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Protocol-based image-guided salvage brachytherapy

Early results in patients with local failure of prostate cancer after radiation therapy

External beam irradiation for prostate cancer has become a well-established treatment for all stages of this tumor. Despite the excellent results of external beam radiation therapy (EBRT), some patients have local relapse. The prostate-specific antigen (PSA) relapse-free survival rates for low-, intermediate-, and high-risk stages are about 88–89%, 78–86%, and 63–67%, respectively [17, 28]. Patients with recurrent prostate cancer after EBRT in most cases receive androgen deprivation therapy as sole treatment with a palliative intention [2]. For example, Agarwal et al. [2] reported that only 4 of 420 patients (0.9%) with treatment failure after primary EBRT underwent salvage prostatectomy and only 2.1% of patients received salvage radiation therapy (1.9% EBRT and 0.2% brachytherapy). Consequently, 93.5% of the patients were treated with androgen deprivation as salvage therapy [2]. Unfortunately, the disease often becomes refractory to this form of treatment. Furthermore, androgen deprivation is not tolerated well by most patients and it has many side effects, e.g., insulin resistance and diabetes, bone loss, fatigue, sexual dysfunction (erectile impotence, loss of libido), symptomatic gynecomastia, hot flushes, anemia, and cardiovascular events [13]. Other palliative treatment possibilities such as cryotherapy or high-intensity focused ultrasonography (HIFU) are useful only for carefully selected patients. In addition, HIFU is currently not recommended as an alternative to accepted curative treatment approaches for localized prostate cancer [20]. Moreover, if local recurrence is detected after radiotherapy, the incidence of distant metastases increases. In an analysis by Fuks et al., the 15-year actuarial distant metastases-free survival in 351 patients with local control was 77% compared to 24% in 328 patients who developed local relapses ($p<0.00001$). Another analysis showed that 68% of patients with local recurrence developed distant metastases compared with 37% of those with no local disease ($p=0.025$) [9, 16]. These data suggest the importance of an aggressive and effective local therapy for local recurrence without distant metastases after EBRT for selected patients.

Favorable factors for salvage brachytherapy are histologically confirmed local recurrence, no clinical or radiologic evidence of distant disease, adequate urinary function, age, overall health indicative of >5- to 10-year life expectancy, prolonged disease-free interval (>2 years) from primary radiation therapy, long prostate-specific antigen (PSA) doubling time (>12 months), Gleason score <6, clinical T1c or T2a tumor status, pretreatment PSA velocity <2.0 ng/ml per year at the time of initial presentation, interval to PSA failure >3 years, and PSA <10 ng/ml at the time of recurrence [5, 21].

In our analysis we could not address all of these factors. It should also be briefly mentioned that we had not treated the patients as part of a prospective or randomized study, but based on an internally defined protocol as mentioned below (see inclusion and exclusion criteria).

However, we believe that aggressive treatment of locally recurrent prostate cancer is necessary for selected patients. In 2005, a prospective protocol was initiated at the University Hospital Erlangen in order to analyze whether salvage pulsed-dose-rate (PDR) brachytherapy as aggressive local therapy for locally recurrent prostate cancer after radiotherapy failure is a well-tolerable and effective salvage therapy. For the present report, data from the first 18 patients who were treated according to this protocol were analyzed, using treatment-related late toxicities as the primary endpoint and PSA-recurrence-free survival as the secondary endpoint.

