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Post-Radical Prostatectomy Erectile Dysfunction Assessed Using the IIEF-5 Questionnaire – A Systematic Literature Review

Tomasz Jurys^a , Bartłomiej Burzynski^b, Anna Potyka^c and Andrzej Paradysz^d

^aDoctoral School, Faculty of Health Sciences in Katowice, Medical University of Silesia in Katowice, Katowice, Poland; ^bDepartment of Rehabilitation, Faculty of Health Sciences in Katowice, Medical University of Silesia in Katowice, Katowice, Poland; ^cInstitute of Education and Communication Research, Silesian University of Technology in Gliwice, Gliwice, Poland; ^dDepartment of Urology, Faculty of Medical Sciences in Zabrze, Medical University of Silesia in Katowice, Poland

ABSTRACT

Erectile dysfunction is common postoperative complication after radical prostatectomy. The aim of this study is to evaluate erectile dysfunction among the population of men who have undergone radical prostatectomy. Finally, 21 articles are included in the current qualitative analysis. The results suggest that recovery in potency occurs after 12 months after surgery, and that different adjuvant treatment can be used to accelerate recovery and increase effectiveness. However, conclusions are not derived from all the selected articles, but are rather based on those which present clear numerical scores according to the IIEF-5 questionnaire.

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prostate cancer;
prostatectomy

Introduction

It is estimated that prostate cancer is responsible for almost 650,000 cases of cancer per year in economically developed countries (Jemal et al., 2011). A patient diagnosed with prostate cancer may be eligible for various types of therapy, depending on his clinical condition. Options include active surveillance, watchful waiting, radical prostatectomy, external beam radiotherapy, brachytherapy, and hormone therapy (Chen & Zhao, 2013). The chosen method of treatment will affect the likelihood of occurrence of complications and the quality of life of the patient. In the case of radical prostatectomy, the most common postoperative symptoms are urinary incontinence and erectile dysfunction (Torvinen et al., 2013). As defined in 1992 by the National Institutes of Health (NIH), erectile dysfunction is the inability to achieve and maintain an erection of sufficient strength for intercourse (“Impotence”, 1993). The frequency of dysfunction after radical prostatectomy may depend on the patient’s clinical condition, the level of experience of the operating surgeon, and the

chosen methods of prostatectomy and of nerve sparing (of the vasomotor bundles) (Ayyathurai et al., 2008; Barocas et al., 2010; Bianco et al., 2005; Zippe et al., 2006). One of the most frequently used tools to assess erectile dysfunction of various etiologies, including patients after radical prostatectomy, is the International Index of Erectile Function-5 (IIEF-5) questionnaire.

The aim of the present systematic review of the literature was to evaluate changes in erectile dysfunction in the population of men who underwent radical prostatectomy before and after surgery using the IIEF-5 questionnaire. When analyzing the phenomenon of erectile dysfunction, variables such as time after surgery and adjuvant treatment were also taken into account.

Materials and methods

For the purpose of conducting a high-quality systematic literature review, the authors of this study used the PRISMA (*Preferred Reporting Items for Systematic Reviews and Meta-Analyses*) protocol (Moher et al., 2009).

Search strategy

The search for literature took place in the period from October 2020 to January 2021 and included searches for studies in the following nine scientific databases: PubMed/MEDLINE, EMBASE, Web of Science, Scopus, the Polish Medical Library, the Cochrane Library, Science Direct, EBSCO, LiSSA. Studies in Polish, English and French were sought using the following keywords or their translation equivalents after taking into account the specificity of the scientific database: (prostate cancer OR prostate carcinoma OR prostate gland cancer OR prostate gland carcinoma) AND (IIEF OR IIEF-5 OR International Index of Erectile Function-5 OR SHIM OR Sexual Health Inventory for Men).

Inclusion and exclusion criteria

Studies found during the initial search were selected for further analysis on the basis of the adopted inclusion criteria, which stipulated that the studies must:

- Concern men suffering diagnosed with prostate cancer and undergoing radical prostatectomy;
- Include assessment of erectile dysfunction using the IIEF-5 questionnaire;
- Include assessment of ED before surgery and at least once after surgery;
- Free full text of the study.

