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TOPIC PAPER

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Anatomic radical retropubic prostatectomy—long-term recurrence-free survival rates for localized prostate cancer

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Abstract Radical prostatectomy remains the mainstay for the treatment of localized prostate cancer. Long-term follow-up data showed excellent cancer control rates in several prostatectomy series. We report biochemical recurrence (BCR) outcomes after radical retropubic prostatectomy (RRP) in a European single center series of patients treated over a 13-year period. Between 1992 and 06/2005, 4,277 consecutive men underwent a RRP at the University Hospital Hamburg Eppendorf, Germany. Kaplan-Meier probabilities of BCR-free survival were determined for those patients with complete preoperative data, postoperative data, and follow-up information. Uni-and multivariate Cox regression models addressed PSA recurrence, defined as a PSA level ≥ 0.1 ng/ml. Overall, BCR-free survival ranged between 84, 70 and 61% for 2, 5, and 8 years, respectively. In univariate and multivariate analyses, except for age and type of nerve-sparing technique, all traditional clinical and pathological variables represented statistically independent predictors of PSA recurrence-free survival (all $P \leq 0.001$). In organ-confined disease, the 10-year recurrence free survival rate was 80 and 30% in non-organ-confined cancers. Our findings confirm excellent long-term biochemical cancer-control outcomes after RRP. High grade prostate cancer at final pathology and seminal vesicle invasion proved to be the strongest risk factors of BCR after surgery.

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Introduction

Early prostate cancer (PCa) detection efforts have been substantially improved by the introduction of prostate-specific antigen (PSA). Specifically, a concomitant shift toward earlier stage and more localized disease at radical prostatectomy known as 'stage migration' has been documented [1, 2]. Additionally, the radical retropubic prostatectomy (RRP) has been substantially refined in the past two decades translating in a highly reliable, oncological safe, and anatomical accurate procedure. Besides improved technique [3–5], improved functional [6–8] and decreased treatment-related morbidity [9], several North American long-term reports have shown excellent cancer control rates [10–15]. However, as indicated by Steuber et al. [16], European PCa men may demonstrate distinct clinical characteristics relative to their North American counterparts. Therefore, we hypothesized that European men may exhibit as well distinct intermediate to long term data after RRP which are currently lacking.

To address this void, we report a large number of patients treated over a period of 13 years with RRP for clinically localized PCa at a single European institution. We provide estimates of PSA recurrence free survival and univariate and multivariate analyses to identify risk factors of BCR.

Materials and methods

Patient population

Between 01/1992 and 06/2005, 4,277 patients underwent a RP at the University Hospital Hamburg-Eppendorf, Germany, by ten surgeons. Clinical and pathological data were on-site logged into a prospective database.

For purpose of analyses, exclusions were made for unavailable time to PSA recurrence information, PSA, biopsy Gleason sum, clinical stage, surgical margin status (SMS), extracapsular extension (ECE), seminal vesicle invasion (SVI), lymph node invasion (LNI), RP Gleason sum, pathologic T stage, age and type of nerve-sparing procedure, and those with neoadjuvant hormonal therapy, which left 2,708 valuable records.

Pathological and clinical evaluation

All prostatectomy specimens were surface inked and processed according to the Stanford protocol [17]. Pathological stage was defined according to the 1992/2002 AJCC staging classification. Histological tumor grading was performed according to the Gleason grading system [18]. A positive surgical margin was defined as cancer cells in contact with the inked specimen surface. The Abbott Axym PSA assay (Abbott Park, Il, USA) was used and pre-treatment PSA was measured prior to digital rectal examination and transrectal ultrasound guided biopsy (TRUSBx).

Operative technique

All patients were treated by a radical retropubic prostatectomy. The indication to perform uni- or bilateral nerve sparing surgery was made using a validated classification and regression tree (CART) analysis that calculates the likelihood of a pathologically organ confined cancer. A nerve sparing procedure on either side was performed if the PSA was less or equal 10 ng/ml and if no more than one core on that side contained any Gleason Grade 4 pattern, resulting in a likelihood of organ-confined PCa of 86% [19].