Patients and methods

Inclusion and exclusion criteria

As selection criteria for the protocol-based image-guided salvage PDR brachytherapy, we defined PSA-confirmed and PET-CT-confirmed macroscopic local recurrence without progressive metastatic disease, prostate size <60 ccm, life ex-

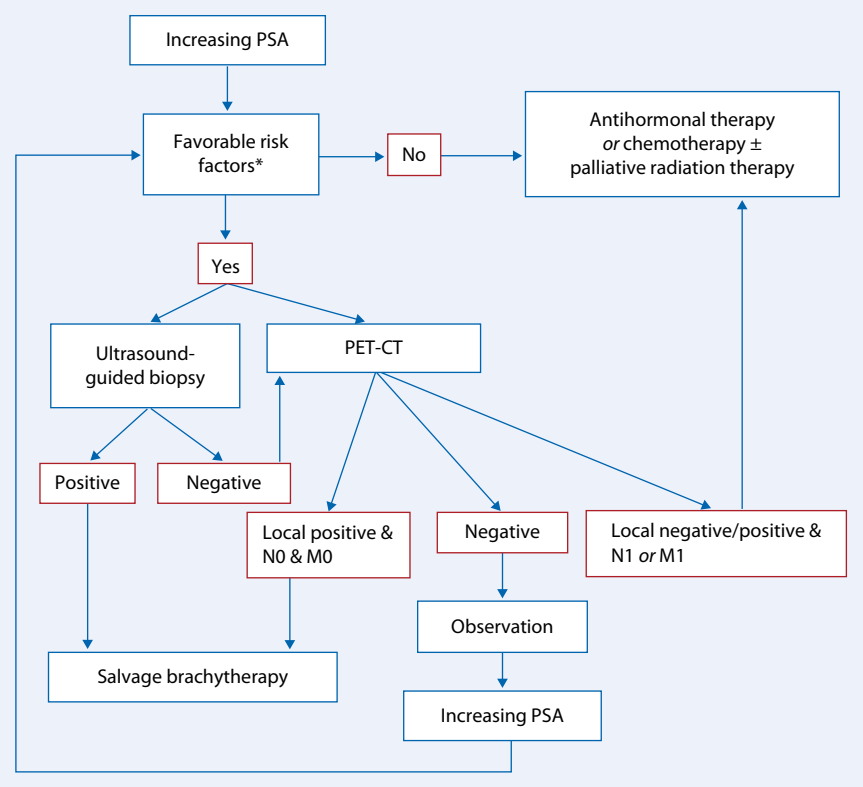

Fig. 1 ▲ Decision tree of a protocol-based salvage brachytherapy. *Favorable factors for salvage brachytherapy: life expectancy >5 years, disease-free interval ≥1–2 years, recurrence of PSA <10–20 ng/ml, PSA doubling time ≥6 months

pectancy more than 5 years, a Karnofsky score of 90–100%, and good compliance.

Patient characteristics

Between March 2005 and March 2011, 18 patients with local failure after EBRT or LDR brachytherapy underwent a protocol-based (**Fig. 1**) salvage interstitial PDR brachytherapy with Ir-192. Of the 18 patients,12 were treated with radiation therapy alone as first-line treatment. For 6 patients (6/18), radical prostatectomy was also performed as initial curative treatment option; for 5 of these patients EBRT was performed after radical prostatectomy for the first recurrence, and in 1 of these patients postoperative EBRT was accomplished owing to positive resection margins.

Regarding the initial radiation therapy techniques, most of our patients (16/18) were treated first with EBRT only, 1 patient (1/18) was treated with EBRT combined with permanent J-125 seed brachytherapy, and 1 patient (1/18) had permanent J-125 seed brachytherapy only as primary radiotherapy. The combination with androgen deprivation (primary treatment or salvage therapy) was diverse.

Both the initial and the salvage therapy characteristics of all patients are described in **Tab. 1**.

The local recurrences were detected mostly by increased PSA level and choline-PET-CT (11 patients). In 6 patients, a histological examination was also performed. In nearly all patients distant metastases were excluded, with two exceptions: One patient had para-aortal lymph nodes metastases, which were treated curatively with EBRT immediately before the salvage brachytherapy, and another patient had nonprogressive bone metastases, which were treated with androgen deprivation and local irradiation. In this patient the PSA level was under control at the last follow-up with androgen deprivation. The median prostate size was 12.4 ccm (range, 3.6–50.2 ccm).

