






# Relationships between erectile dysfunction, prostate cancer treatment type and inflatable penile prosthesis implantation

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**Purpose:** The prevalence of erectile dysfunction (ED) and the utilization of inflatable penile prosthesis (IPP) among prostate cancer patients are understudied. The aim of the study was to examine the relationships between ED, prostate cancer treatment type and IPP implantation in a national cohort.

**Materials and Methods:** We identified a retrospective cohort of Surveillance, Epidemiology, and End Results (SEER)-Medicare patients diagnosed with locoregional prostate cancer between 2006 and 2011 and treated with surgery or radiation. Chi-square tests were used to detect significant differences in ED rates as well as use of IPP among the subset with ED. Multivariable logistic regression was used to examine factors associated with the use of IPP.

**Results:** Among 31,233 patients in our cohort, 10,334 (33.1%) received prostatectomy and 20,899 (66.9%) received radiation. ED within 5 years was significantly more common in the prostatectomy group relative to those the radiation group (65.3% vs. 33.8%,  $p < 0.001$ ). In the subset of 13,812 patients with ED, the radiation group had greater median time to ED diagnosis compared to the prostatectomy group (346 vs. 133 days,  $p < 0.001$ ). IPP implantation was more frequent for prostatectomy patients than for radiation patients (3.6% vs. 1.4%,  $p < 0.001$ ). Cancer treatment type, race, and marital status were significantly associated with IPP utilization.

**Conclusions:** ED is highly prevalent among prostate cancer patients, and IPP implantation is be underutilized. ED rates, time to ED diagnosis and utilization of IPP differed significantly by prostate cancer treatment type.

**Keywords:** Erectile dysfunction; Penile prosthesis; Prostate cancer; Prostatectomy; Radiation

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## INTRODUCTION

Erectile dysfunction (ED) is the inability to achieve or

maintain an erection for sexual intercourse. ED is the most common sexual health problem leading men to seek professional help after cancer treatment, specifically prostate

**Received:** 16 November, 2021 • **Revised:** 15 February, 2022 • **Accepted:** 3 March, 2022 • **Published online:** 18 April, 2022

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cancer, with some studies reporting ED rates as high as 85%. In one study, prostatectomy resulted in failure to regain baseline erectile function in 77% to 90% of males below the age of 60 after one year [1]. A long-term study found that only 28% of post-prostatectomy patients reported erections satisfactory for intercourse after 5 years while a small scale study found that 75% of patients who were potent before radiation therapy (RT) for prostate cancer became impotent [2]. A comparison study found that patients who underwent prostatectomy had a larger decline in sexual function compared to radiation therapy and active surveillance [3].

ED after prostatectomy has been attributed to direct damage to the cavernous nerves or neuropraxia, which can improve over time as the nerves regenerate [4-6]. However, in prostate cancer patients treated with RT, 63% of patients had arteriogenic ED and 32% had a venous leak, determined by Doppler ultrasonography, which does not improve over time [7]. Rates of ED shortly after prostatectomy are high due to damage to the nerves supplying the penis. However, the nerves regenerate and the erection recovers over time. In contrast, RT is often associated with irreversible vascular damage that progresses, resulting in delayed recognition of ED, and thus rates of ED in studies with short follow-up periods are low [8].

Mild to moderate ED may be treated with lifestyle modifications or phosphodiesterase type 5 (PDE5) inhibitors while more severe ED with poor response to PDE5 inhibitors may require non-oral therapies including intracavernosal or intra-urethral injections of alprostadil. These forms of treatment are often less spontaneous and more cumbersome to use with their own set of adverse effects including pain, hematomas, burning, and possible priapism [9-11].

Inflatable penile prosthesis (IPP) is a viable option for ED as primary treatment and in patients who have failed (or cannot tolerate) medical management [12,13]. It has patient satisfaction rates above 90% and is associated with greatly improved erectile function with the mean International Index of Erectile Function-5 (IIEF-5) increasing from 8.2 to 20.6 after 1 year [14,15]. Furthermore, low rates of complications including infection, urethral erosion, and prosthesis extrusion have confirmed penile prosthesis surgery as both safe and efficacious [15]. One study demonstrated improvement in psychosocial well-being along with high levels of patient satisfaction one year after implant surgery [16]. Tal et al. [17] reported excellent long-term mechanical reliability of penile prostheses compared to injectable treatments and PDE5 inhibitors. Furthermore, Stephenson et al. [18] found that of all of the treatments for ED, penile prostheses had the greatest satisfaction and success in maintaining an erection. Importantly,

