Penile haemodynamic changes in post-radical cystectomy patients

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Introduction

Male erectile dysfunction (ED) after radical cystectomy (RC) is a prevalent problem. Various potency rates after nerve-sparing RC have been reported. Some authors indicated that 49–80% of the patients had erection after nerve-sparing radical cystoprostatectomy (Brezza et al., 1989; Austoni et al., 1994; Chiang et al., 1997; Dubbelman et al., 2006, 2008; Miyao et al., 2001). However, Zippe et al. (2004) showed that only 14% of the patients recovered erectile function (EF) after surgery. Moreover, attempted nerve sparing (NS) and younger age are both associated with more frequent recovery of EF (Kessler et al., 2004).

In contrast to radical prostatectomy, few reports discussed the haemodynamic vascular changes in post-radical cystectomy cases. Post-radical pelvic surgery and neuro-vascular factors may be of great importance. The incidence of veno-occlusive dysfunction increases with time in postoperative period with up to 50% in post-prostatectomy impotence (Mulhall et al., 2002). Arteriogenic cause of ED may have a role in non-nerve sparing (NNS) cases.

Different methods such as Rigi scan, cavenosography and cavernosometry are used to assess the penile EF and its vasculature. Colour Doppler ultrasound appears to be the most reliable, non-invasive diagnostic test for ED, especially after radical prostatectomy in patients who do not respond to pharmacotherapy (Dubbelman et al., 2006).

In this study, we aimed to assess the penile haemodynamic vascular changes in post-radical cystectomy patients.
patients using penile duplex ultrasound (PDU). Furthermore, evaluation of the vascular changes and possible vascular aetiology of ED in those patients were additional objectives.

**Material and methods**

Between January 2003 and January 2005, 258 men underwent radical cystectomy for invasive bladder cancer at our centre. A prospective controlled study was performed on 45 preoperative potent men who fulfilled the selection criteria. The study was approved by a local ethical committee. An informed consent was signed.

The selection criteria were patients who were preoperatively potent, married, with invasive bladder cancer. Urethra and prostate were free of carcinoma, free of neurological and penile diseases and age limit between 30 and 60 years.

Nerve sparing (NS) technique was applied in 21 patients. NS technique was applied as described by Schlegel & Walsh (1987) modifications to the standard technique that entails meticulous dissection of the anterior prostate and lateral aspect of the prostate-urethral junction with careful retrograde dissection of the posterior aspect from the rectum. In 24 cases, NS technique could not be applied (NNS group). The possibility of safe dissection of neurovascular bundles was abandoned due to bulky mass, pelvic adhesions, surgeon judgements, basal/near the bladder neck tumour or other intraoperative complications.

Among 60 cases screened, normal PDU indices were detected in 45 (who were included in the study and considered as a control arm). Postoperatively, PDU was carried out at 2, 6 and 12 months.

PDU was carried out using Toshiba colour duplex ultrasound equipment, model SSA-270 A (Toshiba, Tokyo, Japan). The equipment was connected to a multi-format camera to take films and Sony video printers (colour and white & black; Tokyo, Japan). The equipment was connected to a multi-format camera to take films and Sony video printers (colour and white & black; Tokyo, Japan). The equipment was connected to a multi-format camera to take films and Sony video printers (colour and white & black; Tokyo, Japan). The equipment was connected to a multi-format camera to take films and Sony video printers (colour and white & black; Tokyo, Japan). The equipment was connected to a multi-format camera to take films and Sony video printers (colour and white & black; Tokyo, Japan). The equipment was connected to a multi-format camera to take films and Sony video printers (colour and white & black; Tokyo, Japan).

By the same ultrasound radiologist, PDU results were obtained 5, 10 and 15 min after intra-cavernosal injection; the peak systolic velocity (PSV) was assessed as follows: more than 25 cm/sec was considered normal, between 20 and 25 cm/sec mild, between 12 and 20 cm/sec moderate, less than 12 cm/sec as severe arteriogenic impotence (Schwartz, 1992). The end diastolic velocity (EDV): 5 cm/sec or less was considered normal value, more than 5 cm/sec, suggested a veno-occlusive disorder (Knispel & Anderson, 1992). The patients were followed up 2, 6 and 12 months regularly on the same parameters. Formal preoperative and postoperative neurological assessment, by means of a neural root reflex (bulbo-cavernosal and anal reflexes) had been carried out for all cases.

Preoperatively and postoperatively, the potency status was identified by IIEF-5 (international index of EF-5) questionnaire (Rosen et al., 1997).

Cases with more than mild-to-moderate ED (EF domain: 10–25, based on IIEF-5) were advised to take sildenafil citrate 50 mg on demand, while others with EF domain <10 were advised to take intracorporeal injections of prostaglandins 20 μg per dose, on demand.

