



Platinum Priority – Collaborative Review – Sexual Medicine

Editorial by Dimitris Hatzichristou on pp. 287–289 of this issue

Prevention and Management of Postprostatectomy Sexual Dysfunctions Part 1: Choosing the Right Patient at the Right Time for the Right Surgery

Andrea Salonia^{a,*}, Arthur L. Burnett^b, Markus Graefen^c, Kostas Hatzimouratidis^d, Francesco Montorsi^a, John P. Mulhall^e, Christian Stief^f

^aDepartment of Urology, University Vita-Salute San Raffaele, Milan, Italy; ^bThe James Buchanan Brady Urological Institute, The Johns Hopkins Hospital, Baltimore, MD, USA; ^cMartini-Clinic, Prostate Cancer Center, University Hamburg-Eppendorf, Hamburg, Germany; ^d2nd Department of Urology and Center for Sexual and Reproductive Health, Aristotle University of Thessaloniki, Greece; ^eSexual and Reproductive Medicine Program, Urology Department, Memorial Sloan-Kettering Cancer Center, New York, NY, USA; ^fDepartment of Urology, University Hospital Munich-Grosshadern, Ludwig Maximilians University Munich, Munich, Germany

Article info

Article history:

Accepted April 23, 2012
Published online ahead of print on May 2, 2012

Keywords:

Radical prostatectomy
Nerve sparing
Sexual function
Sexual dysfunction
Erectile function
Erectile dysfunction

Abstract

Context: Sexual dysfunction is common in patients following radical prostatectomy (RP) for prostate cancer (PCa).

Objective: To review the available literature concerning prevention and management strategies for post-RP erectile function (EF) impairment in terms of preoperative patient characteristics and intra- and postoperative factors that may influence EF recovery.

Evidence acquisition: A literature search was performed using Google and PubMed database for English-language original and review articles either published or e-published up to November 2011.

Evidence synthesis: The literature demonstrates great inconsistency in what constitutes normal EF before surgery and what a man may consider a normal erection after RP. The use of validated psychometric instruments with recognised cut-offs for normalcy and severity during the pre- and postoperative evaluation should be routinely considered. Therefore, a comprehensive discussion with the patient about the true prevalence of postoperative erectile dysfunction (ED), the concept of spontaneous or pharmacologically assisted erections, and the difference between “back to baseline” EF and “erections adequate enough to have successful intercourse” clearly emerge as key issues in the eventual understanding of the prevention of ED and promotion of satisfactory EF recovery post-RP. Patient factors (including age, baseline EF, and status of comorbid conditions), cancer selection (unilateral vs bilateral nerve sparing), type of surgery (ie, intra- vs inter- vs extrafascial surgeries), surgical techniques (ie, open, laparoscopic, and robot-assisted RP), and surgeon factors (ie, surgical volume and surgical skill) represent the key significant contributors to EF recovery.

Conclusions: The complexity of the issues discussed throughout this review culminates in the simple concept that optimal outcomes are achieved by the careful choice of the correct patient for the correct type of surgery.

© 2012 European Association of Urology. Published by Elsevier B.V. All rights reserved.

* Corresponding author. Department of Urology, University Vita-Salute San Raffaele, Via Olgettina 60, 20132 Milan, Italy. Tel. +39 02 2643 7286; Fax: +39 02 2643 7298.
E-mail address: salonia.andrea@hsr.it, saloniaandrea@yahoo.com (A. Salonia).

1. Introduction

Radical prostatectomy (RP) is a recommended curative procedure for patients with low- and intermediate-risk localised prostate cancer (PCa) and a life expectancy of at least 10 yr (level of evidence [LE]: 1b) [1]. In this context, the most updated European Association of Urology (EAU) guidelines report that either bilateral nerve-sparing radical retropubic prostatectomy (BNSRP; LE: 3) or unilateral nerve-sparing radical retropubic prostatectomy (UNSRP; LE: 4) represents the recommended approach of choice in all men with both a normal preoperative erectile function (EF) and organ-confined disease [1]. Conversely, EAU guidelines suggest as an option a non-nerve-sparing surgical approach for selected patients who suffer from low-volume, high-risk localised PCa and highly selected patients with very high-risk localised PCa in the context of multimodality treatment [1].

Therefore, the population of patients with PCa that may benefit from RP is clearly quite large. More importantly, it is evident that many patients who undergo RP are not receiving an operation with nerve-sparing intent for several reasons, including cancer factors, anatomic factors, technical factors, reduced surgical and technical skill, or a low surgical volume. Yet even these patients have had, keep having, and probably in large part would continue to have satisfactory sexual activity, including at least an adequate level of sexual desire, adequate erections, and an appropriate orgasmic function (OF). Moreover, our unfortunate patient might also feel distress about his own sexuality or might even be bothered by the presence of pain related to sexual activity [2]. It is easy to see that post-RP sexual dysfunction—primarily erectile dysfunction (ED)—remains a challenge for the urologist, and this is increasingly important because the diagnosis of PCa is becoming more frequent in younger patients, who are particularly interested in maintaining an excellent postoperative health-related quality of life (QoL) [3,4].

Similarly, a progressive tendency for the age structure of the population to shift towards the elderly has been observed in all developed countries. People are living longer, are having a steady increase in life expectancy, and, in some parts of the world, healthier lives [5]. Aging is among the most significant risk factors for PCa [1]. The lack of appreciation among both physicians and the general public for the reality of a male biologic clock makes these trends worrisome [6]. In this context, this review aims to define a shareable road map for preventing and managing sexual dysfunction in those patients who wish to continue to be sexually active postoperatively.

2. Evidence acquisition

A literature search for English-language original and review articles either published or e-published up to November 2011 was performed using Google and the National Library of Medicine's PubMed database. Keywords included *radical prostatectomy*, *nerve sparing*, *sexual function*, *sexual dysfunction*, *erectile function*, and *erectile dysfunction*. Of all manuscripts potentially available, we have considered

215 articles with the highest LE (from 1b to 3b). The retrieved articles were gathered and examined. Reference lists of retrieved articles as well as relevant review articles were also studied. This review is the result of an interactive peer-reviewing process by an expert panel of coauthors.

3. Evidence synthesis

3.1. Prevention and management of post-radical prostatectomy erectile dysfunction

The International Consensus of Sexual Medicine (ICSM) 2009 [7] committee on EF rehabilitation after RP has recently compiled a sort of handbook of recommendations precisely intended to better decipher how a patient with PCa who is also a candidate for RP [1], can—and we shall say should—be helped before, during, and after the surgery to promote the preservation and obtain the recovery of his own satisfactory EF. In this direction, it is our deep conviction that well before RP, as correctly stated by the ICSM committee, the patient has the inalienable right to be given realistic expectations regarding his postoperative erectile and sexual function. This will help anyone (ie, physicians and patients) understand how to start with the prevention of damage and his subsequent recovery, reducing possible false expectations and subsequent frustrations. Respectfully, we will build on those recommendations to develop those sections of our collaborative review that are dedicated to postoperative ED.

3.1.1. Prevention is better than cure: claim for intelligible discussion with the patient about the true prevalence of postoperative erectile dysfunction

The conviction that clinicians should comprehensively discuss with the patient—and, whenever possible, with his partner [8]—the locally and internationally published ED prevalence rates at the earliest point in the decision-making process (LE: 4) [7] continues to grow. At the same time, the prevention of a poor functional outcome passes through the objective description of the limitations of current scientific literature in seriously defining postoperative ED prevalence rates [7,9–11].

Recent rigorous reviews about postoperative ED prevalence [9–11] already exist, and a detailed meta-analysis of the most updated postoperative ED rates is not the focus of this review. However, to understand how to prevent and promote recovery of satisfactory EF after RP, we consider it relevant to discuss some key points in terms of prevalence and predictors of postoperative ED. In this sense, it is important to present data in an effort to communicate how difficult it is to approach this issue in a systematic way. Overall, the incidence of post-RP ED varies between 14% and 90% [9,10]. As a whole, the incidence of reported postoperative ED is extremely discrepant among series because of a great variation in the nature of the populations studied and the modality for data collection and reporting [9–11]. The crucial point in this direction is the lack of an objective, reliable, and shareable definition of both *baseline EF* and *postoperative EF*. This means that there is great

inconsistency in what is considered normal EF before surgery and what one may consider a normal erection after RP [9,11]. The results of the meta-analysis conducted by Tal et al. [11] clearly stated that most of the published literature does not meet strict criteria for reporting post-EF recovery. The same meta-analysis found as many as 22 different definitions of *favourable EF outcome*. In this context, the overall fixed-effects EF recovery rate was 58% (95% confidence interval, 56–60%), with significant heterogeneity among effect impacts [11].