the American Urological Association guideline on ED no longer deems it necessary for patients to have failed conservative therapies before deciding to have an IPP [19]. Despite this shift in the “stepped care” model and the favorable statistics, Tal et al. [17] found underutilization of IPPs in prostate cancer patients with only 0.8% of total prostate cancer patients following prostatectomy or external beam radiation receiving an IPP. In one single tertiary care center, Stanley et al. [20] found that the low rate of IPP use could not be attributed solely to increased uptake or effectiveness of oral pharmacotherapies because following the introduction of sildenafil in 1998, the number of implant procedures has remained stable. Current literature is outdated and fails to observe or account for advancements in penile prostheses since 2005. This study describes the current patient demographics who are receiving the IPPs across the United States.

To better characterize utilization of IPP in prostate cancer patients, we examined the relationships between ED, prostate cancer treatment type and IPP implantation in a cohort of older prostate cancer patients diagnosed with local/regional prostate cancer and treated with surgery or radiation. We hypothesize there is an under-utilization of penile prosthesis in the prostate cancer cohort. Specifically patients who undergo radiation treatment are even less likely to receive an IPP. Further, we hypothesize that certain patient characteristics are associated with the use of IPP.

## MATERIALS AND METHODS

### 1. Data source and study cohort

We used the Surveillance, Epidemiology, and End Results (SEER) registry data linked with Medicare claims as the data source for this study. We performed a retrospective analysis of male patients 66 years of age and older who were first diagnosed with primary local/regional stage prostate cancer between 2006 and 2011. Using International Classification of Diseases 9th revision (ICD-9), Current Procedural Terminology (CPT), and Healthcare Common Procedure Coding System (HCPCS) codes, we created a cohort of patients who were treated with either surgery or radiation from one month prior to three months after initial prostate cancer diagnosis. We followed these patients for five years after prostatectomy or RT to investigate the diagnosis of ED. We examined the use of IPP among patients with ED. Detailed inclusion and exclusion criteria are provided in Supplementary Table 1. We did not consider the use of hormonal therapy in our study, because the study design excluded patients who only received androgen deprivation therapy for

**Table 1.** The frequency of each treatment, radiation and prostatectomy, between 2006 and 2011

Treatment within 3 months of diagnosis	2006 (n=5,736)	2007 (n=5,828)	2008 (n=5,290)	2009 (n=5,011)	2010 (n=4,757)	2011 (n=4,832)
Prostatectomy	1,655 (28.9)	1,816 (31.2)	1,794 (33.9)	1,687 (33.7)	1,667 (35.0)	1,715 (35.5)
Radiation	4,029 (70.2)	3,979 (68.3)	3,454 (65.3)	3,291 (65.7)	3,054 (64.2)	3,092 (64.0)

Values are presented as number (%).

**Table 2.** The time from treatment of prostate cancer until ED diagnosis stratified by treatment group among patients who were diagnosed with ED

Variable	Prostatectomy (n=6,743)	Radiation (n=7,069)	Total (n=13,812)	p-value
Days until ED	133 (30–318)	346 (67–799)	208 (36–574)	<0.001

Values are presented as median (interquartile range).

ED, erectile dysfunction.

advanced disease. Furthermore, patients receiving RT who may have received neoadjuvant or even adjuvant androgen deprivation therapy for higher Gleason grade disease would be expected to have, at the minimum, the same degree of ED. We identified the diagnosis of ED based on ICD-9 codes and IPP based on CPT/HCPCS codes (Supplementary File).

## 2. Patient characteristics

We considered many patient characteristics in our analyses including: age, race/ethnicity, marital status at the time of diagnosis, urban/rural status, neighborhood socioeconomic status (census tract median income, census tract percentage with more than high school education, and census tract percentage below poverty level in quartiles) and Medicaid dual eligibility, which indicates low income and limited financial resources. We also included prostate cancer stage at diagnosis and year of diagnosis. Further, we considered patient comorbidities by including the Quan modification of the Charlson Comorbidity Index (CCI) [21] and the type of cancer treatment the patients received (either prostatectomy or radiation).

## 3. Statistical analyses

We investigated the cancer treatment pattern over the years under study and statistically describe the whole study cohort. We also examined the time from cancer treatment to diagnosis of ED among patients diagnosed with ED. We used chi-square tests to examine group differences in the use of IPP. A multivariable logistic regression model was used to examine the association between patient characteristics, treatment received and the use of IPP. Odds ratios (ORs), corresponding 95% confidence intervals (CIs) and p-values were reported.