Studies that met the following exclusion criteria were excluded:

- Not written in English, Polish and French;
- Unable to data extract.

Any differences of opinion between the authors over whether studies qualified for further analysis were resolved through discussion and consensus.

IIEF-5 questionnaire

The International Index of Erectile Function-5 (IIEF-5) is a standardized tool, developed in 1999, for assessing the quality of penile erection and sexual function. The questionnaire consists

of five questions, each of which is answered on a five-point scale. A maximum of 25 points can therefore be obtained, with a score of ≤ 21 indicating erectile dysfunction. The severity of erectile dysfunction is divided into four grades as follows: severe (1–7 points), moderate (8–11 points), mild to moderate (12–16 points), mild (17–21 points) (Albersen et al., 2009; Rosen et al., 1999).

Results

Selection of studies

The search of scientific databases using the abovementioned keywords, as well as a review of other sources, i.e. the tables of contents of key journals and the bibliographies of searched studies, yielded a total of 631 records. Record after duplicates removed was screened through reading the titles and abstracts. Then, each paper was fully read and assessed taking into account eligibility criteria. After further analysis and application of the inclusion and exclusion criteria, 21 articles were finally selected for qualitative analysis. A flow diagram of the search and selection process according to the PRISMA protocol is presented in Figure 1.

Description of studies included

In each of the studies included in the systematic review of the literature, the assessment of erectile dysfunction was made using the IIEF-5 questionnaire. All studies was published in English language. Despite the fact that the questionnaire has existed since 1999, the oldest article that qualified for the final analysis was from 2005. The qualifying studies come from 13 different countries, 13 in Europe, 3 in South America, 3 in Asia and 2 in North America. Eight studies were randomized clinical trials, and the remaining 13 were observational, comparative, or case series. The total number of respondents from all finally selected studies was 17,641. The most common time point for assessing erectile dysfunction was 12 months after surgery, although dysfunction was also assessed with equal frequency at 3 and 6 months after surgery. The mean age of the majority of the study population was over 60 years. The

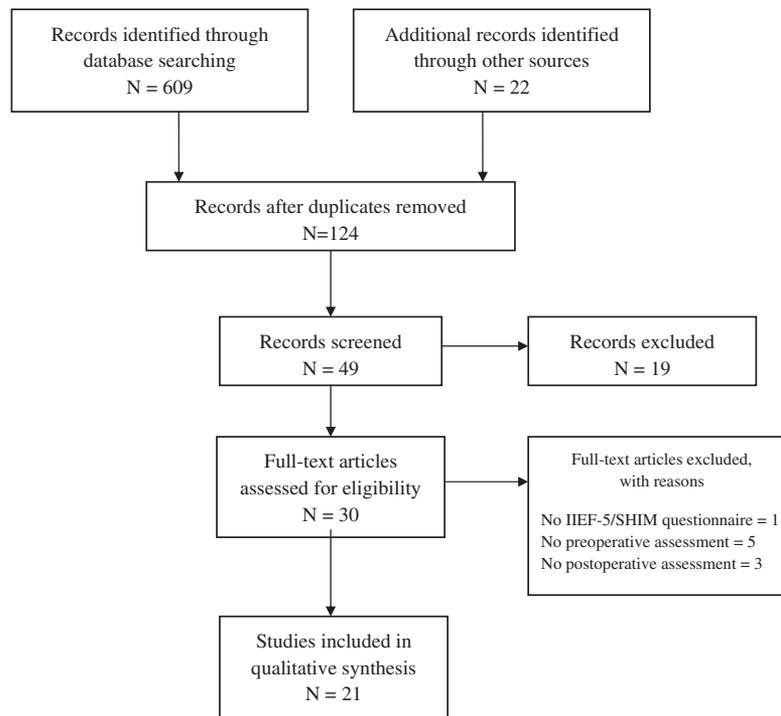


Figure 1. PRISMA Flow diagram.

available information on the clinical tumor grade shows that the cT1, cT2 and cT3 grades were the most common in the prostate cancer population. In turn, the most common pathological stage of the cancers was pT2, pT3 and pT4. The most common surgical techniques used in the studies were radical retropubic prostatectomy and robot-assisted radical prostatectomy, while the most seldom used was laparoscopic radical prostatectomy. The characteristics and a summary of the results of the studies included in the review are presented in Table 1.

