Erectile function after cystectomy with neurovascular preservation

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Abstract
Objectives: To study the utility of neurovascular preservation for postoperative erection in radical cystectomy.
Materials and methods: Retrospective analysis of 44 cystectomies performed at our center between January 2006 and December 2009 in men <65 years. In 11 cases a neurovascular preservation was done. We analyzed age, BMI, indication for surgery, urinary diversion, use of i-PDE5 or alprostadil, and daytime and nighttime continence. Erection Hardness Score (EHS) was used to assess erectile function.
Results: Spontaneous postoperative erectile function in preservation group was 44.4% EHS 4, 33.3% EHS 3 and 22.3% EHS 1 (achieving EHS 3 or 4 with alprostadil). In the non preservation group, 4.5% achieved EHS 4 spontaneously. The other 95.5% had EHS 0 (4.5% achieved EHS 3 with tadalafil 20mg and 9% with intracavernous injections). Variables age (p=0.001) and nerve-sparing surgery (p<0.001) were related to postoperative erectile function recovery. In the multivariate analysis, nerve-sparing surgery remained statistically significant.
Conclusions: The functional results in preserving cystectomy are promising. The preservation should be considered in young patients without erectile dysfunction.

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PALABRAS CLAVE
Cistectomía radical; Función eréctil; Preservación neurovascular; Continencia urinaria

FUNCTION ERECTIL DESPUÉS DE CISTECTOMIA CON PRESERVACIÓN NEUROVASCULAR

Resumen
Objetivos: Estudiar la utilidad de la preservación neurovascular para la erección postoperatoria en la cistectomía radical.
Materiales y métodos: Análisis retrospectivo de 44 cistectomías realizadas en nuestro centro entre enero de 2006 y diciembre de 2009 en hombres menores de 65 años. En 11 casos se hizo preservación neurovascular. Hemos analizado la edad, el índice de masa corporal, la indicación...
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Introduction

Radical cystoprostatectomy (RC) is the treatment of choice for muscle-invasive bladder cancer and non-muscle-invasive bladder cancer with high risk of high risk of tumor progression or after failure of conservative treatments. However, one of the major disadvantages of RC is the frequent postoperative erectile dysfunction (ED). This aspect represents a frequent cause of fear and concern for patients and their partners and has a significant impact on the choice of therapy. Walsh and Donker suggested that ED was produced by injury to the pelvic nerve bundles, which provide innervation to the corpora cavernosa. The preservation of the quality of life is especially important in young sexually active patients with localized disease.

90% of the males showed ED after no nerve-sparing radical cystectomy (NNS RC). Recovery of erectile function (EF) following nerve-sparing cystectomy (NS RC) is between 14% and 80%. Those differences may be due to different levels of skill among surgeons, to surgery technique or to patients’ selection criteria. Based on this information and in order to avoid injuries to the para-prostatic neurovascular branches and to preserve erectile function in patients who underwent to RC, Schlegel and Walsh modified the surgical technique.

The objective of this study was to analyze the postoperative course and functional outcomes of nerve-sparing surgery and to compare these with those obtained after no-nerve-sparing surgery.

Materials and methods

Retrospective review in 44 men under 65 years of age having undergone RC without presurgical erectile dysfunction in our Center was conducted from January 2006 to December 2009. Radical cystectomy was indicated for treatment for muscle-invasive bladder cancer or non-muscle-invasive bladder cancer after intravesical treatment failure with Bacillus Calmette-Guerin (BCG).

NS RC technique was carried out according to standard technique modified by Schlegel and Walsh: careful dissection along anterior and lateral aspects of the prostate and urethra, and careful retrograde dissection of the posterior aspect. Only one surgeon (MJRC) performed the 11 NS RC.

Depending on neurovascular preservation, patients were divided into 2 groups: 11 patients underwent bilateral nerve-sparing cystectomy (NS RC) and the remaining 33 patients underwent no-nerve-sparing cystectomy (NNS RC).

Age, body mass index (BMI), indication for surgery, urinary diversion and recurrence were analyzed retrospectively. Urinary continence was also studied in patients having undergone orthotopic urinary diversion.

Erection Hardness Score (EHS) questionnaire in Spanish language was used to assess preoperative and postoperative erectile function. It is a one-item questionnaire with 5 possible answers: 0 = penis does not change; 1: penis is larger but not hard; 2: penis is hard but not hard enough for penetration; 3: penis is hard enough for penetration but not completely hard; 4: penis is completely hard and fully rigid. This questionnaire is a validated tool compared with International Index of Erectile Function (IIEF).

Those patients who requested assistance with the study and treatment of postoperative erectile dysfunction were referred to the Unit for Sexual Medicine. Postoperative erectile dysfunction was managed with on-demand therapy with 100 mg of sildenafil (Viagra®), 20 mg of vardenafil (Levitra®) or 20 mg of tadalafil (Cialis®). Treatments with intracavernous vasoactive drugs (Caverject® 20 μg) were assayed in those patients who did not respond to phosphodiesterase type-5 (PDE5) inhibitors.