The statistical analyses were conducted in SAS 9.4 (SAS Institute, Cary, NC, USA) and R 4.0.2 (R Core Team, Vienna,

Austria). The Institutional Review Board exempted this study from review because all patients in the database had been de-identified.

## RESULTS

The inclusion/exclusion criteria resulted in 31,233 patients who underwent treatment for prostate cancer for the analysis (Supplementary Table 2). Among these patients, 10,334 (33.1%) patients underwent prostatectomy and 20,899 (66.9%) patients underwent RT. Table 1 shows increasing rates of prostatectomy treatment from 2006 to 2011. Among the patients with prostate cancer who underwent prostatectomy or radiation treatment, 13,812 (44.2%) had an ED diagnosis and 17,421 (55.8%) did not have an ED diagnosis (Supplementary Table 3). Patients who underwent prostatectomy were more frequently diagnosed with ED (6,743 out of 10,334 or 65.3%) within 5 years compared to patients who received RT (7,069 out of 20,899 or 33.8%) ( $p < 0.001$ ). Table 2 shows the time from treatment until ED diagnosis, among patients who were diagnosed with ED. Patients in the RT group had a significantly greater median time to ED diagnosis compared to prostatectomy treatment group (346 vs. 133 days,  $p < 0.001$ ).

Table 3 shows the patient and cancer characteristics stratified by IPP for the subgroup of patients with ED. Among the 13,812 patients with ED, 346 (2.5%) patients were treated with an IPP. Patients who underwent a prostatectomy were significantly more likely to receive an IPP compared to patients with RT (3.6% vs. 1.4%,  $p < 0.001$ ). There was no significant change in IPP procedure rates over the six year time period. Single and younger patients living in a metro area were more likely to receive an IPP ( $p < 0.05$ ). Hispanic and non-Hispanic Black patients had an increase rate of utilization of the IPP compared to non-Hispanic White

**Table 3.** Characteristics for patients who were diagnosed with ED stratified by IPP status

Characteristic	No IPP (n=13,466)	IPP (n=346)	Total (n=13,812)	p-value
Treatment				<0.001
Prostatectomy	6,498 (96.4)	245 (3.6)	6,743 (48.8)	
Radiation	6,968 (98.6)	101 (1.4)	7,069 (51.2)	
Year of diagnosis				0.511
2006	2,185 (16.2)	63 (18.2)	2,248 (16.3)	
2007	2,356 (17.5)	48 (13.9)	2,404 (17.4)	
2008	2,259 (16.8)	63 (18.2)	2,322 (16.8)	
2009	2,270 (16.9)	61 (17.6)	2,331 (16.9)	
2010	2,171 (16.1)	58 (16.8)	2,229 (16.1)	
2011	2,225 (16.5)	53 (15.3)	2,278 (16.5)	
Age at diagnosis (y)	70.9±4.0	69.6±3.1	70.8±4.0	<0.001
Race/ethnicity				0.001
Non-Hispanic White	11,017 (81.8)	258 (74.6)	11,275 (81.6)	
Non-Hispanic Black	1,253 (9.3)	49 (14.2)	1,302 (9.4)	
Hispanic	680 (5.0)	29 (8.4)	709 (5.1)	
Asian	186 (1.4)	Masked <sup>a</sup>	Masked <sup>a</sup>	
Other (and unknown)	330 (2.5)	Masked <sup>a</sup>	Masked <sup>a</sup>	
Marital status at diagnosis				<0.001
Married	10,368 (77.0)	235 (67.9)	10,603 (76.8)	
Single	708 (5.3)	31 (9.0)	739 (5.4)	
Divorced/separated	639 (4.7)	34 (9.8)	673 (4.9)	
Widowed	564 (4.2)	18 (5.2)	582 (4.2)	
Other/unknown	1,187 (8.8)	28 (8.1)	1,215 (8.8)	
Urban/rural code at diagnosis				0.017
Big metro	7,216 (53.6)	155 (44.8)	7,371 (53.4)	
Metro	4,223 (31.4)	133 (38.4)	4,356 (31.5)	
Urban	712 (5.3)	17 (4.9)	729 (5.3)	
Less urban	1,056 (7.8)	36 (10.4)	1,092 (7.9)	
Rural	246 (1.8)	Masked <sup>a</sup>	Masked <sup>a</sup>	
Unknown	13 (0.1)	Masked <sup>a</sup>	Masked <sup>a</sup>	
Stage at diagnosis				0.025
Stage II	11,520 (85.5)	281 (81.2)	11,801 (85.4)	
Stage III	1,499 (11.1)	53 (15.3)	1,552 (11.2)	
Stage IV	150 (1.1)	Masked <sup>a</sup>	Masked <sup>a</sup>	
Stage unknown	297 (2.2)	Masked <sup>a</sup>	Masked <sup>a</sup>	
Charlson Comorbidity Index				0.268
0	9,293 (69.0)	229 (66.2)	9,522 (68.9)	
1	2,288 (17.0)	58 (16.8)	2,346 (17.0)	
≥2	1,885 (14.0)	59 (17.1)	1,944 (14.1)	
Census tract median income (dollars)				0.016
Quartile 1 (≤44,745)	2,947 (23.2)	94 (29.7)	3,041 (23.4)	
Quartile 2 (>44,745 to ≤61,837)	3,054 (24.1)	80 (25.2)	3,134 (24.1)	
Quartile 3 (>61,837 to ≤85,808)	3,248 (25.6)	77 (24.3)	3,325 (25.6)	
Quartile 4 (>85,808)	3,429 (27.0)	66 (20.8)	3,495 (26.9)	
Census tract % with more than high school education				0.002
Quartile 1 (≤48.3)	2,905 (22.9)	102 (32.2)	3,007 (23.1)	
Quartile 2 (>48.3 to ≤62.5)	3,049 (24.0)	66 (20.8)	3,115 (24.0)	
Quartile 3 (>62.5 to ≤75.8)	3,201 (25.2)	73 (23.0)	3,274 (25.2)	
Quartile 4 (>75.8)	3,523 (27.8)	76 (24.0)	3,599 (27.7)	

