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Recovery of erection after pelvic urologic surgery: our experience

L Gallo[1]*, S Perdonã[1], R Autorino[1], E Celentano[1], L Menna[1], G Di Lorenzo[1] and A Gallo[1]

[1]*Division of Urology, National Cancer Institute, 'Fondazione Pascale', Naples, Italy*

The incidence of erectile dysfunction (ED) in patients undergoing pelvic urologic surgery, the efficacy and tolerability of vardenafil-based rehabilitative treatment as first option in these patients, the role of spontaneous erection (SE) as a possible positive predictive factor to erection recovery after such treatment, and the role of second-line therapies in those nonresponders are evaluated. All the patients undergoing pelvic urologic surgery at our Institution between November 2002 and December 2003 were considered. Preoperative erectile function (EF) was evaluated by using the abridged five-item version of the International Index of Erectile Function (IIEF5) questionnaire. Study population was divided into separate groups considering grade of preoperative EF, nerve sparing (NS) surgery and type of procedure (radical prostatectomy, radical cystectomy (RC) or nerve and seminal sparing cystectomy). In total, 86 patients were evaluated. After 6 months, an increase in mean IIEF5 score of 12.9 points was found in those who had undergone a bilateral NSRP after vardenafil therapy, of 8.0 points in those who had undergone unilateral NSRP, of 11.3 in those who had undergone NSRC and of 11.5 in nerve and seminal sparing cistectomies. A better vardenafil response was found in patients with SE + ($P < 0.001$). Among those vardenafil notresponders, 13 were treated by using intracavernous injections, one by vacuum device and three with penile prosthesis implant. In conclusion, in our experience, vardenafil showed to be well tolerated and effective for recovery of EF in patients undergoing pelvic urologic surgery. This drug was particularly effective for those with a normal preoperative EF undergoing an NS procedure. Of course, it should be recognized that the absence of a control group in the study represents an important limitation. However, based on the data from the literature, there is a strong belief that such an approach will lead to an earlier recovery of EF than without rehabilitative treatment.
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Introduction

As a result of improved screening of men over the age of 50 y with digital rectal examination and PSA testing, early diagnosis of prostate cancer (PCa) is possible and makes it a curable disease. Radical prostatectomy (RP) represents a potential definitive therapy in the management of organ confined prostate cancer.[1] On the other hand, this surgical act is burdened by high rates of erectile dysfunction (ED) ranging up to 80%, with a remarkable worsening of quality of life especially in younger patients.[2]

Radical cystectomy (RC) represents the gold standard curative treatment for infiltrating bladder cancers, and it is increasingly advocated for high-risk aggressive superficial bladder cancer.[3] During this surgical procedure, the neurovascular bundles (NVBs) are usually removed or damaged, and it results in a dramatic negative impact on many aspects of the quality of life.[4]

Hence, the preservation of erectile function (EF) after pelvic urologic surgery still represents a major challenge for most urologists.

Since the anatomical studies by Walsh and Donker in the early 1980s, surgeons became aware of the location of the NVBs carrying the cavernous nerves, which are responsible for erection.[5] As a result of this improved understanding of the anatomy, nerve sparing (NS) techniques have become feasible in order to maintain EF without

*Correspondence: L Gallo, Division of Urology, National Cancer Institute, 'Fondazione Pascale', Via Mariano Semmola, Naples 80131, Italy.
E-mail: gigginogallo@tin.it
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compromising cancer control.[6,7] However, the risk of postoperative ED is not eliminated.[8]

Treatment for postoperative ED historically has included the use of vacuum devices, intracavernosal and intraurethral pharmacotherapy or placement of a penile implant. The advent of a new class of drugs, phosphodiesterase type 5 (PDE5) inhibitors, has provided an oral treatment alternative to those patients suffering from this surgery related complication.[9]

Sildenafil was the first agent to be approved in this class.[10] In the last few years, two new molecules, tadalafil and vardenafil, have been introduced and approved as a treatment for ED.[11] The latter is rapidly absorbed, with the time for maximum plasma concentration as short as 0.5–0.6 h and an elimination half-life of 4.8–6.0 h. In *in vitro* essays, it was shown to have a greater selective affinity for receptorial site on PDE5 enzyme than sildenafil.[12] In clinical studies, vardenafil significantly improved erections compared to placebo.[13] At the dosage of 10 and 20 mg, it was more effective than placebo in patients with ED undergoing NSRP.[14]

The objectives of our study were to evaluate the incidence of ED in patients undergoing pelvic urologic surgery, the efficacy and tolerability of vardenafil-based rehabilitative treatment as first option in these patients, the role of spontaneous erection (SE) as a possible positive predictive factor to erection recovery after such treatment, the role of second-line therapies in those nonresponders.

