IJIR: Your Sexual Medicine Journal
https://doi.org/10.1038/s41443-020-00386-4

REVIEW ARTICLE

Neglected side effects to curative prostate cancer treatments

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Received: 18 August 2020 / Revised: 17 November 2020 / Accepted: 24 November 2020

Abstract

In this narrative review we summarize neglected side effects of curative intended treatment for prostate cancer. They include climacturia, arousal incontinence (AI), orgasmic disturbances such as altered orgasmic sensation, anorgasmia, and orgasm-associated pain (dysorgasmia), ejaculatory dysfunction, and morphological penile alterations in the form of shortening and deformity. Even though they have not received as much interest as erectile dysfunction (ED) or urinary incontinence, these side effects have been shown to negatively impact patient's quality of life. They are common and rates of climacturia after radical prostatectomy (RP) range from 20% and 45%, less after external beam radiation therapy (EBRT). Decreased orgasmic sensation ranges from 3.9% to 60% after RP and between 36–57% after EBRT. Dysorgasmia ranges from 9.5–15% for both RP and EBRT. Anejculation after EBRT ranges from 11–71% and rates of penile shortening are reported between 0 and 100%. There are no internationally validated questionnaires that adequately asses these side effects. This is necessary if we are to align patient and partner expectations properly and consequently manage them optimally. Neglected side effects should be discussed with patients and their partners preoperatively, as they are associated with bother and may lead to patient's avoiding sexual activity.

Introduction

Prostate cancer has an estimated worldwide incidence of 1.3 million and mortality of 359,000 [1] per year. Established curative treatments include radical prostatectomy (RP), external beam radiation therapy (EBRT) possibly in combination with androgen deprivation therapy, and brachytherapy. The 10-year prostate cancer specific survival rates for EBRT and RP ~99% [2] so attention should be paid to the adverse effects caused by treatments. Regarding functional outcomes, most attention has gone toward erectile dysfunction (ED), urinary incontinence (UI), and bowel dysfunction [3, 4]. However, there are a wide range of sexual side effects that are often overlooked even though they are common [5, 6] and affect patients' quality of life [5, 7]. They have received increasing interest and are collectively termed "Neglected side effects" [5]. They include climacturia, arousal incontinence (AI), orgasmic and ejaculatory disturbances, and penile anatomical changes. In this narrative review we gave interest to original research reporting on side effects other than only UI and/or ED from January 1990 to April 2020. The aim is to summarize the neglected side effects following the different curative treatments for prostate cancer.

Climacturia

Climacturia is the involuntary loss of urine in relation to orgasm [8]. It was first reported after RP by Koeman et al. [9] ($n = 14$) in 1996 and in 2004 Barnas et al. [10] ($n = 239$) found that 93% experienced climacturia on some occasions and 16% with every orgasm. Since then, several studies have reported rates between 20% and 45% following RP [8, 11–19]. It is associated with worsened quality of life [12] and up to 45% of patients who experience it find it bothersome [19]. Studies on climacturia are summarized in Table 1.

Different mechanisms have been proposed to lead to climacturia [20]. It is likely that surgical alterations following RP, such as a decrease in functional urethral length, nerve damage and trauma to the bladder neck or urethral

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Published online: 14 December 2020

Table 1 Climacturia and arousal incontinence (AI) after curative intended treatment for prostate cancer.

