Hypofractionated Post-Prostatectomy Radiotherapy in 16 Fractions: A Single Institution Outcome

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Article

Hypofractionated post-prostatectomy radiotherapy in 16 fractions: a single institution outcome

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Abstract: Background: Optimal hypofractionated schedule of post-prostatectomy radiotherapy remains to be established. We evaluated treatment outcomes and toxicity of the moderately hypofractionated post-prostatectomy radiotherapy in 16 daily fractions delivered with IMRT/VMAT. The treatment schedule selection was motivated by limited technology resources. Methods: One hundred consecutive M0 patients with post-prostatectomy radiotherapy were evaluated. Radiotherapy indication was adjuvant (ART) in 19%, early salvage (eSRT) in 46% and salvage (SRT) in 35%. The dose prescription for prostate bed PTV was 52.8 Gy in 16 fractions of 3.3 Gy. The Common Terminology Criteria v.4 for Adverse Events scale was used for toxicity grading. Results: The median follow-up was 61 months. Five-year biochemical recurrence-free survival (bRFS) was 78.6%, distant metastases-free survival was 95.7% and overall survival was 98.8%. Treatment indication was the only significant factor for 5-year bRFS in multivariate analysis which was 84.6% *vs.* 67.6% for ART or eSRT *vs.* SRT respectively (HR 0.15, 95% CI 0.05–0.47, p=0.001). Acute GI toxicity grade 2 was recorded in 24%, grade 3 in 2% and acute GU toxicity grade 2 in 10% and no grade 3. Cumulative rate of late GI toxicity grade ≥2 was observed in 9% and late GU toxicity grade ≥2 in 16%. Conclusion: Observed results confirmed efficacy and acceptable toxicity of post-prostatectomy hypofractionated radiotherapy in 16 daily fractions.

Keywords: prostate cancer, moderate hypofractionation, post-prostatectomy radiotherapy

1. Introduction

Post-prostatectomy radiotherapy has been perceived as an intervention improving outcomes of surgery in adjuvant and as the second chance for cure in the salvage setting. Both expectations had been supported by randomized trials for ART [1-3] and by lower-level evidence for SRT [4,5]. Nevertheless, clinical practice has leaned towards SRT, mainly following three randomized trials comparing the both post-prostatectomy indications [6-8] followed by meta-analysis [9] which showed no difference if radiotherapy was reserved for patients with PSA recurrence, thus refraining

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significant proportion of them from extra toxicity. There are two caveats in radiotherapy timing selection. First, patients with multiple risk factors, especially involving International Society of Urological Pathology (ISUP) grade group 4 and 5, might be better addressed with ART [10] and second, optimal results of SRT are secured only when it is delivered early after the PSA rise meets definition for a biochemical failure [11].

Several aspects of radiotherapy delivery including dose escalation, prophylactic pelvic nodal irradiation (PNI) and hypofractionation have been extensively studied in primary prostate radiotherapy. Moderate hypofractionation (2.4 – 3.5 Gy per fraction) in primary setting has been established as the standard treatment option by several phase III studies including three non-inferiority trials [12-14]. Meta-analysis of randomized trials [15] confirmed identical overall survival and clinical and biochemical control as well as acute and late genitourinary (GU) and late gastrointestinal (GI) toxicity with higher acute GI toxicity in moderately hypofractionated primary radiotherapy compared to conventional fractionation. In post-prostatectomy setting, the magnitude of evidence supporting radiotherapy hypofractionation remains limited [16].

Assuming radiobiology basis supporting moderate hypofractionation of primary radiotherapy would be valid after radical surgery we decided to moderately hypofractionate post-prostatectomy radiotherapy in the environment with limited technology resources. This move was motivated by logistical advantage of shortened course of radiotherapy so that more patients could benefit from advanced technology allowing intensity modulated radiotherapy (IMRT) or volumetric modulated arc therapy (VMAT) at our department. We report clinical outcomes of a cohort of patients treated at our institution with post-prostatectomy moderately hypofractionated radiotherapy delivered in 16 fractions.