Pad-test was used to assess UC. Those patients who do not use any pad were considered continent. Urinary incontinent patients were those who used pads for security or necessity (one or more).

Comparative study among men who underwent NS RC and NNS RC was developed. Data analyses were performed using the SPSS 15.0 software (SPSS Inc., Chicago, IL, USA). Values of \( p < 0.05 \) were considered statistically significant. Variables with values of \( p < 0.33 \) in univariate analyses were included in multivariate analysis. Values of \( p < 0.05 \) were considered statistically significant.

Results

Table 1 shows major clinical, pathological and functional data of the 44 males involved in the study. Table 2 shows comparative analyses of clinical, pathological and functional data according to surgical procedure (nerve-sparing vs. no-nerve-sparing). Table 3 shows the results of univariate and multivariate analysis between independent variables and spontaneous erectile function after surgery.
Table 1  Main clinical and pathological data of the 44 men who participated in the study.

<table>
<thead>
<tr>
<th></th>
<th>Preservation (n = 11)</th>
<th>No preservation (n = 33)</th>
<th>Value of p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean ± SD; years)</td>
<td>54.4 ± 7.3</td>
<td>56.1 ± 5.9</td>
<td>0.007</td>
</tr>
<tr>
<td>BMI (mean ± SD; kg/m²)</td>
<td>26.4 ± 4.8</td>
<td>26.5 ± 5.3</td>
<td>0.815</td>
</tr>
<tr>
<td>TNM (post-TUR)</td>
<td></td>
<td></td>
<td>0.730</td>
</tr>
<tr>
<td>Superficial</td>
<td>3/44 (6.8%)</td>
<td>5/33 (15.2%)</td>
<td>0.140</td>
</tr>
<tr>
<td>Muscle-invasive</td>
<td>41/44 (93.2%)</td>
<td>28/33 (84.8%)</td>
<td>0.007</td>
</tr>
<tr>
<td>Neurovascular preservation (yes/no)</td>
<td>11/33</td>
<td>22/33 (66.7%)</td>
<td>0.007</td>
</tr>
<tr>
<td>Urinary diversion (neobladder/Bricker)</td>
<td>38/6</td>
<td>28/33 (84.8%)</td>
<td>0.140</td>
</tr>
<tr>
<td>pTNM (postcystectomy)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>pT0</td>
<td>6/44 (13.6%)</td>
<td>15/33 (45.5%)</td>
<td></td>
</tr>
<tr>
<td>Superficial</td>
<td>18/44 (40.1%)</td>
<td>17/33 (51.5%)</td>
<td></td>
</tr>
<tr>
<td>Muscle-invasive</td>
<td>13/44 (29.5%)</td>
<td>15/33 (45.5%)</td>
<td></td>
</tr>
<tr>
<td>N+</td>
<td>7/44 (16%)</td>
<td>16/33 (48.5%)</td>
<td></td>
</tr>
<tr>
<td>Recurrence (%)</td>
<td>9/44 (20.5%)</td>
<td>17/33 (51.5%)</td>
<td></td>
</tr>
<tr>
<td>Follow-up (months)</td>
<td>21</td>
<td>24</td>
<td></td>
</tr>
</tbody>
</table>

BMI: body mass index; N+: positive nodes; pTNM: final pathological report; TUR: transurethral resection of bladder tumor.

In the multivariate analysis, statistical significance between neurovascular preservation and postoperative erectile dysfunction was maintained. Fig. 1 shows the status of erectile function after surgery depending on surgical technique.

Regarding urinary continence there were no differences in pad test between NS CR group and NNS CR group. Fig. 2 shows daytime and nighttime continence rates depending on the surgery technique.

Discussion

Radical cystectomy is well-established treatment for muscle-invasive bladder cancer. However, it has negative impact on quality of life regarding the sexual activity and the continence. Because we can treat localized disease, issues related to quality of life, such as performance of orthotopic urinary diversion or sexual potency preservation, become important.

Surgical technique and expertise are dominant variables in the disease progression. However, other factors that can affect postoperative sexual function include patient’s age, preoperative sexual function, psychological adjustment to a cancer diagnosis and coexisting medical diseases (i.e. diabetes, hypertension).16

The objective of our study was to assess through validated tool the outcomes of nerve-sparing cystectomy regarding erectile function. Retrospective analysis was carried out comparing our study population with all men who underwent no-nerve-sparing radical cystectomy. The vast majority of papers published up to date use IIEF domain

Table 2  Comparative analysis of 44 patients having undergone radical cystectomy depending on the surgical procedure (nerve sparing vs. non-preservation).