Study	Study design	Number of patients	Assessment of climacturia or AI	Predictors	Curative intended treatment	Prevalence of climacturia or Arousal incontinence (AI)	Key findings related to climacturia or AI
Koeman et al. [9]	Prospective	14	Non-validated questionnaire	NA	RP	Climacturia:64%	55% of patients with Climacturia avoided any sexual contact because of it
Barnas et al. [10]	Prospective	239	Non-validated questionnaire	NA	RP	Climacturia: 93%	16% of the patients with Climacturia reported it with every orgasm.
Lee et al. [8]	Prospective	42	Non-validated questionnaire	Daytime UI, age and time since surgery were not statistically significant predictors of	RP	Climacturia: 45%	47% reported that Climacturia caused significant bother and 21% believed that it was a cause of bother for their partner
Choi et al. [11]	Retrospective cross-sectional	475	Medical interview	Dysorgasmia, PS and time since surgery were statistically significant	Open RP (OPR) Laparoscopic RP (LPR) Cystoprostatectomy (CP)	Climacturia: 20% overall (20% (OPR), 24% (LPR), and 6% (CP))	Climacturia rates dropped from 24% within the first year to 13% after 12 months.
Guay et al. [28]	Retrospective cross-sectional	24 (subgroup)	Non-validated questionnaire	NA	RP	AI: 9 men	All affected reported bother due to AI and 6 men avoided sexual contact. The problem was alleviated by a latex ring for all affected.
Nilsson et al. [12]	Prospective	691 (Only sexually active)	Non-validated questionnaire	Daytime UI, ED, PS, and previous trans-urethral resection of the prostate.	RP	Climacturia: 39%	Climacturia led to less frequent intercourse and a greater risk of low-to-moderate quality of life RR 1.5 (95 C.I 1.3–1.7).
Messaoudi et al. [13]	Prospective	63	Non-validated questionnaire	NA	RP	Climacturia: 25.4%	56.3% reported climacturia to be bothersome
Mitchell et al. [14]	Prospective	1358	UCLA-PCI	Daytime UI	RP	Climacturia or AI: 44% at 3 months 36.1% at 24 months	12.1% of patients reported major bother by Climacturia or AI after 24 months
O'Neil et al. [15]	Retrospective	412 (279 RP, 110 RT and 23 RP + RT)	Non-validated questionnaire	Surgical treatment, UI, use of erectile aides	RP EBRT	Climacturia: 28.3% after RP, 5.2% after RT, and 28.6% after combined RP + RT	Climacturia had no significant impact on orgasmic function and satisfaction
Frey et al. [16]	Retrospective Cross-sectional	256 (subgroup)	Study-specific questionnaire-validated within trial	Daytime UI	RP	Climacturia: 29% AI: 27%(38% combined)	The median bother score caused by either Climacturia or AI was 3 (range 1–10)
Capogrosso et al. [17]	Prospective comparison	749 (395 Open RP (OPR) and 354 Robotic-assisted RP (RARP)	Non-validated questionnaire	RARP and time since surgery were predictors of recovery	ORP RARP	Climacturia: 29.2% at 6 months	Type of surgery showed no significant difference in Climacturia rates at 6 months
Frey et al. [6]	Retrospective	109	Study-specific questionnaire-validated within previous trial	NA	EBRT	Climacturia: 3 men AI: 1 man	Climacturia prevalence was very low after EBRT and ADT was not a significant predictor
Salter et al. [19]	Retrospective Cross-sectional	3207	Non-validated questionnaire	Frequency and quantity of leak and duration of relationship was predictors of bother. Patient bother was predictive of perceived partner bother and vice-versa.	RP	Climacturia: 23%	45% of affected men reported bother due to Climacturia. Perceived partner bother was reported by 15%.
Jimbo et al. [18]	Retrospective	192	Non-validated questionnaire	Time since surgery and daytime UI	RP and EBRT	Climacturia: 14% EBRT 34% RP 52% RP + EBRT	There was a significant reduction in prevalence of climacturia ≥ 1 year.
Bach et al. [29]	Retrospective cross-sectional	226	Non-validated questionnaire on AI	Worsening daytime UI and time since surgery	RP	AI: 49%	76% reported leakage during stimulation, and 24% reported leakage in relation to psychological arousal.
Salter et al. [30]	Retrospective cross-sectional	138 (subgroup)	Non-validated questionnaire on AI	Worsening daytime UI and time since surgery	RP	AI: 53% (41% with current AI and 12% with previous)	Of those with current AI 64% reported perceived partner bother and 41% avoided sexual activity at least a few times

sphincter play a pivotal role [21]. In fact, Nilsson et al. [12] found a slight increased risk of climacturia in patients ($n = 691$) who had previously undergone trans-urethral resection of the prostate. Climacturia may be associated with the severity of UI and potentially improves over time, although, this is not consistent across studies. In a prospective study with 1459 patients, Mitchell et al. [14] found an association between climacturia and daytime UI following RP, which is also reported in other studies [15, 16, 19]. However, in a study by Nilsson et al. [12] 86% of 268 patients with climacturia were otherwise continent. Furthermore, Mitchell et al. [14] found that climacturia declined over time with 22.4% labeling it a major problem after 3 months versus 12.1% after 24 months. A time-dependent decrease has been described in other studies as well [11, 18, 19], however, Lee et al. [8] ($n = 42$) found no association between time since surgery and climaturia in a retrospective survey. Their response rate was 68% and there was a potential recall bias. O'Neil et al. [15] ($n = 412$) also found no association in a mixed cohort of RP and EBRT patients.