Diagnostic staging pelvic lymph node dissection (PLND) of the obturator fossa was performed in 1,589 men. PLND was universally performed in the initial years of the study. In the later years, the indication to perform a staging PLND was made using a validated CART analysis that calculates the likelihood of lymph node metastases. Low risk patients with a predicted likelihood of lymph node metastases of 2.2%, defined according to ≤ 3 biopsies with any Gleason grade 4/5 and no biopsy with predominant high grade cancer, did not undergo PLND [20, 21].

Follow-up

In all patients, PSA values were measured quarterly in the first year, followed by biannual measurements in the second, and annual measurements in the third year after RP. PSA recurrence was defined as a postoperative PSA of 0.1 ng/ml and rising after an initial undetectable PSA. The first PSA value above or equal to 0.1 ng/ml was used to define the time to PSA recurrence. Patients without evidence of PSA recurrence were censored at last follow-up. Patients with evidence of PSA recurrence were censored at the time of PSA recurrence.

Statistical methods

PSA recurrence-free probability after RP was calculated using the Kaplan-Meier method. Further, PSA recurrence-free probability was analyzed in pre- and post-operative univariate and multivariate Cox regression models [22, 23] to assess their prognostic significance. Clinical predictors included PSA, clinical stage, and biopsy Gleason sum. Pathological predictors consisted of PSA, RP Gleason sum, extracapsular extension (ECE), seminal vesicle invasion (SVI), lymph node invasion (LNI), and surgical margin status (SMS). Cox regression coefficients were then used to calculate the predictive accuracy of the two models in a nomogram setting. All statistical tests were performed using S-PLUS Professional, version 1 (MathSoft Inc., Seattle, Washington). Moreover, all tests were two-sided with a significance level at 0.05.

Results

The descriptive statistics of 2,708 men stratified according to the event of PSA recurrence are shown in Table 1. Median (62.5 vs. 62.3 years) and mean (63.2 vs. 62.8 years) age was not statistically different for men with ($n = 558$, 20.6%) or without ($n = 2{,}150$, 79.4%) evidence of BCR (range 43–79 vs. 39–76, $P = 0.36$) which was calculated for 8 years following RRP to include a substantial number of patients at risk. Mean (13.1 vs. 8.0 ng/ml) and median (10.5 vs. 6.5 ng/ml) pre-treatment PSA levels were highly statistically significantly different for those with evidence of BCR versus those without evidence of BCR ($P < 0.001$). In men with BCR versus those without BCR, clinical stages T1c, T2a, T2b, T2c, and T3 were recorded in 228 (40.9%) versus 1,467 (68.2%), 105 (18.8%) versus 387 (18.0%), 198 (35.5%) versus 282 (13.1%), and 27 (4.8%) versus 14 (0.7%) men, respectively ($P < 0.001$). Biopsy (Gleason sum 7–10: n = 345, 78% vs. $n = 564$, 26.2%; $P > 0.001$) and RP Gleason sums (Gleason sum 7–10: $n = 492$, 88.2% vs. $n = 1{,}009$, 47%; $P < 0.001$) were highly, statistically significant in men with evidence of PSA recurrence. According to the 1992/2002 AJCC classification, men with evidence of BCR had statistically, significantly higher stages. Of these, 14 (2.5%) had pT2a, 119 (21.3%) pT2b or pT2c, 184 (33.0%) pT3a, 203 (36.4%) pT3b, and 38 (6.8%) had pT4. Positive pelvic lymph nodes were statistically, significantly, more frequently recorded in 74 (13.3%) versus 25 (1.2%) men with BCR ($P < 0.001$) as well as positive surgical margins ($P > 0.001$). Bilateral nerve-sparing technique was performed more frequently in men without evidence of PSA recurrence ($P = 0.03$) and pre-operative clinical risk

Table 1 Descriptive characteristics of 2,708 patients treated with radical retropubic prostatectomy at the University of Hamburg between 1992 and 06/2005