Primary radiotherapy treatment characteristics

In patients treated previously with EBRT alone (16/18), the median dose was 69.3 Gy (range 49.9–73.8 Gy, fraction dose 1.8–2.0 Gy). In 12 of 17 patients, the EBRT treatment volume included the prostate and seminal vesicles only, in 5 of 17 patients the lymphatic nodes of the small pelvis were included in target volume, up to 50.4 Gy. In no patient was IMRT or IGRT used. In 2 of 18 patients, the previous radiation therapy also included brachytherapy. In 1 patient (1/18) EBRT (36 Gy) and permanent J-125 seed brachytherapy (150 Gy) were performed. In another patient (1/18), primary low-dose-rate brachytherapy using I-125 alone was performed (200 Gy). Detailed dose and volume parameters for the rectum and bladder were not available at the time of salvage brachytherapy. In all, 13 patients received their primary radiotherapy elsewhere (not at the University Hospital Erlangen). Of the remaining 5 patients, the exact dose volume parameters of the bladder and rectum ($D_{2\ ccm}$) were not assessed at the time of primary radiotherapy. We estimated the maximum dose (bladder, rectum) of the primary radiotherapy on the basis of the cumulative dose that was applied.

Salvage treatment characteristics

Brachytherapy

We have described our treatment technique in detail elsewhere [19]. Briefly: All patients were treated with temporary salvage PDR interstitial brachytherapy (PDR-BT) using Ir-192. Titanium afterloading needles were inserted under transrectal ultrasound guidance via a transperineal approach into the prostate. Based on the ultrasound imaging, the treatment planning was performed with the PLATO planning software (Nucletron B.V., The Netherlands). The following structures were delineated in all cases: the prostate or in cases after radical prostatectomy the macroscopic tumor mass as well as the rectal wall and the prostatic urethra.

We prescribed a total dose of 60 Gy divided into two sessions (2×30 Gy) with a time interval between the sessions of

Abstract · Zusammenfassung

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Protocol-based image-guided salvage brachytherapy. Early results in patients with local failure of prostate cancer after radiation therapy

Abstract

Purpose. To assess the overall clinical outcome of protocol-based image-guided salvage pulsed-dose-rate brachytherapy for locally recurrent prostate cancer after radiotherapy failure particularly regarding feasibility and side effects.

Patients and methods. Eighteen consecutive patients with locally recurrent prostate cancer (median age, 69 years) were treated during 2005–2011 with interstitial PDR brachytherapy (PDR-BT) as salvage brachytherapy after radiotherapy failure. The treatment schedule was PDR-BT two times with 30 Gy (pulse dose 0.6 Gy/h, 24 h per day) corresponding to a total dose of 60 Gy. Dose volume adaptation was performed with the aim of optimal coverage of the whole prostate (V_{100} >95%) simultaneously respecting the protocol-based dose volume constraints for the urethra ($D_{0.1\,cc}$ <130%) and the rectum ($D_{2\,cc}$ <50–60%) taking into account the previous radiation therapy. Local relapse after radiotherapy (external beam irradiation, brachytherapy with J-125 seeds or combination) was confirmed mostly via choline-PET and increased PSA levels. The primary endpoint was treatment-related late toxicities—particularly proctitis, anal incontinence, cystitis, urinary incontinence, urinary frequency/urgency, and urinary retention according to the Common Toxicity Criteria. The secondary endpoint was PSA-recurrence-free survival.

Results. We registered urinary toxicities only. Grade 2 and grade 3 toxicities were observed in up to 11.1% (2/18) and 16.7% (3/18) of patients, respectively. The most frequent late-event grade 3 toxicity was urinary retention in 17% (3/18) of patients. No late gastrointestinal side effects occurred. The biochemical PSA-recurrence-free survival probability at 3 years was 57.1%. The overall survival at 3 years was 88.9%; 22% (4/18) of patients developed metastases. The median follow-up time for all patients after salvage BT was 21 months (range, 8–77 months).