Summarizing of included studies

Erectile dysfunction is one of the most common postoperative complications after radical prostatectomy and occurs with a frequency of between 14% and 90% (Park et al., 2013; Saleh et al., 2015). The results of this review indicate that in most of the selected studies, mild or mild to moderate severity of erectile dysfunction had already been observed before surgery. Analysis of those studies which present results in a way that allows the classification of erectile dysfunction into different degrees of severity shows that, up

to 6 months after surgery, the most common level of erectile dysfunction was severe or moderate. However, between 6 and 12 months after radical prostatectomy, moderate, mild to moderate or mild erectile dysfunction was most often observed. At more than 12 months after radical prostatectomy, the distribution of the severity of erectile dysfunction was relatively equal, i.e. there were both severe and no disorders (However, it should be noted that only a small proportion of qualifying studies assessed ED beyond 12 months). Significant improvement in sexual function as measured by the IIEF-5 questionnaire was observed in 7 articles: in one of them the improvement was 6 months after the surgery, the second after 9 months, while in the remaining 5, the improvement was observed at least 12 months after the radical prostatectomy. The improvement took place in studies in which the prostate cancer population was subjected to additional interventions aimed at accelerating the recovery process, including the improvement of sexual function. Among others, the following were used: neurovascular bundle preservation, penile vibratory stimulation, penile rehabilitation, pelvic floor bio-feedback training.

Table 1. Description of Included Studies.

First author, year	Characteristics of population				Pathological stage of tumor	Intervention	Timing of assessment	Main results
	N	Age	Clinical stage of tumor	Pathological stage of tumor				
de Lira et al., 2019	I:16	I:67.3 ± 5.63	NR	I:pT2–pT4 C:pT2–pT4	I:RRP + PFMT C:RRP + TAU	BS, 3 months AS	In the intervention group the average (SD) IIEF-5 score was 16.7 (6.65) and in the control group it was 16.3 (7.64). 3 months after surgery there was no statistically significant difference between groups, but there was a tendency toward lower scores in the control group – 5.73 (7.43) than in the intervention group – 6.70 (6.68).	
	C:15	C:63.53 ± 7.62						
Siltari et al., 2019	I:60	I:64(58–68)*	I:cT1–cT3 C:cT1–cT3	NR	I:RP + 80 mg atorvastatin preoperatively C:RP + placebo preoperatively	BS, 3, 6, 9, 12 months AS	There were no significant differences in IIEF-5 scores between groups at the baseline and at any time point after prostatectomy. However, IIEF-5 scores were higher in the intervention group, and only 22% of the study group have no erectile dysfunction. After surgery at any time point, large decreases in the IIEF-5 scores for both the intervention and control groups—10 pts and 12 pts respectively—were observed.	
	C:58	C:64(58–69)*						
Giberti et al., 2017	G1:100	G1:62.6 ± 6.0	G1:cT1–cT2 G2:cT1–cT2	NR	G1:RARP G2:BT	BS, 3, 6, 9, 12, 18, 24 months AS	Before surgery, there were no differences in the IIEF-5 scores between groups: the average (SD) IIEF-5 score was 22.0 (2.1) in both groups. Significantly lower potency rates were observed in Group 2 at all postoperative time points. At 3, 6, 9, 12, 18 and 24 months after surgery the % of potent patients in Group 1 was 61.00%, 71.40%, 87.00%, 89.60%, 90.90%, 89.60% respectively and in Group 2 was 48.10%, 52.10%, 59.40%, 63.20%, 62.00%, 59.40% respectively.	
	G2:100	G2:63.0 ± 5.4						
Fode et al., 2014	I:42	I:62(46–73)**	NR	NR	I:NSRP + PVS + PFMT + PDES C:NSRP + PFMT + PDES	BS, 3, 6, 12 months AS	There were no statistically significant differences in preoperative IIEF-5 scores between groups. The IIEF-5 score was higher in the intervention group at all time points after surgery, but a statistically significant difference between groups was only reached at 12 months after surgery, resulting in median (range) IIEF-5 scores of 18 (0–25) and 7.5 (0–25) in the intervention and control groups respectively.	
	C:41	C:65(49–76)**						
Bannowsky et al., 2008	I:23	63.6(54–74)**	NR	pT2–pT3	I:NSRP + sildenafil C:NSRP	BS, 6, 12, 24, 36, 52 weeks AS	At baseline, all patients had an IIEF-5 score of > 16 (range 16–25). There was no statistically significant difference between groups at 6, 12 and 24 weeks after surgery. However, there was a significant difference in IIEF-5 score between the	
	C:18							