2. Methods and materials

We conducted a retrospective evaluation based on medical records of 100 consecutive patients treated with moderately hypofractionated post-prostatectomy radiotherapy in 16 fractions.

2.1. Patient workup

All patients had radical prostatectomy, either open or robotic, with or without lymphadenectomy, and were staged M0 with conventional imaging before surgery.

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Adjuvant radiotherapy was indicated for risk factors including pT3, positive surgical margin and/or ISUP grade group ≥4 and undetectable or detectable post-operative PSA. Irradiation was started after continence recovery, up to 6 months after surgery. Salvage radiotherapy was administered in detectable (≥0.1 ng/ml) and rising PSA on 2 consecutive occasions with no specific time limitation. Early salvage radiotherapy was defined as radiotherapy triggered at rising PSA ≤0.5 ng/ml. Biochemical failure after post-prostatectomy radiotherapy was established in case of two rising PSA ≥0.2 ng/ml.

2.2. Treatment

All evaluated patients had radiotherapy prescription to the prostate bed planning target volume (PTV_PB) with the moderately hypofractionated total dose of 52.8 Gy in 16 daily fractions of 3.3 Gy. The calculated equivalent dose of 2 Gy fractionation (EQD2) assuming α/β = 1.5 Gy and 1.9 Gy was 72.4 Gy and 70.4 Gy respectively for prostate cancer response and for α/β = 3 Gy it was 66.5 Gy for late toxicity. The selected treatment schedule allowed substantial reduction of patient workload and radiobiological dose escalation.

Pelvic nodal irradiation (PNI) was indicated in pN1 or high risk pNX situation and was delivered in 11 (11%) patients simultaneously with the total dose prescription (PTV_pelvis) of 40 Gy in 16 fractions of 2.5 Gy with the calculated EQD2 of 46 Gy with the α/β = 1.5 Gy estimate.

Planning target volumes were delineated in 3 mm CT axial slices as follows:

- PTV_PB: prostate bed clinical target volume (CTV_PB) delineation according to RTOG guidelines [17] with 8 mm margin reduced to 7 mm posteriorly,
- PTV_pelvis: pelvic nodal CTV_pelvis according to 2009 RTOG atlas [18] with 5 mm isotropic margin.

Planned dose distribution required at least 95% coverage of 95% of PTVs. Organs at risk (OAR) delineation included femoral heads, bladder, rectum, and bowel bag in case of PNI.

Patients were treated in relaxed supine position with knees bending and feet support with step-and-shoot IMRT or VMAT with daily cone beam CT or orthogonal portal imaging.

The use of androgen deprivation therapy (ADT) was left to the discretion of a treating physician or a urologist and followed the evidence development over time.

After treatment completion, follow-up visits were scheduled in 3-month interval in the first year and every 6 months afterwards. Each visit consisted of a history of symptoms and PSA examination.

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Common Terminology Criteria for Adverse Events v.4 (CTC AE v.4) scoring was used prospectively to assess early and late toxicity. Acute toxicity was evaluated during and up to 3 months after radiotherapy completion and late toxicity at least 3 months after radiotherapy.

2.3. Statistical analysis

The endpoints of analysis were biochemical recurrence-free survival (bRFS), distant metastasis free survival (DMFS) and overall survival (OS). All endpoints were calculated from the date of the first fraction of radiotherapy. To calculate and to compare the rates of bRFS, DMFS and OS the Kaplan – Meier method and the log-rank test were used. Univariate and multivariate analyses using the Cox proportional hazards regression model were performed for the total cohort of patients to determine the prognostic significance of pathological factors including extracapsular extension (ECE), seminal vesicle invasion (SVI), ISUP grade group, surgical margins status (R) and treatment factors including post-prostatectomy radiotherapy indication, PSA at post-prostatectomy radiotherapy (rPSA), PNI and ADT administration. Analyses were performed by the statistical program IBM SPSS Statistics version 25.

3. Results

3.1. Clinical characteristics and treatment

One hundred consecutive patients who commenced irradiation between September 2009 and March 2020 were included into analysis. Patients and treatment characteristics are summarized in *Table 1*.