Based on few studies, climacturia seems less prevalent after EBRT possibly because it is less traumatic to the bladder neck and pelvic floor muscles. However, EBRT can damage pelvic nerves, induce fibrosis, and perhaps even result in loss of functional urethral length [6, 22]. O'Neil et al. [15] reported climacturia in 5.2% after EBRT, 28.3% after RP, and 28.6% following RP + EBRT. Frey et al. [6] ($n = 109$) found UI in relation to sexual activity in 3.7% in sexually active men after EBRT. Androgen Deprivation Therapy (ADT) was not a significant predictor of any of the findings in their study.

Recently, Jimbo et al. [18] ($n = 192$) reported that 14% experienced climacturia after EBRT. The rates were 34% after RP and 52% after EBRT + RP suggesting an additive effect. In the three groups 35%, 33%, and 44% found climacturia to be bothersome, respectively. The higher rate of climacturia after EBRT may be due to patient selection as only patients who were evaluated for sexual dysfunction were included. There was no mention of adjusting for ADT treatment. No time-dependent decrease in climacturia after EBRT was found, similar to O'neil et al. [15].

Potential treatments for climacturia after RP are not widely studied. Bladder emptying prior to sexual activity has been described [8] but no studies have shown significant improvement [23]. A case series by Sighinolfi et al. [24] proposed that pelvic floor muscle exercise (PMFE) might be an option although a systematic review by Kannan et al. [25] found no significant improvement through PMFE alone.

The use of a constriction- or tension ring applied at the base of penis has shown some effect and is recommended at some facilities [23]. Lastly insertion of a urethral sling or artificial sphincter in patients with concomitant daytime UI has been reported to improve climacturia [26, 27]. They apply continuous tension and compress the bulbous urethra to prevent unwanted leakage. Given the time-dependent nature of climacturia studies that include patients with isolated climacturia and control-groups are needed to confirm these findings.

No studies exist regarding treatment following EBRT.

Arousal incontinence

UI during arousal has also been reported, although the literature is scarce. Relevant studies are summarized in Table 1.

Guay et al. [28] ($n = 24$) reported AI in 38% without daytime UI after RP and all found it bothersome. Jain et al. [26] ($n = 11$) reported AI in nine men who had undergone surgery due to daytime UI after RP with seven deeming it to be a major problem. Frey et al. [16] ($n = 316$) reported AI in 29% of 256 sexually active patients following RP. In another recent study [29] ($n = 226$) 49% experienced AI at some point after RP. It was associated with severity of daytime UI and improved over time. Salter et al. [30] looked at a subgroup of 138 patients from the same patient population who were married or cohabitating and reported that 53% had experienced AI at some point following RP and 41% were currently experiencing it. Percieved partner bother was reported by 64% of those with current AI versus 57% with previous AI and bother of any severity was experienced by 87% in total. Only 32% responded to the questionnaire in both studies [29, 30] which introduces a bias and may contribute to the higher prevalence.

There is very little data on AI after EBRT. Frey et al. [6] found that 3.7% had incontinence in relation to sexual activity following EBRT.

Possible mechanisms leading to AI are unknown but likely similar to those suggested for climacturia. In accordance, possible treatments following RP mirror those of climacturia [20, 29].

Orgasmic and ejaculatory disturbances

The male orgasm is a complex mechanism involving a cortical event, subjective experience, neuronal mediation and coinciding muscle contraction, resulting in semen expelled during ejaculation. Orgasm is not dependent on ejaculation and men can achieve orgasm without the ability to ejaculate. which is evident in men who have undergone RP [31, 32].

Orgasmic disturbances include altered sensation of orgasm i.e. more or less intense and/or satisfactory feeling after treatment, anorgasmia, and dysorgasmia in which pain is experienced in relation to orgasm. Ejaculatory dysfunction which includes decreased volume of

ejaculate and anejaculation is also described here as ejaculation may be difficult for patients to distinguish from orgasm.