Variables	Entire cohort ($n = 2{,}708$)	PSA recurrence		
		Yes ($n = 558$)	No ($n = 2150$)	P value
Year of Surgery				
Range	1992–06/2005			–
Age at Surgery				0.36
Mean (median)	62.2 (62.9)	62.5 (63.2)	62.3 (62.8)	
Range	39–79	43–79	39–76	
PSA (ng/ml)				< 0.001
Mean (median)	9.1 (7.0)	13.1 (10.5)	8.0 (6.5)	
Range	0.1–50.0	0.1–50.0	0.1–44.6	
Clinical stage (1992/2002)				< 0.001
T1c	1,695 (62.6%)	228 (40.9%)	1,467 (68.2%)	
T2a	492 (18.2%)	105 (18.8%)	387 (18.0%)	
T2b or T2c	480 (17.7%)	198 (35.5%)	282 (13.1%)	
T3	41 (1.5%)	27 (4.8%)	14 (0.7%)	
Biopsy Gleason sum				< 0.001
≤ 6	1,799 (66.4%)	213 (38.2%)	1,586 (73.8%)	
7	813 (30.0%)	284 (50.9%)	529 (24.6%)	
8–10	96 (3.5%)	61 (10.9%)	35 (1.6%)	
Pathological T stage (1992/2002)				< 0.001
T2a	279 (10.3%)	14 (2.5%)	265 (12.3%)	
T2b or T2c	1,462 (54.0%)	119 (21.3%)	1,343 (62.5%)	
T3a	587 (21.7%)	184 (33.0%)	403 (18.7%)	
T3b	338 (12.5%)	203 (36.4%)	135 (6.3%)	
T4	42 (1.6%)	38 (6.8%)	4 (0.2%)	
Positive nodal disease	99 (3.7%)	74 (13.3%)	25 (1.2%)	< 0.001
Positive surgical margins	582 (21.5%)	214 (38.4%)	368 (17.1%)	< 0.001
Pathologic Gleason sum				< 0.001
≤ 6	1,207 (44.6%)	66 (11.8%)	1,141 (53.1%)	
7	1,443 (53.3%)	448 (80.3%)	995 (46.3%)	
8–10	58 (2.1%)	44 (7.9%)	14 (0.7%)	
Type of nerve-sparing technique[a]				0.03
No	629 (23.2%)	149 (26.7%)	480 (22.3%)	
Unilateral	631 (23.3%)	137 (24.6%)	494 (23.0%)	
Bilateral	1,448 (53.5%)	272 (48.7%)	1,176 (54.7%)	
D'Amico risk groups				< 0.001
Low	1,257 (46.4%)	99 (17.7%)	1,158 (53.9%)	
Intermediate	1,093 (40.4%)	269 (48.2%)	824 (38.3%)	
High	358 (13.2%)	190 (34.1%)	168 (7.8%)	
Follow-up (months)				< 0.001
Mean (median)	31.4 (25.5)	21.5 (16.0)	34.0 (28.7)	
Range	0.1–129.7	0.3–106.7	0.1–129.7	

[a]Information missing in 57 cases

stratification as suggested by D'Amico et al. into low (PSA ≤ 10 ng/ml, clinical stage T1c or T2a and Gleason sum ≤ 6), intermediate (PSA 10.1–20 ng/ml or clinical stage T2b or Gleason sum = 7), and high (PSA > 20 ng/ml or clinical stage T2c or Gleason sum ≥8) reveals statistically, significantly higher patient distribution within intermediate to high risk groups in men with evidence of BCR ($P > 0.001$) as evidenced by PSA, clinical stage, and biopsy Gleason sum distribution.

Overall PSA recurrence

Kaplan-Meier analysis (Fig. 1a and Table 2) showed actuarial 5 and 8-year biochemical progression free probabilities of 70 and 61%. Of all, PSA recurrence after RP was noted in 558 (20.6%) men. Follow-up ranged from 0.1 to 129.7 months (mean 31.4, median 25.5). There were 418 (15.4%) men with at least 60 months' PSA recurrence free follow-up and 248 (9.2%) with at least 72 months' PSA recurrence free follow-up. PSA recurrence beyond the 84-months point is rare in our series. The mean PSA recurrence free survival time was 91.5 months. Median BCR free survival time was not reached and no recurrences were observed later than 108 months.