(continued)

Table 1. Continued.

First author, year	Characteristics of population					Main results
	N	Age	Clinical stage of tumor	Pathological stage of tumor	Intervention	
Giberti et al., 2009	G1:100 G2:100	G1:65(57–74)* G2:66(56–74)*	G1:cT1–cT2 G2:cT1–cT2	G1:pT2–pT3 G2:NR	G1:RRP G2:BT	BS, 6 months, 1, 5 years AS groups at 36 and 52 weeks, resulting in average (SD) IIEF-5 scores of 9.6 (2.37), 14.1 (3.03) respectively in the intervention group and 6.40 (2.08), 9.3 (2.14) respectively in the control group.
Deliveliotis et al., 2005	G1:30 G2:30	G1:55(48–60)** G2:55(49–60)**	G1:cT1–cT2 G1:cT1–cT2	NR	G1:BNS RRP+ betamethasone G2:BNS RRP	BS, 3, 6, 12 months AS Preoperative results showed an average IIEF-5 score greater than 21 points in both groups. After surgery, the differences between groups at any of the follow-up times were not significant, although in Group 2 the results were slightly higher.
Pavone et al., 2020	56	63.6 ± 4.7	NR	pT2–pT3	RRP + sildenafil	BS, before treatment, after treatment (3 months) After surgery, a large decline in IIEF-5 scores was observed, resulting in moderate ED in the assessed population (an average of 8 points). At the end of treatment, a significant improvement was presented by the study group, resulting in mild ED (an average of 18 points).
Zhou et al., 2020	35	63.4 ± 8.1	cT2	pT2	RARP	BS, 12 months AS The median (IQR) preoperative IIEF-5 score was 18 (16.20) and the decline was not statistically significant at 12 months after surgery: the postoperative median (IQR) score was 17 (16.19).
de Carvalho et al., 2020	128	62.6 ± 0.7	cT1–cT3	pT2–pT3	RARP with release of the NVB and DVC preservation	BS, 1, 3, 6, 9, 12 months AS At baseline, 88.3% of patients were potent, with a median (IQR) preoperative IIEF-5 score of 21.5 (20.23). 53.1% of patients presented recovery of potency at 1 month after surgery, 69.9% at 3 months, 82.3% at 6 months, 84.9% at 9 months, and 86.7% at 12 months. Median time (IQR) to recovery of potency was 30 (30.120) days.
Albisinni et al., 2019	584	64 ± 7	cT1–cT4	pT2–pT4	RALP	BS, 1, 3, 12, 24 months AS At baseline, the median (range) preoperative IIEF-5 score was 16 (5–22). After 1 and 3 months after surgery, the median (range)

(continued)

Table 1. Continued.

