Seminal vesicle-sparing perineal radical prostatectomy improves early functional results in patients with low-risk prostate cancer

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INTRODUCTION

Several techniques for radical prostatectomy (RP), including retropubic (RRP), perineal (RPP), laparoscopic or robot-based approaches compete as treatment options for localized prostate cancer. Retropubic approaches are the commonest and since Walsh et al. [1,2] described the nerve-sparing technique the functional results have improved considerably. However, the first RP used the perineal approach, reported by Young in 1905 [3]. The most important difference between RRP and RPP is the possibility for a simultaneous staging lymphadenectomy without extending the procedure. However, the development of preoperative nomograms led to the identification of risk groups in whom the oncological value of a lymphadenectomy is in question [4]. According to the current CaPSURE database, these low-risk patients (PSA level ≤10 ng/mL and Gleason sum ≤7) have a risk of metastasis to regional lymph nodes of <0.87% [5]. This is why the RPP has regained attention and currently is used as the standard approach for ‘low-risk’ patients in many centres [6–8]. Other reasons to prefer RPP are its applicability to extremely obese patients and better cost-effectiveness, as it is faster and uses inexpensive technical equipment.

By comparing the different techniques for oncological effectiveness, surrogate variables, e.g. the rate of positive surgical margins in patients with pT2 disease and PSA relapse, are important, although recently criticised [9]. Due to the long survival times after RP these surrogate variables are nevertheless the most practical means to compare the quality of surgery [10]. Using these data, RRP and RPP yield identical oncological results [7,11,12]. A high surgical volume is correlated with a low rate of positive surgical margins using RRP [13]. The most important secondary aims of the surgical approach is to preserve urinary continence and erectile function. Thus the early continence rate seems to be higher using RRP [6,7]; the data on potency rates after nerve-sparing RPP are sparse [8].

The aim of the present study was to conduct a three-arm, unrandomized, unblinded phase II prospective study, comparing a new and modified (‘seminal vesicle-sparing’, SV) technique of RPP (SV-RPP) with the standard RPP and a standard RRP for early (4 weeks) and late (12 months) continence rates.

METHODS

From July 2003 to July 2006, 507 consecutive unselected patients with a histologically confirmed adenocarcinoma of the prostate had RP. Apart from a few patients with ≥T3 disease (3.7%), all had clinically organ-confined disease and a life-expectancy of >10 years. The patients were divided into three groups: given a calculated risk of lymph node metastasis, according to Partin tables, of >3%, RRP, including bilateral pelvic (iliac and
obturator lymph node dissection) was recommended in 190 men. In these patients the nerve-sparing technique of Walsh [14] was used if possible; 317 patients (62.5%) were treated by RPP, and this (with no lymphadenectomy) was recommended if the PSA level was ≤10 ng/mL, the Gleason sum was ≤7 (3+4 and 4+3) and the prostate volume was ≤50 mL. Rare exceptions were patients with contraindications for RRP or those who wished to have RPP. Within this group of 317 patients we used a random distribution of SV-RPP or classical RPP.

The clinical stage was evaluated from PSA levels and biopsy data from the referring urologists. If data were missing patients had a standardized biopsy protocol with ≥10 cores (at least six of them lateral), all >1.5 cm long (1 mm diameter) with distinct localization within the different prostatic regions. The pathology was evaluated by an experienced uropathologist, providing detailed information on the percentage of tumour and Gleason sum per biopsy.

Of the 317 patients, 171 (53.9%) had a classical RPP, as reported by Gillitzer et al. [7], and 146 had SV-RPP. The technique used was as follows: (i) A reduced, only slightly curved perineal incision (5 cm) was made, without extending to the spine of the os ischii (Fig 1A); (ii) an anatomical preparation of the urethral bulb with careful separation from the pelvic floor by blunt division of the transverse perineal muscle; (iii) a blunt dissection between the two layers of Denonvilliers' fascia, to dissect the rectum off the prostate and expose the prostate using only two small blades of a self-retractor system ventrally and dorsally; (iv) leaving the SVs and parts of the ducts in situ (Fig. 1C); (v) preparation directly on the prostatic capsule, leaving the levator fascia intact, to separate and carefully dissect both nerve bundles infrasfacially exclusively using microclips, with no cauterization (Fig. 1D).