The pathophysiology of orgasmic disturbances after RP is not fully understood. One theory regarding dysorgasmia is that bladder neck contraction during orgasm translates into a spasm of the vesicourethral anastomosis or pelvic floor dystonia [10]. This does not, however, explain dysorgasmia following EBRT. Anorgasmia and dysorgasmia have also been suggested to result from neuropraxia. Lastly, the psychological distress associated with prostate cancer and its treatment may lead to orgasmic disturbances [31, 33]. Studies reporting on orgasmic function are depicted in Table 2.

Altered orgasmic sensation and anorgasmia

Studies report decreased orgasmic sensation ranging from 3.9% to 70% in selected groups after RP [9, 10, 13, 16, 32, 34]. In a large prospective study, Hollenbeck et al. [34] ($n = 671$) found rates of diminished ability to achieve orgasm or anorgasmia ranging from 16%, for men under 58 years who had undergone nerve sparing RP, to 70% for men over 69 years who had undergone non-nerve sparring RP. They did not adjust for men who could not attain erections. Nerve sparing technique and lower age were also protective in other studies [13, 32, 35, 36]. In Barnas et al. [10] 37% experienced anorgasmia after RP and another 37% experienced decreased orgasm intensity. Interestingly, 4% reported intensified orgasms, which has also been reported in other studies [13, 16, 37]. Frey et al. [16] reported anorgasmia in 5% after RP and decreased intensity in 60%. Furthermore, 57% experienced a prolonged time and 5% a decreased time to reach orgasm. Furthermore, regaining orgasmic function seems to be positively correlated with increased time since surgery [17, 38, 39].

The first study to assess orgasm following EBRT was Helgason et al. [40] ($n = 53$) where 57% experienced decreased orgasm frequency after treatment, 25% were categorized as much decreased, which fell to 21% after adjusting for hormonal treatment. Almost half of those who could achieve orgasm felt diminished pleasure and 46% felt that overall decreased orgasmic function reduced their quality of life. Olsson et al. [41] ($n = 518$) reported that 29.6% of patients after EBRT and 23.7% after EBRT + high dose brachytherapy had orgasms less than half of the time and 46.2% and 36% reported a weaker sensation at least half the time, respectively. Findings did not differ when adjusting for hormonal treatment. Following EBRT Frey et al. [6] reported anorgasmia in 24%, decreased intensity in 44% and longer time to reach orgasm in 40% of patients.

One study by Gay et al. [42] ($n = 573$) looked at EBRT and low-dose brachytherapy and found that 43.9% reported poor, very poor, or no ability to achieve orgasm after brachytherapy alone vs. 23.3% at baseline. The contrasting rates, for men treated with EBRT as monotherapy, were 39.1% at 24 months vs. 30.4% at baseline. Finally, Sullivan et al. [43] ($n = 364$) investigated men who had undergone either EBRT or brachytherapy and found that orgasm domain scores decreased with time since therapy.

Dysorgasmia

Painful orgasms have been reported in 9.5–14% of all men following RP [16, 17, 28, 36, 39, 44] and between 14–17% for men able to achieve orgasm after RP [9, 36].

Matsushita et al. [39] ($n = 702$) reported dysorgasmia in 12% after RP and found that it decreased over time. Most men felt pain in the penis but 22% reported pain in the testis and 8% in other areas. Tewari et al. [32] found a rate of only 3.2% among 156 patients ≤60 years who had undergone bilateral nerve sparring robot-assisted RP (RARP). Mogorovich et al. [36] ($n = 834$) reported dysorgasmia in 18% following RARP and found that sparring of the seminal vesicles increased the risk. Frey et al. [16] reported dysorgasmia in 9% occurring at least a few times and lasting up to 5 min in most men. Worse daytime UI was predictive for orgasmic dysfunction. Capogrosso et al. [17] ($n = 749$) found dysorgasmia in 9.5%. RARP was protective of dysorgasmia compared to open RP and patients had recovery rates of 10% and 30% at 12 and 60 months, respectively.

Few studies have addressed dysorgasmia following EBRT. Olsson et al. [41] found that 10% of men following EBRT and 12% after EBRT + high-dose brachytherapy experienced painful ejaculation. Similarly, Frey et al. [6] found that 15% reported pain in relation to orgasm at least a few times after EBRT.