<table>
<thead>
<tr>
<th></th>
<th>Preservation (n = 11)</th>
<th>No preservation (n = 33)</th>
<th>Value of p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean ± SD; years)</td>
<td>49.4 ± 9.1</td>
<td>56.1 ± 5.9</td>
<td>0.007</td>
</tr>
<tr>
<td>BMI (mean ± SD; kg/m²)</td>
<td>26.1 ± 3.2</td>
<td>26.5 ± 5.3</td>
<td>0.815</td>
</tr>
<tr>
<td>TNM (post-TUR)</td>
<td></td>
<td></td>
<td>0.730</td>
</tr>
<tr>
<td>Superficial</td>
<td>1 (9.1%)</td>
<td>2 (6.1%)</td>
<td></td>
</tr>
<tr>
<td>Muscle-invasive</td>
<td>10 (90.9%)</td>
<td>31 (93.9%)</td>
<td></td>
</tr>
<tr>
<td>Urinary diversion</td>
<td>11/0</td>
<td>27/6</td>
<td>0.128</td>
</tr>
<tr>
<td>(orthotopic/heterotopic)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recurrence</td>
<td>2/11 (18.2%)</td>
<td>7/31 (22.6%)</td>
<td>0.140</td>
</tr>
<tr>
<td>Spontaneous EHS</td>
<td>7/9 (77.8%)</td>
<td>1/21 (4.5%)</td>
<td>0.000</td>
</tr>
<tr>
<td>3/4 with treatment</td>
<td>9/9 (100%)</td>
<td>5/22 (22.7%)</td>
<td>0.000</td>
</tr>
<tr>
<td>Daytime continence</td>
<td>10/11 (90.9%)</td>
<td>20/22 (90.9%)</td>
<td>0.999</td>
</tr>
<tr>
<td>Nighttime continence</td>
<td>6/11 (54.5%)</td>
<td>11/22 (50%)</td>
<td>0.805</td>
</tr>
</tbody>
</table>

Continence: no pads. Using one pad was classified as incontinence; EHS 3/4 with treatment: presence of erections sufficient for intercourse with treatment; spontaneous EHS 3/4: presence of erections sufficient for sexual intercourse without treatment; BMI: body mass index; TUR: transurethral resection of bladder tumor.

Figure 1  Graphical representation of erectile function after radical cystectomy. The first and second columns show the erectile function of men having undergone NNS-RC (spontaneous and after treatment, respectively). The third and fourth columns show the erectile function of the group of men with nerve sparing (spontaneous and after treatment, respectively).
of erectile function. EHS questionnaire is a useful, reproducible and reliable tool.

Several studies about sexual function following RC reported erection rates sufficient for intercourse in 17–82%. Results regarding erectile function reported in medical literature are diverse. The factors that explain the variations between studies include: experience of the surgeon, surgical technique and inclusion criteria of patients. Other possible factors are: assessment method and definition of the potency. The majority of papers published up to date use IIEF to assess sexual function. Our study has used EHS questionnaire. It is one-item questionnaire, robust and useful to assess erection hardness. Psychometric analysis supports the use of the EHS as a simple, reliable and valid tool to assess erection hardness. Generally, our study confirmed the hypothesis that NS RC is essential to the return of natural erections after surgery.

The use of a validated tool to analyze erectile function showed that younger age and nerve-sparing technique were factors associated with a more favorable sexual outcomes in order to the recovery of post-surgical erectile function. Surprisingly, 45% of patients who underwent NS RC achieved their normal erectile function (EHS 4). Furthermore, EHS 3 was achieved by 30% of patients. Only 25% of men did not achieve spontaneous erection sufficient for sexual intercourse, but all of them were able to maintain sexual intercourse after oral treatment or intracavernous injection.

On the contrary, only 4.5% of men in NNS RC subgroup returned spontaneously to normality in terms of erectile function. It is noteworthy that only 20% of 95% remaining patients treated either with iPDE-5 or intracorporeal prostaglandin regained functional erections (EHS 3 or 4). Furthermore, NNS RC group was difficult to manage, because only 20% of its patients responded to therapy.

From our point of view, some factors for proper return of erectile function after surgery are: (a) normal erectile function before surgery; (b) younger men and (c) quality of preservation of the neurovascular branches by development of refined technique in the hands of experienced surgeon.

Urinary continence after RC was studied too. Due to the lack of literature about postoperative continence regarding neurovascular preservation after RC, the studies carried out in the University of California with patients having undergone radical prostatectomy were taken as reference. In these studies, urinary continence was typically defined as: no use of pads, use of one pad for security, continuous use of one pad per day. Recent studies conclude that the association between those men who use pad for security and those who have a continuous use is stronger than with those men who use no pads. In general, in our series both types of continence (daytime and nighttime) were comparable to those in previous publications about RC. According to our experience, neurovascular preservation was not related with continence differences.

Some study limitations should be mentioned. Firstly, given the limitations of small size and being a retrospective study, our report may show statistical bias. However, although the number of patients in NS RC group was small, we have achieved statistical significance. Furthermore, the retrospective way of collecting functional data (erectile dysfunction and continence) reduces the conclusions of the
study. In our opinion, prospective data collection using validated instruments should be extended to confirm the promising benefits in nerve sparing radical cystectomy.

Conclusion

Functional results related to erection after nerve sparing radical cystoprostatectomy are promising. Preservation of neurovascular bundles would be considered in selected young patients with localized disease and without previous sexual dysfunction.

Further studies are necessary in order to confirm the real impact of nerve sparing on functional aspects as erectile function and urinary continence.

Conflict of interests

The authors declare that they have no conflict of interest.

References

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