Table 3. Continued

Characteristic	No IPP (n=13,466)	IPP (n=346)	Total (n=13,812)	p-value
Census tract % below poverty level				0.007
Quartile 1 ( $\leq 4.9$ )	3,265 (25.8)	56 (17.7)	3,321 (25.6)	
Quartile 2 ( $>4.9$ to $\leq 9.2$ )	3,368 (26.6)	85 (26.8)	3,453 (26.6)	
Quartile 3 ( $>9.2$ to $\leq 16.6$ )	3,063 (24.2)	86 (27.1)	3,149 (24.2)	
Quartile 4 ( $>16.6$ )	2,982 (23.5)	90 (28.4)	3,072 (23.6)	
Medicaid dual-eligible				<0.001
No	12,658 (94.0)	305 (88.2)	12,963 (93.9)	
Yes	808 (6.0)	41 (11.8)	849 (6.1)	

Values are presented as number (%) or mean $\pm$ standard deviation.

ED, erectile dysfunction; IPP, inflatable penile prosthesis; SEER, Surveillance, Epidemiology, and End Results.

<sup>a</sup>:Masked per SEER-Medicare user agreement for confidentiality.

patients ( $p=0.001$ ).

Table 4 shows ORs from the multivariable logistic regression model for IPP among patients with ED. Compared to patients who received prostatectomy, those who received radiation were significantly less likely to receive IPP (OR, 0.41; 95% CI, 0.31–0.53). Non-Hispanic Black were significantly more likely to receive IPP compared to White (OR, 1.61; 95% CI, 1.14–2.27); single (OR, 1.82; 95% CI, 1.23–2.71) or divorced patients (OR, 2.06; 95% CI, 1.40–3.02) were more likely to undergo IPP compared to married patients. Patients with higher CCI scores had higher odds of receiving IPP treatment, but the p-value did not reach statistical significance (OR, 1.32; 95% CI, 0.98–1.78 for comorbidity index  $\geq 2$  vs. 0).

## DISCUSSION

Overall, we found that 44% of older patients with prostate cancer had an ED diagnosis within 5 years of cancer treatment. Only 25% of the males with an ED diagnosis in this study underwent IPP. Although low, this rate is higher than those previously reported [17,18]. For example, Tal et al. [17] showed a utilization rate of 0.8% and Stephenson et al. [18] reported IPP utilization rate of 1.9% in prostate cancer patients. These studies reported much lower rates possibly because they were conducted between 1998 and 2005, just before key innovations to the penile implant devices. Between 2004 and 2008, AMS and Coloplast redesigned the device for easier inflations, easier deflations, and a flattened reservoir design to make it less palpable (Supplementary Table 4) [22]. Our study, from 2006 to 2011, assessed IPP implantation rates after implementation of these major innovations. It is conceivable that these improvements, or perhaps increased coverage of these changes at various scientific meetings and journals, may have resulted in higher IPP utilization in our study.

