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ORIGINAL ARTICLE

Erectile function after radical prostatectomy: Do patients return to baseline?

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ABSTRACT

Objective: The aim of this study was to assess postprostatectomy erectile function compared to preoperative status by subjective patient perception and the abbreviated International Index of Erectile Function (IIEF-5) questionnaire. *Materials and methods*: The study used data from a prospectively collected database and a cross-sectional, questionnaire-based study in patients following radical prostatectomy. Erectile function was assessed with the IIEF-5 and the question "Is your erectile function *as good* as before the surgery (yes/no)". Patients were included if they were sexually active before surgery and had at least 1 year of follow-up. The main outcome measure was the proportion of patients returning to self-perceived baseline erectile function. Secondary outcome measures included the proportion of patients returning to baseline erectile function according to the IIEF-5 and predictors of return to baseline function. *Results*: Questionnaires from 210 patients were available. Overall, 14 patients (6.7%) reported that their erections were as good as before surgery. Bilateral nerve-sparing was the only significant predictor of a return to baseline erectile function ($p = 0.004$). Forty-three patients (20.5%), who did not report use of erectile aids, showed no decline in IIEF-5 score. When including patients who used erectogenic aids, 69 (32.9%) maintained their preoperative IIEF-5 score. On multivariate analysis a low preoperative IIEF-5 score was a significant predictor of return to baseline IIEF-5 score ($p < 0.0001$). *Conclusions*: Return to subjective baseline erectile function following radical prostatectomy is rare. The IIEF-5 questionnaire may not adequately reflect patients' experience. This should be considered in preoperative patient counselling.

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Erectile dysfunction, IIEF-5, patient perception, prostate cancer, radical prostatectomy, sexual dysfunction

Introduction

Prostate cancer is estimated to account for almost 650,000 yearly cancers in the economically developed world [1] and radical prostatectomy is often employed for localized cancer [2]. The treatment may improve survival [3] but there is often a cost in the form of urinary and sexual side-effects, which can reduce the patient's quality of life significantly [4]. Erectile dysfunction (ED) is recognized as the most common side-effect even when nerve-sparing techniques are used [5]. However, large variations in study methodology and ED definitions have resulted in controversies regarding the true incidence [6]. Several questionnaires regarding erectile function exist, but few have been validated specifically in a postprostatectomy population and there is no general consensus on how they should be used [7]. The confusion may lead to poor preoperative management of patients' expectations and it may adversely affect the postoperative management if the occurrence of side-effects is underestimated.

To increase the understanding of the patients' experience, the current study aimed to assess postprostatectomy erectile function compared to the preoperative status by the subjective patient perception. For comparison, the study also reports on postoperative erectile capacity as assessed by a conventional questionnaire.

Materials and methods

The data used in this study are derived from the Herlev Hospital prostate cancer survivor database, on which this group has previously reported. In brief, it consists of combined data from a cross-sectional, questionnaire-based study conducted between December 2012 and February 2013, in patients following radical prostatectomy [8], and from a prospectively collected database with information on disease characteristics, surgeries and baseline sexual/urinary function [9]. Preoperative erectile function was evaluated using the abbreviated International Index of Erectile Function (IIEF-5) questionnaire [10]. For assessment of postoperative erectile function, the cross-sectional questionnaire included the IIEF-5 and the question "Is your erectile function *as good* as before the surgery (yes/no)". Patients were included in the current analysis if they reported having engaged in sexual intercourse within the last 3 months before their surgery and had at least 1 year of follow-up.

The main outcome measure was the proportion of patients returning to self-perceived baseline erectile function. Secondary outcome measures included the proportion of patients returning to baseline erectile function according to the IIEF-5 questionnaire and predictors of return to baseline function.