Three studies looked at brachytherapy and dysorgasmia. Merrick et al. [45] ($n = 34$) found that 26% experienced dysorgasmia at some point after treatment, with a decrease over time. Similarly, Finney et al. [46] ($n = 96$) reported dyorgasmia in 40% and saw a time-dependent decrease. Huyghe et al. [47] retrospectively evaluated 241 men treated with brachytherapy. Ejcaulatory pain was reported by 30.3% of 198 still sexually active men with 10.1% experiencing pain often. In contrast, 12.9% had experienced pain prior to treatment.

Few treatment options have been studied for dysorgasmia, however, based on the theory that muscle spasms may play a role in dysorgasmia after RP, Barnas et al. [44] studied the effect of tamsulosin on dysorgasmia and found that 77% had an improvement in pain. By relaxing smooth muscle of the bladder neck and prostate, tamsulosin

Table 2 Orgasmic disturbances; diminished orgasmic sensation and dysorgasmia.

Reference	Study design	Number of patients	Assesment of orgasmic disturbances	Predictors	Curative intended treatment	Prevalence altered orgasmic sensation or dysorgasmia	Key findings in related to Orgasmic disturbances
Helgason et al. [40]	Prospective	40	Questionnaire developed through 30 in-depth interviews	NA	EBRT	Diminished orgasm frequency: 57%	47% found that decreased frequency affected their quality of life.
Koeman et al. [9]	Prospective	14	Non-validated questionnaire	NA	RP	Decreased orgamic sensation: 7/14 Dysorgasmia: 2/14	8/14 patients reported that anejaculation had reduced their pleasure of orgasm
Merrick et al. [45]	Retrospective Cross-sectional	34	Non-validated questionnaire	Times since therapy	Brachytherapy	Dysorgasmia: 26% Diminshed orgasmic function: 38%	Diminished orgasm and dysorgasmia was quite common following treatment, the latter subsided over time.
Hollenbeck et al. [34]	Retrospective	671	Validated Epic Questionnaire	Age, nerve sparing technique and prostate weight	RP	Diminished orgasmic function:16-70%	Younger age and use of nerve sparing technique was protective and orgasm was achieved at a higher rate than EF.
Barnas et al. [10]	Prospective	239	Non-validated questionnaire	NA	RP	Anorgasmia: 37% Diminished orgasmic function: 37% Increased intensity: 4% Dysorgsmia: 14%	68% reported pain with dysorgasmia felt in the penis and 24% located the pain to the rectum
Finney et al. [46]	Retrospective Cross-sectional	92	Combination of validated questionnaire UCLA prostate Cancer Index and single validated questions	Time since therapy	Brachytherapy	Dysorgasmia: 40%	Dysorgasmia persisted in approx.. 15% after follow up
Guay et al. [28]	Retrospective	24	Non-validated questionnaire	NA	RP	Dysorgasmia: 3 (12%)	
Dubbelman et al. [35]	Prospective	458(subgroup)	Non-validated questionnaire	Severity of daytime UI, age, nerve sparing technique	RP	Anorgasmia: 33.2%	Younger age and use of nerve sparing technique was associated with the ability to attain orgasm
Messaoudi et al. [13]	Prospective	63	Non-validated questionnaire	NA	RP	Anorgasmia: 39.7% Decreased orgasmic: 38%	Diminished orgasmic function was common as was anejaculation and more than half found that bothersome
Tewari et al. [32]	Prospective	408	Expand prostate cancer index composite (EPIC), IIEF and Non-validated questionnaire	Age, nerve sparing technique, Post-op EF	RP	Anorgasmia: 14.2% Diminished orgasmic function: 3,9% Better orgasm: 1,2%	Men <60 recovered their preoperative orgasmic function best
Matsushita et al. [39]	Retrospective	702	Non-validated questionnaire	Time since surgery	RP	Dysorgasmia 12%	Dysorgasmia decreased in degree and frequency over time
Mogorovich et al. [36]	Retrospective Incl. control group	1288	Study-specific questionnaire-validated within trial	Nerve sparing technique, removal of seminal vesicles	RP	Anorgasmia: 35.3% Dysorgasmia: 11%	Sparing seminal vesicles were associated with dysorgasmia
O'Neil et al. [15]	Retrospective	412(279 RP, 110 RT and 23 RP + RT)	Non-validated questionnaire	NA	RP and EBRT	Anorgasmia: 28,6% RP 31.8% RT 47.8% RP + EBRT	Diminished orgasm was common for both RP and RT