The rates of ED in prostatectomy patients were almost double the rates in RT patients (66.9% vs 33.1%). These rates are similar to previously reported rates of ED in the prostate cancer cohort. The CaPSURE study found that 1 year after prostatectomy, 80% of males suffered from ED [23] while the Prostate Cancer Outcomes Study found that 59.9% of men self-reported ED after a prostatectomy [24]. Potosky et al. [25] compared five-year functional outcomes after prostatectomy and external beam radiotherapy and found that there was a statistically increased rate of erectile function in males treated with prostatectomy (79.3% compared to 63.5%). Of significance, there was improvement in sexual function between 6 months and 2 years post-prostatectomy while there was a slight decline in function over time in patients receiving radiation. Another study showed that the rate of ED after RT increased over time from 4% to 47% in 5 years, secondary to irreversible, slowly progressing vascular damage [26]. These findings are in line with our study results showing a much longer time span from treatment of prostate cancer to ED diagnosis for patients with radiation compared to patients with prostatectomy (median 346 vs. 133 days). The rate of ED in the radiation group in our study may still be underestimated due to the slow progression of ED.

We found that patients who underwent prostatectomy were more likely to undergo IPP compared to RT (3.6% vs. 1.4%). Interestingly, Tal et al. [17] also found that there was unequal usage of IPP between prostatectomy and RT patients (2.3% vs. 0.3%). The discrepancy in utilization rates between the two groups may be explained by different practice patterns and discussion focus between urologists and radiation oncologists. The delayed onset of ED among those receiving RT compared to prostatectomy, as shown above, may have also played an important role. Specifically, a sizeable percentage of patients undergoing RT may be followed solely by radiation oncologists, and while ED may be

**Table 4.** Results from a multivariable logistic regression model for IPP

Parameter	Odds ratio (95% confidence interval)	p-value
<b>Treatment group</b>		
Prostatectomy (ref)	1	
Radiation	0.41 (0.31–0.53)	<0.001
Year of diagnosis, 1-year increase	0.98 (0.92–1.05)	0.58
Age at diagnosis, 5-year increase	0.75 (0.63–0.89)	0.001
<b>Race/ethnicity</b>		
Non-Hispanic White (ref)	1	
Non-Hispanic Black	1.61 (1.14–2.27)	0.007
Hispanic	1.47 (0.96–2.26)	0.08
Asian	0.87 (0.31–2.44)	0.79
Other/unknown	0.78 (0.34–1.78)	0.56
<b>Marital status at diagnosis</b>		
Married (ref)	1	
Single	1.82 (1.23–2.71)	0.003
Divorced/separated	2.06 (1.40–3.02)	<0.001
Widowed	1.60 (0.97–2.63)	0.06
Other/unknown	1.31 (0.88–1.97)	0.19
<b>Urban/rural location</b>		
Big metro (ref)	1	
Metro	1.48 (1.16–1.90)	0.002
Urban	1.22 (0.72–2.07)	0.47
Less urban	1.60 (1.05–2.42)	0.028
Rural	0.97 (0.38–2.47)	0.95
<b>Stage at diagnosis</b>		
Stage II (ref)	1	
Stage III	1.03 (0.75–1.40)	0.87
Stage IV	1.36 (0.62–2.97)	0.44
Unknown	0.71 (0.29–1.75)	0.46
<b>Charlson Comorbidity Index</b>		
0 (ref)	1	
1	1.07 (0.80–1.45)	0.63
≥2	1.32 (0.98–1.78)	0.07
<b>Census tract median income</b>		
Q1 (≤44,745 [ref])	1	
Q2 (>44,745 to ≤61,837)	0.95 (0.65–1.38)	0.77
Q3 (>61,837 to ≤85,808)	1.09 (0.68–1.73)	0.72
Q4 (>85,808)	1.07 (0.60–1.89)	0.82
<b>Census tract % above high school education</b>		
Q1 (≤48.3 [ref])	1	
Q2 (>48.3 to ≤62.5)	0.77 (0.55–1.07)	0.12
Q3 (>62.5 to ≤75.8)	0.77 (0.52–1.12)	0.17
Q4 (>75.8)	0.77 (0.49–1.20)	0.25
<b>Census tract % below poverty level</b>		
Q1 (≤4.9 [ref])	1	
Q2 (>4.9 to ≤9.2)	1.38 (0.96–1.99)	0.08
Q3 (>9.2 to ≤16.6)	1.41 (0.94–2.12)	0.10
Q4 (>16.6)	1.14 (0.68–1.90)	0.61
Medicaid dual-eligibility	1.48 (1.01–2.17)	0.048

IPP, inflatable penile prosthesis.

diagnosed, radiation oncologists may not be as comfortable discussing IPPs as a treatment option.