First author, year	Characteristics of population				Intervention	Timing of assessment	Main results
	N	Age	Clinical stage of tumor	Pathological stage of tumor			
Huang et al., 2019	G1:97 G2:71 G3:179	G1:63.6 ± 5.2 G2:64.2 ± 4.1 G3:63.5 ± 5.6	G1:cT1–cT2 G2:cT1–cT2 G1:cT1–cT2	G1:pT1–pT4 G2:pT1–pT4 G3:pT1–pT4	G1:ORP G2:LRP G3:RRP	BS, 12 months AS	IIEF-5 scores showed a major decline in the study group and were 1 (1–4) and 2 (1–6) respectively. After 12 and 24 months follow-up, an improvement in the median (range) IIEF-5 score was observed, with scores of 4 (1–13) and 5 (1–16) respectively. Before surgery, there was no significant difference among the groups in the average (SD) IIEF-5 scores: 18.1 (5.7), 19.1 (4.9) and 19.4 (4.1) in Group 1, Group 2 and Group 3 respectively. At 12-month follow-up, there was also no significant difference between groups. However, in Group 3, the average (SD) IIEF-5 score was the highest among the groups, at 7.1 (5.6) points.
Nason et al., 2017	G1:107 G2:100 G3:85	G1:63.2 ± 10.9 G2:62.7 ± 6.4 G3:59.1 ± 5.7	G1:cT1–cT3 G2:cT1–cT3 G3:cT1–cT3	G1:pT2–pT3 G2:pT2–pT3 G3: pT2–pT3	G1:ORP G2:LRP G3:RRP Each group received PFMT after surgery	BS, 3, 6, 9, 12 months AS	Before surgery, there were no differences in the average (SD) IIEF-5 scores between groups, at 17.8 (2.4), 17.7 (2.7) and 17.9 (2.5) points in Group 1, Group 2 and Group 3 respectively. In each group, deterioration was observed in the average (SD) IIEF-5 scores at: 3 months – 9.2 (1.9), 6 months – 10.7 (2.7), 9 months – 12.3 (2.9), and 12 months – 13.3 (3.5). No significant difference between groups was noted at any follow-up time.
Sridhar et al., 2016	G1:365 G2:135 G3:51	63(44–77)**	NR	pT2–pT4N1	G1:RRP + N-NBP G2:RRP + U-NBP G3:RRP + B-NBP Each group received PR after surgery	BS, 3, 6, 12, 24, 36, 48 months AS	There was a significant increase in the median IIEF-5 score in Group 3 from 3 to 18 months postoperatively, from 12 to 22 points on the IIEF-5 scale. This increase continued up to 3 years but was not statistically significant after 18 months. In Group 2, there was no significant increase in median IIEF-5 score from 3 to 18 months, but a significant increase was seen from 18 to 36 months, from 5 to 18 points on the IIEF-5 scale. There was no significant increase in IIEF score in Group 1 from 3 to 36 months.
Putora et al., 2016	G1:252 G2:135 G3:91	G1:65(44–77)** G2:63(49–76)** G3:72(53–84)**	G1:cT1–cT2 G2:cT1–cT2 G3:cT1–cT3	NR	G1:RRP or ORP G2:BT G3:EBRT	BS, 6 weeks, 6 months, 1, 2, 3 years AS	Baseline IIEF-5 scores indicated mild ED in Group 1 (19.0) and Group 2 (21.0), and moderate ED in Group 3 (10.0). The average results at 1.5–36 months showed that Group 2 was on average 7.8 points higher than Group 1, while Group 3 was on average 4.7 points higher than Group 1.

(continued)

Table 1. Continued.

