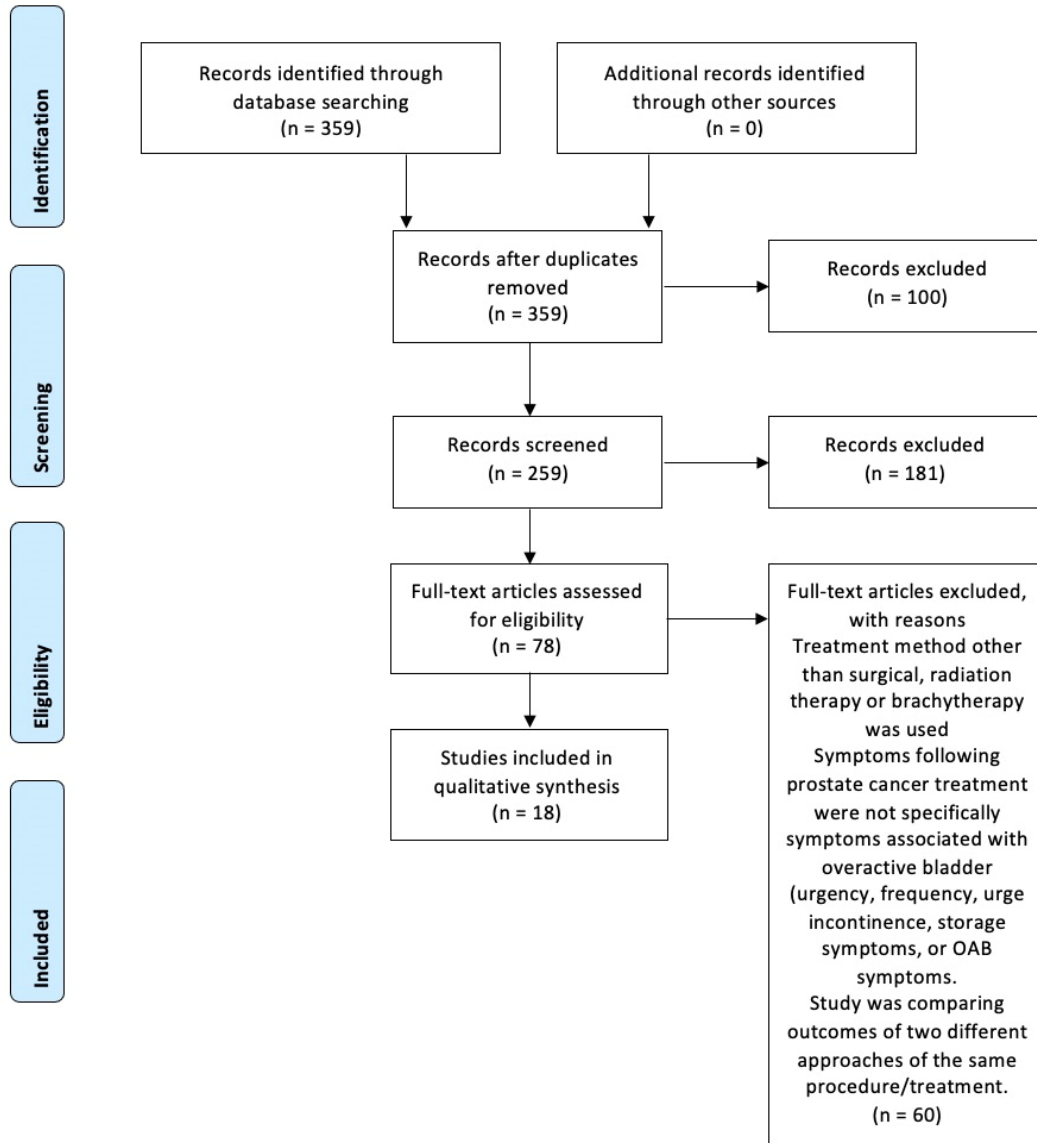
Fig. 2. Flowchart of study selection (overactive bladder [OAB] symptoms following prostate cancer treatment).

Table 1. PICO search terms		
	Research question 1	Research question 2
Population or problem	Prostate cancer	Prostate cancer
Intervention or exposure	Overactive bladder	Radical prostatectomy/ brachytherapy/external beam radiotherapy
Comparison	Not relevant	Not relevant
Outcome	Not relevant	Overactive bladder
Study type	No restrictions	No restrictions