Similar results were discussed by Burnett et al. [9] as a side analysis of outcomes assessed as part of an update of the American Urological Association PCa guidelines. They reported how, in many instances, only qualitative and subjective determinations were used, thus interpretable at best as erectile ability insufficient for sexual intercourse (complete ED), somewhat functional for sexual intercourse (partial EF), or regularly sufficient for sexual intercourse (intact EF). Moreover, it has been well observed that EF data from the largest series often refer only to a small fraction of the total RP population, and the evaluable number of patients represents but a fraction of the total exposed to surgery [11]. These are the most significant obstacles to the accurate interpretation of the incidence and prevalence of post-RP ED, when considering all study types and all technical approaches [7,9–11].

To our knowledge, there are no randomised prospective well-designed head-to-head comparative studies that prove EF outcomes are significantly different (namely, better) between open and laparoscopic or robotic RP (LE: 4) [10–13]. In this context, laparoscopic and, even more, many large series of robot-assisted approaches are mature enough and have demonstrated that EF outcomes are at least equivalent to those obtained with open retropubic RP (LE: 2B, 3, 4) [10–18]. Given the huge discrepancy in the definition of the outcome in question, Tal et al. reported that differences were found in EF recovery among open (57%), laparoscopic (58%), and robotic RP (73%) [11]. A more thorough and critical discussion of this aspect is reported across this review.

Accordingly, the words of the ICSM committee sound even wiser (LE: 4): “[P]atients should be given individualised outcomes based on surgical technique, patient, and surgeon factors, thus including accurate data on EF recovery from their own patient population” [7]. This last aspect, which seems polemic against a certain type of behaviour, actually allows clinicians to bypass the errors of the scientific literature, eventually providing patients with more realistic expectations.

3.1.2. *Prevention is better than cure: defining what is meant by (adequate) postoperative erectile function passes through the objective assessment of the baseline condition*

It has been widely demonstrated that preoperative EF is an important predictor of EF recovery after RP [19–27]. To this specific purpose, it is mandatory to verify how the definition of *baseline EF* was created; indeed, numerous means of assessment have been reported in the literature, including patients’ subjective self-reports, partner-corroborated function, and validated psychometric instruments. In a recent

critical reappraisal of the literature, Mulhall reported that a clear mention of baseline EF was only given in 16 (66%) of 24 studies considered as representative of the experience of large-volume worldwide centres [10].

It was a further recommendation of the ICSM committee that clinicians use a validated psychometric instrument with recognised cut-offs for normalcy and severity during the pre- and postoperative evaluation of their patients [7]. Among the other available psychometric tools, the International Index of Erectile Function (IIEF) [28], with a dedicated EF domain, or the Sexual Health Inventory for Men (SHIM) [29]—with cut-off scores for “normal” EF of 26 and 21, respectively [28–30]—continue to be highly recommended and widely used to define EF.

Baseline EF assessment is still problematic, and the most reliable timing of this assessment is even more poorly defined [7]. Indeed, on the one hand, some patients might overestimate their previous EF; on the other hand, proximity to the surgery may reduce the sexual activity or desire of the patient, his partner, or the couple as a whole [20,22]. PCa diagnosis and cancer-related or treatment-associated psychological distress may also significantly impair the real-time assessment of EF immediately prior to RP; therefore, this “late” real-time evaluation might not be fully representative of the patient’s true sexual functioning [7,20,22]. Kim et al, for instance, recently reported that to accurately assess the pre-diagnostic baseline EF in candidates for RP, the psychometric tools should be administered before prostate biopsy rather than before robot-assisted laparoscopic RP (RARP) because cancer diagnosis-related symptoms and depression can ultimately affect sexual function and index scores [31].

The US National Institutes of Health (NIH) consensus conference defined ED as “the consistent inability to obtain and/or maintain an erection sufficient for satisfactory sexual performance” [32]. This definition was not designed to be applied to a specific population and even less for a complex population—that is, patients undergoing RP. This is of particular importance today because such a widely used definition does not include any mention of the role or use of erectogenic aids or other assistance. In this context, data from clinical studies show that phosphodiesterase type 5 inhibitors (PDE5-Is) are efficacious in the treatment of post-RP ED [7,33]; even more importantly, in any series reporting postoperative EF outcomes, the proportion of patients using PDE5-Is—or second-line therapies—is of great relevance [1,7,33]. Likewise, in many reported series, it is extremely difficult to define whether the patients are having spontaneous, unassisted, or PDE5-I-assisted erections when assessing both preoperative EF and post-RP EF recovery. Thus it must be certainly emphasised that the definition of *adequate EF* in post-RP studies is unique for the ED literature because most studies include PDE5-I responders as those with adequate EF [33,34].

Adequate knowledge of the potential use of any preoperative or post-RP erectogenic aid and what proportion of data in any given series was collected from patients using these agents is of major importance in allowing an accurate interpretation of the findings. These aspects make

giving a proper definition of *postoperative EF* extremely difficult in addition to accurately defining a rate of post-RP ED [7,9–11].

The ICSM committee interestingly outlined a further crucial aspect: It is not always possible to take EF “back to baseline” postoperatively [7]. This last aspect is considered the keystone of the whole matter of prevention and maintenance of postoperative EF. Overall, a significantly small proportion of preoperative potent men appear to return spontaneously to baseline EF after surgery [9–11,35]. To the best of our knowledge, this last sentence could easily be applied to open RP series, but the item has scarcely been investigated for laparoscopic RP [11,34,36] and probably even less so for RARP [11]. So, with the clear intention of limiting false patient expectations, it is important that clinicians comprehensively discuss the objective of regaining an erection equivalent to that prior to RP, especially using data from their own RP population. If we start from the NIH definition of ED, the focal point would become the fact that adequate postoperative erections may be “at least” sufficient for satisfactory sexual performance [32]. Mulhall [10] reported that *adequate EF* was defined as the “ability to have successful intercourse by patient self-report” in 42% out of the series. Unfortunately, overall, 37% of the series did not even report how the authors define *adequate erections* [10]. Satisfactory sexual relations is a complex issue; simplistically, it can be considered an expression of the relationship of several factors, including patient age, preoperative sexual activity, pre- and post-RP libido, baseline (namely, immediately preoperative) and previous EF (that is, remote from the diagnosis of disease) [22], preoperative and post-RP use of erectogenic aids, penile morphology issues, OF, mental health of the patient, continence, and micturition disorders [10].

Certainly, the important aspects of cancer control outcomes cannot be overlooked; therefore, we cannot overlook the possibility that the patient might also receive androgen-deprivation therapy or radiation therapy as an adjuvant treatment, with all the negative implications that these therapies may have on the sexual functioning of the patient. No less important is the impact of the partner and the couple’s relationship [8,10,37–39].

In an attempt to combine the two concepts of getting EF “back to baseline” and being able to achieve erections sufficient for satisfactory sexual intercourses as defined by the NIH [32], it becomes important to consider the potential misinterpretation of the established cut-offs for normalcy as well as the grading of ED severity (mild, moderate, and severe) of both the IIEF-EF domain and SHIM. Indeed, using the usual cut-offs for normal function, which are generally considered for the broad-spectrum ED population, might be overly stringent for post-RP populations; indeed, there are patients who still consider themselves fully functional while having lower scores [9,40,41]. To try to define a cut-off value as close as possible to the real-life setting, Briganti et al. [41] considered a relatively small cohort of preoperatively fully potent patients (IIEF-EF ≥ 26) treated with retropubic BNSRP at a single institution. All patients reached an IIEF-EF ≥ 17 following surgery, which should

be usually considered as mild to moderate ED. Moreover, the authors considered intercourse satisfaction (IS) and overall satisfaction (OS) as assessed by the corresponding domains of the IIEF administered prior to and after surgery; after a 26.7-mo mean follow-up, findings demonstrated that mean postoperative IIEF-OS and IIEF-IS domain scores, assessed at the time of EF recovery, were comparable for patients reaching an IIEF-EF of 22–25 points and for those men scoring postoperatively ≥ 26 . Conversely, mean IIEF-OS and IIEF-IS domain scores of these patients were significantly higher compared with patients reaching an IIEF-EF domain score < 22 after surgery. Therefore, based on the results of their analysis, the authors concluded that a cut-off of IIEF-EF ≥ 22 may represent a reliable score for defining EF recovery after BNSRP (LE: 4) [41].

