



Long Term Follow-up of Prostate Cancer Patients Who Fail Salvage Radiation Therapy and Radical Prostatectomy

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ABSTRACT

Introduction: Salvage radiation therapy (SRT) is an effective treatment for prostate cancer (PCa) that has recurred after radical prostatectomy. Long term follow up in men who developed biochemical recurrence (BCR) after SRT is less well described in literature. This study follows the natural history of patients treated with SRT > 13 years ago.

Materials/Methods: 61 patients with PCa treated with SRT during 1992-2000 at UT Southwestern were identified. Survival was calculated using the Kaplan-Meier method. Log-rank test and Cox regression were used to determine significance of clinical parameters with outcome.

Results: Median follow-up for the 61 patients was 126 months (3-238). Median age at SRT was 62 (46-83), 15% of patients had pathologic Gleason score (pGS) 8-10 disease, 14% had pre-surgical PSA > 20, 63% had pT3+ disease, 59% had positive margin at time of surgery. Of 61 patients, 34 (56%) had treatment failure after SRT. 5 y and 10 y freedom from PSA failure (FFPF) were 51% and 33% respectively. pGS significantly correlated with FFPF (p=.0042) and overall survival (OS) (p=.0022). Seminal vesicle invasion (p=.0357, HR 2.07, 1.0-4.2), lymphovascular invasion (p=.035, HR 5.28, 0.9-32.2), and pre-SRT PSA (p=.015, HR 2.27, 1.14-4.5) were associated with decreased FFPF. For the 34 patients who had BCR, median follow-up was 157.5 months (13-238). Median time to BCR following SRT was 30 months (3-138). 19 (56%) received androgen deprivation therapy (ADT). Median time from BCR to initiating ADT was 48 months (0-151). Outcome after BCR is as follows. OS at 5 and 10 y were 79% and 59% (median 13.6 y). PCa-specific survival (PCSS) at 5 and 10 y were 89% and 73%. Distant metastasis free survival at 5 and 10 y were 75%. Castration resistant free survival at 5 and 10 y were 81% and 70%. Time to BCR after SRT < 1 year (p=.0005, HR 3.92, 2.7-33.6) and < 2 years (p=.021, HR 2.52, 1.2-9.2) significantly correlated with decreased OS, compared to < 3 years (p=.054) and < 5 years (p=.073).

Conclusions: Clinical parameters predictive of treatment failure after SRT are presented. Unfortunately, 25% of patients who fail SRT developed distant metastases within 5 yrs of failure. 56% of those who failed eventually also required ADT. Such events could have significant emotional impact, affect quality of life, and lead to morbidity related to salvage therapy. However, while up to 27% of patients died from PCa after BCR at 10 years, only patients who failed SRT in less than 2 years had a significantly worse OS. Overall, patients who fail SRT treatment can have a prolonged median overall survival of 13.6 years.

INTRODUCTION

➤ In the United States, prostate cancer (PCa) is the most common cancer in men--with an estimated 238,590 new cases expected in 2013. [1]

➤ PCa is also the second leading cause of cancer death in men--with an estimated 29,720 men who will die of PCa in 2013. 1 in 6 men is expected to be diagnosed with PCa in his lifetime. [1]

➤ Radical prostatectomy (RP) is one of the major techniques for treating PCa, but in up to one third of the cases, disease recurs within 10 years. [2]

➤ After RP failure, timely administration of salvage radiation therapy (SRT) can be an effective treatment method for local control, prevention of distant metastasis, and increased cancer-free survival. [2] However, biochemical recurrence (BCR) after SRT can occur.

➤ Long term follow up in men who develop BCR post-SRT is less well described in literature.

MATERIALS/METHODS

➤ 61 patients with PCa treated with post-RP SRT during 1992-2000 at the University of Texas Southwestern Medical Center.