Conclusion. Salvage PDR-brachytherapy of the prostate following local failure after radiation therapy is a treatment option with a low rate of genitourinary side effects and no late gastrointestinal side effects. The treatment efficacy in the first 3 years is promising.

Keywords

Salvage brachytherapy · Side effects · Tumor response · Recurrent prostate cancer · Re-irradiation

Protokollbasierte bildgesteuerte Salvage-Brachytherapie. Frühe Ergebnisse von Prostatakrebspatienten mit lokalem Rückfall nach Strahlentherapie

Zusammenfassung

Ziel der Arbeit. Ziel der Arbeit ist die Beurteilung des klinischen Gesamtergebnisses der protokollbasierten bildgestützten Salvage-PDR-Brachytherapie bei lokal rezidiviertem Prostatakarzinom nach durchgeführter Radiotherapie mit Hauptaugenmerk auf die Durchführbarkeit und die Nebenwirkungen.

Patienten und Methoden. Insgesamt 18 Patienten (medianes Alter 69 Jahre) mit lokal rezidiviertem Prostatakarzinom nach bereits durchgeführter Strahlentherapie wurden im Zeitraum von 2005–2011 mittels interstitieller PDR-Brachytherapie (PDR-BT) in Form einer Salvage-Brachytherapie behandelt. Das Behandlungsschema bestand aus PDR-BT mit 2-mal 30 Gy (Einzelpulsdosis 0,6 Gy/h, 24 h pro Tag) bis zu einer Gesamtreferenzdosis von 60 Gy. Das Bestrahlungsvolumen wurde mit dem Ziel einer optimalen Volumenabdeckung der gesamten Prostata (V_{100} >95%) bei gleichzeitiger Einhaltung der Dosis-Volumen-Restriktionen für die Urethra ($D_{0,1\,cc}$ <130%) und für das Rektum ($D_{2\,cc}$ <50–60%) unter Beachtung der bereits vorangegangenen Strahlentherapie durchgeführt. Das Lokalrezidiv nach Strahlentherapie (perkutane Strahlentherapie, Brachytherapie mit Jod-125-Seeds oder Kombinationstherapie) wurde meist mittels Cholin-PET-CT und steigendem PSA-Wert gesichert. Der primäre Endpunkt war die behandlungsassoziierte Spättoxizität – im besonderen Proktitis, Stuhlinkontinenz, Zystitis, Harninkontinenz, Harndrang und Harnverhalt – gemäß der „Common Toxicity Criteria". Sekundärer Endpunkt war das PSA-rezidivfreie Überleben.

Ergebnisse. Wir verzeichneten nur Toxizitäten bezüglich des Harntrakts. Grad-2- und Grad-3-Toxizitäten wurden bei 11,1% (2/18) bzw. bei 16,7% (3/18) der Patienten beobachtet. Die häufigste Grad-3-Spättoxizität war Harnverhalt bei 3 der 18 Patienten (17%). Es traten keine gastrointestinalen Spättoxizitäten auf. Die Wahrscheinlichkeit für das biochemische PSA-rezidivfreie Überleben nach 3 Jahren betrug 57,1%. Das Gesamtüberleben nach 3 Jahren betrug 88,9%. Metastasen entwickelten 22% (4/18) der Patienten. Die mediane Nachbeobachtungszeit für alle Patienten nach Salvage-BT lag bei 21 Monaten (Spannweite 8–77 Monate).

Schlussfolgerung. Die Salvage-PDR-Brachytherapie des Prostatakarzinomrezidivs nach bereits durchgeführter Strahlentherapie ist eine Behandlungsoption mit einer niedrigen Rate an urogenitalen Nebenwirkungen und ohne gastrointestinalen Spätnebenwirkungen. Die Behandlungseffektivität für die ersten 3 Jahre ist vielversprechend.