Materials and methods

Patient recruitment

All the patients undergoing pelvic urologic surgery at our Institution between November 2002 and December 2003 were considered.

Preoperative EF was evaluated by using the abridged five-item version of the International Index of Erectile Function (IIEF5) questionnaire.[15] Based on this questionnaire, study population was divided into four groups: group a (normal EF: score 21–25), group b (mild ED: score 15–20), group c (moderate ED: score 9–14), group d (severe ED: score 1–8). Only patients in the groups a and b (ie normal EF or mild ED) were submitted to an NS surgery.

For those with PCa, a bilateral or unilateral NSRP was performed when lateral biopsy cores were negative at both sides or at one side only, respectively. On the other hand, bilateral excision of NVBs was chosen in any cases where older (>65 y) patients or when PSA ≥ 20 ng/ml and/or Gleason score ≥ 7 were involved. The NSRP technique was the one described by Walsh.[16]

For the patients with bladder cancer, we performed a NS cystoprostatectomy, as described by Brendler *et al*.[17] A nerve and seminal sparing radical cystectomy, as described by Colombo *et al*,[18] was performed in selected cases (<65 y, strongly motivated patients, with multifocal T1 G3 or unifocal, extratrigonal T2 cancer, with PSA ≤ 4 ng/dl and urethral negative biopsy).

The study was approved by Ethics Committee and Scientific Board of our Institution and all patients signed an informed consent form.

Study design (Figure 1)

At 1 month after catheter removal, the possibility of participating in an EF recovery protocol was offered to all patients. For those interested in the protocol, we administered again the IIEF5, considering the scores, the questionnaire obtained at first visit as a baseline for evaluation of results. Moreover, we investigated the presence of SEs during the period subsequent to surgery, defining '*spontaneous erection*' as the ability to achieve a partial or total penile tumescence during the period immediately after the surgery without pharmacological aids (ie before the beginning of rehabilitative protocol). This aspect was investigated asking the patient: 'Did you notice in the period following catheter removal any modification of your penis rigidity determined by any type of sexual stimulation?'. Those answering 'yes' were classified as SE+.

Then, a rehabilitative therapy was started by using vardenafil 20 mg at least three times a week taken on demand. Patients were encouraged to have sexual activity.

The follow-up consisted in a visit every 3 months up to 12 months. During each visit, the tolerance to the treatment and the EF was evaluated by using the IIEF5 questionnaire. We considered as '*vardenafil responders*' patients totalizing a score ≥ 3 to both questions 2 and 3 of the questionnaire. Practically, these were the ones able to penetrate partners' vagina and to keep erection in the most part of the sexual intercourses.

At second visit (6 months), we performed a diagnostic test using intracavernous injection (ICI) with alprostadil 20 μg to all patients. We also gave a questionnaire asking grade of satisfaction for this therapeutic option (see Appendix A). The *vardenafil responders* were invited to choose between oral therapy and ICI. In case of preference for vardenafil, based on the previous grade of response to the drug, we considered modifying dosage to 10 or 5 mg (dose setting) or eventually abolishing therapy. Vacuum constriction device (VCD) was offered as an alternative to ICI for vardenafil not-responders. As the last option, we proposed surgical intervention of penile prosthesis implant to those not satisfied with