The nerve-sparing approach was only used if a tumour-free frozen-section analysis of the prostatic capsule was obtained at the location where the nerve bundles had been attached. All RPs were done by only three experienced surgeons, with a balanced frequency of procedures.

Patients having salvage RP after radiotherapy and those who had TURP before RP (21; 7.4% of SV-RPP, 2.5% of RPP and 5.2% of RRP) were excluded from the analysis. The baseline variables and patients' characteristics are shown in Table 1.

After surgery, patients were recommended for 'fast-track' mobilization on the day of surgery if they had RPP, and on the day after surgery for RRP. All patients were put on a normal diet from the day after RP, and drains were also removed then (RPP) or when there was <100 mL/day lymphatic drainage (RRP). The anastomosis was checked during RP and 10 days later on drain removal, if there were no leaks.

Patients were evaluated before and 3-monthly after RP for erectile function using the International Index of Erectile Function instrument (IIEF), voiding symptoms (IPSS), continence (number of pads), and for

<table>
<thead>
<tr>
<th>Variable</th>
<th>SV-RPP</th>
<th>RPP</th>
<th>RRP</th>
</tr>
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<tbody>
<tr>
<td>No. of patients</td>
<td>146</td>
<td>171</td>
<td>190</td>
</tr>
<tr>
<td>Clinical stage, %</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>≤cT1c</td>
<td>75.3</td>
<td>74.2</td>
<td>68.8</td>
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<tr>
<td>cT2</td>
<td>24.7</td>
<td>25.8</td>
<td>22.7</td>
</tr>
<tr>
<td>≥cT3</td>
<td>0</td>
<td>0</td>
<td>8.51</td>
</tr>
<tr>
<td>Gleason sum, %</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>&lt;7</td>
<td>83.6</td>
<td>82.3</td>
<td>62</td>
</tr>
<tr>
<td>7</td>
<td>14.4</td>
<td>16.5</td>
<td>25</td>
</tr>
<tr>
<td>&gt;7</td>
<td>2.1</td>
<td>1.2</td>
<td>13</td>
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<tr>
<td>Prostate volume, mL</td>
<td></td>
<td></td>
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<tr>
<td>mean</td>
<td>38.7</td>
<td>36.7</td>
<td>42.4</td>
</tr>
<tr>
<td>median (range)</td>
<td>35 (15–115)</td>
<td>35 (16–80)</td>
<td>35 (10–115)</td>
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<td>Age, years</td>
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<tr>
<td>mean</td>
<td>63.0</td>
<td>64.3</td>
<td>64.3</td>
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<tr>
<td>median (range)</td>
<td>63 (38–79)</td>
<td>65 (45–78)</td>
<td>65 (46–78)</td>
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<tr>
<td>Body mass index, kg/m²</td>
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<td></td>
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<tr>
<td>mean</td>
<td>27.1</td>
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<tr>
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<tr>
<td>range</td>
<td>21.6–33.7</td>
<td>20.7–41.3</td>
<td>19.1–36.3</td>
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</table>
data were assessed on-line using an Internet-based data bank of the Berlin Tumor Center (www.prostata-ca.net). Groups were compared using Student’s t-test after analysing for equal distribution using the F-test; differences were considered significant at $P < 0.05$.

RESULTS

The pathology after RP is shown in Fig. 2a–c; according to the selection criteria before RP, more patients with pT2 disease had RPP (70.5% SV-RPP, 69.6% RPP, 57.4% RRP). Of patients with stages pT3b (SV-RPP 5.5%) before and during RP, the SVs were resected after intraoperative frozen-section analysis to achieve a complete resection. The Gleason sum was upgraded to >7 in SV-RPP, RPP and RRP samples in 8.3%, 5.3% and 28.4%, respectively.

The surgical margins in pT2 patients treated by SV-RPP, RPP and RRP were positive in 1.9%, 6.7% and 9.2%, respectively; this was significantly different between SV-RPP and RRP ($P = 0.023$).