First author, year	Characteristics of population				Intervention	Timing of assessment	Main results
	N	Age	Clinical stage of tumor	Pathological stage of tumor			
Nakano et al., 2014	G1: 35 G2: 68	G1: 61.8 ± 13.2 G2: 64.2 ± 12.8	NR	G1:pT2–pT3 G2:pT2–pT3	G1:RP + PR G2:RP	BS, 12 months AS	1, and the results of Group 2 were on average 3.1 points higher than Group 3. 12 months AS. The proportion of potent patients in Group 1 was significantly greater (60.0%) than in Group 2 (38.2%), but there was no significant difference between groups in the IIEF-5 results.
Fode et al., 2013	G1:435 G2:585	G1:66(45–76)** G2:65(43–76)**	G1:cT1–cT3 G2:cT1–cT3	G1:pT0–pT4 G2:pT0–pT4	G1:RRP G2:RALP	BS, 3, 6, 12 months AS	Patients in Group 1 had significantly lower preoperative IIEF-5 scores compared with patients in Group 2. The proportion of potent patients in Group 1 was 12.5%, 15.4% and 28.9% at 3, 6 and 12 months after surgery respectively. The proportion of potent patients in Group 2 was 20.6%, 26.2% and 36.3% at 3, 6 and 12 months after surgery respectively.
Becker et al., 2014	G1:443 G2: 12825	G1: <50 G2: ≥50	G1:cT1–cT3 G2:cT1–cT3	G1:pT2–pT4 G2:pT2–pT4	RARP or RRP	BS, 12 months AS	At baseline, the difference in IIEF-5 scores between Group 1 and Group 2 was less than 2 points. 12 months after surgery, the IIEF-5 score in Group 1 was significantly higher (19.0) than in Group 2 (13.7).
Rogers et al., 2013	69	73(71–74.5)*	cT1–cT3	pT2–pT4	RARP	BS, around 26.2 months AS	The mean (SD) preoperative scores were 14.5 (9.1) and mean postoperative scores were 5.2 (7.2). Of 32.3% men who had a preoperative IIEF-5 score greater than 21, only 7 were able to achieve erections after surgery.
Prota et al., 2012	I:26 C:26	I:62.4 ± 6.4 C:64.0 ± 8.0	I:cT2–cT3 C:cT2–cT3	NR	I:RRP + PFBT C:RRP + TAU	BS, 1, 3, 6, 12 months AS	In the intervention group the time taken to recover potency was significantly lower than in the control group. At 12 months after surgery, 47.1% of the intervention group but only 12.5% in the control group were able to achieve erections.
Choi et al., 2011	G1:94 G2:70 G3:19	G1:59.7 ± 7.2 G2:60.8 ± 6.2 G3:60.8 ± 6.1	G1:cT1–cT2 G2:cT1–cT2 G3:cT1–cT2	G1:pT0–pT3 G2:pT0–pT3 G3:pT0–pT3	RARP	BS, around 10 months AS	Patients were divided into three subgroups according to their AUA-SS results. Patients with AUA-SS values 0–7 were assigned to Group 1, with values 8–19 (moderate) to Group 2, and with values 20–35 (severe) to Group 3. Around 10 months after surgery the % of potent patients were: Group 1 (56%), Group 2 (47%), Group 3 (26%). These results were statistically significant.

Discussion

These observations could find support in the literature, as results of studies on potency recovery indicate that the average time required for potency recovery after radical prostatectomy is between 12 and 24 months (Albersen et al., 2009; Saleh et al., 2015; Salonia et al., 2012). However, only a third of the included studies followed the population for more than 12 months.

Complementary therapies are useful in accelerating and increasing the efficiency of the erectile function recovery process (Park et al., 2013; Saleh et al., 2015; Salonia et al., 2012). In 10 of the selected studies, complementary treatments were applied, i.e. pelvic floor muscle training, pharmacotherapy, or penile rehabilitation. In most of these studies, a better sexual functioning was observed in the groups in which such adjuvant therapies were applied. Nevertheless, studies that use adjuvant therapy represent only half of the articles included in the systematic review.

The results of this review should be considered with certain limitations in mind. First, as a result of limited translation facilities, the literature search was restricted to articles published in English, Polish and French. Therefore, articles in other languages were not included. Second, a significant number of the qualifying studies did not provide full information about the clinical and/or pathological stage of the cancer or about raw results on the IIEF-5 scale which could form a basis for a comparison of the studied populations, thus making it impossible to attempt a meta-analysis of the studies.

After making a qualitative analysis of the included studies, some implications for further research can be drawn. The most important of these concerns the observation time of the studied patients, which should be at least 12 months. In contrast, research on the use of supportive treatments should be conducted more frequently and be planned in a way that allows their results to be included in a possible future meta-analysis.

Conclusions

Erectile dysfunction is a common complication after surgery which has a significant impact on

the quality of life of patients. Assessment of ED should therefore be used as one of many tools for evaluating the effectiveness of treatment after radical prostatectomy.

The results of this review suggest that recovery of potency can be enhanced by the use of various types of additional treatment which can shorten the recovery process and increase its effectiveness. Nevertheless, analysis of qualifying studies and contemporary literature indicates that the recovery period has an average duration minimum 12 months.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

ORCID

Tomasz Jurys  <http://orcid.org/0000-0002-9961-5157>

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