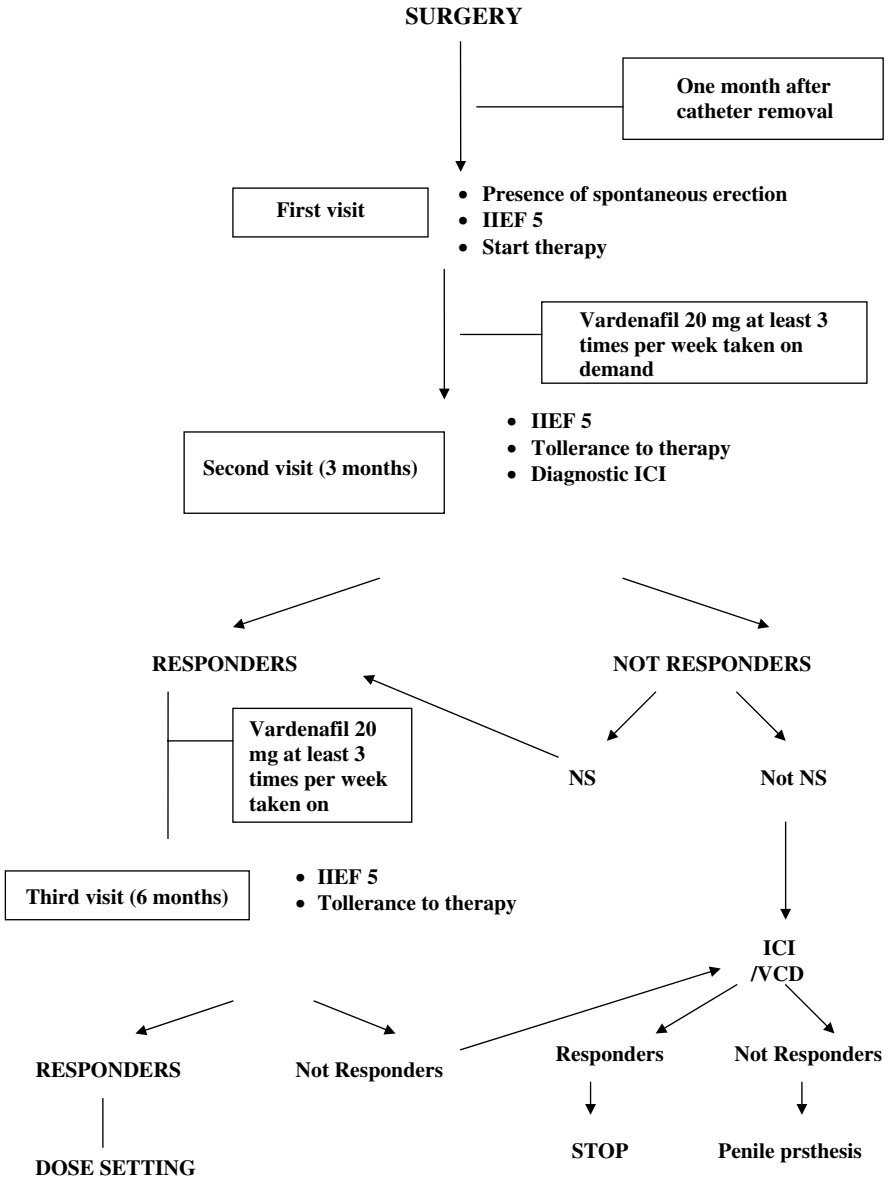

Figure 1 Scheme of study.

any of the previous by mentioned therapeutic options.

In those patients who were *not-responders*, and previously submitted to NS surgery, initial therapy was prolonged at least for 6 months, before defining a patient as a *vardenafil responder* or not. In those *not-responders* who were not submitted to NS, we directly offered an alternative treatment option (ie ICI or VCD), after the initial three months.

In the evaluation of the data, study population was divided into separate groups considering the grade of preoperative EF, the type of surgery (NS or not), the type of procedure (RP, RC or nerve and seminal sparing RC).

Moreover, among the patients who underwent an NS surgery, we separated those who already had an SE in the immediately postoperative period (SE+) from those who had not (SE−). In these two groups, we evaluated the different percentages of *vardenafil responders*, oral therapy dose setting or abolishment, and treatment switch to ICI.

Statistical analysis

Frequency distributions of IIEF5 scores were analysed at different times for each subgroup. Student's *t*-test was used to compare distributions of scores at different times (1, 3, 6, 9, 12 months) in those *vardenafil responders*, data analysis in each

subgroup could not be performed, because of the small samples.

To evaluate the efficacy of vardenafil therapy over 6 months, differences in IIEF5 scores at 6, 9, 12 months on postoperative scores were calculated and transformed in categories of five points' difference to perform analysis of concordance of these differences through *Cohen k* test.

Pearson χ^2 test was used to compare, in the groups of patients with or without SE, proportions of those *vardenafil-responders*, those reducing the dose, those abolishing the therapy and those preferred alternative options.

All the tests were considered statistically significant when *P*-values were less than 0.01. All statistical analyses were performed using SPSS for Windows statistical package (SPSS Inc., Chicago).

Results

Demoghrapics

Overall, 95 patients underwent pelvic urologic surgery, 58 RPs and 37 RCs. Mean age was 59.4 (range 50–76 y, SD 9.6). In total, 40 patients had normal EF (42.1%), 31 mild ED (32.6%), 11 moderate ED (11.5%) and 13 severe ED (13.6%). We found the incidence of the following risk factors in moderate and severe ED: eight cases of hypertension (30%), five cases of diabetes (20.8%), 12 cases of chronic smoking (50%) and five cases of hyperlipidemy (20.8%).