Nerve-sparing was possible in 90.4%, 62.0% and 57.4% of patients undergoing SV-RPP, RPP and RRP, respectively. The mean (range) operative duration was 90 (50–280), 141 (75–255) and 164 (70–294) min for SV-RPP, RPP and RRP, respectively; the differences between each procedure were significant ($P < 0.001$). As a measure of anastomotic leakage, the duration of transurethral catheter drainage over 13 days differed significantly among SV-RPP (6.6%), RPP (13.6%) and RRP (33.3%) ($P < 0.001$); the catheter was removed routinely at 10 days.

Surgical revisions due to bleeding were necessary in 10 patients (SV-RPP, two; RPP, six; RRP, two). The transfusion rate was 3.4%, 10.5% and 10.0% for SV-RPP, RPP and RRP; the difference between SV-RPP and RPP ($P = 0.016$), and SV-RPP and RRP ($P = 0.014$), was significant. One patient had a revision because of a severe wound infection; two patients needed an artificial sphincter as they had stress incontinence grade III after RP. Lymphoceles requiring surgical intervention occurred in 8.9% of patients after RRP. Four patients had major complications: one had to be temporarily diverted with a colostomy consequent to a rectourethral fistula after a revision for bleeding (SV-RPP); and another three had major pulmonary embolism after deep vein thromboses. Rectal lesions occurred during RP in eight patients (SV-RPP, two; RPP, four; RRP, two), none requiring additional procedures. Temporary voiding problems were reported in six patients, and one of them (RRP) needed a stricture revision.

There were no deaths during or after surgery; after a mean (range) follow-up of 12 (0–24) months there was no significant difference in stage-related PSA relapse rates. Overall, there was PSA recurrence in 14.3%, 17.5% and 13.5% of patients after SV-RPP, RPP and RRP, respectively. In patients with pT2 RO tumours after SV-RPP, RPP and RRP, the PSA relapse rates were 10.2%, 14.7% and 9.7%, respectively.

After 4 weeks, full continence (0–1 pad/24 h) was achieved in 61.7% of patients after SV-RPP, vs 45.0% after RPP ($P = 0.023$) and 43.8% after RRP ($P = 0.007$) (Fig. 3a); these rates improved to 96.3%, 85.7% and 85.6% after 12 months, respectively (Fig. 3b). The differences between SV-RPP and RPP ($P = 0.005$), and SV-RPP and RRP ($P = 0.008$) were significant.

Potency rates were available after 12 months from 306 patients with fully completed

comorbidity and quality of life (QLO C-30), using validated questionnaires. Follow-up data were either provided by the follow-up urologists or by telephone. It was decided not to use a formal pad test for continence, as patients were followed by telephone calls to their office urologists, and a complete analysis of all patients demanded an easily conducted assessment. Continence was defined as the use of no or one pad per day (24 h). A subdivision of no pad vs one pad was used but not reported, as this is mostly influenced by patients’ preferences. Potency was defined as erectile function with an IIEF score of >21; potency rates were analysed only if patients had a follow-up of >12 months.

PSA recurrence was defined as an increasing value after RP, from undetectable values to $>0.2$ ng/mL and rising (two consecutive values). Patients with adjuvant treatment with no increasing PSA levels were excluded from the analysis.

Data before and after RP were assessed by a study assistant and transferred into an online data bank (Table 1). Since January 2005 all

FIG. 2. The percentage for pT categories in; a, SV-RPP; b, RPP; and c, RRP.

FIG. 3. The percentage continence rates at a, 4 weeks and b, 12 months after surgery.
DISCUSSION

For younger patients with clinically relevant but organ-confined prostate cancer, RP is the treatment of choice. With RRP, simultaneous lymph node staging is possible, and thus RRP has become the most widely used technique worldwide. However, there is growing evidence that with preoperative risk stratification, a subgroup of ‘low-risk’ patients can be identified in whom the risk of lymph node metastasis is <1% [5]. Even large- and medium-volume centres that favour RRP have changed their practice and currently avoid lymphadenectomy in this group of patients [1,15]. If there is an indication for lymphadenectomy (‘high-risk’ patients), many surgeons favour the extended lymphadenectomy [16]. This can even be done using RRP [17] by considerably extending the surgical approach.