DRAFT

Study	Sample	Time point	Symptoms	Measured	Outcome
Collin et al ¹⁵	2467	Baseline initial checkup	LUTS PCa incidence	ICS male questionnaire DRE, repeat PSA test, and TRUS-guided biopsy	LUTS and elevated PSA (≥ 3 ng/mL): More likely to be diagnosed with benign disease than PCa
Martin et al ¹⁶	518	Baseline (LUTS), median 9.3 years followup	LUTS PCa incidence	IPSS Localized or advanced PCa	IPSS (20–35): 2.26 times higher risk of localized (HR 4.61; 2.23–9.54), but not advanced (HR 0.51; 0.15–1.75) PCa
Borre ¹⁷	538	Baseline consultation with GP	LUTS PCa Prevalence	DAN-PSS PSA, fraction of tumour-positive biopsy cores, Gleason score, clinical T classification	188 (34.9%) patients were asymptomatic at diagnosis, while 350 (65.1%) were diagnosed because of LUTS
Porter et al ¹⁸	569	Baseline consultation with urologist	LUTS PCa diagnosis	AUASS TRUS-guided prostate needle biopsy	Low AUASS score (<8): Independent predictor of positive prostate biopsy result ($p < 0.05$)
Matsubara et al ¹⁹	51	Baseline consultation	LUTS PCa diagnosis	IPSS PSA test, TRUS-guided 6-core biopsy	IPSS (8–36) and high PSA: Not at higher risk of PCa when compared with asymptomatic men (IPSS 0–7).
Cicione et al ²⁰	1366	Baseline consultation	LUTS PCa diagnosis	IPSS Ultrasound-guided transrectal PBx	Patients with PCa: Significantly lower IPSS (10.6 ± 7.4 vs. 12.7 ± 8.1) than those with benign diagnosis

Ito et al ²¹	1159	Baseline consultation	LUTS PCa diagnosis	IPSS TRUS-guided systematic extended biopsy protocols	Absent or mild lower urinary tract symptoms: Significant increased risk of PCa and high-grade disease (OR 1.64 and 1.70, p= 0.0007 and 0.0121, respectively)
Oh et al ²²	3107	Baseline consultation	LUTS PCa diagnosis	IPSS TRUS-guided biopsy	There was no significant difference for mean IPSS scores between patients with PCa and without (mean IPSS; 13.02 vs. 12.41, p=0.436, respectively).
Frånlund et al ²³	7625	Baseline consultation	LUTS PCa diagnosis	Study-specific, self-administrated questionnaire DRE and TRUS-guided biopsy	Absence of voiding symptoms and elevated PSA (>3.0 ng/mL): Independent risk factor for PCa detection
Kitagawa et al ²⁴	1739	During prostate biopsy	LUTS PCa diagnosis	IPSS Transrectal ultrasonography-guided prostate biopsy	IPSS≤7: Cancer detection probability of 27.4%. IPSS≥8: Cancer detection probability of 32.7% (not a statistically significant difference)
Hosseini et al ²⁵	233	Following PCa diagnosis	LUTS PCa diagnosis	IPSS DRE, PSA test	Significant difference in IPSS score between cases and noncancerous males (16.1±10.9 vs. 6.7±6.6. p<0.0001)

DRE: digital rectal exam; HR: hazard ratio; ICS: International Continence Society; IPSS: International Prostate Symptom Score; LUTS: lower urinary tract symptoms; OAB: overactive bladder; OR: odds ratio; PCa: prostate cancer; PSA: prostate-specific antigen; TRUS: transrectal ultrasound.

Table 3. Characteristics of studies related to the incidence of OAB-related symptoms in prostate cancer patients					
Study	Measured	Time point	Treatment(s)	Symptoms studied	Outcome
Hosier et al ²⁶	Clinical assessment	Baseline treatment, median followup time of 2.7 years	RP	OAB symptoms	19% incidence following treatment
				UI	6% incidence following treatment
				Nocturia	22% Incidence following treatment
				Frequency	21% incidence following treatment
				Urgency	19% incidence following treatment
Albkri et al ²⁷	Retrospective self-administered questionnaire	The median followup period was 58.1 months	RP	Frequency	24.5% incidence following treatment (p=0.007)
			RT	Frequency	53.5% incidence following treatment (p=0.007)
Daugherty et al ²⁸	Validated 2-item incontinence severity index	N/A	RP	UI	Prevalence of 27.3% following treatment (not significantly different from controls [24.0%]) and RT
			RT	UI	35.9% of patients, however not significantly different compared to controls (24.0%) and RP
Leapman et al ²⁹	IPSS	Median 6.4-year followup	BRT	UI	Prevalence of 72.2% (urge predominant leakage) following treatment