Subgroups analysis

In total, 86 patients were included in the study, since nine patients refused to enter in the protocol. As previously mentioned, the results were evaluated considering preoperative EF, type of procedure and surgical technique:

- Bilateral NSRP group (22 patients): 12 had a normal preoperative EF, 10 a mild ED. The results were as follows (Figure 2):
  - *Normal EF*: 75% already had SE without therapy during the first month after surgery. We found an increase of 12.9, 13, and 12.6 points in the mean IIEF5 scores compared to baseline after 6, 9 and 12 months, respectively. In seven of them, we could reduce dosage to 10 mg and in 2–5 mg. Only three patients were able to have sexual intercourse without therapy. None required a second-line treatment. We did not find differences in IIEF 5 score after 6, 9 and 12 months of therapy even after dose setting.
  - *Mild ED*: 40% had SE during the first month. The increase of mean IIEF5 scores after 6 months was of 8.2. In none, was dose setting possible. One patient preferred ICI.
- Unilateral NSRP group (18 patients): 10 had a normal EF, while eight presented a mild ED. The results were as follows (Figure 2):
  - *Normal erection:* two were SE+. Mean IIEF5 score increased by 8.0 at 6 months, 10.2 at 9 months and 10.5 at 12 months. In one patient we could lower dosage to 10 mg and two patients preferred ICI.
  - *Mild ED*: only one patient was SE+. Increase of IIEF5 mean score was of 4.8, 10.6 and 10.8 points at 6, 9 and 12 months, respectively. No diminution of dosage was required and four patients preferred ICI.
- NSRC group (20 patients): 12 presented a normal EF before surgery, eight had a mild ED.
  - *Normal erection:* one-third of them was SE+. After 6 months of therapy, mean IIEF5 increased of 11.3 points. In four patients we could provide dose setting and in two abolish therapy. No one of these preferred other forms of treatment.

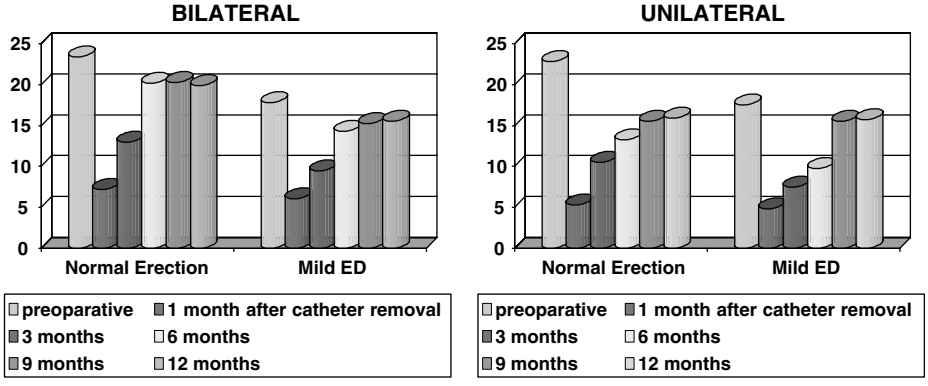

Figure 2 Mean IIEF5 score variations after vardenafil therapy in bilateral and unilateral nerve sparing radical prostatectomies.

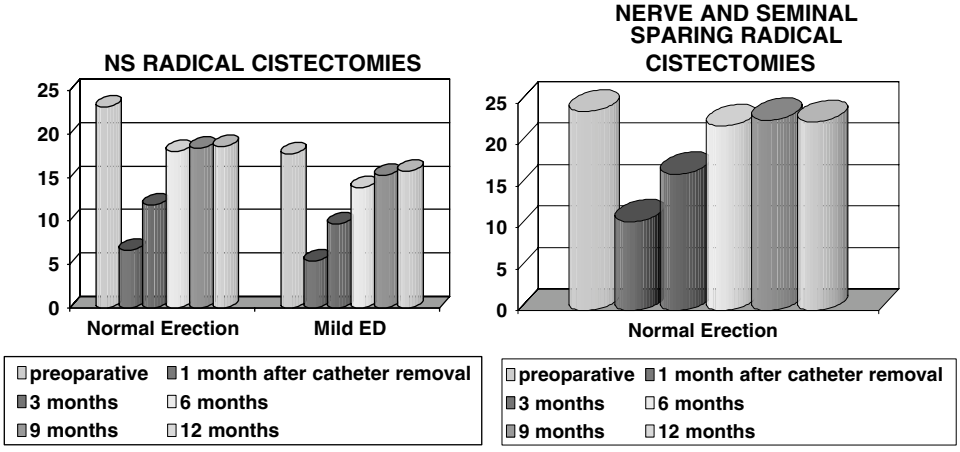

Figure 3 Mean IIEF5 score variations after vardenafil therapy in NS radical cistectomies and in nerve and seminal sparing cistectomies.