***Table 1**. Patient and treatment characteristics*

Characteristics		**n = 100**
Age, years	Median	64
	Range	47 - 77
Initial PSA [ng/ml]	Median	9.8
	Range	1 - 91
pT, n (%)	pT2	48 (48)
	pT3a	31 (31)
	pT3b	19 (19)
	pTX	2 (2)
ECE, n (%)	No	53 (53)
	Yes	44 (44)
	NA	3 (3)
SVI, n (%)	No	78 (78)
	Yes	19 (19)

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	NA	3 (3)
ISUP Grade group (Gleason score), n (%)	1 (≤6)	27 (27)
	2 (3+4)	41 (41)
	3 (4+3)	15 (15)
	4 (8)	7 (7)
	5 (9-10)	9 (9)
	NA	1 (1)
Surgical margin, n (%)	R0	27 (27)
	R1	60 (60)
	NA	13 (13)
pN, n (%)	pN0	29 (29)
	pN1	8 (8)
	pNX	63 (63)
rPSA [ng/ml], n (%)	<0.2	25 (25)
	0.2 – 0.5	33 (33)
	0.5 – 2.0	29 (29)
	≥2.0	13 (13)
RT indication, n (%)	Adjuvant	19 (19)
	Early salvage	46 (46)
	Salvage	35 (35)

NA: not available

Median time between prostatectomy and post-operative radiotherapy initiation was 10 months (range 1.6 – 110 months). In 19 adjuvant radiotherapy indications postoperative PSA was <0.2 ng/ml, 0.2 – 0.5 ng/ml and >0.5 ng/ml in 12, 4 and 3 patients respectively. Urine continence recovery before radiotherapy was recorded in 43%, occasional incontinence with up to one pad per day in 48%, incontinence with multiple pads in 8% and the total loss of urine control in 1%.

Step-and-shoot IMRT was delivered in 32% and VMAT in 68%. The total dose was reduced in 5 (5%) (to 26.4 Gy in 1 patient and to 49.5 Gy in 4 patients) due to toxicity or patient`s preference. No ADT was used in 42%, short-term LHRH antagonist/agonist in 30%, 2-year bicalutamide 150 mg o. d. in 12% and long-term LHRH antagonist/agonist in 16%.

3.2. Treatment outcomes

With the median follow up of 61 months (range 25 to 156 months) the PSA recurrence was identified in 22 (22%) patients. Clinical recurrence was found in pelvic nodes in 4 (4%) (all in PB only irradiation) and distant bone metastases in 5 (5%) patients. All recurrences were treated with ADT and all patients with pelvic nodes recurrence had salvage re-irradiation. Five patients died of intercurrent diseases and none of prostate cancer.

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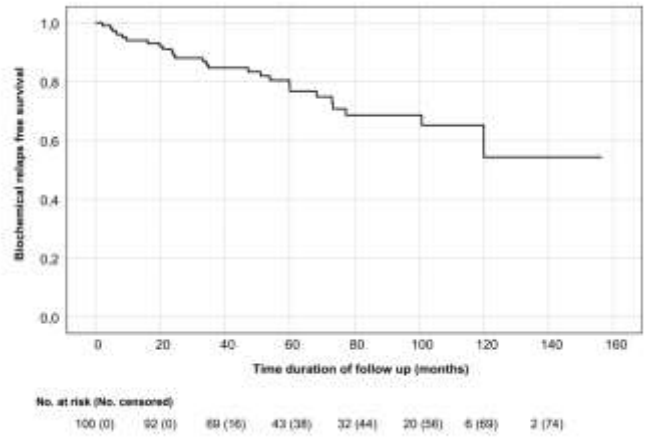
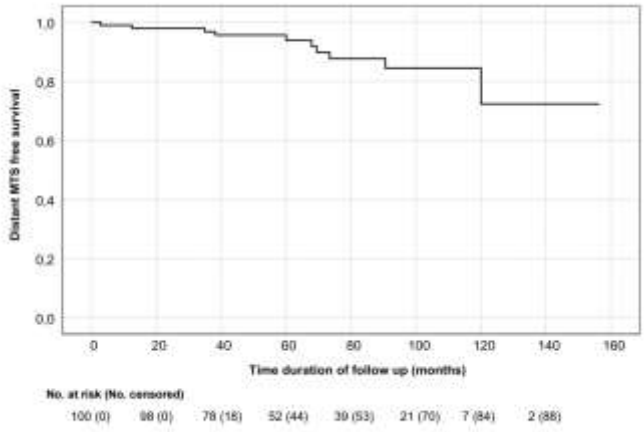
Five-year bRFS, DMFS and OS were 78.6%, 95.7% and 98.8% respectively (*Fig. 1*).