3.1.3. Prevention is better than cure: defining time to recovery and postoperative quality of erection is a compulsory task for the clinician Facing the various aspects of EF recovery with the candidate for RP or with the patient after his operation, the issue of the chronology of events has to be addressed. Burnett et al. [9] rightly commented that in the modern era of RP, most men usually achieve resumption of all physical activities, recovery of urinary control, and normalisation of bowel function within a few months after surgery. In contrast, postoperative EF continues to improve over time, at least up to 24 mo and in some series up to 48 mo post-RP [9,10,19,42–45]. In this context, studies limiting follow-up assessment to < 24 mo likely underestimate EF recovery [10]. Tal et al. [11] showed that studies reporting ≥ 18 -mo follow-up outlined somewhat higher EF recovery (60%) rates compared with studies with < 18 -mo follow-up (56%) ($p = 0.02$). Overall, RARP seems to promote a more rapid EF recovery as compared with open RP (LE: 4) [34]. A growing amount of data are published almost daily to reinforce and better specify this type of widespread feeling.

Time of erection recovery does not uniformly occur in all cases, and several predictors of EF recovery have been identified, including patients’ age at surgery (ie, the younger, the better), better preoperative EF, extent of neurovascular bundle (NVB) preservation, and erectile haemodynamic changes after surgery [7]. In this context, surgery (ie, type, quality, surgical volume, and the actual nerve-sparing approach) probably emerges as the most compelling aspect. For instance, Tal et al. reported that BNSRP was certainly associated with higher EF recovery (namely, 60% vs 47%; $p = 0.01$) than UNSRP [11]. However, as perfectly stated by the ICSM committee [7], when dealing with preservation of the NVBs, most patients—and, unfortunately, a number of clinicians—do not have an adequate understanding of the concept of nerve sparing. Indeed, they think that nerve sparing always leads to complete preservation of the nerves and, consequently, to the absence of any transient postoperative ED. Even when surgeons believe that they have achieved complete bilateral cavernous nerve preservation, there is inevitably some trauma to the nerves. As outlined, to prevent false and unrealistic expectations, clinicians must provide patients with a realistic time frame for EF recovery; experts suggest

that a potential period of 6–36 mo would be necessary, although most individuals experience functional recovery within 12–24 mo after RP [7].

Interestingly enough, Katz et al. showed that the recovery of functional erections in the early postoperative phase, especially without the need for PDE5-Is, is a good prognostic indicator for EF at 12-mo assessment [46]. However, a distinct cohort of men lose functional erections within 6 mo after surgery, with a time to nadir in postoperative EF not immediately after RP but more likely around 3 mo after surgery [46]. In terms of postoperative management, it is important to inform patients of this possibility, as it has an impact on their QoL and, potentially, on their compliance with post-RP therapy for ED. Similarly, it should be stated that the ability to have either a spontaneous or a pharmacologically assisted functional erection (namely, PDE5-I sustained) within 3 mo of RP is an excellent prognostic indicator [10].

Overall, the fact that it can take a long time until the first spontaneous erections occurs should not lead the physician to wait inactively. Conversely, the patient should start with supportive medication therapy for EF recovery as early as possible [7,33,47].

As a second major aspect, the clinician should debate issues concerning the quality of erection. Unfortunately, science has only a few parameters that may help to characterise this aspect, for which the patient's actual perception is always a key point, although often not clearly decipherable. In this sense, capacity of recovering an erection sufficient for successful intercourse has caused the neglect of two important concepts: the quality of the erection itself, otherwise defined as *erection hardness*, and the consistency of functional erections.

3.1.3.1. Hardness of erection. Once more, there is no unique and unequivocal way to define *hardness of erection*. For instance, we can use a 10-point rigidity scale (where 0 = completely flaccid and 10 = fully rigid, with 6 being adequate for vaginal penetration) or a 4-point scale such as the Erectile Hardness Score [48]. However, erection hardness is a simple concept that is easy for the clinician to use, easy for the patient to understand, and gives the clinician and patient a goal to aim for after RP (LE: 4). Indeed, although a patient may postoperatively have functional erections that allow him to have sexual intercourse, a more or less severe loss of erection hardness may lead to erection dissatisfaction for that man. Consequently, he might need erectogenic compounds for greater erection hardness or even a second- or third-line treatment if that man was already using an erectogenic medication [7,10]. A significant correlation between erection hardness and patient's satisfaction has been demonstrated for patients complaining of ED of broad-spectrum aetiology [49], but reports regarding RP populations are still lacking.

3.1.3.2. Consistency of functional erections. This parameter represents the second point of value of any erection, meaning how consistently a functional erection can be obtained (LE: 4) [10]. Data regarding RP populations are still lacking.

3.1.4. Prevention is better than cure: choosing the right patient at the right time for the right surgery

The complexity of the issues we have touched on throughout this review leads us to suggest that prevention and management of EF in patients treated with RP necessarily is heavily predicated on a careful choice of the correct patient for the correct type of surgery. This fits perfectly with what has recently been highlighted by the ICSM committee [7]: Clinicians should comprehensively discuss the recognised predictors of EF recovery with any candidate for RP. Although this would seem implicit, it is of paramount importance to note that this discussion should be taken into account both considering and regardless of the oncologic indication [1]—in other words, all patients with PCa who might benefit from RP as a curative treatment should also receive appropriate counselling regarding the possibility of being subjected to RP (see, in this context, the most updated EAU guidelines [1]) and the possibility of being subjected to NSRP or, conversely, the need to be treated with non-NSRP, according to the baseline oncologic condition [1]. Interestingly, Imbimbo et al. [50] investigated factors related to patients' desire to preserve post-RP sexual activity and those determinants for surgeons' final decision to eventually perform NSRP. Out of a multicentre cohort of 2408 men, 1667 (69%) were interested preoperatively in preserving their sexual activity. Of the entire cohort, 13% were not interested but suitable for BNSRP, 18% were neither interested nor suitable, 39% were both interested and suitable, but up to 31% were interested but not suitable. Age ($p = 0.001$) and normal preoperative sexual function parameters (all $p \leq 0.008$) emerged as independent determinants of patients' desire to preserve postoperative sexual functioning. Overall, 318 (13%) underwent UNSRP and 856 (36%) BNSRP. Along with oncologic indications, age ($p = 0.026$) and patients' desire to preserve sexual activity ($p < 0.001$) were among the main independent determinants of surgeon's final decision for NSRP. Overall, findings from this study underlined the existence of discrepancies among patient's desire to preserve postoperative sexual function, guideline indications for NSRP, and surgeons' final decision for a nerve-sparing approach [50].

Once it has been established that the patient can receive NSRP, counselling should focus on the patient's baseline functional situation along with the potential predictors of postoperative EF recovery. Preoperatively, these factors necessarily include age at surgery, baseline EF, and comorbidities. Likewise, type of surgery, coupled with surgical volume and surgical skill, and nerve-sparing status achieve the role of significant contributors to EF recovery [7].

As seen, baseline EF is related to several different variables, including age and comorbid conditions status. In this context, Rabbani et al. [19], for instance, demonstrated that at 36-mo follow-up, approximately 70%, 45%, and 30% of patients had recovered EF when ≤ 60 yr of age, between 60 and 65 yr of age, and > 65 yr of age, respectively. More recently, Penson et al. [51] confirmed those previous findings using data from a cohort of 1288 patients from the Prostate Cancer Outcomes Study, with a postoperative

5-yr follow-up. The authors observed a significant trend effect of age on sexual function following BNSRP, with 61% of men ≤ 55 yr of age compared with 49% of those between 55 and 59 yr of age, 44% of those 60–64 yr of age, and 18% of those > 65 yr of age having functional erections ($p < 0.001$) [51]. As a point of criticism, both of the previous two studies clearly detailed a long list of comorbid conditions at baseline, but they did not consider them during any multivariate analysis. In contrast, Solomon et al. [25] recently reported that baseline age and comorbidity-dependent ED affects up to 48% of all patients prior to open RP. The importance of the result is that although comorbidities were not considered for their actual weight as obtainable using a validated index, age, body mass index, type 2 diabetes mellitus, and depression emerged as independent predictors of baseline ED (all $p \leq 0.005$) [25].

Overall, it is certainly true that the presence, number, and potentially severity of those comorbidities (eg, vascular risk factors such as dyslipidemia, diabetes mellitus, hypertension, coronary artery disease) afflicting the patient well before the RP will likely afflict that man even after surgery, adversely affecting EF recovery, just as usually happens in the general population [52].