- *Mild ED*: two of eight were SE+. Mean IIEF5 increase was of 8.5 points after 6 months. In no one did we considere lower dosage. Only one patient preferred ICI (Figure 3).

- Prostate and seminal sparing RC group (four patients): all had normal preoperative EF and were SE+. In all patients, rehabilitative treatment was not necessary. Mean IIEF 5 scores before and after the surgery were not significantly different (Figure 3).
- Standard RP (12 patients): seven had normal EF or a mild ED. Five patients had a severe or moderate ED before surgery. In this, group we tried oral therapy just for 3 months. None showed a response to the treatment: four patients abandoned the study, four responded to ICI, one accepted VCD and in three penile prosthesis was implanted.
- Standard RC (10 patients): none had a normal preoperative EF. We found no IIEF5 scores improvement. Nine abandoned the protocol and one pateint was successfully treated with ICI.

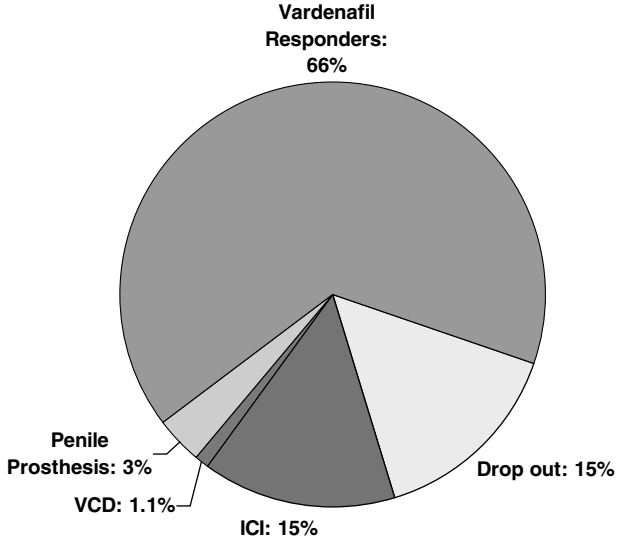

Figure 4 Overall results of protocol.

Overall analysis

In total, 13 out of 86 evaluable patients (13%) abandoned the protocol, 13 preferred ICI (15%), one preferred VCD (1.1%) and three (3.4%) were submitted to penile prosthesis implantation. Overall, independent of the type of surgery and preoperative EF, 57 patients (66%) were *vardenafil responders* and none of them chose alternative therapeutic options (Figure 4).

After the first 6 months, in 12 of 57 patients (21%) we could provide a dose setting and in nine (15.7%) no further treatment was required. Considering the modification of mean IIEF5 scores in the 57 *vardenafil responder*, patients over the time, after 6, 9, and 12 months with respect to baseline of therapy, statistical analysis showed that no further improvement of EF with vardenafil is obtained at 9 and 12 months. The comparison between score distributions at different times in this group of patients is represented in Figure 5. Student's *t*-test values, calculated in pairs of value at 6, 9, and 12 months in respect of 1 month scores, were respectively 31.5, 30.8, and 32.8 (all with *P*-value <0.001). Analysis of concordance between calculated IIEF5 scores differences at 6 *versus* 1 month, at 9 *versus* 1 month and at 12 *versus* 1 month resulted in *Cohen K* of 0.75 and 0.82, respectively ($P<0.001$).

In total, 25 out of 64 patients undergoing NS surgery (39%) were SE+ after catheter removal. All these finally responded to vardenafil treatment. In this group, nine patients (36%) did not require further therapy and eight (32%) could be treated

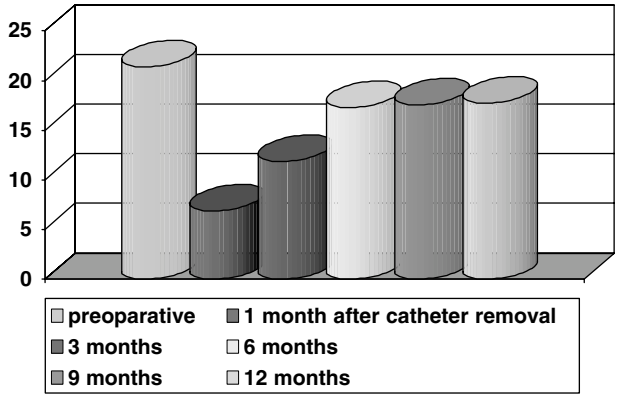

Figure 5 Mean IIEF5 variations in vardenafil responders group.