Schlüsselwörter

Salvage-Brachytherapie · Nebenwirkungen · Tumoransprechen · Wiederkehrendes Prostatakarzinom · Re-Bestrahlung

about 4 weeks. The biological equivalence dose (EQD2) calculated for this PDR schedule and for a repair half-time of 1.9 h [8] and for α/β 1 or 3 corresponded to 79.1 and 71.5 Gy, respectively [19]. As quality parameters for dose distribution by CTV we defined that for all patients V100 >90% (optimal >95%) and D90 >100% should be achieved. For organs at risk (OAR), we considered in particular the values of $D_{0.1\,cc(urethra)}$ and $D_{2\,cc(rectum)}$. As constraints for OAR, we intended first that the dose which affects 0.1 ccm of the urethra [$D_{0.1\,cc(urethra)}$] should not be higher than 130% of the total dose, and second for the rectum that $D_{2\,cc(rectum)}$ should be lower than 50% of the total prescribed dose.

Tab. 1 Initial and salvage therapy characteristics of patients

Characteristic	At initial presentation	At salvage therapy
Age (years)	Median, 60.5 (range, 49–70)	69 (range, 58–81)
Time between primary radiation therapy and salvage brachytherapy (months)	Median, 64.5 (range, 27–271)	
PSA, ng/ml	Median, 8.25 (range, 3.73–1290)	4.46 (range, 0.54–46.3)
≤10	7/18 patients	17/18 patients
>10–20	3/18	0
>20	2/18	1/18
Unknown	6	0
Gleason score	Median, 8 (range, 4–9)	Median, 8 (range, 8–9)
≤6	5 patients	1 patient
7	1	n.a.
8–10	6	5
Unknown	6	12
No histology	1	12
T stage		
≤ T2a	1/18 patients	0 patients
T2b	2	4
≥ T2c	14	8
Unknown	1	
Recurrent		6
Hormone use	12/18 patients	2/18 patients
Prostatectomy		
Yes	6/18 patients	
No	12/18	
Radiation technique		
EBRT alone	16/18 patients	0 patients
EBRT + J-125 seeds BT	1	0
J-125 seeds BT alone	1	0
PDR-BT	0	18

Tab. 2 Summary of the most important dose parameters for CTV and organs at risk

	V150 (%)	V100 (%)	D90 (%)	D90 (Gy)	D2rectum (%)	D2rectum (Gy)	D0.1urethra (%)	D0.1urethra (Gy)
Median	38.52	93.90	105.4	63.30	38.85	24.54	122	74.61
Range	21.2–65.28	80–98.5	79.5–118.4	31.0–72.32	16.88–61.1	10.07–36.11	75–133.6	50.31–78.1

Antihormonal therapy

At the time of salvage PDR brachytherapy, 2 of 18 patients received antihormonal therapy and 12 did not. In 1 patient the androgen deprivation therapy consisted of bicalutamide and in the other patient of buserelin. For 4 patients, we had no information on antihormonal therapy. No other treatment modalities were performed.

Endpoints

Patients were followed up for disease-related parameters and adverse side effects every 3 months in the first 2 years, and in 6-month intervals for the next 3 years. For toxicity scoring, we used the CTC scoring system NCI 1988 with modifications according to EORTC 1992 [25]. The toxicity was scored prospectively at 3-month intervals for the first 2 years and thereafter at 6-month intervals. In particular we documented the following side effects: proctitis, anal incontinence, cystitis, urinary incontinence, urinary frequency/urgency, and urinary retention. We dispensed with detection of erectile dysfunction, because in our experience it is very difficult to obtain truthful information from the patients about erectile dysfunction.

Overall survival (OS) and biochemical PSA-recurrence-free survival were defined as the period from the date of salvage brachytherapy until the date of death and as the period from the date of salvage brachytherapy until PSA increase >2 ng/ml over nadir (Phoenix definition), respectively. Progression-free survival (PFS) was defined as no progression of disease after salvage brachytherapy.