Recently, Briganti et al. [47] developed a preoperative risk-stratification tool aimed at assessing the probability of EF recovery after open BNSRP. They used routinely available baseline data such as patient age and preoperative EF as psychometrically objectified with the IIEF; moreover, as a proxy for general health status, the authors scored health-significant comorbidities using the Charlson Comorbidity Index (CCI) [53]. For the specific purpose of the analysis, CCI was categorised as a score of 0, 1, or ≥ 2 . The resulting tool was able to stratify patients into three groups according to the relative risk of ED after surgery: low risk (≤ 65 yr of age, IIEF-EF ≥ 26 , CCI ≤ 1), intermediate risk (66–69 yr of age or IIEF-EF 11–25, CCI ≤ 1), and high risk (≥ 70 yr of age or IIEF-EF ≤ 10 or CCI ≥ 2). Overall, the EF recovery rate was 58% at 3-yr follow-up; however, the 3-yr EF recovery rate significantly differed among the three groups, being 85%, 59%, and 37% in patients at low, intermediate, and high risk of postoperative ED, respectively ($p < 0.001$). More recently, Novara et al. [26] applied the same risk-stratification categories to a cohort of 208 patients treated with bilateral nerve-sparing RARP who were assessed at a minimum 12-mo follow-up. Data showed that 62% of the entire cohort was potent 12 mo after surgery, with age at surgery (hazard ratio [HR]: 2.8; $p < 0.001$), CCI (HR: 2.9; $p = 0.007$), and baseline EF (HR: 0.8; $p < 0.001$) achieving independent predictor status for potency recovery. According to the risk group stratification proposed by Briganti et al, the 12-mo EF recovery rate was 82%, 57%, and 29% in the low-risk, intermediate-risk, and high-risk groups, respectively ($p < 0.001$) [26].

Overall, prevention and management of postoperative EF necessarily pass through rigorous selection of the patients who may benefit from RP; this should not be seen as a kind of discrimination against some patients but rather a strong awareness by the clinician and the most respectful form of aid that the patient can receive. Data in hand so as to avoid

generating false expectations [54,55], the clinician must clearly say to the patients that NSRP does not ensure the recovery of erections at all and, because it may be potentially subjected to a number of sequelae, a nerve-sparing approach should be reserved for young patients without significant comorbidities and an adequate preoperative EF [7,19,26,47,25,56,57].

In this context, it is certainly important to remember that there are literature data that seem to suggest that bilateral nerve-sparing surgery could also significantly contribute to the preservation of postoperative urinary continence. Indeed, Burkhard et al. [58] reported that in their series of 536 patients who underwent open RRP, the incidence of postoperative urinary incontinence was lower and continence was highly associated with a nerve-sparing technique. Therefore, they concluded that nerve sparing should be attempted in all patients if the principles of oncologic surgery are not compromised [58]. However, whether this association equals causation is unclear. It is possible that nerve-sparing surgery is a surrogate for meticulous apical dissection, which may be the pathway to continence preservation.

In the general sense, however, for patients who cannot undergo a nerve-sparing approach, a technically flawless surgery without preservation of NVBs has to be suggested, with the specific aim of allowing them to have a satisfactory sexual activity assisted by second- and third-line therapies [7,59–62].

3.1.5. *Prevention is better than cure: choosing the right cancer for the right surgery*

Since NSRP was introduced, it has continuously been accompanied by the discussion about the right indication for this surgical modification [63,64]. Nerve sparing should not compromise the effectiveness of RP by producing artificial surgical margins that could have been avoided if a non-nerve-sparing approach had been chosen. Therefore, an estimation of organ confinement of the cancer is crucial, with the idea that in such cancers, nerve sparing could be safely indicated. Tailoring the NSRP approach according to the cancer extension of each subject is important for saving as many NVBs as possible to improve outcome with respect to sexual function.

Despite recent improvements, the reliability of imaging techniques to securely identify microscopic extracapsular extension is still limited [65]. In this context, Graefen et al. [66] published the first nomogram that specifically estimated the likelihood of extracapsular cancer growth to aid the indication of nerve sparing. Since then, several other statistical models have been created incorporating readily available information of the cancer to estimate organ confinement [67,68].

However, all available models deliver only a likelihood of organ confinement while leaving the patient and the surgeon with a degree of uncertainty. Therefore, several institutions have introduced intraoperative frozen sections to identify cancer tissue at the resection margin during NSRP [69]. This approach may allow surgeons to tailor the surgical approach during the procedure (eg, secondary

resection of an initially preserved NVB). Even though this procedure seems to be the safest approach for indicating nerve sparing without the risk of an artificial surgical margin, it certainly remains time consuming. It is recognised that the positive predictive value of frozen-section analysis for positive surgical margins (PSM) is high; however, the sensitivity is too low to expect that a policy of routine frozen-section analysis will be offered outside specialised centres [70]. However, to preserve as many NVBs as possible, it is crucial that a reproducible approach indicating whether a nerve bundle will be preserved be used to give the patient a clear idea of the sexual function he can expect postoperatively.

3.2. Recent findings in terms of functional and topographic anatomy of the prostate: what has changed the way we conceive radical prostatectomy?

Even after it is clear who the right candidate for NSRP is, controversies still exist about the surgical approach to the NVBs that may provide the best EF results. A growing body of evidence concerning the potential consequences of cavernous nerve injury [71–73] from any type of surgical procedure (including pinch, compression, percussion, traction, cautery, and even transection), the importance of the accessory pudendal arteries [74–78], and the eventual subsequent impact on cavernous smooth muscle have stimulated a large amount of basic research and clinical trials aimed at evaluating different strategies to promote the preservation of and the fastest recovery of post-RP EF [7]. To improve cancer control and concurrently prevent and, when necessary, treat post-RP sexual disorders, it clearly emerged that having an adequate idea of the anatomy and topography of pelvic organs—the prostate and adjacent tissues—as well as having some familiarity with aspects of the functional anatomy of erection and ejaculation are of major importance.

After the description by Walsh and Donker in 1982 of the cavernous nerves along the prostate, which subsequently enabled nerve-sparing surgery [71] and the discovery of the importance of nitric oxide in the physiologic pathway of erection, the characteristics of the fascia surrounding the prostate itself emerged as one of the major relevant discoveries in anatomic and functional terms [72]. This fascia is multilayered, either fused with or clearly separated from the prostatic capsule, depending on interindividual variations. In its context, we recognise the visceral component of the endopelvic fascia, which in its entirety covers the pelvic organs, including the prostate, bladder, and rectum, and it is fused with the anterior fibromuscular stroma of the prostate at the upper ventral aspect of the gland [73]. The fascia on the outer surface of the prostate, called the *periprostatic fascia* (PPF) throughout this review according to Walz et al. [73], is mostly ordered in several layers over the prostate. Neglecting the interesting discrepancies in the description of the relationship between the NVB and prostatic fascia [73], these fasciae represent important surgical planes because numerous technical variations are possible according to the dissection plane the surgeon

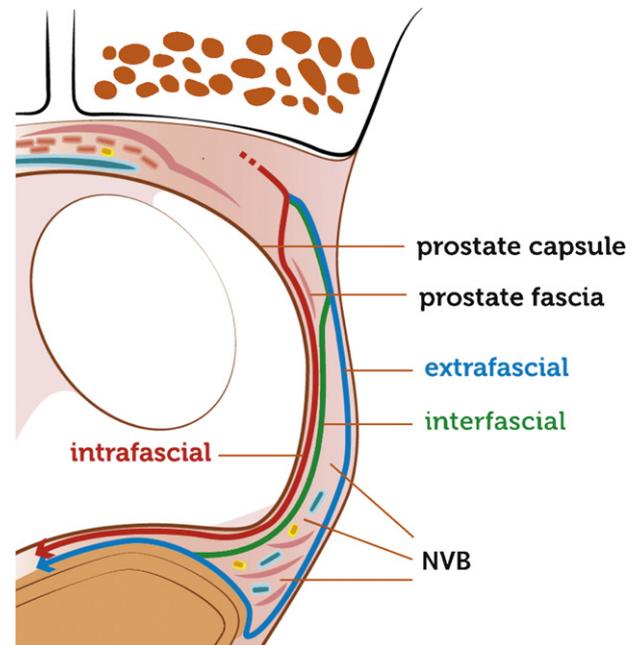


Fig. 1 – Schematic representation of the axial section of prostate and periprostatic fasciae at midprostate with three different dissection planes (intrafascial [red line], interfascial [green line], and extrafascial [blue line]). NVB = neurovascular bundle.

chooses during the procedure. Regardless of the technology (laparoscopic or robot-assisted RP) and the type of intervention chosen (open, laparoscopic, or robot-assisted RP), the recognition of three surgical approaches that ultimately refer to the relationship between the NVB and the PPF (Fig. 1) [72,73] is compulsory for functional outcome:

- **Intrafascial dissection of the NVB.** The dissection follows a plane close to the prostate capsule throughout its path, leaving lateral the prostatic fascia at the anterolateral and posterolateral aspect of the prostate and remaining anterior to the posterior prostatic fascia–seminal vesicles fascia network [72]. This surgical approach allows a whole-thickness preservation of the lateral prostatic fascia, which is completely lateralised together with a virtually intact NVB.
- **Interfascial dissection of the NVB.** The dissection combines a first part that outside or lateral to the prostatic fascia at the anterolateral and posterolateral aspects of the prostate with a second part that develops medial to the NVB at the 5 o'clock and 7 o'clock positions. This approach eventually allows the posterolateral prostate to remain completely covered with the fascia [73]. This dissection might not necessarily allow the preservation of all the nerve fibres dispersed on the anterolateral surface of the prostate [77].
- **Extrafascial dissection of the NVB.** The dissection is carried lateral to the levator ani fascia and the Denonvilliers' fascia, thus completely resecting the NVBs [73].