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Descriptive statistics were performed and a multivariate linear regression analysis including nerve-sparing (non-nerve-sparing or unilateral nerve-sparing versus bilateral nerve-sparing), preoperative erectile function, age, time since surgery, known cardiovascular disease, D'Amico classification, robotic versus open surgery and surgeon was used to identify predictors of higher postoperative IIEF-5 scores. Owing to limited statistical power, univariate logistic regression analyses with the same parameters were used to identify possible predictors of return to baseline erectile function, and multivariate analyses were planned in case of multiple statistically significant covariates. Two-sided p values less than 0.05 were considered statistically significant. Statistical analyses were performed using SAS statistical software version 9.3 (SAS Institute, Cary, NC).

The study was approved by the Danish Data Protection Agency and received a waiver from the regional ethics committee. Informed consent was obtained from all participants.

Results

Overall, 210 questionnaires from patients who fulfilled the inclusion criteria were available for analyses. The flow of patients is shown in Figure 1. The mean age was 65 years (range 45–77 years) and the mean time since surgery was 22.6 months (range 12–36 months). The mean preoperative IIEF-5 score was 21.7 [95% confidence interval (CI) 20.6–22.8]. Other patient characteristics are listed in Table 1. Seven surgeons contributed patients, and the number of patients for each surgeon was 104, 48, 26, 15, 14, two and one. The first two surgeons had experience with more than 500 radical prostatectomies each before the time of data collection and were involved as direct supervisors during procedures performed by the less experienced surgeons.

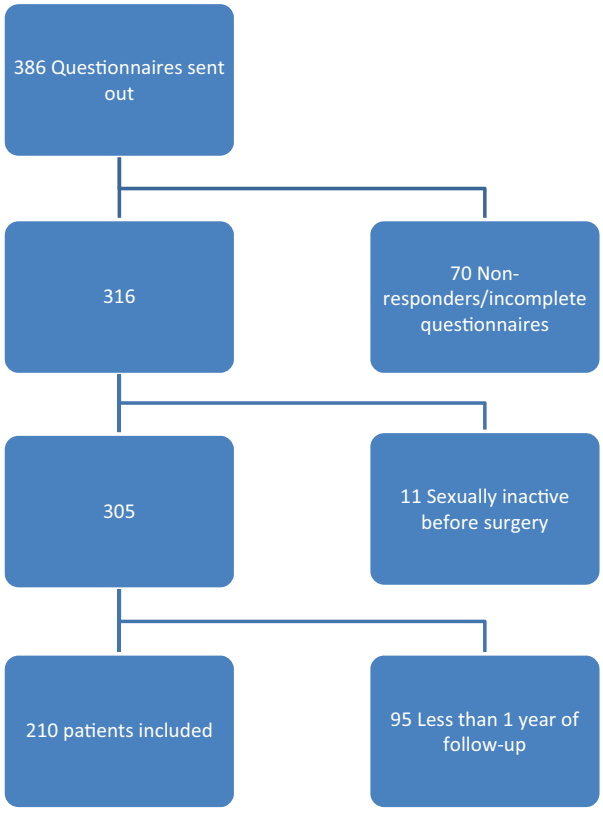

Figure 1. Flow of patients through the study.

At the time of the study, the mean IIEF-5 score had dropped to 9.9 (95% CI 8.6–11.3). Nerve-sparing ($p = 0.0018$), higher preoperative IIEF-5 scores ($p = 0.0025$) and age ($p = 0.019$) were significant predictors of a higher score, while the absence of cardiovascular disease almost reached significance ($p = 0.06$). Preoperatively, 21 participants used phosphodiesterase-5 inhibitors (PDE5-Is) and no patients used other forms of erectogenic aid. Of the 189 patients who did not use erectogenic aids preoperatively, 51 patients had started using a PDE5-I, 11 used alprostadil injection therapy and three used the Medicated Urethral System for Erection® (MUSE). Five patients used a combination of a PDE5-I and injection therapy while two patients combined a PDE5-I and MUSE. One patient used both injection therapy and a vacuum erection device. Two had received a penile implant at the time of the study. Of the 135 patients who did not use erectogenic aids at the time of the study, 65 had previously attempted at least one type of treatment. The most commonly stated reasons for discontinuation were lack of effect (27%), side-effects (12%) and return of spontaneous erectile function (4%).