Statistical analysis

The data of patients who underwent complete salvage brachytherapy (see eligibility criteria) were analyzed. For the analysis, the SPSS program was used (PASW Statistics 18) applying the Kaplan–Meier method and log rank test. Kaplan–Meier parameters were calculated at 3 years.

Results

Dose parameters of salvage brachytherapy

The total doses prescribed on the prostate capsule and the D_{90} were 60 and 63.30 Gy (median), respectively. The median of V_{100} was 94±4.2%.

Detailed information on the dose parameters for CTV and OARs is presented in **Tab. 2**.

Side effects

We registered only urinary toxicities. Grade 2 and grade 3 toxicities were observed in up to 11.1% (2/18) and 16.7% (3/18) of patients, respectively. For details, see **Tab. 3**.

Most often we registered grade 3 urinary retention as a new event after salvage brachytherapy in approximately 17% (3/18) of patients. It is noteworthy that 2 other patients, who had suffered grade 3 urinary retention, had a suprapubic catheter before salvage brachytherapy. In these 2 patients, radical prostatectomy was performed as first-line therapy. One of the 3 patients, who suffered grade 3 urinary incontinence, was treated in the course of the primary radiotherapy with an estimated dose of 196 Gy (combination of EBRT + J-125).

Tab. 3 Side effects according to the Common Toxicity Criteria scale

	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	n.a.
Proctitis	16/18 88.89%	0/18 0%	0/18 0%	0/18 0%	0/18 0%	Ø	2/18 11.11%
Anal incontinence	16/18 88.89%	0/18 0%	0/18 0%	0/18 0%	0/18 0%	0/18 0%	2/18 11.11%
Cystitis	13/18 72.22%	1/18 5.56%	2/18 11.11%	0/18 0%	0/18 0%	0/18 0%	2/18 11.11%
Urinary incontinence	12/18 66.67%	1/18 5.56%	1/18 5.56%	2/18 11.11%	0/18 0%	Ø	2/18 11.11%
Urinary frequency/urgency	11/18 61.11%	1/18 5.56%	1/18 5.56%	1/18 5.56%	Ø	Ø	4/18 22.22%
Urinary retention	10/18 55.56%	1/18 5.56%	0/18 0%	3/18 16.67%	0/18 0%	0/18 0%	2/18 11.11%
Total (%)	**56–89%**	**0–6%**	**0–11%**	**0–17%**	**0%**	**0%**	**11–22%**

Tab. 4 Salvage series

Study, year	Salvage therapy	N	Median f/u (months)	Grade 3/4 toxicity	Urinary retention	Urinary incontinence	Rectal injury	Outcome
Stephenson et al., 2004 [26]	RP	100	60	13–33%	30%	43–32%	2–15%	42–66% pfp
Heidenreich et al., 2009 [14]	RP	55	23	15%	9%	18%	4%	0–35% recurrences
Amling et al., 1999 [4]	RP	108	120	n. a.	15–27%	50%	6%	43% pfs
Rogers et al., 1995 [24]	RP	40	39	n. a.	28%	58%	15%	33±24% PSA-npr
Grado et al., 1999 [12]	BT	49	64	16%	n. a.	6%	4%	34% bdfs
Allen et al., 2007 [3]	BT	12	45	0%	n. a.	23%	0	63% bdfs
Aaronson et al., 2009 [1]	BT	24	30	4%	4%	4%	13%	88% bdfs
Burri et al., 2010 [6]	BT	37	86	11%	5%	5%	5%	54% bdfs
Present series	BT	18	21	0–17%	17%	22%	0	57% PSA-rfsp

f/u follow-up, *pfp* progression-free probability, *PSA-rfsp* PSA-recurrence-free survival probability, *Pfs* progression-free survival, *PSA-npr* PSA nonprogression rate, *bdfs* biochemical disease-free survival, *sBT* salvage brachytherapy

Regarding gastrointestinal side effects, the salvage brachytherapy was tolerated very well. No grade 1–5 side effects occurred.