The scientific literature still largely lacks studies that rigorously compare the currently available surgical

techniques (eg, open, laparoscopic, and robot-assisted RP). The number of prospective randomised studies of the type of surgical aggression (ie, intrafascial to interfascial) is even more limited. In this context, we attempt to summarise a number of key points.

3.2.1. Open nerve-sparing radical prostatectomy is still common

Open NSRP—mainly retropubic RP—is still a common surgical approach for operable PCa [79–82]. Budäus et al. reported the most updated description of open intrafascial NVB dissection coupled with the 12-mo postoperative functional outcome [82]. They used the abridged five-item version of the IIEF to assess EF, and patients were asked to complete the tool before surgery and 12 mo after RP [25,82]. The analyses excluded those men with a preoperative IIEF score <19, indicating some degree of ED, and the patients who stated that they had not had sexual stimulation within the past 6 mo, according to question 2 of the IIEF-5 questionnaire. Defining as *potent* those men who reported erection sufficient for penetration after sexual stimulation, EF recovery rates varied from 84% to 92% in men who underwent BNSRP and from 58% to 70% following UNSRP. The authors also reported that the use of PDE5-Is was left to the patient's discretion, and 80% of men who completed the questionnaire did not use such medications, thus ultimately meaning spontaneous recovery of postoperative EF. Moreover, Budäus rigorously outlined that if a "strict" definition of EF was applied (namely, a postoperative IIEF score >19), the corresponding potency rates were 25–59% [82]. One must presume that if higher EF domain scores were used as a cut-off, EF recovery would be even lower.

3.2.2. Laparoscopic nerve-sparing radical prostatectomy can be performed extraperitoneally or transperitoneally

Laparoscopic or endoscopic NSRP can be performed extraperitoneally or transperitoneally [83,84], and this further heterogeneity is responsible for an even more complex objective assessment of the functional outcomes across the literature. Greco et al. [85] reported the results of a retrospective, parallel-arms study comparing the 12-mo follow-up functional outcomes in patients undergoing intrafascial retropubic and laparoscopic NSRP, both performed by high-volume surgeons. At the time of assessment, 66% of patients in the laparoscopic group and 51% in the open group reported being able to engage in sexual intercourse, respectively ($p < 0.05$). A comparison between intrafascial and interfascial laparoscopic extraperitoneal BNSRP in preoperatively potent patients was recently reported by Stolzenburg et al. [86]. Considering as *potent* those men responding positively to several specific questions on the sexual encounter profile diary, 12-mo postoperative potency rates were 94% (<55 yr of age), 83% (55–65 yr of age), and 60% (>65 yr of age) in the intrafascial group compared with 77%, 50%, and 40%, respectively, for men who underwent interfascial BNSRP according to the same age stratification. The authors thus concluded that intrafascial laparoscopic BNSRP overall provides significantly better EF recovery rates [86].

More recently, using the dichotomous definition of *erections satisfactory or unsatisfactory for intercourse*, Stewart et al. confirmed this significant difference between the two dissections, also highlighting that men <60 yr of age may certainly achieve the highest functional results with the intrafascial laparoscopic approach [87,88]. Conversely, Neill et al. [89] did not find a significant difference in terms of either continence or EF recovery rate after intrafascial versus interfascial extraperitoneal laparoscopic NSRP. Overall, the rates of men who actually have spontaneous erections were not even considered in most of the previous studies. This does not permit us to provide any clear-cut conclusion either concerning the type of surgery (namely, laparoscopic RP) or the appropriateness of the selected anatomic dissection.

3.2.3. Intrafascial vs interfascial bilateral nerve-sparing radical retropubic prostatectomy outcomes have also been considered for robot-assisted laparoscopic radical prostatectomy

The outcomes of intrafascial versus interfascial BNSRP techniques have more recently been considered for RARP, as well. Potdevin et al. [90] reported that EF recovery rates at 3, 6, and 9 mo in the intrafascial group were 24%, 82%, and 91%, respectively, whereas in the interfascial group, they were 17%, 44%, and 67%, respectively, at the same follow-up time points. *Erectile function* was defined as being able to achieve erection adequate for penetration more than half of the time (namely, Expanded Prostate Cancer Index Composite [91] questions 18 and 19) with or without PDE5-Is. As a major point, the authors outlined that the intrafascial technique was associated with higher PSM rates in patients with pT3 disease, although no significant differences emerged in pT2 disease [90].

Xylinas et al. recently supported the idea that a formal robot-assisted intrafascial approach provided early (ie, 1-mo assessment) satisfactory functional results with respect to postoperative continence and potency [92]. Interestingly, these authors outlined that 60% of their 50 consecutive patients exhibited erection sufficient for intercourse; of these latter patients, 50% did not need to use any PDE5-I while 50% required an oral compound [92]. Asimakopoulos et al. [36] reported the results of a prospective randomised study aimed at comparing the functional results of 128 consecutive patients treated by a single experienced surgeon with either laparoscopic RP or RARP with the intent of using intrafascial bilateral nerve sparing in all cases. The 12-mo evaluation of patients' EF—defined as capability for sexual intercourse—showed that RARP scored significantly better ($p < 0.0001$) than laparoscopy. Men in the RARP group also showed a faster time to capability for intercourse ($p = 0.0001$) and a higher rate of return to baseline IIEF-EF domain scores ($p = 0.0002$) than those operated on with laparoscopic RP [36]. Conversely, a similar rate of patients with functional erections did use PDE5-Is within the two groups (55% vs 47%, respectively; $p = 0.58$).

Despite the belief that there are no sufficient prospective randomised and rigorously conducted clinical trials to confirm this unequivocally—especially with external validation of the data already published—there is an increasing

school of thought that RARP eventually may be shown to be the most potency-protective surgical approach [13,36]. In this context, the circumferential extent of fascia preservation—otherwise known as *intrafascial surgery*—and patient age [93] as well as preoperative EF and patient comorbidity [26] emerged as the best independent predictors of postoperative EF even for RARP.

3.2.4. The importance of intraoperative preservation of erectile haemodynamics

Accumulating evidence suggests that a certain amount of men have vascular abnormalities after RP [75]. These abnormalities can generally be traced to two main forms: arterial insufficiency and venous leakage [75,76,94]. In this context, Mulhall et al. clearly showed that in a cohort of men who underwent open BNSRP, had ED, and never received any pharmacotherapy, up to 75% had some form of vascular alteration. Overall, 59% of the patients had arterial insufficiency, and 26% had venous leakage [75].

Arterial insufficiency has been attributed to the trauma to one of two types of accessory pudendal arteries: a lateral or aberrant pudendal artery that runs along the fascial tendinous arch of the pelvis in the groove between the bladder, prostate, and pelvic sidewall, and an apical accessory pudendal artery that is located inferiorly and laterally to the Denonvilliers' fascia, in proximity to the anterolateral aspect of the prostate apex [74]. Between 4% and 75% of all men have accessory or aberrant pudendal arteries [74,77,95,96], depending on which type of series is reviewed (cadaveric, angiographic, or operative). These aberrant arteries may originate from the internal or external iliac or obturator arteries (see, in this context, Walz et al. [73] for a more comprehensive review). Although still controversial [24,78,96] when reconsidering the way we surgically perform BNSRP, the importance of preserving accessory pudendal arteries comes from several observations that support the concept that they could be solely responsible for arterial blood supply to the corpora cavernosa [75,77]; if this were the case, preservation of these arteries during any surgical approach (open, laparoscopic, or robot assisted) would be compulsory to avoid ED secondary to penile arterial insufficiency [74,76]. Ohebshalom et al, indeed, clearly showed a significant difference in terms of self-reported erectile rigidity ($p=0.013$) and IIEF-EF domain scores ($p=0.025$) at 18-mo follow-up between those patients who had normal postoperative penile haemodynamics and those with abnormal haemodynamics [97]. Likewise, the percentage of patients with normal EF domain scores ($p < 0.01$), the percentage of patients positively responding to sildenafil ($p=0.03$), and the percentage of patients with functional erections permitting pharmacologically unassisted sexual intercourse ($p=0.018$) were significantly higher in men with normal haemodynamics [97]. Overall, published data support the concept that accessory pudendal arteries may have a role in preserving post-RP EF as well as in promoting postoperative recovery of EF [76]. Surgical approaches with a clear intrafascial goal have been postulated to eventually allow a more stringent preservation of any accessory pudendal artery [98].