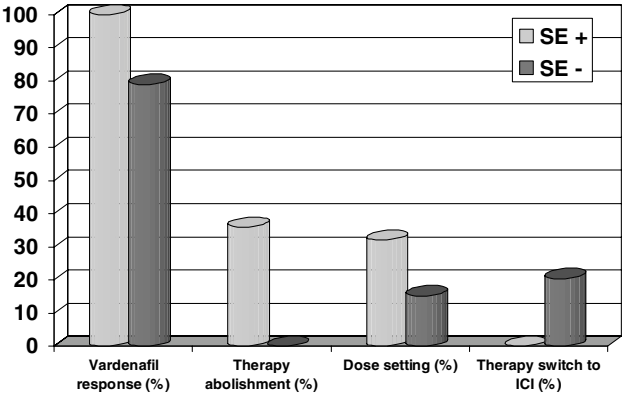

Figure 6 SE+ and SE− groups: different percentages of oral therapy response, therapy abolishment, dose setting and switched therapy.

with a lower dosage of the drug; no patient had to switch to ICI. In those SE−, 31 patients (74.5%) responded to oral therapy, in only six cases (15.3%), a lower dosage could be used, while eight patients switched to ICI (20.5%) (Figure 6). Statistical comparison between these two groups (SE+ *versus* SE−) showed that there was a significant difference in those requiring no further therapy after the initial period (χ^2 value 16.337 with $P<0.001$), in those allowing a reduced dosage (χ^2 value 2.461 with P not significant) and in those switching to ICI (χ^2 value 5.861 with $P<0.001$).

Oncological outcome

In 38/40 patients (95%), who had undergone an NSRP, cancer was pT2. In the two cases (5%) with a pT3 tumor, gleason score was <5. Both patients are under hormonal therapy with bicalutamide 150 mg, without libido problems and no PSA relapse at follow-up.

Among the 20 patients who underwent RC, we had one case of incidental PC. Among the four patients who underwent nerve and seminal sparing RC, none had PSA values elevation at follow-up.

Safety

Adverse events related to vardenafil were: headache (8.8%), flushing (7.5%), dyspepsia (4.5%), nasal congestion (3.2%), diarrhoea (2.6%), dizziness (2.2%), and arthralgia (2.0%). In the 13 patients treated with ICI, adverse reactions were found in three cases: one with painful erections and two with priapism, resolved with α-adrenergic agonist injection. Nine patients agreed to try the VCD, but only one regularly used it.

Discussion

Why to treat and prevent ED following pelvic surgery?

RP is a potentially definitive therapy, but, at same time, it is burdened by complications such as ED and urinary incontinence, with rates ranging up to 80 and 25%, respectively.[19] While an increasing number of studies have reported very satisfactory postoperative rates of urinary continence, the preservation of EF after surgery remains the most important challenge for urologists.[20] It has already been demonstrated that there is a significant and sustained effect of ED on quality of life after RP.[21] On the other hand, although surgical cure is always the priority in the patients undergoing RC, ED will become a more accountable end point in the future management of bladder cancer. Similar to what occurred in PCa, better screening and monitoring protocols for bladder cancer will cause stage migrations and provide earlier indications for RC.[4]

Clinical evaluation of ED after PUS

We used the abridged five-item version of IIEF questionnaire to define and validate the degree of ED in our surgical population. This diagnostic tool was found to be very useful. It consists of a five question schedule exploring all the aspects of sexual activity including erection quality, penetrating ability, difficult to keep erection and sexual intercourse pleasure.[15] Moreover, we consider the question 2 and 3 (penetrating and maintenance ability) to be the more appropriate to evaluate the response to the oral therapy.

We think that for this category of patients IIEF5 is preferable to more expensive and invasive studies such as eco-colour-doppler or Rigiscan. Moreover, the aetiology of this kind of ED is well understood (Surgical damage or complete excision of NVBs[22]) and for this reason further diagnostic assessment is not required.

