04. The percentage

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Submission date: 14-May-2023 12:50PM (UTC+0800)
Submission ID: 2092460319
File name: 04._The_percentage.PDF (1.09M)
Word count: 5056
Character count: 26601

ORIGINAL ARTICLE

Bali Medical Journal (*Bali MedJ*) 2023, Volume 12, Number 1: 283-290
P-ISSN.2089-1180, E-ISSN: 2302-2914

The percentage of positive biopsy cores in predicting biochemical recurrence and adverse pathology in prostate cancer patients after radical prostatectomy: a systematic review and meta-analysis

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Received: 2022-10-25
Accepted: 2022-12-29
Published: 2023-01-20

ABSTRACT

Background: Biochemical recurrence (BCR) occurs in more than one-third of prostate cancer (PCa) patients 10 years after radical prostatectomy. The percentage of positive biopsy cores (PPBC) obtained from prostate needle biopsy is suggested as one of the predictors of BCR. We aim to investigate the role of PPBC in predicting BCR and adverse pathology in PCa patients after RP.

Methods: A systematic search was conducted based on PRISMA guidelines from Pubmed, Scopus, and Cochrane Library databases up to July 2022. We screened studies that met our inclusion criteria and NOS (Newcastle-Ottawa Scale) was utilized as the quality assessment tool. The primary outcome was BCR measured as Hazard Ratios (HRs). The secondary outcome was adverse pathology, including positive surgical margin (PSM), Extra-prostatic disease (EPD), and seminal vesicle invasion (SVI). Review Manager®5.4 was used as the statistical analysis tool.

Results: A total of 5971 patients were included from eleven eligible studies with overall good quality scores. Eleven studies were included in the qualitative synthesis and five of them were analyzed in the meta-analysis. The pooled analysis demonstrated that higher PPBC has a 2.77 times risk of BCR (OR 2.77 (95% CI: 1.97, 3.9; p<0.00001) after RP. Similarly, it has significant results in SVI (OR 2.61 (95% CI: 1.19, 5.73; p=0.02). However, there were insignificant results in terms of EPD (p=0.17) and PSM (p=0.33).

Conclusion: This systematic review and meta-analysis (SRMA) indicate that a high PPBC is strongly correlated with a greater risk of BCR and SVI, but not EPD and PSM in patients following RP.

Keywords: percentage of positive prostate biopsy core, biochemical recurrence, adverse pathology, radical prostatectomy, prostate cancer.

Cite This Artide: Fitra, A.F., Yogiswara, N., Djatisoesanto, W., Chung, E., Hakim, L. 2023. The percentage of positive biopsy cores in predicting biochemical recurrence and adverse pathology in prostate cancer patients after radical prostatectomy: a systematic review and meta-analysis. *Bali Medical Journal* 12(1): 283-290. DOI: 10.15562/bmj.v12i1.4075

INTRODUCTION

Prostate Cancer (PCa) is the second most common solid organ malignancy with a high mortality rate among men.[1-3] The prognosis of cancer survival is related to their stage at diagnosis and treatment.[4-6] Contemporary literature supported radical prostatectomy (RP) as an effective treatment for localized disease.[7-10] However, about thirty percent of all patients undergoing RP will have a biochemical recurrence (BCR) and high serum PSA levels within ten years.[11] Furthermore, pathological examination of RP specimens revealed that almost 50% of patients are under-staged clinically.[12] Although considered as standard of care for localized PCa, RP is often not offered in high-risk PCa patients due to potentially higher adverse effects and rates of BCR.[5,13,14]

Additional information in prostate needle biopsy had been evaluated to enhance the preoperative and postoperative prediction of pathological stage in patients undergoing RP, such as quantitative nuclear grade, percentage of biopsy cores, and the number of positive cores.[15-18] In several studies, tumor volume, extracapsular extension, and seminal vesicle invasion have been predicted using the percentage of positive biopsy cores (PPBC).[19-21] Current research also used PPBC to predict biochemical failure after RP. However, the role of PPBC for predicting BCR and adverse pathology is still unclear and not yet stated in the recent guidelines. We created this SRMA to analyze the role PPBC in predicting BCR and adverse pathology in PCa patients after RP.

METHODS

Study design

This review was conducted in accordance with the Cochrane Handbook for

Systematic Reviews of Interventions and Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA).[23,24] The protocol of this review has been registered in PROSPERO (CRD42022337620).[25]

Systematic search strategy

A systematic search was performed in Scopus, Cochrane Library, and Pubmed databases for studies published up to July 2022. The keywords used in this review were summarized in table 1.