Failure to recover EF after RP may also result from venous leakage as a sequela of neuropraxia-induced and possibly the absence of cavernosal oxygenation-associated erectile tissue damage [78]. Overall, data seem to suggest a strong clinical correlation between postoperative time and interval of EF recovery and the incidence of venous leakage [75,76], with previous findings showing an incidence of 14% at <4 mo postoperatively that becomes 35% at 9–12 mo post-RP [75]. As a whole, these reports suggest that venous leakage portends a poor prognosis for EF recovery, with a high probability of never recovering preoperative EF, to a poor response to PDE5-Is and even an unsatisfactory outcome with intracavernosal injection therapy (ICI) [78,97]. All of these observations outline the importance of performing nerve-sparing surgery whenever possible. Therefore, surgeons should not only consider those men who might either preserve or recover spontaneous, pharmacologically unassisted postoperative erections but also all of those individuals who are destined to need second-line erectogenic pharmacotherapy, who still deserve preservation of the cavernous tissue to ensure continued excellent response to ICI [78]. This ultimately would mean that, with the specific aim of preserving viable neural tissue while reducing the risk of long-term venous leakage, a bilateral approach should always be attempted when PCa characteristics allow BNSRP without compromising cancer control. Conversely, UNSRP should be at least provided when the oncologic characteristics do not allow a bilateral nerve-sparing surgery [78].

Interestingly, a recent suggestion for more precisely predicting postoperative EF outcomes comes from the use of a subjectively assigned intraoperative nerve-sparing score that allows the surgeon to self-define the quality of intraoperative nerve sparing (1 = complete preservation, 4 = complete resection) for each patient [99]. In this context, in multivariate analyses, lower nerve-sparing scores achieved independent predictor status for 24-mo EF recovery ($p=0.001$), as did age ($p=0.001$) and baseline IIEF-EF domain score ($p=0.02$) [99].

4. Conclusions

The literature offers great inconsistency in the definition of what is considered *normal EF* before surgery and what a man may consider normal erection after RP. Validated psychometric instruments with recognised cut-offs for normalcy and severity during the pre- and postoperative evaluation have to be routinely considered. Therefore, a comprehensive discussion with the patient about the true prevalence of postoperative ED, the concept of “back to baseline,” and spontaneous or pharmacologically assisted erections clearly emerge as key issues for eventually understanding how to promote recovery of satisfactory post-RP EF. In this context, patients should be given individualised outcomes based on surgical technique, patient factors, and surgeon factors. Despite the literature lacking comprehensive data, type of surgery (ie, intrafascial vs interfascial vs extrafascial) and surgical technique (ie, open, laparoscopic, and robot assisted) achieve the role

of significant contributors to EF recovery. The complexity of the issues discussed throughout this review precisely outlines that prevention and possible management of EF in patients treated with RP necessarily passes through a careful choice of the right patient at the right time for the correct type of surgery.

Author contributions: Andrea Salonia had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Salonia, Burnett, Graefen, Hatzimouratidis, Montorsi, Mulhall, Stief.

Acquisition of data: Salonia, Burnett, Graefen, Hatzimouratidis, Montorsi, Mulhall, Stief.

Analysis and interpretation of data: Salonia, Burnett, Graefen, Hatzimouratidis, Montorsi, Mulhall, Stief.

Drafting of the manuscript: Salonia, Burnett, Graefen, Hatzimouratidis, Montorsi, Mulhall, Stief.

Critical revision of the manuscript for important intellectual content: Salonia, Burnett, Graefen, Hatzimouratidis, Montorsi, Mulhall, Stief.

Statistical analysis: Salonia, Burnett, Graefen, Hatzimouratidis, Montorsi, Mulhall, Stief.

Obtaining funding: None.

Administrative, technical, or material support: Salonia, Burnett, Graefen, Hatzimouratidis, Montorsi, Mulhall, Stief.

Supervision: Salonia, Burnett, Graefen, Hatzimouratidis, Montorsi, Mulhall, Stief.

Other (specify): None.

Financial disclosures: Andrea Salonia certifies that all conflicts of interest, including specific financial interests and relationships and affiliations relevant to the subject matter or materials discussed in the manuscript (eg, employment/affiliation, grants or funding, consultancies, honoraria, stock ownership or options, expert testimony, royalties, or patents filed, received, or pending), are the following: None.

Funding/Support and role of the sponsor: None.

References

- Heidenreich A, Bellmunt J, Bolla M, et al. EAU guidelines on prostate cancer. Part 1: screening, diagnosis, and treatment of clinically localized disease. *Eur Urol* 2011;59:61–71.
- Nelson CJ, Deveci S, Stasi J, Scardino PT, Mulhall JP. Sexual bother following radical prostatectomy. *J Sex Med* 2010;7:129–35.
- Merrill RM, Sloan A. Risk-adjusted incidence rates for prostate cancer in the United States. *Prostate* 2012;72:181–5.
- Sidana A, Hernandez DJ, Feng Z, et al. Treatment decision-making for localized prostate cancer: What younger men choose and why. *Prostate* 2012;72:58–64.
- National Institutes of Health, National Institute on Ageing Web site. <http://www.nia.nih.gov/NR/rdonlyres/9E91407E-CFE8-4903-9875D5AA75BD1D50/0/WPAM.pdf>. Accessed August 29, 2011.
- Fisch H. Older men are having children, but the reality of a male biological clock makes this trend worrisome. *Geriatrics* 2009;64:14–7.
- Mulhall JP, Bella AJ, Briganti A, McCullough A, Brock G. Erectile function rehabilitation in the radical prostatectomy patient. *J Sex Med* 2010;7:1687–98.
- Salonia A, Zanni G, Gallina A, et al. Unsuccessful investigation of preoperative sexual health issues in the prostate cancer “couple”: results of a real-life psychometric survey at a major tertiary academic center. *J Sex Med* 2009;6:3347–55.
- Burnett AL, Aus G, Canby-Hagino ED, et al. American Urological Association Prostate Cancer Guideline Update Panel. Erectile function outcome reporting after clinically localized prostate cancer treatment. *J Urol* 2007;178:597–601.
- Mulhall JP. Defining and reporting erectile function outcomes after radical prostatectomy: challenges and misconceptions. *J Urol* 2009;181:462–71.
- Tal R, Alphs HH, Krebs P, Nelson CJ, Mulhall JP. Erectile function recovery rate after radical prostatectomy: a meta-analysis. *J Sex Med* 2009;6:2538–46.
- Ficarra V, Novara G, Artibani W, et al. Retropubic, laparoscopic, and robot-assisted radical prostatectomy: a systematic review and cumulative analysis of comparative studies. *Eur Urol* 2009;55:1037–63.
- Ficarra V, Novara G, Fracalanza S, et al. A prospective, non-randomized trial comparing robot-assisted laparoscopic and retro-pubic radical prostatectomy in one European institution. *BJU Int* 2009;104:534–9.
- Rassweiler J, Hruza M, Teber D, Su L-M. Laparoscopic and robotic assisted radical prostatectomy—critical analysis of the results. *Eur Urol* 2006;49:612–24.
- Tooher R, Swindle P, Woo H, Miller J, Maddern G. Laparoscopic radical prostatectomy for localized prostate cancer: a systematic review of comparative studies. *J Urol* 2006;175:2011–7.
- Ficarra V, Cavalleri S, Novara G, Aragona M, Artibani W. Evidence from robot-assisted laparoscopic radical prostatectomy: a systematic review. *Eur Urol* 2007;51:45–56.
- Menon M, Shrivastava A, Kaul S, et al. Vattikuti Institute prostatectomy: contemporary technique and analysis of results. *Eur Urol* 2007;51:648–58.
- Orvieto MA, Coelho RF, Chauhan S, Mathe M, Palmer K, Patel VR. Erectile dysfunction after robot-assisted radical prostatectomy. *Expert Rev Anticancer Ther* 2010;10:747–54.
- Rabbani F, Stapleton AM, Kattan MW, Wheeler TM, Scardino PT. Factors predicting recovery of erections after radical prostatectomy. *J Urol* 2000;164:1929–34.
- Salonia A, Zanni G, Gallina A, et al. Baseline potency in candidates for bilateral nerve-sparing radical retropubic prostatectomy. *Eur Urol* 2006;50:360–5.
- Michl UH, Friedrich MG, Graefen M, Haese A, Heinzer H, Huland H. Prediction of postoperative sexual function after nerve sparing radical retropubic prostatectomy. *J Urol* 2006;176:227–31.
- Salonia A, Gallina A, Briganti A, et al. Remembered International Index of Erectile Function domain scores are not accurate in assessing preoperative potency in candidates for bilateral nerve-sparing radical retropubic prostatectomy. *J Sex Med* 2008;5:677–83.
- Papadoukakis S, Kusche D, Stolzenburg JU, Truss MC. Reconsidering the use of the International Index of Erectile Function questionnaire in evaluating the preoperative erectile function status of patients undergoing radical prostatectomy. *BJU Int* 2007;100:368–70.
- Dubbelman YD, Wildhagen MF, Dohle GR. Penile vascular evaluation and sexual function before and after radical retropubic prostatectomy: 5-year follow-up. *Int J Androl* 2008;31:483–9.
- Salomon G, Isbarn H, Budaeus L, et al. Importance of baseline potency rate assessment of men diagnosed with clinically localized prostate cancer prior to radical prostatectomy. *J Sex Med* 2009;6:498–504.
- Novara G, Ficarra V, D’Elia C, et al. Preoperative criteria to select patients for bilateral nerve-sparing robotic-assisted radical prostatectomy. *J Sex Med* 2010;7:839–45.
- Hisasue S, Hashimoto K, Kobayashi K, et al. Baseline erectile function alters the cavernous nerve quantity and distribution around the prostate. *J Urol* 2010;184:2062–7.