Overall, 14 out of 210 patients (6.7%, 95% CI 4.4–10.1%) reported that their erections were as good as before the surgery. Bilateral nerve-sparing was the only significant predictor of a return to baseline erectile function, with an odds ratio of 5.4 (95% CI 1.7–16.9, $p = 0.004$). Among patients who had undergone bilateral nerve-sparing 15.5% reported having erections equivalent to baseline, while the proportion was 3.3% in those who had not undergone bilateral nerve-sparing.

Forty-three patients (20.5%, 95% CI 15.6–26.4%), who did not report use of any erectile aids, showed no decline in IIEF-5 score. When including patients who did use erectogenic aids, the total number of patients who maintained their preoperative IIEF-5 score was 69 (32.9%, 95% CI 26.9–39.5%). On univariate analyses, a low preoperative IIEF-5 score ($p < 0.0001$) and longer time since surgery ($p = 0.01$) were significant predictors of return to baseline IIEF-5 score without erectogenic aids. In a multivariate model, only the low preoperative IIEF-5 score remained significant ($p < 0.0001$).

Table 1. Patient characteristics.

Mean age (years)	65 (range 45–77)
Mean time since surgery (months)	22.6 (range 12–36)
Known heart disease	
Yes	18
No	192
D'Amico score	
1	20
2	140
3	50
Method of surgery	
Robot assisted	160 patients
Open surgery	50 patients
Bilateral nerve-sparing	
Yes	58 patients
No	152 patients

None of the 14 patients who reported ''back to baseline erections'' showed a decline in IIEF-5 score. On the other hand, 28 men who showed no decline in IIEF-5 score did not report being back to baseline function.

Discussion

Reported rates of postoperative ED range between about 15% and 95%, with the definition of ED and data collection methods being important decisive factors [11]. Known physiological factors which influence postoperative erectile quality include nerve-sparing status, patient age, preoperative erectile function and comorbidities. When considering a return to baseline erectile capacity, Levinson et al. published a study in 2011 in which they used the Extended Prostate Cancer Index Composite. Here, 27% of preoperatively potent men returned to baseline erectile function at 24 months after surgery [12]. Using the IIEF-5 questionnaire, Woo and co-workers found that 21.4% of preoperatively potent men fully recovered their erectile quality at 12 months after surgery [13]. Likewise, Nelson and colleagues published a report on patient return to preoperative erectile function as assessed by the IIEF-5 questionnaire in 2013 [14]. They showed that this was achieved by 36% (95% CI 28–44%) of patients with the use of PDE5-Is and by 16% (95% CI 11–23%) without the use of medication at 24 months after surgery.

The present study showed similar results using the IIEF-5 questionnaire. However, when addressing the issue with a simple subjective ''yes'' or ''no'' question, less than 7% reported a return to baseline erections at least 1 year after radical prostatectomy. Even with bilateral nerve-sparing the figure only reached 15.5%. The implications of this are that patients' perception of sexual problems following radical prostatectomy may be greater than generally reported and that the most commonly used questionnaires may not reflect the patients' experience. More specifically, if the IIEF-5 score is maintained there is no guarantee that the subjective assessment is positive. This may be related to the fact that the IIEF-5 score has not been validated specifically in a postprostatectomy population [7]. Furthermore, the instrument is designed to measure improvements in erectile function with erectogenic medications and not to measure functional deterioration [10,15].

This study is the first of its kind to evaluate the rate of return to baseline erectile capacity in the current way, which makes comparison with the available literature difficult. Therefore, the results require confirmation in trials from other centres. In particular, the specific rate of subjective return to baseline erectile capacity may not be generalizable. However, the similarities between these IIEF-5 results and those seen in other trials imply that this patient population did not differ significantly from those of other centres. This notion is supported in a very well-designed randomized trial investigating the role of nightly sildenafil in the return of spontaneous erections [16]. In this trial, a vigorous definition of satisfactory erections was used as patients needed to have a combined score of at least 8 for question 3 (''Over the past 4 weeks, when you attempted sexual intercourse, how often were you able to penetrate your partner?'') and question 4 (''Over the past 4 weeks, during sexual intercourse, how often were you able to maintain your erection after you had penetrated your partner?'') on the IIEF questionnaire. Only one patient out of 25 (4%) in the placebo group fulfilled these criteria at approximately 12 months after surgery.