➤ PSA failure after RP, defined as: 1) persistently detectable PSA; 2) two consecutive PSA \geq 0.1 ng/mL; or 3) initiation of salvage treatment for disease recurrence.

➤ BCR after SRT was defined as: 1) two consecutive PSA \geq 0.2 ng/mL above nadir; 2) PSA \geq 2 ng/mL above nadir; 3) initiation of salvage systemic therapy; 4) clinical recurrence.

Statistics

➤ Freedom from PSA failure (FFPF), overall survival (OS), PCa-specific survival (PCSS), distant metastasis-free survival (DMFS), and castration resistant-free survival (CRFS) were estimated using the Kaplan-Meier method. The univariate log-rank test and Cox regression were used to determine the significance of clinicopathological parameters with survival endpoints.

➤ Prostate cancer-specific death was defined as death due to PCa, SRT toxicity, or unknown cause with distant metastasis or castration resistance.

➤ Castration resistance was defined as 2 consecutive rises in PSA while on hormone therapy with testosterone level \leq 50 ng/dL.

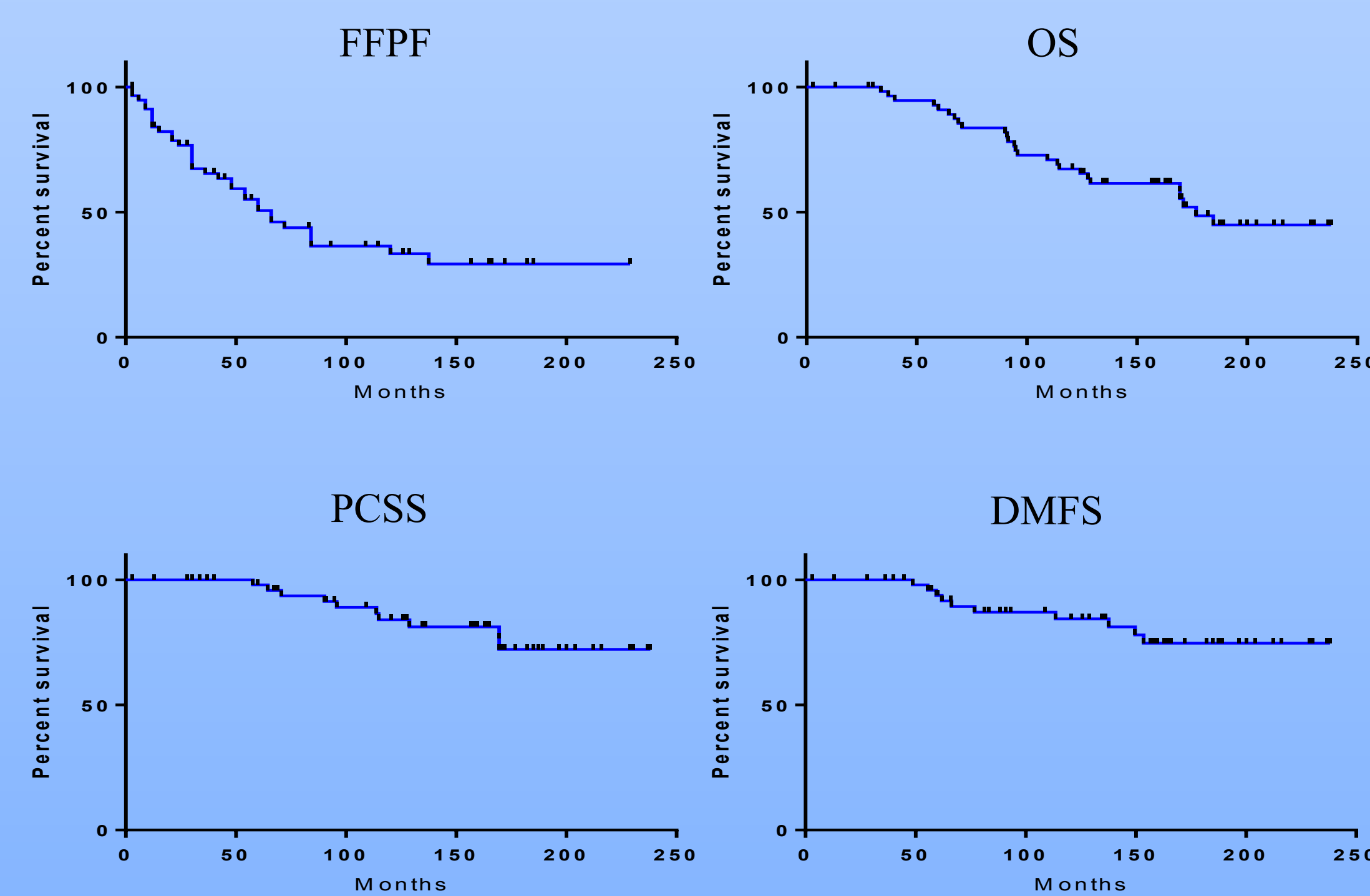
RESULTS

Patient characteristics of 61 patients

➤ The median post-SRT follow-up was 126 months (range 3-238).

➤ 26 (42.6%) died, including 10 (16.4%) of PCa.

➤ Of the 61 patients, 34 (56%) had PSA failure after SRT.



Kaplan-Meier survival after SRT (n=61)

➤ FFPF at 5 and 10 years were 51% and 33% (median 5.5 years)

➤ OS at 5 and 10 years were 91% and 67% (median 14.7 years)

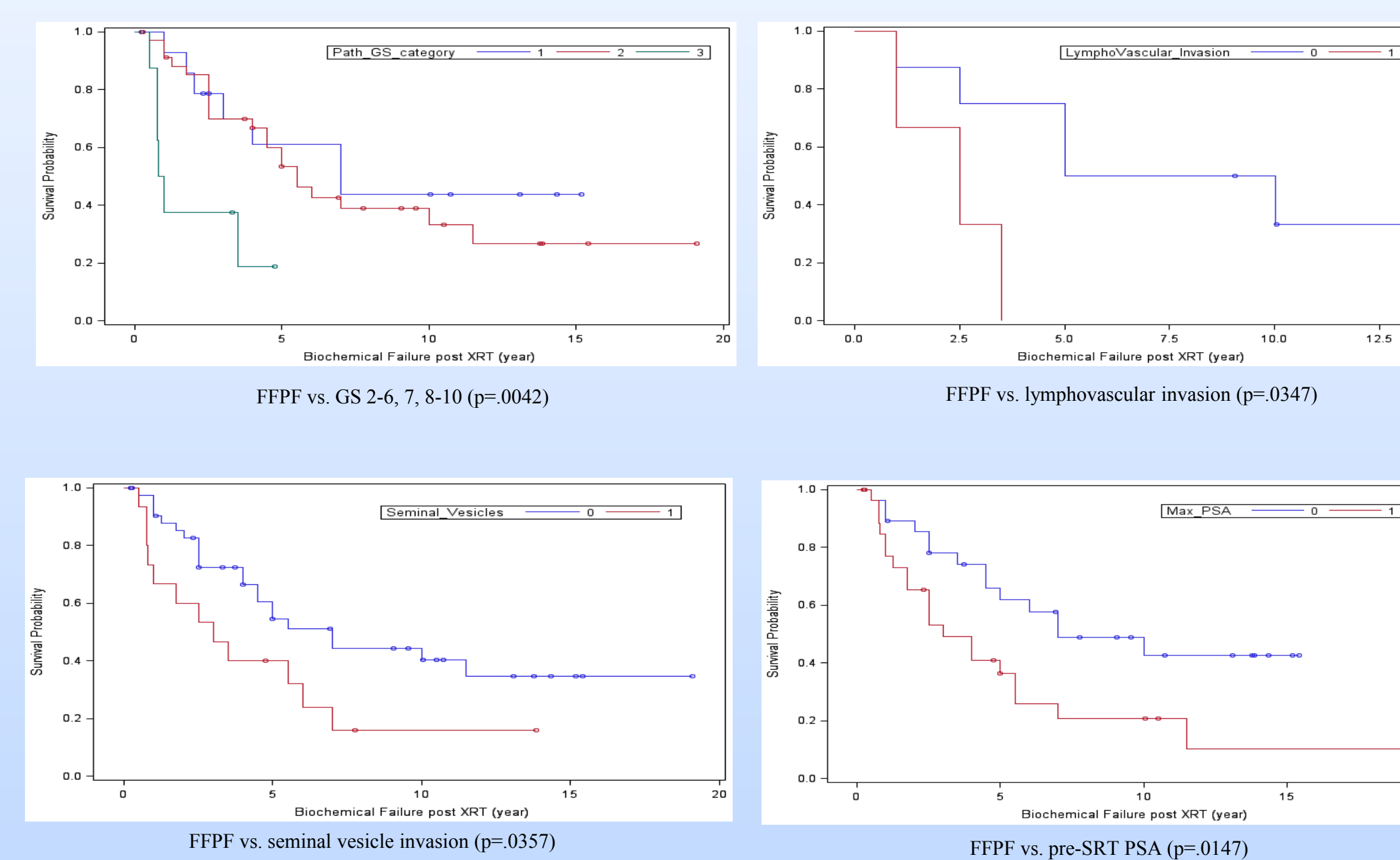
➤ PCSS at 5 and 10 years were 98% and 84%