Survival and freedom from tumor progression

The median follow-up time after salvage brachytherapy was 21 months (range, 8–7 months). The local tumor control after salvage brachytherapy was 94.4%. Only in 1 case did we observe locoregional recurrence in the right seminal vesicle. This area was on the edge of the brachytherapy target volume.

During follow-up, 6 of 18 patients experienced biochemical PSA recurrence. The 3-year biochemical PSA-recurrence-free survival probability was 57% (**Fig. 2**). The 3-year overall survival was 89%. Two patients had died at the time of the last follow-up. No death was attributable to prostate cancer. One patient died of a heart attack and the other died of pancreatic cancer.

Six patients developed metastases; of them, 2 patients were known to have metastasis before salvage brachytherapy, as mentioned above. Thus, 4 of 18 (22%) patients developed metastases after brachytherapy. The median time for development of metastases after brachytherapy in these 4 patients was 11 months (range, 2–33 months).

Discussion

As generally known, for local recurrence of previously irradiated prostate cancer there are only two curative treatment options: salvage prostatectomy or salvage brachytherapy, with very similar efficacy but different toxicities (**Tab. 4**). Accordingly, the frequency and grade of side effects of salvage prostatectomy or salvage brachytherapy are of utmost importance both for the patient and for the physician in charge.

The most frequent toxicity of salvage prostatectomy is urinary incontinence—typically between 29 and 50% [22]. Most reports on salvage prostatectomy show urinary incontinence rates between 18 and 58% [4, 16, 26, 28] (see also **Tab. 4**), which are distinctly higher than in our analysis. The rates of urinary retention differ between 9 and 30%. These side effects are on average higher than in salvage brachytherapy series (**Tab. 4**). In our analysis, we saw grade 3 urinary incontinence in 2 patients (2/18; 11%), in 1 patient grade 3 urinary frequency/urgency (1/18; 5.5%), and 3 patients experienced grade 3 urinary retention as a new event (3/18; 17%). Recently, Gotto et al. [11] reported a higher probability of medical and surgical complications, including urinary tract infection (20.4% vs. 2.8%), bladder neck contracture (47.0% vs. 5.8%), urinary retention

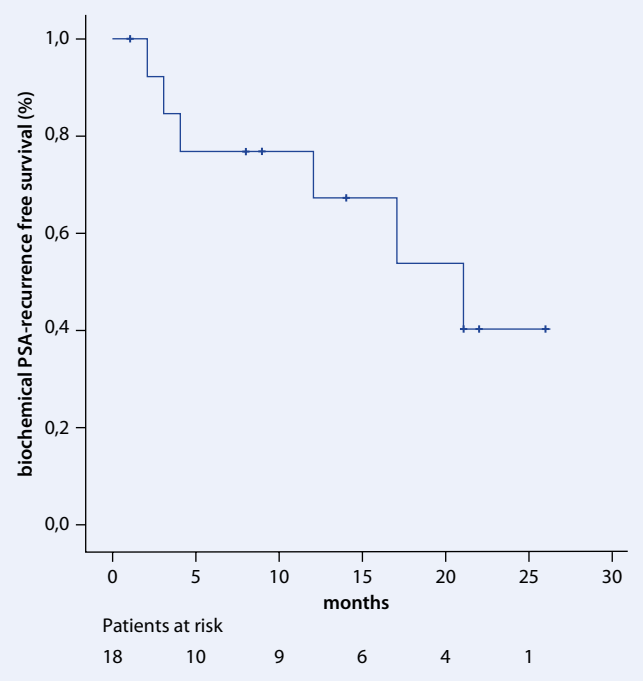

Fig. 2 ◀ Biochemical PSA-recurrence-free survival (%)

(25.3% vs. 3.5%), urinary fistula (4.1% vs. 0.06%), abscess (3.2% vs. 0.7%), and rectal injury (9.2% vs. 0.6%) after salvage radical prostatectomy in comparison to radical prostatectomy without prior radiotherapy. In the analysis of Gotto et al. [11], only 1 of 4 potent patients with salvage prostatectomy who underwent bilateral nerve sparing recovered adequate erection function for intercourse, and the 3-year actuarial recovery of continence was 30%.