Regarding predictors of postoperative erectile function as measured directly by the IIEF-5 questionnaire, the present analysis confirmed the importance of well-known factors including nerve-sparing, patient age and preoperative erectile function. However, nerve-sparing was the only significant predictor for subjective return to baseline erectile function in this study. This may be because other factors influencing erectile function did not change with surgery and thus did not play a role in the relationship between preoperative and postoperative function. However, this should be interpreted with caution owing to the low number of patients reporting a return to baseline function, and the finding needs confirmation in larger trials.

Surprisingly, a low preoperative IIEF-5 score was the only predictor of return to baseline IIEF-5 score on multivariate analysis. This observation was also made by Nelson et al. [14]. Taken at face value, this could mean that good preoperative erections are more prone to damage while erections are damaged less if the function is already compromised. However, as the factor was not a predictor of subjective return to baseline and as no physiological parameter played a role, the finding is likely to signify a quality of the IIEF-5 questionnaire, which may be more sensitive to changes at the high end of the spectrum. The discrepancy could also be caused by a natural regression towards the mean, i.e. that good scores are likely to decrease when repeated while bad scores are likely to increase [17].

The main strengths of this study are the simple design and the novel patient-centred approach. In addition, the assessment of erectile function by a commonly used questionnaire allows for meaningful comparisons with the general literature. The major weaknesses of the study are the potential for recall bias when asking the subjective ED question and the lack of an objective measurement of erectile function. Thus, the study has no way of determining the ''true'' return to physiological erectile function and it must be stressed that the results reflect the subjective patient experience following surgery. Another commonly discussed aspect of postprostatectomy erectile function is the concept of ''penile rehabilitation''. This entails the idea that scheduled postoperative treatment with erectogenic aids, not necessarily related to actual sexual activity, can improve spontaneous erectile capacity in the long term. In this study, about two-thirds of patients had tried at least one erectogenic aid, with about half abandoning it before the time of the study. This inconsistency in ED treatment in this patient cohort can be considered a weakness of the study. However, although penile rehabilitation strategies are commonly used, the majority of randomized trials have been unable to confirm their effectiveness and no standardized recommendations exist [18]. Moreover, previous studies suggest that the pattern seen in this patient cohort is likely to reflect the clinical reality. Thus, an Italian study by Salonia and co-workers found that 49% of patients decided not to start any ED treatments after radical prostatectomy while about 73% of patients who started

therapy discontinued it within an 18 month period [19]. Finally, the choice of a follow-up period of 1–3 years could be criticized, since some studies have implied that erectile capacity may improve beyond 1 year. However, this is unlikely to have influenced the results as time since surgery did not significantly influence return to baseline erectile function. Importantly, none of the limitations negates the discrepancy between subjective patient assessment and the IIEF-5 questionnaire, which is arguably the major finding of the study.

In conclusion, this study suggests that a return to subjective baseline erectile function is rare following radical prostatectomy. In addition, it shows that one of the most commonly used questionnaires may not adequately reflect the patients' experience. Clinicians should be aware of these issues both when advising patients about surgery and in postoperative management.

Declaration of interest

Mikkel Fode: consultant and speaker for Eli Lilly, Astellas and Menarini; speaker for Bayer and Coloplast. Anders Frey: none. Henrik Jakobsen: consultant and speaker for Astellas and Sanofi Aventis; speaker for Jannsen-Cilag. Jens Sønksen: consultant and speaker for Eli Lilly, Menarini and Coloplast; speaker for Astellas; board member and shareholder in Multicept, Denmark.

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