➤ DMFS at 5 and 10 years were 94% and 84%

RESULTS

Univariate analysis

➤ pGS (2-6, 7, 8-10) significantly correlated with FFPF (p=.0042) and OS (p=.0022). Seminal vesicle invasion (p=.0357, HR 2.07, 1.0-4.2), lymphovascular invasion (p=.035, HR 5.28, 0.9-32.2), and pre-SRT PSA (p=.015, HR 2.27, 1.1-4.5) were associated with decreased FFPF.



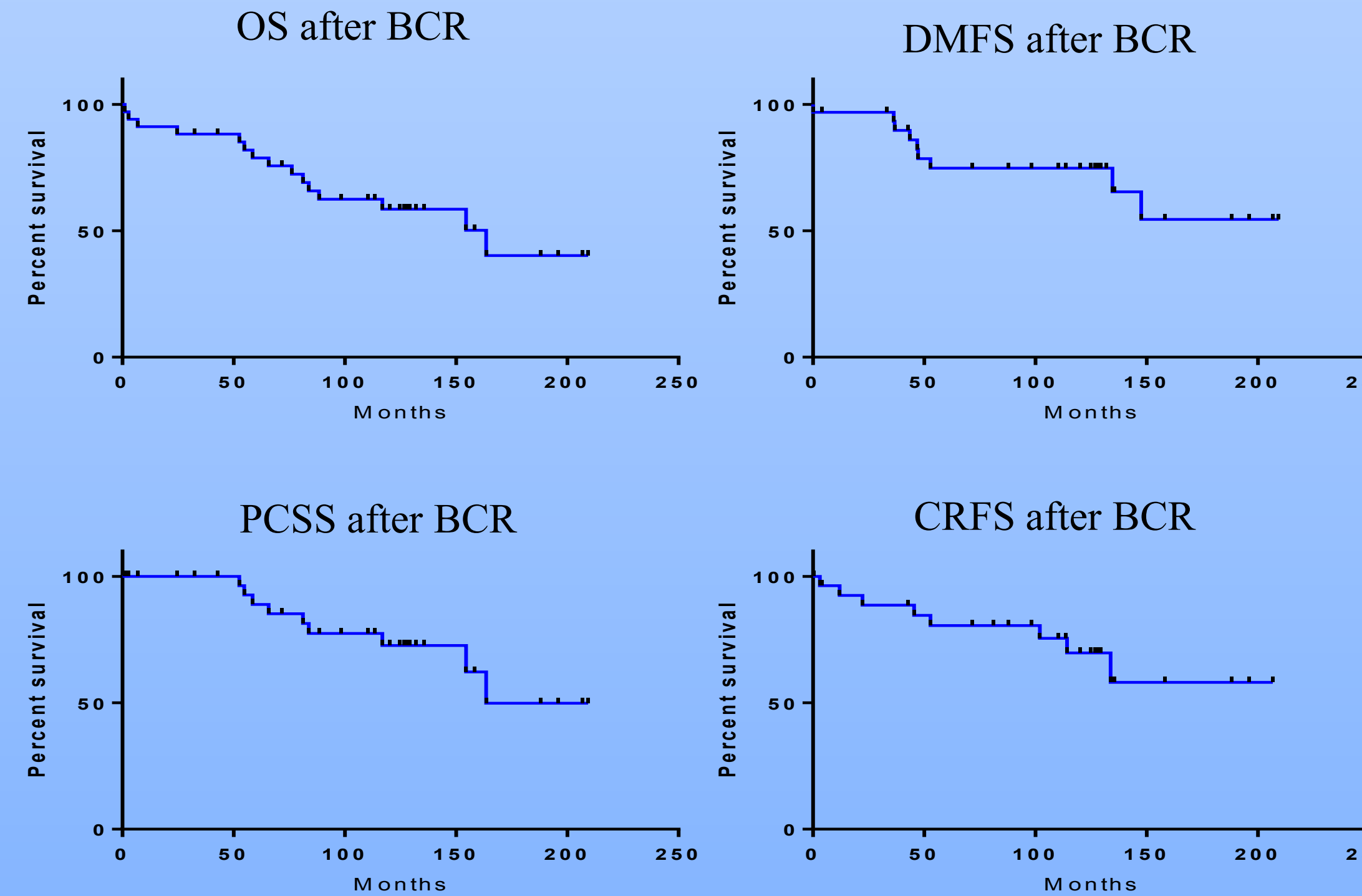
Patient characteristics of 34 patients who had BCR

➤ Median follow-up after SRT was 157.5 months (13-238)

➤ Median follow-up after BCR was 112 months (0-209).

➤ Median time to BCR following SRT was 30 months (3-138).

➤ Median time from BCR to initiating ADT was 48 months (0-151).



Kaplan-Meier survival after BCR (n=34)

➤ OS at 5 and 10 years were 79% and 59% (median 13.6 years)

➤ PCSS at 5 and 10 years were 89% and 73%

➤ DMFS at 5 and 10 years were 75%.

➤ CRFS at 5 and 10 years were 81% and 70%.