In univariate analysis the 5-year bRFS was not significantly different in extracapsular extension ($p = 0.39$), R status ($p = 0.41$), ADT administration ($p = 0.107$) and volume irradiated ($p = 0.39$). A trend was found for ISUP grade group ($p = 0.079$). Significant difference was found in seminal vesicle invasion ($p \leq 0.01$), rPSA ($p = 0.002$) and treatment indication ($p=0.001$) (*Table 2*).

Treatment indication was the only independent factor in multivariate analysis with HR 0.15 (95% CI 0.05 – 0.47; $p = 0.003$) and 5-year bRFS 84.6% and 67.6% for adjuvant or early salvage and salvage radiotherapy respectively *(Fig. 2)*.



(a)



(b)

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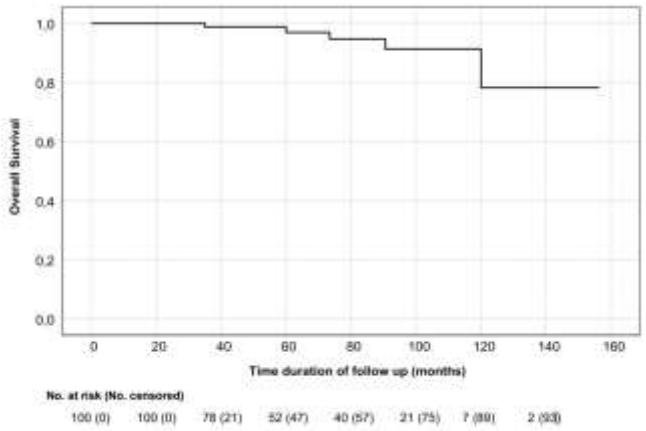

(c)

Fig. 1 (a) *Biochemical relapse-free survival (bRFS),* ***(b)*** *Distant metastases-free survival (DMFS) and* ***(c)*** *Overall survival (OS)*

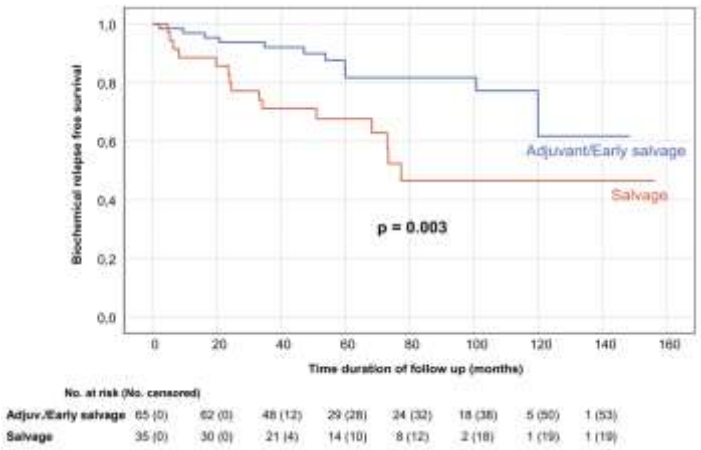

Fig.2 *Biochemical progression-free survival for adjuvant and early salvage radiotherapy (blue line) and for salvage radiotherapy (red line)*

Table 2*. Univariate analysis for biochemical recurrence-free survival (bRFS)*

Independent variable	**5-year bRFS (%)**	***p* value**
Extracapsular extension		0.69
Yes	80	
No	79.5	
Resection margin status		0.40
R1	80.5	
R0	72.8	
ADT administration		0.11
Yes	70.4	
No	85.7	
Volume irradiated		0.75
Prostate bed only	78	
Prostate bed and pelvic nodes	NA	
ISUP grade group		0.079