- [28] Rosen RC, Riley A, Wagner G, Osterloh IH, Kirkpatrick J, Mishra A. The International Index of Erectile Function (IIEF): a multidimensional scale for assessment of erectile dysfunction. *Urology* 1997;49:822–30.
- [29] Cappelleri JC, Rosen RC. The Sexual Health Inventory for Men (SHIM): a 5-year review of research and clinical experience. *Int J Impot Res* 2005;17:307–19.
- [30] Cappelleri JC, Rosen RC, Smith MD, Mishra A, Osterloh IH. Diagnostic evaluation of the erectile function domain of the International Index of Erectile Function. *Urology* 1999;54:346–51.
- [31] Kim DS, Chung YG, Kim DJ, et al. Optimal timing to evaluate prediagnostic baseline erectile function in patients undergoing robot-assisted radical prostatectomy. *J Sex Med* 2012;9:602–7.
- [32] NIH Consensus Conference. Impotence. NIH Consensus Development Panel on Impotence. *JAMA* 1993;270:83–90.
- [33] Hatzimouratidis K, Burnett AL, Hatzichristou D, McCullough AR, Montorsi F, Mulhall JP. Phosphodiesterase type 5 inhibitors in post-prostatectomy erectile dysfunction: a critical analysis of the basic science rationale and clinical application. *Eur Urol* 2009;55:334–47.
- [34] Kim SC, Song C, Kim W, et al. Factors determining functional outcomes after radical prostatectomy: robot-assisted versus retro-pubic. *Eur Urol* 2011;60:413–9.
- [35] Levinson AW, Lavery HJ, Ward NT, Su LM, Pavlovich CP. Is a return to baseline sexual function possible? An analysis of sexual function outcomes following laparoscopic radical prostatectomy. *World J Urol* 2011;29:29–34.
- [36] Asimakopoulos AD, Pereira Fraga CT, Annino F, Pasqualetti P, Calado AA, Mugnier C. Randomized comparison between laparoscopic and robot-assisted nerve-sparing radical prostatectomy. *J Sex Med* 2011;8:1503–12.
- [37] Descazeaud A, Debré B, Flam TA. Age difference between patient and partner is a predictive factor of potency rate following radical prostatectomy. *J Urol* 2006;176:2594–8.
- [38] Shindel A, Quayle S, Yan Y, Husain A, Naughton C. Sexual dysfunction in female partners of men who have undergone radical prostatectomy correlates with sexual dysfunction of the male partner. *J Sex Med* 2005;2:833–41.
- [39] Moskovic DJ, Mohamed O, Sathyamoorthy K, et al. The female factor: predicting compliance with a post-prostatectomy erectile preservation program. *J Sex Med* 2010;7:3659–65.
- [40] Teloken P, Valenzuela R, Parker M, Mulhall J. The correlation between erectile function and patient satisfaction. *J Sex Med* 2007;4:472–6.
- [41] Briganti A, Gallina A, Suardi N, et al. What is the definition of a satisfactory erectile function after bilateral nerve sparing radical prostatectomy? *J Sex Med* 2011;8:1210–7.
- [42] Litwin MS, Flanders SC, Pasta DJ, Stoddard ML, Lubeck DP, Henning JM. Sexual function and bother after radical prostatectomy or radiation for prostate cancer: multivariate quality-of-life analysis from CaPSURE. *Cancer of the Prostate Strategic Urologic Research Endeavor*. *Urology* 1999;54:503–8.
- [43] 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.
- [44] Rabbani F, Schiff J, Piecuch M, et al. Time course of recovery of erectile function after radical retro-pubic prostatectomy: does anyone recover after 2 years? *J Sex Med* 2010;7:3984–90.
- [45] Bannowsky A, Schulze H, van der Horst C, Seif C, Braun PM, Jünemann KP. Nocturnal tumescence: a parameter for postoperative erectile integrity after nerve sparing radical prostatectomy. *J Urol* 2006;175:2214–7.
- [46] Katz D, Bennett NE, Stasi J, et al. Chronology of erectile function in patients with early functional erections following radical prostatectomy. *J Sex Med* 2010;7:803–9.
- [47] Briganti A, Gallina A, Suardi N, et al. Predicting erectile function recovery after bilateral nerve sparing radical prostatectomy: a proposal of a novel preoperative risk stratification. *J Sex Med* 2010;7:2521–31.
- [48] Mulhall JP, Levine LA, Jünemann KP. Erection hardness: a unifying factor for defining response in the treatment of erectile dysfunction. *Urology* 2006;68(Suppl 3):17–25.
- [49] Lowy M, Collins S, Bloch M, et al. Quality of erection questionnaire correlates: change in erection quality with erectile function, hardness, and psychosocial measures in men treated with sildenafil for erectile dysfunction. *J Sex Med* 2007;4:83–92.
- [50] Imbimbo C, Creta M, Gacci M, et al. Patients' desire to preserve sexual activity and final decision for a nerve-sparing approach: results from the MIRROR (Multicenter Italian Report on Radical Prostatectomy Outcomes and Research) Study. *J Sex Med* 2011;8:1495–502.
- [51] Penson DF, McLerran D, Feng Z, et al. 5-year urinary and sexual outcomes after radical prostatectomy: results from the Prostate Cancer Outcomes Study. *J Urol* 2008;179(Suppl 5):S40–4.
- [52] Dwyer ME, Nehra A. Defining sexual function after radical retro-pubic prostatectomy. *Urol Oncol* 2010;28:469–72.
- [53] Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987;40:373–83.
- [54] Giuliano F, Amar E, Chevallier D, et al. How urologists manage erectile dysfunction after radical prostatectomy: a national survey (REPAIR) by the French Urological Association. *J Sex Med* 2008;5:448–57.
- [55] Chartier-Kastler E, Amar E, Chevallier D, et al. Does management of erectile dysfunction after radical prostatectomy meet patients' expectations? Results of a national survey (REPAIR) by the French Urological Association. *J Sex Med* 2008;5:693–704.
- [56] Nehra A. Erectile dysfunction and cardiovascular disease: efficacy and safety of phosphodiesterase type 5 inhibitors in men with both conditions. *Mayo Clin Proc* 2009;84:139–48.
- [57] Rogers CG, Su LM, Link RE, Sullivan W, Wagner A, Pavlovich CP. Age stratified functional outcomes after laparoscopic radical prostatectomy. *J Urol* 2006;176:2448–52.
- [58] Burkhard FC, Kessler TM, Fleischmann A, Thalmann GN, Schumacher M, Studer UE. Nerve sparing open radical retro-pubic prostatectomy—does it have an impact on urinary continence? *J Urol* 2006;176:189–95.
- [59] Gontero P, Fontana F, Bagnasacco A, et al. Is there an optimal time for intracavernous prostaglandin E1 rehabilitation following non-nerve sparing radical prostatectomy? Results from a hemodynamic prospective study. *J Urol* 2003;169:2166–9.
- [60] Prasad MM, Prasad SM, Hevelone ND, et al. Utilization of pharmacotherapy for erectile dysfunction following treatment for prostate cancer. *J Sex Med* 2010;7:1062–73.
- [61] Yuan J, Hoang AN, Romero CA, Lin H, Dai Y, Wang R. Vacuum therapy in erectile dysfunction—science and clinical evidence. *Int J Impot Res* 2010;22:211–9.
- [62] Hellstrom WJ, Montague DK, Moncada I, et al. Implants, mechanical devices, and vascular surgery for erectile dysfunction. *J Sex Med* 2010;7:501–23.
- [63] Walsh PC. Radical prostatectomy, preservation of sexual function, cancer control. The controversy. *Urol Clin North Am* 1987;14:663–73.
- [64] Graefen M, Hammerer P, Michl U, et al. Incidence of positive surgical margins after biopsy-selected nerve-sparing radical prostatectomy. *Urology* 1998;51:437–42.
- [65] Wang L, Hricak H, Kattan MW, Chen HN, Scardino PT, Kuroiwa K. Prediction of organ-confined prostate cancer: incremental value of MR imaging and MR spectroscopic imaging to staging nomograms. *Radiology* 2006;238:597–660.