Positive predicting factors to erection recovery

It has been suggested that positive predicting factors for recovery of EF after RP are young patient age, preoperative EF, preservation of NVBs and early beginning of rehabilitative therapy.[23]

In our experience, the two main predicting factors were preoperative EF and NVBs preservation: when these two elements were concomitant, we observed the maximum positive response to vardenafil therapy, evaluated as an increase of mean IIEF5 scores. When only one NVB was spared or when preoperative EF was not complete, we did not find the same positive results. Hence, we believe therapy must be conducted only in men without ED or affected by mild ED before operation. Oral therapy is useless for patient with preoperative ED and/or for ones that did not undergo NS surgery. For this reason, providing different therapeutic options is suitable in these cases. Anyway we chose to start with oral treatment as recommended by the EAU guidelines, which consider PDE5 inhibitors as the first-line therapeutic option.[24]

About NS surgery, it is not always possible to preserve both NVBs for oncological reasons and, above all, it is not always possible to be sure to have preserved them. Devices such as Cavermap® could help surgeons for this purpose.[25] Unfortunately, this device is not yet widespread and its definitive results are not yet available. Therefore, only the clinical evidence of EF after surgery could confirm the achievement of this goal.

The role of PDE5 inhibitors

The introduction of PDE5 inhibitors revolutionized the therapeutic approach for ED.

Their role is much more important in patients undergoing unilateral NS surgery or presenting mild preoperative ED, in which it is necessary to maximize all residual neurovascular function to ensure the best cavernous tissue response. In our experience, no patient with these characteristics was able to have sexual activity without vardenafil and few of them could have dose diminution.

For patients who underwent bilateral NS surgery, PDE5 inhibitors accelerate erection recovery working as an incentive to maintain sexual interest. Commonly after an NSRP with the slow return of SEs, a dysfunctional sexual dynamic may develop in couples, the patient withdraws sexually as he is increasingly discouraged with his lack of EF, which is a constant reminder of cancer. The female partner, relieved that the patient has survived the surgery, may be satisfied with his companionship and is not anxious to upset him by making sexual overtures that may frustrate him. Successful rehabilitative therapy early after surgery may contribute to break this negative cycle.[26]

It is preferable to start the therapy always with maximal dosage and providing dose setting at follow-up in cases of good response. Previously published data with sildenafil suggest that the highest available dose of a PDE5 inhibitor is usually necessary to treat ED following surgery.[27]

We could not provide a control group for ethical reasons: the same drug already showed to be more active than placebo for this same indication in a study by Brock *et al*.[14] It remains unclear whether patients who did not receive oral therapy, especially in the most favourable groups, would not have otherwise recovered function over time with observation alone. The question as to whether vardenafil or related oral drugs truly rehabilitate erection remains open. However, there is a strong belief that such treatment will lead to earlier recovery of erections than without treatment.[28] As yet data on the efficacy of early postoperative erectile treatment rely on very few randomized trials.[29] As the natural recovery of EF has been reported to take as long as 2 years,[26] it is possible that the erectile rehabilitation may simply bring forward the natural healing time of potency rather than saving patients from permanent erectile failure. Larger randomized trials with at least 2 y of follow-up are required before a definite conclusion can be drawn on the true efficacy of rehabilitative sexual therapy.[30]

Among the PDE5 inhibitors, we chose to use vardenafil because it has been introduced recently into the Italian market and for its pharmacological profile. We thought it was the most suitable molecule for this difficult category of patients. However, comparative studies are necessary, since all the three available molecules showed to be more effective than placebo to treat DE after pelvic urologic surgery.[31] In particular, vardenafil has been tested in patients treated with ED following a uni- or bilateral NSRP in a multicentre, prospective, placebo controlled, randomized study. This was a 12-week parallel arm study comparing placebo to vardenafil 10 and 20 mg. In total, 71 and 60% of patients treated with a bilateral NS procedure reported an improvement of EF following the administration of vardenafil 20 and 10 mg, respectively. A positive answer to SEP2 question (were you able to insert your penis into your partner's vagina) was seen in 47 and 48% of patients using vardenafil 10 and 20 mg, respectively. A positive answer to the

more challenging question SEP3 question (did your erections last enough to have successful intercourse?) was seen in 37 and 34% of patients, respectively.[14]

When to start oral therapy and how long to wait before providing alternative options?

It has been suggested that rate of success strongly depends on early beginning of therapy and used dosage.[9] Starting the therapy as early as possible is a very important issue since several reports showed how '*penis is not a muscle, but behaves like a muscle*': the better understanding of pathophysiology of post prostatectomy ED including the concept of tissue damage induced by poor corporeal oxygenation paved the way to the application of pharmacological regimens aimed at improving early postoperative corporeal blood filling.[32]

We chose to begin treatment 1 month after catheter removal to verify the presence of SE and to reduce the influence of urinary incontinence that could alter the results of rehabilitative therapy.

In a previous experience, sildenafil appeared to be ineffective in the first 9 months following surgery; therefore, it was suggested to wait this time after evaluating treatment.[33] We think this period to be excessive: in our experience, we found concordance in vardenafil responders considering mean IIEF5 scores at 6, 9 and 12 months. Practically, vardenafil achieves its maximum effect already at 6 months of treatment. After this time it is possible to provide a dose setting to vardenafil responders and to counsel to try a second-line of treatment to those not responding.