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1+2+3	82.5	
4+5	54.6	
Seminal vesicle invasion		≤ 0.01
Yes	56.8	
No	82.6	
Recurrent PSA [ng/ml]		0.002
<0.2	95.2	
0.2 – 0.5	79.3	
0.5 – 2.0	67.3	
≥2.0	68.4	
Treatment indication		0.001
Adjuvant or early salvage	84.6	
Salvage	67.6	

NA: not applicable

3.3. Toxicity

Acute GI toxicity grade 2 was recorded in 24% (rectal mucositis, rectal pain, rectal hemorrhage, and fecal incontinence), grade 3 in 2% (one small intestine obstruction after completion of adjuvant radiotherapy and one diarrhea) and acute GU toxicity grade 2 in 10% (urinary urgency, cystitis, urinary frequency, hematuria, urinary tract pain and urinary incontinence) and no grade 3.

Cumulative rate of late GI toxicity grade ≥2 was 9%. Six (6%) patients developed grade 2 (rectal hemorrhage requiring cauterization in 4 and rectal mucositis with medical treatment in 2), and 3 (3%) patients had grade 3 toxicity (fecal incontinence limiting daily activities in 2, and rectal hemorrhage with repeated cauterization and transfusion in 1) *(Fig. 3)*.

Cumulative rate of late GU toxicity grade ≥2 was 16%. In 8 (8%) patients grade 2 (in 5 urinary urgency requiring long-term medication and in 3 hematuria with cystoscopy) and in 8 (8%) patients grade 3 (urinary retention with repeated urethral dilatation and direct visual internal urethrotomy of a urethral stricture in 5, hematuria with transfusion and hospitalization in 2 and urinary incontinence progression with surgical intervention in 1) toxicity was observed *(Fig. 4)*.

Metachronous malignancies were found in 6% (non-muscle invasive bladder cancer in 2, colon cancer in 2, lung cancer in 1 and pancreatic cancer in 1).

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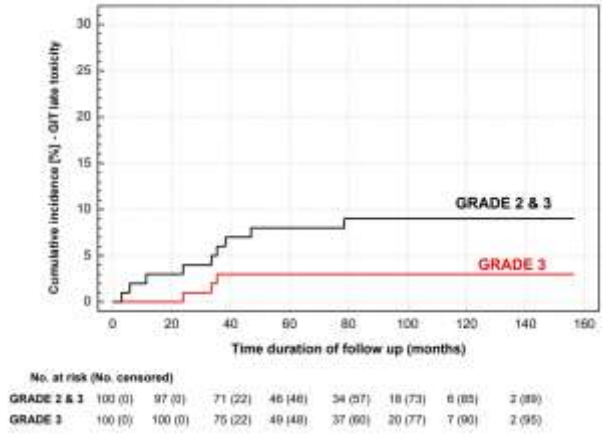

Fig. 3. *Cumulative incidence of grade 2 and 3 (black line) and grade 3 (red line) late GI toxicity*

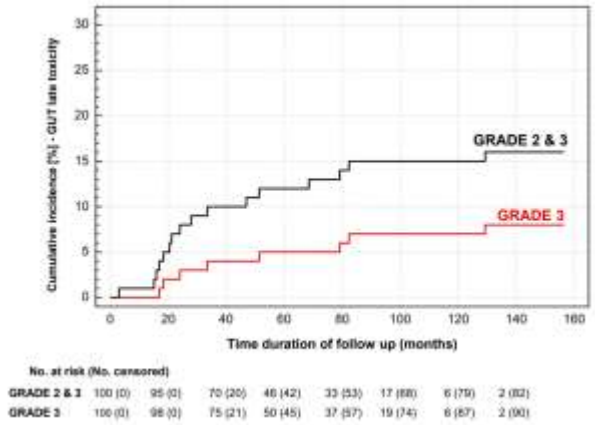

Fig. 4. *Cumulative incidence of grade 2 and 3 (black line) and grade 3 (red line) late GU toxicity*

4. Discussion

In contrary to primary prostate irradiation, the role of moderate hypofractionation of post-prostatectomy radiotherapy has yet to be established. Outcomes data is based on analyses of small cohort studies and systematic reviews [16]. Until final analyses of ongoing randomized studies are available, we may rely only on indirect comparison with conventionally fractionated radiotherapy.