PSA recurrence as a function of clinical characteristics

Kaplan-Meier analyses of PSA recurrence free survival probabilities stratified according to nine main classifying variables are illustrated in Fig. 1b–j.

Figure 1b shows PSA recurrence free survival probabilities by PSA strata between 0.1–2.5, 2.6–4.0, 4.1–10.0, 10.1–20.0 and > 20 ng/ml. Actuarial 5 and 8 year recurrence free probabilities were 74 and 69% for PSA ≤ 2.5 ng/ml, 81 and 61% for PSA between 2.5–4.0 ng/ml, 79 and 70% for PSA between 4.1–10.0 ng/ml, 59 and 54% for PSA between 10.1–20.0 ng/ml, and 37 and 24% for PSA > 20 ng/ml. Except for the comparisons between 4.1–10.0 versus

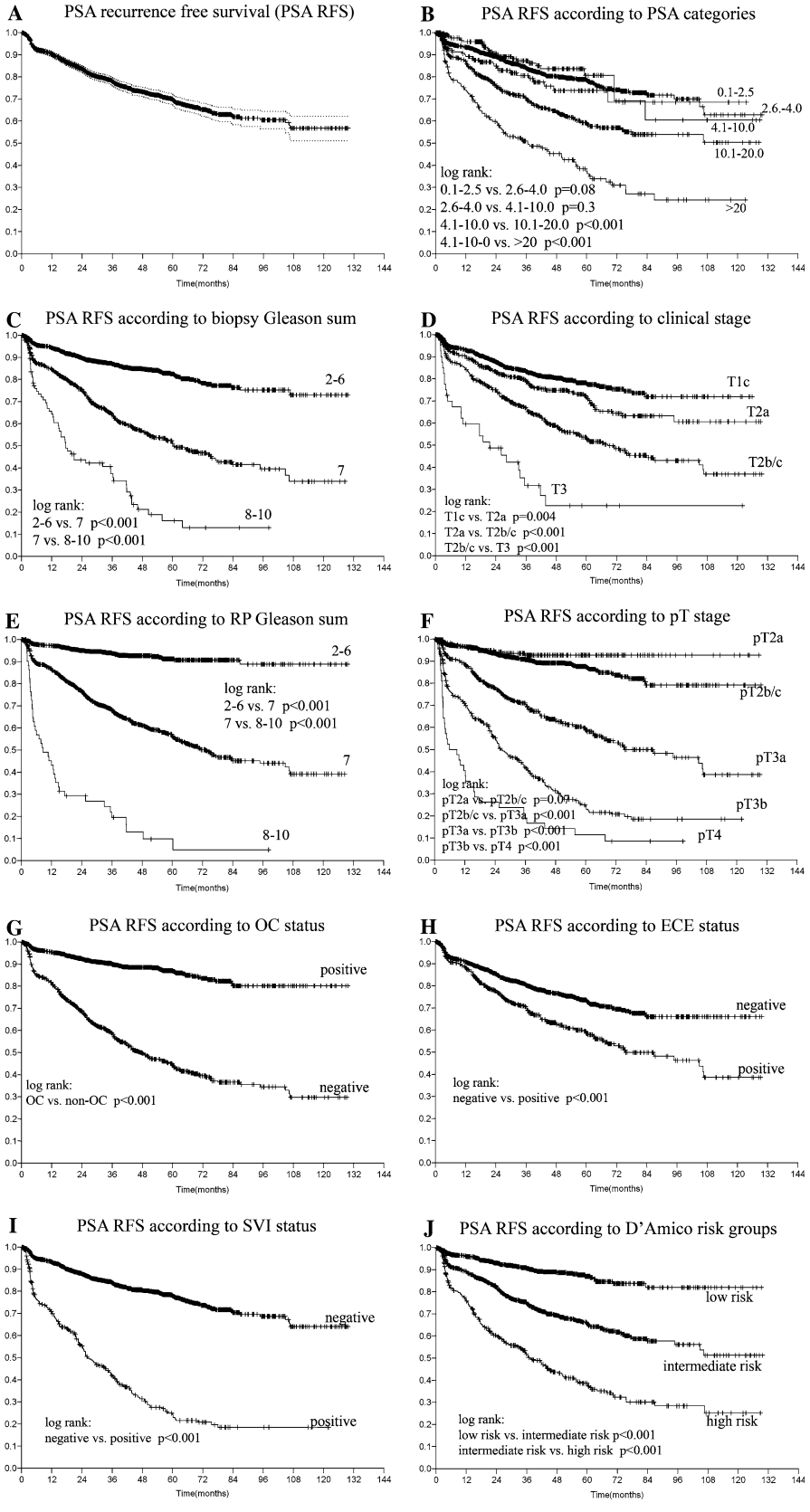

Fig. 1 Kaplan-Meier estimates of overall biochemical recurrence free survival and stratified according to nine main classifying variables that were included in univariate and multivariate analyses for 2,708 radical retropubic prostatectomy patients from the University of Hamburg-Eppendorf (1992–06/2005). Mean and median follow-up was 31.4 and 25.5 months (range 0.1–129.7). The *X-axis* shows the time since radical retropubic prostatectomy and the *y-axis* the PSA recurrence-free probability. The *solid line* represents the overall PSA recurrence-free survival and PSA recurrence-free survival stratified according to nine main classifying variables, the *dotted lines* represent the 95% confidence intervals. **a** Kaplan-Meier estimates of PSA recurrence-free survival. **b** Kaplan-Meier estimates of PSA recurrence-free survival according to PSA categories. **c** Kaplan-Meier estimates of PSA recurrence-free survival according to biopsy Gleason sum. **d** Kaplan-Meier estimates of PSA recurrence-free survival according to clinical stage. **e** Kaplan-Meier estimates of PSA recurrence-free survival according to RP Gleason sum. **f** Kaplan-Meier estimates of PSA recurrence-free survival according to pathologic T stage. **g** Kaplan-Meier estimates