Our study also demonstrated that patients who were younger, Hispanic, Non-Hispanic Black, single, divorced were more likely to undergo implant surgery. It can be hypothesized that males who are younger and single are more motivated to seek more efficacious and satisfactory treatment options for ED since they are more likely to have younger partners and a higher sexual drive. In contrast, our analysis indicated that patients with a higher CCI had an increased rate of IPP utilization. It may be speculated that these patients have high rates of diabetes and hypertension, and are therefore more refractory to more conservative treatments or have contraindications to PDE5 inhibitors [27]. Our dataset does not inform the possibility of a racial disparity in the usage of IPP since other confounding patient factors such as sexual drive and access to care were not available for inclusion in the analysis. Consideration for these factors (age, race, location, marital status, comorbidities, and treatment modality) when a patient is first assessed for ED will help guide urologists in offering the best treatment.

IPPs have one of the highest satisfactions rates of all ED treatment modalities and yet have the lowest utilization rate with only 2.5% of patients receiving prostheses [4]. On the other hand, for the general ED population not limited to prostate cancer patients, studies have shown that intracavernosal injection (ICI) have a 11% to 31% dropout rate due to pain and lack of efficacy. Furthermore, several studies reported a disappointing 30% success rate of ICI in post-prostatectomy patients [4,28,29]. In a meta-analysis, Corona et al. [30] found that there was roughly a 50% PDE5 inhibitor dropout rate each year due to lack of efficacy, adverse events, and contraindications. Since PDE5 inhibitors are often the first treatments prescribed for ED, the high failure rate leaves thousands of Americans untreated. With a 50% dropout rate and a 30% success rate of PDE5 inhibitors and ICIs respectively, it is estimated that about 4,700 (34%) of the patients in our database likely remained untreated for ED. The substantial underutilization of IPP detected in our analysis might be addressed by further educating patients on ED as an adverse event of prostate cancer therapy. Providing the full gamut of treatment options including IPP and their effectiveness will potentially help restore erectile function to those who may not respond to non-surgical therapies.

While our study strengths lie in the large sample size, long follow-up time and the inclusion of a large number of demographic, clinical and socioeconomic factors, there are some limiting factors. The major limitation of this study is that we only evaluated Medicare patients 66 and older.

Therefore the study may not be generalizable to all men undergoing treatment for prostate cancer. The rate of IPP utilization may have been higher had a younger cohort been included, as shown by Tal et al. [17]. Although we have included a large number of factors, there are still many other factors not captured in the database. For example, there may be variability in the ED rates since we cannot account for the radiation dose or the surgical technique. Furthermore, the severity of the ED pathology was not evaluated in this study, since ED was determined by CPT coding rather than chart review and symptomatology. Sexual interest was not gauged and thus its influence on the rate of IPP implantation could not be assessed in this study. Another limitation of the study is the absence of rates of different medical managements for ED. We did not investigate the success and failure rates of other ED treatment options and thus cannot conclude if patients simply opted out of surgical management or if they were not offered the option due to success with medical management. Finally the patients in our study sample are heterogeneous covering a very diverse population. However, the large sample size allowed us to adjust for a large number of factors including patient characteristics at the time of diagnosis (age, race/ethnicity, marital status at the time of diagnosis, urban/rural status, neighborhood socioeconomic status, and Medicaid dual eligibility), comorbidities, stage of cancer, and year of prostate cancer diagnosis in our multivariable analyses.

## CONCLUSIONS

This study filled the knowledge gap about the utilization rate of IPP and factors associated with usage since 2005. We showed the underutilization of IPP among older patients with prostate cancer persisted. Such under-utilization may be due to greater clinical focus on cancer treatment rather than quality-of-life issues. We also observed discrepancies in IPP utilization rates between those treated with radiation versus surgery, which may be partially explained by variations in follow-up protocols between these two treatment modes, different progression trajectories, and highly variable sexual dysfunction reporting. These findings highlight the importance of thorough counseling about all treatment options for ED and providing patients the option of the penile prosthesis implantation for ED after treatment for prostate cancer.