Biochemical recurrence-free survival, a frequently used endpoint in post-prostatectomy radiotherapy studies, would be acceptable for relative efficacy comparison and is also well suited for subgroup analyses. More robust endpoints like DMFS, an accepted surrogate for overall survival [19] or overall survival would require long follow-up and large cohorts of patients to identify a reasonable number of events.

In our series of the mixed population of post-prostatectomy patients, the 5-year bRFS was 78.6% suggesting high effectiveness of the intervention. Indirect comparison with other series is limited by differences in patients' characteristics, mostly in Gleason score, timing of treatment, use of ADT or extent of target volumes. Nevertheless,

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observed biochemical control in our series fits in the range reported in other hypofractionated cohort studies (67 – 86.5%) [20-30].

Treatment was well tolerated in our series with grade 3 GI acute toxicity in 2 patients, one grade 3 diarrhea resulting in significant dose reduction and one surgery for small bowel obstruction shortly after the course of radiotherapy. This condition might have been also attributable to prostatectomy with lymphadenectomy. The last radiotherapy fraction was not administered in 4 patients for various reasons, though the total dose they had received (49.5 Gy in 15 fractions) might have been considered curative.

Our institutional policy of post-prostatectomy radiotherapy has been the preference of SRT in most cases except of the presence of several pathology risk factors, pN1 or persistent PSA. This approach is in accord with cautious recommendation for eSRT suggested by ARTISTIC meta-analysis [9] for patients with Gleason score 9 -10 and persistent PSA. Similarly, the large analysis (*N*=26,118) of ART versus eSRT found ART superior in terms of all-cause mortality among men with pN1 or Gleason score 8 to 10 and pT3/4 [31]. The only significant pathology risk factor for bRFS identified in our series was SVI, suggesting more aggressive approach including early post-prostatectomy radiotherapy timing, and the addition of ADT and PNI should be considered in this situation, especially when it is combined with other adverse pathology factor.

The radiotherapy indication (ART vs. eSRT vs. SRT) as well as rPSA were significant with rPSA <0.2 ng/ml predicting the best outcome with the 5-year bRFS of 95.2% in our cohort of patients. It was shown earlier in the meta-analysis of SRT studies that bRFS was a function of rPSA level with 2.6% decrease for every rPSA increment of 0.1 ng/ml [32]. The known risk of biochemical recurrence might be greatly increased (up to 10% for every 0.1 ng/ml) in case of presence of at least two pathologic risk factors [33]. Very early SRT initiated below 0.2 ng/ml is supported also by the large study analyzing bRFS according to rPSA level in 2,460 multi-institutional patients [34].

Systematic review of postoperative hypofractionated studies with mostly IMRT point at very low or zero occurrence of serious grade 3 GI or GU acute toxicity [16]. A major concern for hypofractionated postoperative radiotherapy is the large amount of bladder that intentionally receives radiotherapy to ensure adequate coverage of the prostate bed. This concern was studied in comparative analysis of acute GU toxicity of conventionally fractionated primary and post-prostatectomy radiotherapy. Patients randomized to the radiation-alone arms of two trials; RTOG 94-08 with primary prostate irradiation of 68.4 Gy and RTOG 96-01 with prostatic fossa treated to 64.8 Gy were compared. Grade ≥2 acute urinary toxicity was significantly higher in primary compared with postprostatectomy radiotherapy (30.8% *vs.* 14.0%; *P*<0.001) [35].