of PSA recurrence-free survival according to OC status. **h** Kaplan-Meier estimates of PSA recurrence-free survival according to ECE status. **i** Kaplan-Meier estimates of PSA recurrence-free survival according to SVI status. **j** Kaplan-Meier estimates of PSA recurrence-free survival according to D'Amico risk groups

≤ 2.5 ($P = 0.2$) and 2.6–4.0 ($P = 0.3$), the log rank test across the PSA strata was statistically significant (all $P \leq 0.004$)

Figure 1c and e shows progression free survival functions by Gleason pattern. Biopsy versus RP low (Gleason sum ≤ 6), intermediate (Gleason sum = 7),

Table 2 Actuarial 24, 60, and 96-months overall PSA recurrence-free survival probabilities and stratified according to biopsy and RP specimen characteristics

Outcome	24 Months probability (CI) [number of patients at risk]	60 Months probability (CI) [number of patients at risk]	96 Months probability (CI) [number of patients at risk]
PSA recurrence free survival	0.836 (0.819–0.851) [1,418]	0.696 (0.671–0.720) [418]	0.605 (0.565–0.643) [79]
RP Gleason			
≤ 6	0.950 (0.934–0.962) [680]	0.912 (0.886–0.933) [193]	0.888 (0.834–0.925) [39]
7	0.767 (0.741–0.790) [725]	0.563 (0.527–0.598) [223]	0.440 (0.388–0.492) [39]
8–10	0.293 (0.176–0.420) [13]	0.098 (0.028–0.219) [2]	0.049 (0.005–0.179) [1]
OC status			
Positive	0.924 (0.908–0.937) [955]	0.871 (0.847–0.892) [271]	0.802 (0.753–0.843) [49]
Negative	0.688 (0.654–0.719) [463]	0.442 (0.400–0.483) [147]	0.345 (0.292–0.398) [30]
SVI status			
Negative	0.880 (0.864–0.894) [1,279]	0.780 (0.755–0.802) [382]	0.687 (0.641–0.728) [72]
Positive	0.553 (0.493–0.609) [139]	0.243 (0.187–0.303) [36]	0.185 (0.130–0.248) [7]
D'Amico[ref] risk groups			
Low	0.930 (0.912–0.945) [655]	0.871 (0.840–0.896) [160]	0.820 (0.760–0.866) [31]
Intermediate	0.820 (0.793–0.844) [588]	0.656 (0.616–0.693) [201]	0.561 (0.500–0.618) [35]
High	0.604 (0.548–0.655) [175]	0.380 (0.319–0.440) [57]	0.284 (0.214–0.357) [13]