Carlsson et al ³⁰	Validated patient self-reported questionnaire*	Median (IQR) time of 12 years after diagnosis	RT	Urgency	Elevated risk after RT (OR 1.32, 95% CI 1.06–1.64), but lower after RP (OR 0.79, 95% CI 0.66–0.94)
Ervandian et al ³¹	DAN-PSS	Questionnaire between April and June 2010 after treatment from 2005–2007	RP	Frequency Nocturia Urgency UI	Prevalence of 8.50% Prevalence of 9.00% Prevalence of 27.00% Prevalence of 9.50%
Boettcher et al ³²	EORTC, IPSS, ICS	Baseline (before treatment) and 6, 12, 24, and 36 months after treatment	RP BRT	OAB symptoms OAB symptoms	Prevalence of 11% at 36 months post-treatment Prevalence of 30% at 36 months post-treatment
Blaivas et al ³³	IPSS	≤6 months after treatment	BRT	OAB symptoms	Prevalence of 79% post-treatment
Miyake et al ³⁴	S-IPSS OABSS	Median followup of 72 months Median followup of 72 months	BRT BRT	Storage LUTS UI	Elevated S-IPSS at 24 months. Heightened OABSS 3 (urge incontinence) for over 48 months
Haga et al ³⁵	N-QOL (Japanese version)	Baseline (before treatment), 3 and 12 months after treatment	RP	Nocturia	N-QOL scores (continent vs incontinent) at 3 (85.3% vs. 74.2%, p=0.006) and 12 (90.3% vs. 82.2%, p=0.04) months post-treatment. Significantly lower score in incontinent patients

Katayama et al ³⁶	EORTC	Before treatment, 10 weeks, and 6, 12, and 24 months after treatment	RT	UI	Grade 1 UI prevalence increased from 2.6% to 23.1% 10 weeks post-treatment.
Gore et al ³⁷	AUASI	Baseline (before treatment) and 11 different times during 48-month period following treatment	RP, EBRT, BRT	Storage LUTS	Higher burden of storage symptoms among those who underwent BRT than among those treated with EBRT or RP (p<0.001)
Ponholzer et al ³⁸	Bristol-LUTS questionnaire	Mean time-interval 4.6 years for RPE and 4.4 years for EBRT	EBRT, RP	Urgency Nocturia	Prevalence of 73% vs. 58.5% (however not statistically significant) Incidence of 35.6% after RP, 48.2% after EBRT (not statistically significant)
Teishima et al ³⁹	IPSS	Baseline (before treatment), and 1, 3, 6, 9, and 12 months following treatment	BRT	Urgency Nocturia	IPSS (0–1): 67.3% of patients IPSS (2–5): 32.7% of patients IPSS (0–1): 30.8% of patients IPSS (2–5): 69.2% of patients
Majoros et al ⁴⁰	Urodynamic examination	3–7 days before and 2 months following treatment	RP	UI	3.2% patients with pre-treatment LUTS/voiding difficulty displayed urge incontinence following treatment
Namiki et al ⁴¹	IPSS	Baseline (before treatment), 3, 6, 12, 18, and 24 months after treatment	RP	Storage LUTS	39% increased symptom score following treatment.
Fransson ⁴²	EORTC – QLQ-C30 Version 2	4, 8, and 15 years after treatment	EBRT	UI	Mean score of 2.1 with SD of 2.8 in patients compared to mean score of 1.1 with SD of 2.1 in controls at 15 years

				Nocturia	Mean score of 1.7 with SD of 1.2 in patients compared to mean score of 1.8 with SD of 1.8 in controls at 15 years
				Urgency	Mean score of 1.6 with SD of 2.4 in patients compared to mean score of 1.6 with SD of 2.8 in controls at 15 years
Johansson et al ⁴³	Study-specific questionnaire (validated)	Median followup of 12.2 years after treatment	RP	Nocturia (twice a night or more)	Prevalence of 49% compared to 42% in the control group
				Urgency (once a day or more)	Prevalence of 15% compared to 8% in the control group

AUASI: American Urological Association Symptom Index; BRT: brachytherapy; CI: confidence interval; DAN-PSS: Danish Prostatic Symptom Score; EBRT: external beam radiation therapy; EORTC: European Organisation for Research and Treatment of Cancer; ICS: International Continence Society; IPSS: International Prostate Symptom Score; IQR: interquartile range; LUTS: lower urinary tract symptoms; N-QOL: Nocturia Quality of Life questionnaire; OAB: overactive bladder; OABSS: OAB Symptom Score; OR: odds ratio; QRQ-C30: EORTC Core Quality of Life questionnaire; RP: radical prostatectomy; RT: radiation therapy; SD: standard deviation; UI: urinary infection.

Appendix 1. Full search strategy

Prevalence of LUTS/OAB at PCa diagnosis

("lower urinary tract symptoms" OR "overactive bladder") AND (prostatic neoplasms[MeSH Terms]) AND (Epidemiologic Methods[MeSH Terms] OR Epidemiology[MeSH Terms] OR Prevalence[MeSH Terms])

Prevalence, incidence, exacerbation or resolution of OAB-related symptoms after PCa treatment

(prostatectomy[MeSH Terms] OR brachytherapy[MeSH Terms] OR radiotherapy[MeSH Terms]) AND (prostatic neoplasms[MeSH Terms]) AND (Urinary bladder, overactive[MeSH Terms] OR "urgency" OR "nocturia" OR "urgency incontinence" OR "urge incontinence" OR "frequency" OR "storage symptoms" OR "detrusor overactivity" OR "quality of life" OR "patient reported outcomes") AND (lower urinary tract symptoms[MeSH Terms])