The current study should clarify whether SV-RPP improves early continence after 4 weeks; in this unrandomized, three-arm phase II trial, ‘low-risk’ patients were prospectively offered RRP, and ‘intermediate’ and ‘high-risk’ patients were recommended to have RRP with extended lymph node dissection. Within the group of RPPs about half the patients were randomly assigned to SV-RPP. Because this trial was not randomized it inevitably includes some selection bias for patients recommended to have SV-RPP or RPP. As patients with adverse factors were selected for RRP this might also have influenced early continence rates. However, the group sizes were comparable and allowed a valid statistical analysis of differences within the groups.

The published pT2 positive surgical margin rates for RRP differ from 0% for an extended RPP [18] to 8–21.5% [1,8], depending on technique and surgical volume. In the present series this rate was significantly lower for RRP (SV-RPP 1.9%, RPP 6.7%) than for RRP (9.2%). This difference in this stage-stratified group is probably due to selection bias, as patients in the RRP group with pT2 had adverse factors precluding them from RRP. In addition, some authors question the relevance of a positive surgical margin for PSA-free recurrence rates [9]. Overall, SV-RPP did not increase the positive surgical margin rate over more extensive resections.

In a reference series of RPP the PSA-free survival rate was 83.6% after 2 years [1]. Patients with pT2pN0 tumours had a 2-year PSA-free survival rate of 95.4% [1]. Long-term data for PSA-free survival with RPP were 88%, 81% and 69% after 5, 10 and 15 years, respectively, for the whole group of patients, serving as another reference [19]. In series of RPP the comparable 5-year PSA-free survival rates were 65–80% for specimen-confined tumours [8,20].

Analysing the whole group, the present series showed no significant short-term differences in PSA recurrence for SV-RPP, RPP and RRP, at 14.3%, 17.5% and 13.8%, respectively. The SV-RPP was no worse for PSA-free survival rates within the first year; hence, a longer follow-up is needed to confirm this observation.

Severe complications with either RRP or RRP are rare [12]; the rate of rectal lesions is higher for RPP, but the overall blood loss is lower [21]. This is also true in contemporary series of nerve-sparing RPP [6]. Compared with previous reports the present series showed a significant improvement in transfusion rates (3.4%) and reduction in anastomotic leaks (6.6%) using RPP. With generally quicker surgery, the minimal approach further speeds the surgery, to a mean of 90 min. Especially compared with endoscopic or robotic techniques, this is definitely a major advantage of SV-RPP.

Reported continence rates at 18 months after RP are 90–93%, with or without nerve-sparing [22,23]; RPP has identical continence rates of 87–94% [8,18]. The early continence rate after 1–3 months was reported to be higher using RPP than RRP [6,7]. In the present study we focused on the 4-week continence rates after SV-RPP, RPP and RRP; the rates of both RPPs were higher at 4 weeks and at 12 months than after RRP. This might be partly due to the more advanced stages in patients having RRP. For the primary endpoint of the trial, SV-RPP significantly outperformed the other techniques, with early continence rates of 62% after 4 weeks. Again, compared with RRP, this might be due to selection bias. However, the comparison within patients having RRP favours SV-RPP.

Reported potency rates differ considerably; for RRP the rates are 52–86% [23,24] and for RPP 52–80% [8,25]. In both techniques the potency rates are difficult to interpret because there are many variables for which these data have not been stratified (e.g. surgeon, rate of use of erectile aids). In the present series these problems are apparent; there were few patients with complete data and the follow-up was short. Therefore it is difficult to make firm conclusions about SV-RPP.

The limitations of the present study are the rather short follow-up for PSA recurrence and the few patients with sufficient follow-up to be analysed for potency. With these limitations, the SV-RPP represents a technical
improvement of RPP for early functional variables, especially the 4-week continence rates; a longer follow-up for PSA relapse rates is needed to confirm this factor.

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CONFLICT OF INTEREST

None declared.

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Abbreviations: (R)R(P)P, (retropubic) radical (perineal) prostatectomy; SV, seminal vesicle (-sparing); IIEF, International Index of Erectile Function.