Table 2 (continued)

Reference	Study design	Number of patients	Assesment of orgasmic disturbances	Predictors	Curative intended treatment	Prevalence altered orgasmic sensation or dysorgasmia	Key findings in related to Orgasmic disturbances
Frey et al. [16]	Retrospective Cross-sectional analysis	256(subgroup)	Study-specific questionnaire-validated within trial	None	RP	Anorgasmia: 5% Decreased orgasm: 60% Increased orgasm: 6% Dysorgasmia: 9%	Orgasmic disturbances as a whole affected 2/3 of patients
Huyghe et al. [47]	Retrospective Cross-sectional	518	Non-validated questionnaire	Dry ejaculation predictive of anorgasmia Number of implants predictive of dysorgasmia	Brachytherapy	Anorgasmia: 10% Diminished orgasm: 16.6% Dysorgasmia: 30.3% after treatment vs. 12.9% before treatment Anejaculation: 18.7%	Dysorgasmia was prevalent in every third man
Olsson et al. [41]	Prospective	518	Non-validated questionnaire	Time since treatment (5–7.5 years)	EBRT EBRT + Brachytherapy	Diminished orgasm: 46,2% EBRT 36% EBRT + Brachytherapy Dysorgasmia: 5.2% EBRT 6.4% EBRT + Brachytherapy	Diminished orgasm affected almost half of the patients after RT
Capogrosso et al. [17]	Prospective comparison	749	Non-validated questionnaire	Time since srugery	OPR RARP	Dysorgasmia: 9.5%	Dysorgasmia decreased over time (60 mo)
Frey et al. [6]	Retrospective	109	Study-specific questionnaire-validated within previous trial	None	EBRT	Anorgasmia: 24% Dimished orgasm: 44% Dysorgasmia: 15%	>50% had orgasmic disturbances and ADT was not a significant predictor
Gay et al. [42]	Prospective	573	EPIC-26 Instrument	Time since treatment	EBRT Brachytherapy	Diminished orgasm: Increased by (%) after 24 months: Brachytherapy: 20.6% Brachytherapy + ADT: 21.4% RT: 9.3% RT + ADT: 31.2%	Diminished orgasm was most prevalent after RT + ADT at 6 months and then it decreased.

potentially disrupts or prohibits muscle spasm or dystonia after a prostectomy. However, further studies are needed to investigate and confirm tamsulosin's effect on dysorgasmia.

Ejaculatory dysfunction

Anejaculation is a consequence of RP, however, one study reported that more than 60% of patients were not aware of this [48]. Messaoudi et al. [13] reported bother due to anejaculation in 54% after RP and 8.2% avoided intercourse. Koeman et al. [9] found that anejculation decreased pleasure at orgasm in 8 of 14 men.

Ejaculatory dysfunction is prevalent after EBRT. In a study by Helgason et al. [40] decrease in ejaculate volume was reported by 91% with retained orgasm following treatment. Sullivan et al. [43] found that 71% experienced anejaculation and rates increased over time until 5 years. ADT and age over 65 were predictors of anejaculation. In contrast, Olsson et al. [41] and Frey et al. [6] found rates of 37% and 11%, respectively. The large difference between Sullivan and Frey et al. may partially result from selection differences. Frey et al. excluded men who were not sexually active, Sullivan et al. did not.

Following brachytherapy, Finney et al. [46] reported decreased ejaculate volume in 88.5% and Huyghe et al. [47] in 71.2%. They also reported dry ejaculation in 18.7%.

Penile anatomical changes

Penile shortening after RP has been linked to ED and the suggested pathophysiology is that hypoxia in the penile tissue due to neuropraxia or direct arterial damage results in smooth muscle loss and fibrosis which causes penile shortening [49–53].