CI 95% confidence interval, *PSA* prostate specific antigen, *Bx* biopsy, *RP* radical prostatectomy, *OC* organ confinement, *SVI* seminal vesicle invasion

and high grade (Gleason sum 8–10) actuarial 5-year recurrence free probabilities were 83 versus 91, 51 versus 56, and 16 versus 10%. The log rank test comparing survival functions across biopsy and RRP Gleason patterns was highly, statistically significant (all $P < 0.001$).

Figure 1d shows BCR free survival functions for clinical stage. Actuarial 5-year recurrence free probabilities were 78, 72, 53, and 22% for cT1c, cT2a, cT2b/c, and cT3. The log rank test comparing survival functions across the clinical stage categories was highly, statistically significant (all $P < 0.004$).

Figure 1f shows progression free survival functions by pathologic T stages T2a versus T2b/c, T3a, T3b, and T4. For these stages, actuarial 5-year recurrence free probabilities were 93, 88, 59, 24, and 11%. Except for comparison between pT2a versus pT2b/c ($P = 0.06$), the log rank test comparing survival functions across pathologic T stages was highly, statistically significant (all $P < 0.001$).

Figure 1g and H shows PSA progression free survival functions according to Partin stages of OC, ECE, and SVI. Actuarial 5-year recurrence free probabilities were 43, 58, and 25% for non-OC disease, positive ECE, and SVI status. The log rank test comparing survival functions across Partin stages was highly, statistically significant (all $P < 0.001$).

Figure 1J shows a risk stratification suggested by D'Amico et al. [24] into low, intermediate, and high-risk groups. Actuarial 5-year recurrence free probabilities were 87, 66, and 38% for low, intermediate, and high-risk patients, respectively. The log rank test across all three strata was highly, statistically significant ($P < 0.001$).

Table 2 summarizes the actuarial PSA recurrence free survival estimates and PSA recurrence free survival stratified according to RP Gleason sum, OC, SVI, and D'Amico risk groups.

Table 3 shows pre- and post-operative univariate and multivariate Cox regression analyses predicting PSA recurrence. In univariate analyses, all pre- and postoperative predictor variables including the type of nerve-sparing technique were statistically significant (all $P = 0.005$), except for age ($P = 0.39$) and type of nerve-sparing technique ($P = 0.10$). In multivariate analyses, all pre- and postoperative predictor variables were independently associated with PSA recurrence ($P < 0.001$) after RP, except for the type of nerve-sparing technique ($P = 0.83$) and age ($P = 0.57$).

Discussion

During the last 20 years, the anatomic RP has become the surgical treatment of choice for localized PCa. By enforced serum PSA testing, men at risk are diagnosed at an earlier age and stage of disease. Consequently, more men are surgical candidates for definitive treatment. Moreover, new anatomic insight, refined surgical technique, improved tumor characterization, and patient selection translates into less treatment-associated morbidity [3–8]. Augustin et al. [9] reported earlier that 80.2% ($n = 996$) of our patients were not affected by any kind of complication and that the mortality rate was 0%. Despite excellent long-term outcome control after RRP, mainly North American data have been reported. [10–13, 15] As substantiated by Steuber et al. [16], European and North American RP patients may show significantly different tumor characteristics. Therefore, we hypothesized that long-term outcome assessment may vary in European men relative to their North American counterparts. In this analysis, the authors

Table 3 Univariate and multivariate Cox regression models addressing biochemical recurrence after radical retropubic prostatectomy