## CONFLICTS OF INTEREST

The authors have nothing to disclose.

## FUNDING

None.

## ACKNOWLEDGMENTS

This study used the linked SEER-Medicare database. The interpretation and reporting of these data are the sole responsibility of the authors. The authors acknowledge the efforts of the Applied Research Program, NCI; the Office of Research, Development and Information, CMS; Information Management Services (IMS), Inc; and the Surveillance, Epidemiology, and End Results (SEER) Program tumor registries in the creation of the SEER-Medicare database. Dr. Helmer is supported by the Center for Innovations in Quality, Effectiveness and Safety (VA HSRD CIN 13-413), Michael E. DeBakey VA Medical Center, Houston, Texas, USA. The views expressed in this article are those of the authors and do not necessarily reflect the position or policy of the Department of Veterans Affairs or the United States government.

## AUTHORS' CONTRIBUTIONS

Research conception and design: Chan Shen and Hossein Sadeghi-Nejad. Data acquisition: Chan Shen. Statistical analysis: Chan Shen, Eric Schaefer, and Shouhao Zhou. Data analysis and interpretation: all authors. Drafting of the manuscript: all authors. Critical revision of the manuscript: all authors. Supervision: Chan Shen and Hossein Sadeghi-Nejad. Approval of the final manuscript: all authors.

## SUPPLEMENTARY MATERIALS

Supplementary materials can be found via <https://doi.org/10.4111/icu.20210445>.

## REFERENCES

1. Castiglione F, Ralph DJ, Muneer A. Surgical techniques for managing post-prostatectomy erectile dysfunction. *Curr Urol Rep* 2017;18:90.
2. Kendirci M, Bejma J, Hellstrom WJ. Update on erectile dysfunction in prostate cancer patients. *Curr Opin Urol* 2006;16:186-95.
3. Barocas DA, Alvarez J, Resnick MJ, Koyama T, Hoffman KE, Tyson MD, et al. Association between radiation therapy, surgery, or observation for localized prostate cancer and patient-