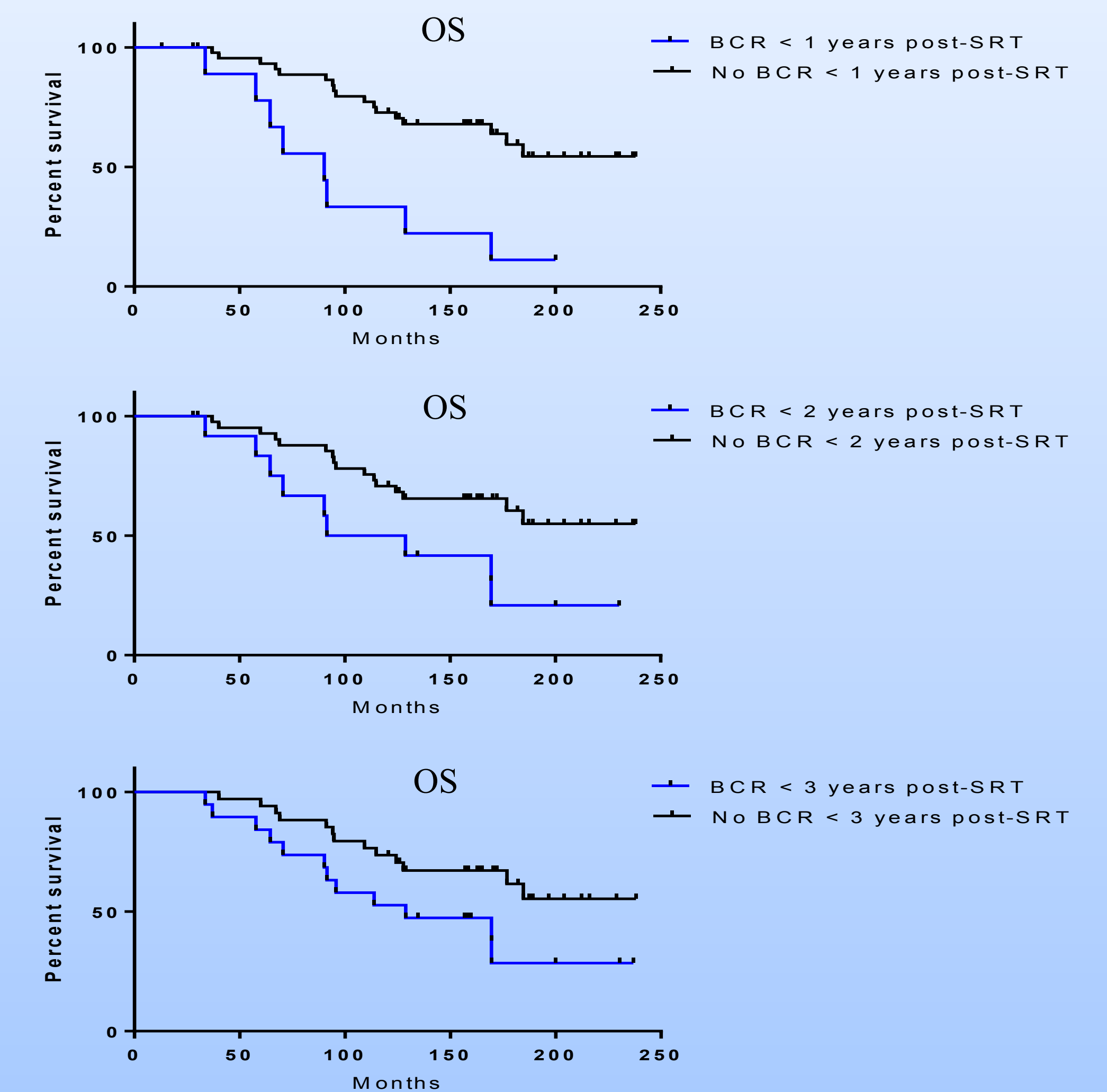
RESULTS

Significance of time to BCR after SRT

➤ Time to BCR after SRT < 1 year correlated with decreased OS (p=.0005, HR 3.92, 2.7-33.6). Median OS = 90 months after SRT.

➤ Time to BCR < 2 years correlated with a decreased OS (p=.021, HR 2.52, 1.2-9.2). Median OS of 110 months after SRT.

➤ Time to BCR < 3 years (p=.054) and < 5 years (p=.073) were not significant, having median OS after SRT of 129 months and 169 months, respectively.



CONCLUSIONS

➤ Clinical parameters predictive of treatment failure after SRT are presented.

➤ Unfortunately, 25% of patients who fail SRT developed distant metastases within 5 yrs of failure. 56% of those who failed eventually also required ADT. Such events could have significant emotional impact, affect quality of life, and lead to morbidity related to salvage therapy.

➤ However, while up to 27% of patients died from PCa after BCR at 10 years, only patients who failed SRT in less than 2 years had a significantly worse OS. Overall, patients who fail SRT treatment can have a prolonged median overall survival of 13.6 years.

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