Clinical parameter	UVA Relative risk (*P* value)	MVA Relative risk (*P* value)
Pre-operative model		
Age (years)	1.01 (0.387)	1.00 (0.569)
PSA (ng/ml)	1.06 (< 0.001)	1.04 (< 0.001)
Clinical stage (1992/2002)	– (< 0.001)	– (< 0.001)
T1c versus T2a	1.40 (0.005)	1.15 (0.233)
T1c versus T2b/c	2.44 (< 0.001)	1.48 (< 0.001)
T1c versus T3	5.80 (< 0.001)	1.99 (0.002)
Biopsy Gleason	– (< 0.001)	– (< 0.001)
≤ 6 versus 7	3.18 (< 0.001)	2.64 (< 0.001)
≤ 6 versus 8–10	7.93 (< 0.001)	5.26 (< 0.001)
Post-operative model		
PSA (ng/ml)	1.06 (< 0.001)	1.03 (< 0.001)
Pathological Gleason sum	– (< 0.001)	– (< 0.001)
6 versus 7	6.23 (< 0.001)	3.55 (< 0.001)
6 versus 8–10	27.84 (< 0.001)	10.56 (< 0.001)
Surgical margin status: positive versus negative	2.80 (< 0.001)	1.67 (< 0.001)
Extracapsular extension	1.70 (< 0.001)	1.71 (< 0.001)
Seminal vesicle invasion	4.96 (< 0.001)	2.77 (< 0.001)
Lymph node invasion	6.53 (< 0.001)	2.03 (< 0.001)
Type of nerve-sparing technique	– (0.104)	– (0.830)
No versus unilateral	0.86 (0.193)	0.98 (0.872)
No versus bilateral	0.81 (0.034)	0.94 (0.564)

UVA univariate analyses, *MVA* multivariate analyses, *PSA* prostate specific antigen

report the 8-year follow-up results for a large European cohort of men who underwent radical retropubic prostatectomy for localized prostate cancer.

The overall PSA recurrence free probabilities in our series were 84, 70, and 61% at 2, 5, and 8 years after RRP. Further risk assessment of PSA recurrence according to clinical and pathological factors (Fig. 1) confirmed that high pre-treatment PSA levels, as well as high clinical stage biopsy or RP Gleason sum, positive SM, ECE, SVI, and LNI are associated with an increased risk of BCR after RRP [10–15, 22, 23]. Moreover, we confirm that neither the type of nerve sparing nor age at surgery did represent an independent risk factor of BCR [25]. Taken together, our intermediate-term results confirm that excellent cancer control can be achieved by radical retropubic prostatectomy in European men with a clinically localized prostate cancer.

Hull et al. [12] reported long-term cancer control on 1,000 patients. Their 5-year biochemical progression free estimate was 78%. However, compared to our series, Hull et al. did not include cT3 patients in their analyses, their median PSA was slightly lower but most importantly their rate of positive surgical margins was lower due to the inclusion of a higher percentage of patients at an early disease stage. These variables represented were shown to represent independent risk factors of biochemical recurrence after RRP, which we were able to confirm in our findings. Moreover, Hull et al. used a different PSA cutoff of 0.4 ng/ml to define BCR. Consequently, these may be plausible explanation for the reported differences compared to our findings. Another group recently updated their series on 3,478 men treated with RRP [13]. They reported a 5-year BCR free survival of 80%. Similarly to our findings using a PSA cutoff of 0.2 ng/ml, they report the aforementioned clinical and pathological variables to be risk factors of PSA recurrence. Besides similar PSA and clinical stage distribution, their reported high-grade prostatectomy Gleason sums (7–10) was 37 versus 55.4% in the present series. Conversely, further comparisons with other North American groups [11, 13, 22] showed similar 5-year actuarial PSA recurrence free survival results (69–73%). D'Amico et al. [24] have used risk stratification consisting of low, intermediate, and high-risk patients according to pre-treatment PSA, biopsy Gleason, and clinical stage to analyze results of radical prostatectomy, external beam therapy, and brachytherapy with and without neoadjuvant hormonal treatment. Our 5-year BCR free survival was 87, 66, and 38% for low, intermediate, and high-risk patients, respectively. These findings are comparable to the RP results of D'Amico. Moreover, we are able to confirm that high PSA, biopsy Gleason sum, and/or clinical stage are risk factors of PSA recurrence after RRP, which was substantiated in our multivariate analysis. Finally, in our uni- and multivariate analyses, we demonstrate that the type of nerve-sparing technique is not a risk factor of BCR after RRP. Our findings are corroborated by Palisaar et al. [25], who reported earlier that a nerve-sparing technique was not associated with BCR ($P = 0.798$) in multivariate analyses.