Efficacy and compliance of second-line treatments

In patients who did not undergo NS surgery, independently on their preoperative EF, it is necessary to start immediately with alternative options. In particular, we agree with the fact that ICI is the best treatment.[34] Delaying treatment with ICI could determine cavernous tissue fibrosis. To avoid this dangerous complication we provided to all our study population ICI diagnostic test independently from response to therapy. Furthermore, early ICI could help patients psychologically, making them understand that oral therapy is not the only option and even when it fails other forms of treatment are available. Our experience confirmed that patients preferred ICI to VCD as reported in other experiences in literature.[35]

Other studies reported different types of therapies showing to be successful in recovery of erection after pelvic urologic surgery: MUSE (Medicated Urethral System for Erection), combination of MUSE and sildenafil,[36] VCD and penile prosthesis implant.[37] Among these options, MUSE is an interesting technique for its lower invasivity, but unfortunately it is not yet available in Italy at the moment.

Could spontaneous postoperative erections be considered as a positive predicting factors to oral therapy?

We found the presence of SE after catheter removal in our study as a positive predictive factor to vardenafil therapy response and final erection recovery. Indeed, there were statistically significant differences in SE+ and SE− groups regarding the percentages of those in which we could abolish therapy (36 *versus* 0%, respectively) and of those who had to use ICI to have sexual intercourse (0 *versus* 20.5%, respectively). SE had the same role also in patients treated with tadalafil, as reported by Montorsi *et al*.[31] We think it is always necessary to consider this aspect for its clinical utility.

NS surgery is not always possible: correct case selection and respect of oncological criteria

Recovery of EF is certainly an important goal for urologists. Anyway we do not have to forget that the main purpose of uro-oncological surgery remains the cancer control. In a previous study, patients interviewed about their expectations were interested more to quality of life and absence of complications than to overall survival.[38]

We think both goals can be achieved if correct oncological criteria on cases selection are respected: NS prostatectomy determines an excision of the gland very close to its lateral aspect and for this reason there is the risk to leave tumoral tissue in the field. In our experience, this complication occurred only in 5% of the cases and in all of them we could manage the problem by using antiandrogen monotherapy with bicalutamide without consequences on libido and EF.

Conclusions

In our experience, vardenafil showed to be well tolerated and effective for recovery of EF in patients undergoing pelvic urologic surgery. This drug was particularly effective for those with a normal preoperative EF undergoing an NS procedure.

A 6-month period can be considered sufficient for a correct evaluation of oral therapy. After this time, not-responder patients should be counselled to try second-line treatments.

Of course, it should be recognized that the absence of a control group in the study represents an important limitation to the proof of our rehabilitative therapy on EF recovery after surgery. However, based on the data form the literature, there is a strong belief that such approach will lead to an earlier recovery of EF than without rehabilitative treatment.

The presence of SE after catheter removal is a useful clinical instrument to predict response to oral therapy and final EF recovery. Among the second-line therapies, ICI showed to be more effective and better tolerated.

Acknowledgements

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Appendix A

Intracavernous injection diagnostic test (ICIDT)

Dear Sir

In order to evaluate your problem properly and assess the best therapy for you, it is very important that you bring back this questionnaire filled on your next visit. In case of persistent erection for more than 4 h, please avoid any erotic stimulation and soak your penis in cold water. If erection persists do not hesitate to contact us.

INJECTION_____ **DATE**_____ **TIME**_____

QUESTIONNAIRE

1. Did you have any erection after the injection? NO ☐ YES ☐
2. How much time elapsed between injection and erection?_____
3. How long did it last?_____
4. What was it like? Complete rigidity ☐ Partial rigidity ☐
5. How was it compared with your spontaneous penile tumescence?
   Better ☐ Worse ☐ Similar ☐
6. Did you attempt any sexual activity with your partner? NO ☐ YES ☐
   - Was it satisfactory for you? NO ☐ YES ☐
   - And for your partner? NO ☐ YES ☐
   - Did sexual stimulation increase your erection? NO ☐ YES ☐
7. Did it last more than 4 hours ? NO ☐ YES ☐
   if yes, what did you do? _____
8. Did any other complications occur ?
   NO ☐ YES ☐ Specify_____
9. In conclusion, do you think you will use this kind of injection regularly for sexual activity when it is needed? NO ☐ YES ☐
10. Comments _____

(Please do not forget to take this questionnaire on the day of your next visit.)