The data were processed using spss 11.0 for Windows (SPSS Inc, Chicago, IL, USA). Statistical analysis of the means of continuous variables was performed through use of non-parametric two independent samples test (Mann–Whitney test). Analysis of the significance of categorical variables was performed using chi-square test. A p-value <0.05 was considered statistically significant.

**Results**

Forty five preoperative potent males (had been proven by PDU) were divided into two groups based on surgical intervention, NS group (n = 21 cases) and NNS group (n = 24 cases). Both groups were comparable in preoperative demographic features (p > 0.05) (Table 1).

The urinary diversion was orthotopic (ileal W neo bladder) in 37 (82.2%) cases, 17 and 20 cases in NS and NNS respectively, continent cutaneous diversion in 5 (11.2% cases, 4 and 1 in NS and NNS respectively) in view of short mesentery, and ileal loop conduit of Bricker’s in 3 (6.6%) cases only in NNS group. Regarding the oncological outcome, we have no recurrence among our patients within the mean oncological follow-up period of 16.4 months (range: 12–24 months). In all patients (in both groups), no neural defects were observed through

<table>
<thead>
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<th>Parameters</th>
<th>Total number</th>
<th>Nerve sparing</th>
<th>Non-nerve sparing</th>
<th>p-value</th>
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</thead>
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<tr>
<td>Age</td>
<td>45</td>
<td>31–54</td>
<td>45–64</td>
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<tr>
<td>Smoking n (%)</td>
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<td>11</td>
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<td>Hypertension n (%)</td>
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<td>Diabetes Mellitus n (%)</td>
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<td>2</td>
<td>5</td>
<td>0.363</td>
</tr>
<tr>
<td>Related surgery* n (%)</td>
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<td>3</td>
<td>8</td>
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</table>

*Preoperative related surgeries as pelvic ureterolithotomy, cystolithotomy or any similar pelvic surgery could induce pelvic adhesions.
testing sacral root mediated reflexes pre- and postoperatively.

Among patients with NS cystectomy, 78.8% were potent postoperatively; 12 cases (57.8%) with spontaneous complete tumescence (EF domain of IIEF more than mild ED), and 5 cases (21%) with partial tumescence (EF domain of IIEF mild-to-moderate ED) on PDE-5i as erectogenic aid, while 4 cases required intracorporeal prostaglandin E1 injection. In contrast, none in the NNS group had a spontaneous erection (EF domain <10) and all of them failed to respond to sildenafil and required prostaglandin intracorporeal injection as erectogenic aid.

On first postoperative visit, none of NS cases demonstrated any arterial insufficiency, while two cases of NNS (8.3%) had PSV < 30 cm/sec in comparison with control arm. Moreover, all cases of both groups showed an early increase in EDV > 5 cm/sec.

In NS group, there were statistically non-significant changes in PSV (mean: 42.8, 52.1 and 43.6 cm/sec on 2, 6 and 12 months respectively) compared with preoperative (control) measures [(mean: 50 ± 2.6 cm/sec), p > 0.05]. The EDV was high at the early follow-up visit followed by gradually statistically significant decrease on the following visits (i.e. improvement) (mean values: 10.1, 7.7, 5.9 cm/sec on 2, 6 and 12 months, respectively) in comparison with control [(mean: 2.9 ± 0.2 cm/sec), p < 0.05] (Table 2).

On the other hand, the NNS cases also showed insignificant changes in PSV; but poorer than NS cases (mean values: 56.1, 46.6, 42.3 cm/sec on 2, 6 and 12 months respectively). In contrast to NS cases, the EDV of NNS group deteriorated and did not improve with time, [p > 0.05 (mean: 12.7, 11, 13.1 cm/ sec on 2, 6 and 12 months respectively)] (Table 2).

Figures 1 and 2 show the comparison between the mean values of PSV and EDV of the both groups. The comparison shows a significant difference between the groups regarding EDV (venogenic mechanism) rather than PSV (arteriogenic mechanism).

**Table 2** The comparison of penile Doppler ultrasound in both groups

<table>
<thead>
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<th>Nerve sparing group</th>
<th>Non-nerve sparing group</th>
<th>p-value</th>
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<tr>
<td></td>
<td>Mean</td>
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<td>Mean</td>
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<tr>
<td>PSV Control</td>
<td>50.096</td>
<td>2.6932</td>
<td>48.000</td>
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<td>2 months</td>
<td>42.8783</td>
<td>3.4903</td>
<td>56.1500</td>
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<td>6 months</td>
<td>52.1000</td>
<td>2.8006</td>
<td>46.6739</td>
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<td>12 months</td>
<td>43.6381</td>
<td>2.0372</td>
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<td>EDV Control</td>
<td>2.9840</td>
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<td>3.2656</td>
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<td>2 months</td>
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<td>0.96702</td>
<td>12.7826</td>
</tr>
<tr>
<td>6 months</td>
<td>7.7826</td>
<td>0.89420</td>
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<td>12 Months</td>
<td>5.9500</td>
<td>0.85767</td>
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PSV, peak systolic velocity; EDV, end diastolic velocity.