However, PSA recurrence after RP does not represent the most important outcome after surgery. Very long-term data spanning more than two decades are available now. Five different North American studies [10–13, 15] have been reported that include the following endpoints: prostate cancer-specific, overall survival, PSA progression free, local and distant progression free survival. For the most mature series from Seattle, WA [15] which spans for about 25 years show that prostate cancer-specific, overall survival, PSA progression free, local and distant progression free survival ranged from

99.0 to 81.5, 93.5 to 19.3, 84.8 to 54.5, 95.3 to 87.8, and 95.2 to 78.2% at 5 and 25 years. Further, Porter et al. identified a high grade Gleason pattern and the delivery of hormonal therapy as independent risk factors for prostate-cancer specific survival. Moreover, they demonstrate that very long-term PSA recurrence outcomes after RP might be suboptimal, as nearly 50% of men are at risk of developing PSA recurrence at 25 years after surgery. However, their data demonstrate excellent local and distant control as well as excellent cancer specific mortality-free outcomes. On average, 80% of RP patients will remain free of these adverse events 25 years after surgery.

This study demonstrates that cancer control data depend for example on clinical and pathological patient characteristics, era of surgery (pre- or post PSA era) but most importantly rely on sufficient length of follow-up. Dependent on follow-up time, risk factors of disease recurrence may change. For example, a +SM seemed to play a crucial role in previous long-term series. However, Porter et al. showed that in multivariate analyses, SM status was no longer an independent risk factor of prostate-cancer specific survival. However, more very long-term series are needed to prove their findings. Therefore, data maturity and extent of follow-up are most important factors for reliable long-term results.

Several weaknesses are associated with our study. Despite prospective data collection, this study was not randomized. We report a single center experience of radical retropubic prostatectomy for clinically localized prostate cancer. Additionally, our mean follow-up was limited to 31.4 months. This is mainly due to the fact that in recent years the number of RPs substantially increased with 788 RPs in 2005 compared to 69 RPs in 1992. This leads to the inclusion of a large number of patients with a short-term follow-up period and a consecutive statistical decrease of follow-up time. Therefore, our observations are limited to a single outcome, PSA recurrence, and biochemical progression free survival can be predicted up to 8 years. In order to compare our results with long-term North American series, the data need to mature. Finally, further evaluation is needed to confirm our intermediate-term cancer control results. However, we are unaware of any other European center that has presented its long-term BCR data. The data represent PSA recurrence outcome after RRP from a single institution over 13 years involving ten surgeons, who performed 4,277 consecutive surgeries. Thus, patient selection may have differed and may have possibly introduced a variation in cancer control rates [17]. Moreover, reported actuarial biochemical outcome percentages after prostatectomy have been shown to be dependent on the chosen PSA threshold [26]. Detectable but low PSA levels after RP that fail to increase may more likely represent residual benign glands, or may be due to different PSA assays used. Therefore, lower PSA cut offs translate into a shift of the Kaplan-Meier curve to the left, higher PSA cut offs shift the Kaplan-Meier curve to the right. Consequently, reported actuarial percentages for BCR after RP may seem more favorable using a high cut off than series that use a low PSA cutoff. Our series used a cutoff of 0.1 ng/ml. Conversely, Amling et al. [26] suggested after testing four different PSA cut offs, a PSA level of 0.4 ng/ml to be best suited for BCR definition after RP. Therefore, our findings most likely overestimate the actual rate of BCR. These factors should be taken into account when evaluating our intermediate-term cancer specific survival rates.

Conclusions

Our results in a consecutive series of 2,708 patients confirm the excellent intermediate to long-term cancer control of anatomic radical retropubic prostatectomy. Besides low treatment-associated morbidity, a nerve-sparing technique does not adversely affect PSA recurrence free survival. Finally, we confirm that traditional clinical and pathological variables represent risk factors of PSA recurrence.

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