Other parameters regarding side effects in these studies are perioperative complications and rectal injuries. Heidenreich et al. [14] presented the lowest rates of perioperative complications (9%) and rectal injuries (3.6%). Some prostatectomy series show rectal injury rates between 4 and 15% (**Tab. 4**). We are happy that we can report a very low incidence of late side effects. No gastrointestinal discomforts resulted from salvage brachytherapy. Moreover, the rectal injuries in our paper are lower than the best salvage prostatectomy series with a rate of 3.6% [14]. One reason for the low rectal injuries can be that there is a learning curve effect for the implantation of the brachytherapy implant, which caused a lower radiation dose at the rectal wall and therefore led to the low rate of rectal injuries [18]. If the physician has expert knowledge in brachytherapy for prostate cancer, we believe that he should also be an expert in salvage brachytherapy, because the technical implementation is in principle the same. In an analysis of 150 patients undergoing treatment, Le Fur et al. [18] reported a learning curve that led to a decrease in rectal dose. We can state that we have treated more than 400 patients with brachytherapy for prostate cancer in our department from 2000 to 2012, and the data from first 130 patients have already been published [19].

Regarding perioperative complications, different grades were reported by 9–27% patients treated with salvage prostatectomy [10, 14, 26, 27]. In contrast to these reports, in our analysis only 1 of 18 patients (5.6%) suffered from these complications. This patient had a known coronary artery disease and acute coronary syndromes occurred immediately after the insertion of the brachytherapy needles for the second brachytherapy session. It is self-explanatory that time-consuming surgery like salvage prostatectomy will be indicated in such cases with restraint.

Regarding the efficacy of salvage therapy, only a limited comparison of salvage prostatectomy and salvage brachytherapy is possible. A lengthy report from Heidenreich et al. [14] showed that 4.4% of patients developed bone metastases after salvage prostatectomy and up to 35% of patients developed recurrences. In comparison to the report of Heidenreich et al., in our analysis the biochemical PSA recurrence rate after 3 years was 43%. Altogether the PSA-recurrence-free survival probability of salvage brachytherapy is comparable to salvage prostatectomy (see **Tab. 4**). In our patients, only 4 of 18 (22%) developed metastases after brachytherapy—1 of them immediately at 2 months after salvage brachytherapy and a second patient at 8 months after salvage brachytherapy. In this second patient, the PSA level never decreased. We believe that these 2 patients had an occult metastatic disease at the time of salvage brachytherapy. Consequently, only 2 (11.1%) patients developed a new metastatic disease at the time of analysis and 88.9% of patients did not. In a recently published analysis by Chade et al. [7], the biochemical recurrence-free survival was 48% and the metastasis-free and cancer-specific survival rates after salvage radical prostatectomy were 77 and 83% after 10 years, respectively. Unfortunately, Quin et al. [23] commented that the complications of salvage prostatectomy are not documented by Chade et al. [7]. In the present analysis, none of our patients died because of prostate cancer. The limiting fact here is that the number of our patients in the current analysis is small and the follow-up period is relatively short. But we are optimistic that the rates of side effects decrease to a low constant level. At least from EBRT it is known that late complications after radiotherapy for prostate cancer approach a constant level after 5 years and they do not increase further [15].

Conclusion

PDR salvage brachytherapy for recurrent previously irradiated prostate cancer is associated with a very low rate of side effects and probably also with good intermediate-term efficacy. Compared with the results of salvage prostatectomy, salvage PDR brachytherapy seems to offer similar or lower genitourinary toxicities and apparently no late gastrointestinal side effects.

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Conflict of interest. On behalf of all authors, the corresponding author states that there are no conflicts of interest.

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