- [66] Graefen M, Haese A, Pichlmeier U, et al. A validated strategy for side specific prediction of organ confined prostate cancer: a tool to select for nerve sparing radical prostatectomy. *J Urol* 2001;165:857–63.
- [67] Steuber T, Graefen M, Haese A, et al. Validation of a nomogram for prediction of side specific extracapsular extension at radical prostatectomy. *J Urol* 2006;175:939–44.
- [68] Ohori M, Kattan MW, Koh H, et al. Predicting the presence and side of extracapsular extension: a nomogram for staging prostate cancer. *J Urol* 2004;171:1844–9.
- [69] Eichelberg C, Erbersdobler A, Haese A, et al. Frozen section for the management of intraoperatively detected palpable tumor lesions during nerve-sparing scheduled radical prostatectomy. *Eur Urol* 2006;49:1011–8.
- [70] Tsuboi T, Ohori M, Kuroiwa K, et al. Is intraoperative frozen section analysis an efficient way to reduce positive surgical margins? *Urology* 2005;66:1287–91.
- [71] Walsh PC, Donker PJ. Impotence following radical prostatectomy: insight into etiology and prevention. *J Urol* 1982;128:492–7.
- [72] Awad A, Alsaïd B, Bessedé T, Droupy S, Benoît G. Evolution in the concept of erection anatomy. *Surg Radiol Anat* 2011;33:301–12.
- [73] Walz J, Burnett AL, Costello AJ, et al. A critical analysis of the current knowledge of surgical anatomy related to optimization of cancer control and preservation of continence and erection in candidates for radical prostatectomy. *Eur Urol* 2010;57:179–92.
- [74] Mulhall JP, Slovick R, Hotaling J, et al. Erectile dysfunction after radical prostatectomy: hemodynamic profiles and their correlation with the recovery of erectile function. *J Urol* 2002;167:1371–5.
- [75] Mulhall JP, Secin FP, Guillonneau B. Artery sparing radical prostatectomy—myth or reality? *J Urol* 2008;179:827–31.
- [76] Nehra A, Kumar R, Ramakumar S, Myers RP, Blute ML, McKusick MA. Pharmacangiographic evidence of the presence and anatomical dominance of accessory pudendal artery(s). *J Urol* 2008;179:2317–20.
- [77] Secin FP, Touijer K, Mulhall J, Guillonneau B. Anatomy and preservation of accessory pudendal arteries in laparoscopic radical prostatectomy. *Eur Urol* 2007;51:1229–35.
- [78] Tal R, Valenzuela R, Aviv N, et al. Persistent erectile dysfunction following radical prostatectomy: the association between nerve-sparing status and the prevalence and chronology of venous leak. *J Sex Med* 2009;6:2813–9.
- [79] Box GN, Kaplan AG, Rodriguez Jr E, et al. Sacrifice of accessory pudendal arteries in normally potent men during robot-assisted radical prostatectomy does not impact potency. *J Sex Med* 2010;7:298–303.
- [80] Montorsi F, Salonia A, Suardi N, et al. Improving the preservation of the urethral sphincter and neurovascular bundles during open radical retropubic prostatectomy. *Eur Urol* 2005;48:938–45.
- [81] Kessler TM, Burkhard FC, Studer UE. Nerve-sparing open radical retropubic prostatectomy. *Eur Urol* 2007;51:90–7.
- [82] Budäus L, Isbarn H, Schlomm T, et al. Current technique of open intrafascial nerve-sparing retropubic prostatectomy. *Eur Urol* 2009;56:317–24.
- [83] Stolzenburg JU, Schwalenberg T, Horn LC, Neuhaus J, Constantinides C, Liatsikos EN. Anatomical landmarks of radical prostatectomy. *Eur Urol* 2007;51:629–39.
- [84] Stolzenburg JU, Rabenalt R, Do M, Schwalenberg T, Winkler M, Dietel A, et al. Intrafascial nerve-sparing endoscopic extraperitoneal radical prostatectomy. *Eur Urol* 2008;53:931–40.
- [85] Greco F, Wagner S, Hoda MR, et al. Laparoscopic vs open retropubic intrafascial nerve-sparing radical prostatectomy: surgical and functional outcomes in 300 patients. *BJU Int* 2010;106:543–7.
- [86] Stolzenburg JU, Kallidonis P, Do M, et al. A comparison of outcomes for interfascial and intrafascial nerve-sparing radical prostatectomy. *Urology* 2010;76:743–8.
- [87] Stewart GD, El-Mokadem I, McLornan ME, Stolzenburg JU, McNeill SA. Functional and oncological outcomes of men under 60 years of age having endoscopic surgery for prostate cancer are optimal following intrafascial endoscopic extraperitoneal radical prostatectomy. *Surgeon* 2011;9:65–71.
- [88] Stolzenburg JU, Kallidonis P, Minh D, et al. Endoscopic extraperitoneal radical prostatectomy: evolution of the technique and experience with 2400 cases. *J Endourol* 2009;23:1467–72.
- [89] Neill MG, Louie-Johnsun M, Chabert C, Eden C. Does intrafascial dissection during nerve-sparing laparoscopic radical prostatectomy compromise cancer control? *BJU Int* 2009;104:1730–3.
- [90] Potdevin L, Ercolani M, Jeong J, Kim IY. Functional and oncologic outcomes comparing interfascial and intrafascial nerve sparing in robot-assisted laparoscopic radical prostatectomies. *J Endourol* 2009;23:1479–84.
- [91] Wei JT, Dunn RL, Litwin MS, et al. Development and validation of the expanded prostate cancer index composite (EPIC) for comprehensive assessment of health-related quality of life in men with prostate cancer. *Urology* 2000;56:899–905.
- [92] Xylinas E, Ploussard G, Salomon L, et al. Intrafascial nerve-sparing radical prostatectomy with a laparoscopic robot-assisted extraperitoneal approach: early oncological and functional results. *J Endourol* 2010;24:577–82.
- [93] van der Poel HG, de Blok W. Role of extent of fascia preservation and erectile function after robot-assisted laparoscopic prostatectomy. *Urology* 2009;73:816–21.
- [94] Mulhall JP, Graydon RJ. The hemodynamics of erectile dysfunction following nerve-sparing radical retropubic prostatectomy. *Int J Impot Res* 1996;8:91–4.
- [95] Polascik TJ, Walsh PC. Radical retropubic prostatectomy: the influence of accessory pudendal arteries on the recovery of sexual function. *J Urol* 1995;154:150–2.
- [96] Droupy S, Hessel A, Benoît G, Blanchet P, Jardin A, Giuliano F. Assessment of the functional role of accessory pudendal arteries in erection by transrectal color Doppler ultrasound. *J Urol* 1999;162:1987–91.
- [97] Ohebsshalom M, Parker M, Waters B, Flanagan R, Mulhall JP. Erectile haemodynamic status after radical prostatectomy correlates with erectile functional outcome. *BJU Int* 2008;102:592–6.
- [98] Galfano A, Ascione A, Grimaldi S, Petralia G, Strada E, Bocciardi AM. A new anatomic approach for robot-assisted laparoscopic prostatectomy: a feasibility study for completely intrafascial surgery. *Eur Urol* 2010;58:457–61.
- [99] Moskovic DJ, Alphas H, Nelson CJ, et al. Subjective characterization of nerve sparing predicts recovery of erectile function after radical prostatectomy: defining the utility of a nerve sparing grading system. *J Sex Med* 2011;8:255–60.