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Indirect comparison of acute toxicity might be confounded by retrospective nature of some data, interobserver variability and differences in grading scales. We identified two cohort studies with toxicity evaluation based on CTC AE v4.0. Genitourinary and GI grade 2 acute toxicity rates of 10.3% and 11%, respectively and no grade 3 symptoms were observed in the phase II trial evaluating 40 patients with prostate bed irradiation in the total dose of 54 Gy in 18 daily fractions [36]. Similar rate of grade 2 and 3 GU toxicity 12.8% and 0,8% respectively and grade 2 GI acute toxicity 8.8% and no grade 3 was also recorded in retrospective cohort of 125 patients with median dose to the prostate bed of 66 Gy and pelvic nodes of 52.5 Gy in 28 – 30 fractions [37]. In view of these data the rate of acute GU toxicity was comparable (10% grade 2) and rate of acute GI toxicity (24% grade 2 and 2% grade 3) could be considered somewhat increased in our series.

The rate of late GI toxicity, determined by rectal injury, could be anticipated at the similar level as in the case of primary radiotherapy with the similar dose constrains. Calculated $BED2Gy_3$ was 66 Gy in our study with grade ≥2 GI late toxicity 9%. Meta-analysis of 5 studies of 369 patients with moderate hypofractionation and calculated $BED2Gy_3$ below 70 Gy reported grade ≥2 GI late toxicity in 3% (95% CI: 1-5) [27]. In the SAKK 09/10 salvage radiotherapy dose-escalation trial, the late GI toxicity grade 2 and 3 was observed in 7.3% and 4.2% in the 64 Gy arm, and in 20% and 2.3% in the 70 Gy arm, respectively ($p = 0.009$) [38].

Late GU toxicity and mainly the symptoms related to urethral strictures is of major concern in post-prostatectomy irradiation. We observed grade ≥2 GU toxicity in 16% with urethral strictures which required repeated endoscopic interventions and therefore were assigned grade 3 in 5%. Symptomatic urethral strictures may develop also after radical prostatectomy without any radiotherapy and were identified in 9.5% in observational arm of SWOG 8794 study, with higher rate of 17.8% in the ART arm [1]. Treatment schedules employing $EQD2Gy_{1.5}$≥70 Gy were significantly associated with worse grade ≥2 GU toxicity which was grade 2 in 6% of 412 evaluated patients in the meta-regression analysis of 5 moderately hypofractionated studies [27]. Higher than anticipated rate of gross hematuria was identified in the cohort study of 54 men with early salvage PB IMRT with the total dose of 65 Gy in 26 fractions of 2.5 Gy. With the median follow-up of 48 months, grade 3 persistent gross hematuria was recorded in 28% [28]. On the other side, there was no difference in late grade 2 and 3 GU toxicity in the SAKK 09/10 study which was observed in 21% and 7.9% in the 64 Gy arm, and in 26% and 4% in the 70 Gy arm [38].

Treatment outcomes of post-prostatectomy radiotherapy might be improved by treatment intensification which includes addition of ADT, PNI and the dose escalation. We could not identify any difference for ADT and PNI due to uncontrolled indication, in most cases preferred in less favorable pathology. Recently, data regarding ADT duration in

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RADICALS HD study, the part of RADICALS protocol, randomizing 492 pN0 patients with ART or eSRT to no ADT, 6 months ADT and 24 months ADT were reported. There was no difference in DMFS for none versus 6 months, but there was a significant improvement in 10-years DMFS for the 24 months compared to 6 months (HR 0.77; CI: 0.61-0.97; 72% vs 78%). Despite improved time to salvage ADT with ADT prolongation, the absolute DMFS improvement of 6% might be viewed as little added value of long-term ADT as overall survival was not improved [39]. Similarly, NRG Oncology/RTOG 0534 SPPORT three-arm trial randomized 1,792 patients into three groups: PB irradiation alone (group 1), PB plus 6 months of ADT (group 2) and PB and PNI plus 6 months of ADT (group 3). At the median follow-up among survivors of 8.2 years, the 5-year freedom from biochemical progression rates were 70.9% in group 1, 81.3% in group 2, and 87.4% in group 3. Treatment with PB and PNI plus 6 months ADT was superior per protocol criteria, at the cost of higher acute grade ≥2 toxicity, though late toxicity except of bone marrow events did not differ.