Eligibility criteria

The included studies in this review focus on the PPBC in predicting BCR and adverse pathology in patients undergoing RP, including open, laparoscopic, and robotic-assisted procedures. We included studies with randomized trial designs and observational studies with at least one outcome of interest. Meta-analysis, systematic reviews, editorials, commentaries, letters, animal studies, abstract-only studies, case reports and case series without control, carcinoma in situ studies, and non-English language studies were excluded.

Data extraction and quality assessment

Two authors reviewed the titles or abstracts of studies found in the initial search while ruling out irrelevant studies. Full-text relevant studies were then collected and evaluated to find the one that matched the inclusion criteria. Both authors also evaluated the method of randomization and the adequacy of allocation concealment. The authors resolved internal disagreements related to study selection with discussion. The bias was evaluated by using Newcastle-Ottawa Scale (NOS).[26]

Statistical analysis

The primary outcome analyzed in this study was BCR measured as Hazard Ratios (HRs) and secondary outcomes comprised of adverse pathology measured as Odds Ratios (ORs) with 95% Confidence Interval (95% CI).[27,28]

Heterogeneity was assessed using the I^2 test. If the I^2 was less than 50%, the analysis indicated a low heterogeneity among the studies, hence a fixed-effects model was selected for analysis. Otherwise, the random-effects model was selected for this analysis.[29] Review Manager® 5.4 (Cochrane Collaboration, UK) was used as the statistical analysis tool.

Table 1. Systematic search keywords.

Databases	Keywords
PubMed	((percent OR percentage) AND (positive cores OR positive biopsy OR positive biopsy cores)) AND prostate cancer AND ("biochemical recurrence" OR "adverse pathology" OR "seminal vesicle invasion" OR "positive surgical margin" OR "extraprostatic disease")
Cochrane Library	((percent OR percentage) AND (positive cores OR positive biopsy OR positive biopsy cores)) AND prostate cancer AND ("biochemical recurrence" OR "adverse pathology" OR "seminal vesicle invasion" OR "positive surgical margin" OR "extraprostatic disease")
Scopus	TITLE-ABS-KEY (((percent OR percentage) AND (positive AND cores OR positive AND biopsy OR positive AND biopsy AND cores)) AND prostate AND cancer AND ("biochemical recurrence" OR "adverse pathology" OR "seminal vesicle invasion" OR "positive surgical margin" OR "extraprostatic disease"))