**Discussion**

Erectile dysfunction is common after prostate and bladder cancer surgery. The aetiology of changes in sexual potency after radical cystectomy (RC) is probably multifactorial, including neurogenic, vascular and psychosexual factors.

The ED in patients after RC is important and relatively less investigated in comparison with ED after radical prostatectomy.

Psychosexual factor has a significant role in such cases after pelvic surgeries and should be corrected as a
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A penile haemodynamic study on patients after nerve-sparing radical prostatectomy who had no pharmacological support in the initial year after surgery revealed a progressive incidence of venous leakage varying from 14% at 4 months to 50% at >12 months (Mulhall et al., 2002). Similarly, in the study of Montorsi et al. (1997), eight of 15 patients who did not self-inject with alprostadil in the first 4 months after surgery had a colour Doppler diagnosis of venous leakage, compared with only two of 12 of the treatment group. These findings corroborate the hypothesis that erectile rehabilitation prevents the occurrence of vasculogenic ED during the process of nerve healing after nerve-sparing radical prostatectomy.

In addition to other studies, we documented that spontaneous EF is absent for most of our patients soon after NS surgery, but there was a progressive return over 12 months in a variable proportion of them. This temporary delay could be explained by the hypothesis of the so-called ‘neuropaxia’ phenomenon, a temporary deficit in the cavernosal nerves which prevent any form of erection (Leungwattanakij et al., 2003). Moreover, corporeal fibrosis and subsequent ED may be induced by low oxygen tension in cavernosal tissue because of decrease in nitric oxide, which is significantly reduced during hypoxia following the surgery, which leads to vasoconstriction and corporeal fibrosis (Saenz de Tejada & Moreland, 1993).

The comparison of the Doppler indices before and early after surgery in all patients included in this study (45 cases; 21 NS and 24 NNS) showed that PSV remains the same or slightly insignificantly lower in both surgical groups (Fig. 1) and EDV deteriorated first and then improved progressively in NS group. These findings are consistent with that of Penson et al. (2003) and Leungwattanakij et al. (2003). Furthermore, in Dubbelman et al. (2008), surgical technique did not influence penile arterial blood flow after the operation as colour Doppler ultrasound did not show any significant reduction in mean peak systolic flow velocity and mean response index.

Based on our results, we found that early deterioration of penile haemodynamic (whatever the surgical technique) may be caused by early neuropaxia (Leungwattanakij et al., 2003), postoperative morbidity and/or psychosexual trauma. These haemodynamic changes were mainly in diastolic velocity on PDU (most probably suggestive of venogenic incompetence defect). On consecutive PDU, progressive improvement was noticed in NS cases which can be attributed to better and fast nerve recovery in NS cases rather than to a subsequent improvement in psychosexual trauma.
Thus, in post-radical cystectomy cases, the diagnosis of ED should be attributed to vascular defect (which indeed is venogenic in nature rather than arteriogenic).

However, a venogenic ED is caused by cavernous insufficiency. Indeed, patients who underwent extensive intrapelvic surgery, the cavernous insufficiency in turn is caused by a neurogenic lesion (because of neuropraxia of the cavernous tissue innervation, whether partial or complete). However, there seems to be tremendous potential of neuronal recovery within 12 months.

Therefore, the treatment should be directed towards improvement in the venogenic competence mechanism by avoidance of prolonged neuropraxia (by NS technique and early resuming of sexual relationship) and improvement in corporeal oxygenation to avoid corporeal fibrosis (by early rehabilitation programmes with PDE-5 Inhibitor).

Among our patients, T3a–b was the predominant radiological staging; heterogeneity of the surgical technique may hinder the outcome of EF. These may be considered the limitations of our study. Another study on homogenous surgical techniques over a larger number of cases is warranted to attain a more conclusive outcome.

Conclusion

According to our study, the main significant penile vascular haemodynamic changes were in EDV (venogenic mechanism) in post-cystectomy patients, whatever the surgical technique used. This may be the reason behind ED, which develops in these patients.

There was a gradual progressive improvement in venogenic competence mechanism in NS cases with insignificant deterioration in arteriogenic mechanism in both groups and this is manifested as regain of EF in NS cases.

Our recommendation is to improve the venogenic competence mechanism by avoidance of prolonged neuropraxia and improvement in corporeal oxygenation to avoid corporeal fibrosis and subsequently, permanent ED.

References