- reported outcomes after 3 years. *JAMA* 2017;317:1126-40. Erratum in: *JAMA* 2017;317:2134.
4. Lima TFN, Bitran J, Frech FS, Ramasamy R. Prevalence of post-prostatectomy erectile dysfunction and a review of the recommended therapeutic modalities. *Int J Impot Res* 2021;33:401-9.
  5. Masterson TA, Serio AM, Mulhall JP, Vickers AJ, Eastham JA. Modified technique for neurovascular bundle preservation during radical prostatectomy: association between technique and recovery of erectile function. *BJU Int* 2008;101:1217-22.
  6. Glickman L, Godoy G, Lepor H. Changes in continence and erectile function between 2 and 4 years after radical prostatectomy. *J Urol* 2009;181:731-5.
  7. Zelefsky MJ, Eid JF. Elucidating the etiology of erectile dysfunction after definitive therapy for prostatic cancer. *Int J Radiat Oncol Biol Phys* 1998;40:129-33.
  8. Yildirim HC, Ergen SA, Sedef E, Sahin M, Karacam SC, Senocak MS, et al. Erectile dysfunction in prostate cancer patients treated with intensity-modulated radiation therapy. *Indian J Cancer* 2020;57:70-5.
  9. Miller TA. Diagnostic evaluation of erectile dysfunction. *Am Fam Physician* 2000;61:95-104, 109-10.
  10. Feldman HA, Goldstein I, Hatzichristou DG, Krane RJ, McKinlay JB. Impotence and its medical and psychosocial correlates: results of the Massachusetts Male Aging Study. *J Urol* 1994;151:54-61.
  11. Mobley DF, Khera M, Baum N. Recent advances in the treatment of erectile dysfunction. *Postgrad Med J* 2017;93:679-85.
  12. Levine LA, Becher EF, Bella AJ, Brant WO, Kohler TS, Martinez-Salamanca JI, et al. Penile prosthesis surgery: current recommendations from the International Consultation on Sexual Medicine. *J Sex Med* 2016;13:489-518. Erratum in: *J Sex Med* 2016;13:1145.
  13. Bennett N, Huang IS. Inflatable penile prosthesis in the radical prostatectomy patient: a review. *F1000Res* 2018;7:770.
  14. Çayan S, Aşçı R, Efesoy O, Bolat MS, Akbay E, Yaman Ö. Comparison of long-term results and couples' satisfaction with penile implant types and brands: lessons learned from 883 patients with erectile dysfunction who underwent penile prosthesis implantation. *J Sex Med* 2019;16:1092-9.
  15. Antonini G, Busetto GM, De Berardinis E, Giovannone R, Vicini P, Del Giudice F, et al. Minimally invasive infrapubic inflatable penile prosthesis implant for erectile dysfunction: evaluation of efficacy, satisfaction profile and complications. *Int J Impot Res* 2016;28:4-8.
  16. Tefilli MV, Dubocq F, Rajpurkar A, Gheiler EL, Tiguert R, Barton C, et al. Assessment of psychosexual adjustment after insertion of inflatable penile prosthesis. *Urology* 1998;52:1106-12.
  17. Tal R, Jacks LM, Elkin E, Mulhall JP. Penile implant utilization following treatment for prostate cancer: analysis of the SEER-Medicare database. *J Sex Med* 2011;8:1797-804.
  18. Stephenson RA, Mori M, Hsieh YC, Beer TM, Stanford JL, Gilliland FD, et al. Treatment of erectile dysfunction following therapy for clinically localized prostate cancer: patient reported use and outcomes from the Surveillance, Epidemiology, and End Results Prostate Cancer Outcomes Study. *J Urol* 2005;174:646-50; discussion 650.
  19. Burnett AL, Nehra A, Breau RH, Culkin DJ, Faraday MM, Hakim LS, et al. Erectile dysfunction: AUA guideline. *J Urol* 2018;200:633-41. Erratum in: *J Urol* 2022;207:743.
  20. Stanley GE, Bivalacqua TJ, Hellstrom WJ. Penile prosthetic trends in the era of effective oral erectogenic agents. *South Med J* 2000;93:1153-6.
  21. Quan H, Li B, Couris CM, Fushimi K, Graham P, Hider P, et al. Updating and validating the Charlson comorbidity index and score for risk adjustment in hospital discharge abstracts using data from 6 countries. *Am J Epidemiol* 2011;173:676-82.
  22. Le B, Burnett AL. Evolution of penile prosthetic devices. *Korean J Urol* 2015;56:179-86.
  23. Hu JC, Elkin EP, Pasta DJ, Lubeck DP, Kattan MW, Carroll PR, et al. Predicting quality of life after radical prostatectomy: results from CaPSURE. *J Urol* 2004;171(2 Pt 1):703-7; discussion 707-8.
  24. Stanford JL, Feng Z, Hamilton AS, Gilliland FD, Stephenson RA, Eley JW, et al. Urinary and sexual function after radical prostatectomy for clinically localized prostate cancer: the Prostate Cancer Outcomes Study. *JAMA* 2000;283:354-60.
  25. Potosky AL, Davis WW, Hoffman RM, Stanford JL, Stephenson RA, Penson DF, et al. Five-year outcomes after prostatectomy or radiotherapy for prostate cancer: the prostate cancer outcomes study. *J Natl Cancer Inst* 2004;96:1358-67.
  26. Rogers MJ, Ramirez-Fort MK, Kashanian JA, Broster SA, Matta J, Mahase SS, et al. Prostatic irradiation-induced sexual dysfunction: a review and multidisciplinary guide to management in the radical radiotherapy era (Part II on Urological Management). *Rep Pract Oncol Radiother* 2020;25:619-24.
  27. Kouidrat Y, Pizzol D, Cosco T, Thompson T, Carnaghi M, Bertoldo A, et al. High prevalence of erectile dysfunction in diabetes: a systematic review and meta-analysis of 145 studies. *Diabet Med* 2017;34:1185-92.
  28. Linet OI, Ogrinc FG. Efficacy and safety of intracavernosal alprostadil in men with erectile dysfunction. The Alprostadil Study Group. *N Engl J Med* 1996;334:873-7.
  29. Virag R, Shoukry K, Floresco J, Nollet F, Greco E. Intracavernous self-injection of vasoactive drugs in the treatment of impo-



- tence: 8-year experience with 615 cases. *J Urol* 1991;145:287-92; discussion 292-3.
30. Corona G, Rastrelli G, Burri A, Serra E, Gianfrilli D, Mannucci E, et al. First-generation phosphodiesterase type 5 inhibitors dropout: a comprehensive review and meta-analysis. *Andrology* 2016;4:1002-9.