Studies on penile shortening after RP are numerous and rates range from 0% to 100% [5, 49, 52, 54–59]. In a pilot study by Munding et al. [49] ($n = 31$) penile length was measured preoperatively and 3 months after surgery. Length was measured to the nearest 0.5 cm and 48% had a loss in stretched penile length in excess of 1 cm. Savoie et al. [54] ($n = 63$) found that 12% had a decrease of 15% in stretched penile length at 3 months. In a prospective study, Gontero et al. [52] ($n = 126$) reported a loss of 1.34 cm and 2.3 cm for flaccid and stretched penile length at 12 months. Nerve sparing surgery, recovery of erectile function, and younger age were predictors of retaining length. Contrary, Briganti et al. [55] ($n = 33$) found no decrease measured penile length at 6 months postoperatively.

Engel et al. [56] ($n = 127$) reported that stretched penile length returned to normal 9 months after bilateral nerve sparing RP and change in length was significantly associated to return of sexual function. Kwon et al. [57] ($n = 507$) found that 59.4% had flaccid and 60.2% had stretched penile length return to normal at 12 months. Vasconcelos et al. [53] ($n = 105$) reported a return to preoperative baseline length after 36 months. These findings contradict the fibrosis theory as a cause of penile shortening since such a change would not be reversible. However, selection bias is a possible explanationas there were substantial drop-out rates and Kwon et al. did not exclude patients who received adjuvant or salvage radiation therapies.

In studies where penile length was self-reported Carlsson et al. ($n = 1288$) [60], Frey et al. [16] and Capogrosso et al. [58] ($n = 134$) reported rates of decrease in length ≥1 cm at 55%, 47% and 56%, respectively. In the study by Capogrosso et al., better preoperative erectile function, postoperative retainment of erectile function and RARP were protective against penile shortening, while Carlsson et al. found nerve sparring to be protective. Frey et al. found that increasing BMI and ED significantly increased the risk of penile shortening and furthermore, that 10% noted an altered curvature. In a study by Tal et al. [61] ($n = 1011$) 15% developed Peyronie's disease within 3 years after RP, they used intracavernosal injections to induces erection. Younger age and white race were predictors. Contrary to this, Berookhim et al. [62] ($n = 63$) only reported 1 patient with penile curvature at 6 months after RP.

There is little data on penile shortening or altered curvature following EBRT. Radiation toxicity can possibly result in penile fibrosis [6]. Haliloglu et al. [59] reported decrease in stretched penile length from 14.2 to 8.6 cm, 18 months after EBRT and ADT. There was a tendency toward greater shortening with longer pre-treatment length. Frey et al. [6] reported a subjective loss of ≥1 cm in 42% and altered curvature in 12%. No independent risk factors were identified.

Interventions to preserve penile length do not demonstrate a clear effect. Kohler et al. [63] found a significant difference in the proportion of men with a mean loss of penile length >2 cm between two groups who started treatment with a Vacuum Erection Device after 1 and 6 months, respectively. Yet, the delayed group did not differ significantly from preoperative measures. Raina et al. [64] found that successful use of Vacuum Erection Device yielded a lesser decrease in penis size compared to no treatment. However, this was self-assessed in a retrospective study and should be interpreted with caution. Lastly Montorsi et al. [65] found that the PDE5-inhibitor tadalafil amiliorated penile length for men on tadalafil once daily vs. placebo. However, the mean difference was only 4.1 mm, so it is debatable whether the finding is clinically significant.

The only two studies evaluating sensory changes unrelated to orgasm were by Frey et al. [6, 16]. Following RP 21% reported decreased sensitivity, 4% experienced paresthesia, 3% experienced the sensation of hot/cold and 3%

reported increased sensitivity. After EBRT 27% reported decreased sensitivity, 2% experienced paresthesia, and 2% experienced the sensation of hot/cold.

Discussion

Neglected side effects after curative intended treatment for prostate cancer have received more attention in recent years. It is difficult to compare studies as there are big discrepancies in study methodology and general use of non-validated questionnaires. Furthermore, when used in this setting the validated questionnaires, such as the IIEF-OD and the UCLA-PCI, do not adequately assess the neglegted side effects. A few study-specific questionnaires have been validated as with Frey et al. [16] who tested face-to-face validity and did test–retest questionnaires, but there is no broad use of these in other studies. In addition, many studies were prone to selection biases and/or recall bias [17, 53, 54].