We believe that in view of the potential toxicity of long-term ADT and good tolerance of PNI with IMRT/VMAT delivery the post-prostatectomy radiotherapy of PB and PNI with 6 months of ADT might be considered as the preferred approach in terms of optimal biochemical control in most pN0 and pNX patients [40].

The assessment of biochemical response to the PB dose based on metanalysis and systematic review of SRT studies suggested 2% gain in bRFS per incremental 1 Gy [32]. This assumption may not be correct if patients with low rPSA are treated as shown by SAKK 09/10 trial pointing at no difference in biochemical progression with the dose escalation to 70 Gy in men with early biochemical progression after radical prostatectomy (median PSA 0.3 ng/ml) [38].

Data from randomized studies supporting post-prostatectomy radiotherapy hypofractionation are still awaited. The RADICALS phase II trial evaluating adjuvant versus early salvage radiotherapy along with the inclusion and duration of ADT permitted a conventionally fractionated course of 66 Gy in 33 fractions or a moderately hypofractionated regimen of 52.5 Gy in 20 fractions [41]. The subgroup analysis of this trial may provide comparative information of hypofractionation versus conventional fractionation.

Patients reported outcomes were reported in the randomized phase III NRG oncology GU-003 trial of hypofractionated versus conventional post-prostatectomy radiotherapy which compared toxicity of PB radiotherapy in the total dose of 66.6 Gy in 37 fractions of 1.8 Gy (N=133) with 62.5 Gy in 25 fractions of 2.5 Gy (N=100). Hypofractionated radiotherapy was associated with greater patient-reported GI toxicity at the completion of radiotherapy but was non-inferior to conventionally fractionated radiotherapy at 2 years with no statistical differences in the Expanded Prostate Cancer Index Composite (EPIC) for both GI and GU toxicities at 2 years (p=0.12) [42].

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Optimal hypofractionated schedule in post-RP setting remains to be established. Based on current data, radiobiological $EQD2Gy_{1.5}$ close to 64 Gy rather than ≥70 Gy may be preferred to control anticipated microscopic disease in the PB especially in adjuvant and early salvage indication. Aiming at improved long-term PSA control, other strategies than dose escalation might be preferred addressing regional and distant spread with PNI and ADT. More assertive treatments like local PB boost for avid lesions or metastases directed treatment based on molecular imaging may potentially improve outcomes even further and are subject of current research.

Our study showed high 5-year bRFS at the cost of grade 3 GU toxicity in 8% which seems to be higher than in similar retrospectively evaluated studies and might be the result of high $EQD2Gy_{1.5}$ = 72.4 Gy of our treatment schedule. The radiobiological high total dose might have been relevant in our case as a significant proportion of our patients had PSA before radiotherapy >0.5 ng/ml. Nevertheless, statistical analysis confirmed significance of adjuvant or early salvage and low PSA level as predictors of higher bRFS. Retrospective nature of our study and indirect comparison with other studies with inherent methodological differences limit any firm conclusions. Outcome of our institutional cohort should be considered in the context of apparent logistical advantage of the treatment schedule providing irradiation in 16 fractions.

5. Conclusion

Observed results confirmed efficacy and acceptable toxicity of post-prostatectomy hypofractionated radiotherapy in the total dose of 52.8 Gy in 16 daily fractions. Adjuvant and early salvage radiotherapy indication was an independent predictor of favorable long-term biochemical control.

Author Contributions: Conceptualization and writing, Pavol Dubinsky; formal analysis, validation, and writing-review Vladimir Vojtek; investigation and data collection, Katarina Belanova and Natalia Janickova; formal analysis Noemi Balazova, data collection Zuzana Tomkova; All authors have read and agreed to the published version of the manuscript.

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Institutional Review Board Statement: The study was conducted in accordance with the Declaration of Helsinki and approved by Ethics Committee of East Slovakia Institute of Oncology (protocol code ZEK009-11-2022 on November 22, 2022).

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: The data presented in this study are openly available at Mendeley Data, V1, https://data.mendeley.com/datasets/trctb5gwbf/1

Conflicts of Interest: The authors declare no conflict of interest. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript; or in the decision to publish the results.

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