Recently there has been a move toward recommending a standardized methodology for reporting on erectile function after pelvic surgery [66]. Likewise, methodology must be applied in a rigorous fashion when reporting usually neglected disorders This is crucial in order to provide adequate pre-treatment information for patients, to track possible changes over time, and especially when comparing the side effect profile of different prostate cancer treatment modalities [67]. Neglected side effects after EBRT are less investigated and few studies have examined the situation following brachytherapy.

Even with these limitations, several conclusions can be made. Climacturia is common and should be a part of preoperative counseling as recently proposed by the American Urological Association [68]. Data on AI after RP are scarce, however, prevalence seems to be comparable to that of climaturia, which arguably justifies its inclusion in preoperative counseling as well. UI in relation to sexual activity can be detrimental for some patients, especially those for whom oral sex is a big part of their sexual life. Even with utilities such as variable tension rings, there is a need for randomized clinical trials regarding treatments for climacturia and AI.

Altered orgasmic sensations seem to be more common after RP than after EBRT with or without ADT. Yet, they only appear to decrease over time following RP not EBRT. Decreased orgasmic intensity is the most prevalent form of altered orgasmic sensation with some losing the ability to reach orgasm completely. However, patients seem to retain orgasmic sensation more often than erectile function [31, 33]. As orgasmic function plays a big part in sexual health patients should be encouraged to seek orgasm and sexual pleasure even when erections cannot be obtained. They may not be aware of this and should therefore be counseled on this preoperatively. Dysorgasmia is less prevalent than decreased sensation but rates seem to be the same after RP and EBRT. There is a need for more high-quality data on the subject to discern the nature and course of altered orgasmic sensations after curative intended treatment. Likewise, well documented treatments are warranted.

Anejaculation always follows RP but ejaculatory dysfunction is also quite prevalent after EBRT. However, rates of anejaculation differ significantly between studies and they tend to increase over time. It is bothersome for roughly half the afflicted. Only three studies have reported isolated on brachytherapy, all regarding ejaculatory dysfunction [45–47].

Penile shortening is common in the first 6–9 months following RP but then diminishes. There is no obvious physiological explanation for this. The underlying mechanism could be associated with those proposed for ED, which includes fibrotic changes, which could also account for the findings after EBRT. The use of nerve sparing surgery, PDE5i's, and retained erectile function seem to protect against penile shortening but findings are not universal. Furthermore, rates vary greatly between studies and patient-reported shortening is more prevalent than objectively measured shortening. Therefore, other factors may be obscuring the impression of penile shortening, such as high BMI [5], where the pre-pubic fat pad covering the proximal part of the penis may account for this. Measuring penile length prior to and after surgery as a standard may help shed light on the matter and could also offer console to patients who are bothered by, possibly, only perceived shortening. Other penile alterations are far less investigated.

Limited data exist regarding impact on quality of life among non-heterosexual men. Some studies show that side effects of prostate cancer treatment impact differently depending on sexual orientation. Ejaculatory dysfunction is reported to have greater negative impact on quality of life for non-heterosexual men [69, 70]. One reason proposed by Wassersug et al. [69] is that ejaculation is important as a measure of sexual gratification for men who have sex with other men. Further, the specific treatment related sexual side effects that concern non-heterosexual men may differ from that of heterosexual men, e.g., impact of radiation on bowel function for a man who enjoys anal stimulation [71]. This gap in knowledge may lead to difficulty managing expectations of sexual rehabilitation for non-heterosexual men both preoperatively and postoperatively. In fact, studies have shown a discrepancy between expectations and sexual side effects following prostate cancer treatment [72].

Conclusion

With the wide range of different sexual side effects, it seems obvious that too much emphasis is put on ED and so-called penile rehabilitation after curative treatment for prostate cancer. There is a need adequate for internationally validated questionnaires. Further, more research is needed to identify possible treatments and studies on brachytherapy are warranted to compare side effects across treatments and inform patients properly. More importantly, the post-treatment focus needs to be shifted to much broader sexual rehabilitation programs. As similar side effects may cause different degrees of bother, such programs need to incorporate the needs and wishes of patients and their partners and consider the specific sexual practices of individual men. The main goal is to facilitate a feasible and pleasurable sexual life.

Compliance with ethical standards

Conflict of interest MF is a speaker for Astellas Pharma and an advisor for Ferring Pharmaceuticals. The remaining authors declare no conflict of interest.

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