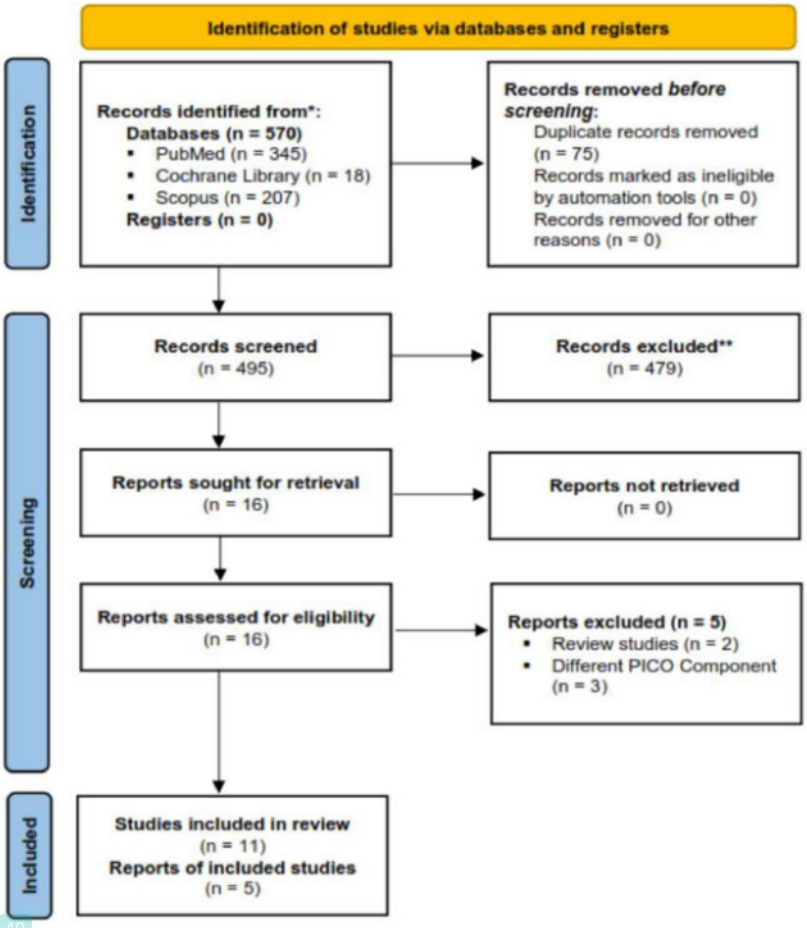

Figure 1. PRISMA Flow diagram of the screening process.

RESULTS

Systematic search results

A total of 570 initial studies were obtained from the systematic search. The number of articles found from each database is

Table 2. **Study Characteristics.**

No.	Author	Study Design	n	Age (years)	Clinical Stage	Pre-operative GS	Core-biopsy	Variable of PPBC
1.	Antunes et al. 2005	Cohort Retrospective	534	63	T1c, T2, T3	2-6: 423 (79.2) 7: 76 (14.2) 8–10: 35 (6.6)	TRUS, 6-18	Continous
2.	Freedland et al. 2003	Cohort Retrospective	1094	62.6	T1, T2, T3	2–6: 752 (68) (3+4): 216 (19) >4+3: 145 (13)	US-guided, 6-30	Continous
3.	Memis et al. 2011	Cohort Retrospective	156	62.1	T1c, T2a, T2b	5.2 ± 1.6	TRUS, ≥6	Dichotomous with cut-off 40%
4.	Russo et al. 2014	Cohort Retrospective	750	65.5	T1c, T2	NR	US-guided, 10-24	Dichotomous with cut-off 40%
5.	Suekane et al. 2007	Cohort Retrospective	117	66	T1c, T2a, T2b, T3c	NR	US-guided, ≥6	Continous
6.	Mortensen et al. 2009	Cohort Retrospective	390	NR	T1c, T2a, T2b, T3	2-4: 62 5: 58 6: 138 7-10: 101	TRUS, ≥6	Continous
7.	Oikawa et al. 2020	Cohort Retrospective	386	68	T1c, T2a, T2b, T2c, T3	NR	TRUS, 10-12	Continous
8.	Grossfeld et al. 2002	Cohort Retrospective	1265	63.8	T1,T2,T3	2-6: 996 (78.9) 7(3+4): 128 (10) 7 (4+3): 46 (3.6) 8-10: 69 (6.5)	NA, ≥6	Continous
9.	Otsuka et al. 2018	Cohort Retrospective	198	69	T3a, T3b	6: 3 (2) 7: 93 (47) 8-10: 102 (51)	NA, 12-16	Dichotomous with cut-off 50%
10.	San Fransisco et al. 2004	Cohort Retrospective	476	61	T1a, T1b, T1c, T2a, T2b	3-5: 10 (2.1) 6: 342 (71.9) 7: 92 (19.3) 8: 22 (4.6) 9: 10 (2.1)	TRUS, 3-16	Dichotomous with cut-off 28%
11.	Lotan et al. 2004	Cohort Retrospective	605	60.4	T1, T2	4-6: 399 (66%) 7: 168(22%) 8-10: 36 (6%)	NA	Continous

RRP: Radical Retropubic Prostatectomy; RP: Radical Prostatectomy; RARP: Robotic-assisted Radical Prostatectomy; GS: Gleason Score; NR: Not-recorded; TRUS: Trans-rectal ultrasonography; US: ultrasound; PPBC: Percentage of Positive Biopsy Core

Table 3. **Profiles after Treatment.**

No.	Author	Treatment	pTNM Status (n)	Post-operative GS	PSA Cut-off Recurrence	The average duration of Follow-up	Outcome(s)
1.	Antunes et al. 2005	RP	T2 (401) T3 (133)	NR	0.4 ng/mL	60.5 months	BCR, EPD, SVI
2.	Freedland et al. 2003	RP	T2 (765) T3 (208) T4(23)	2-6: 589 (53) 3+4: 321 (29) >4+3: 203 (18)	0.2 ng/mL	29.5 months	BCR, PSM, EPD, SVI
3.	Memis et al. 2011	RP	T2a (41) T2b (47) T3a (23) T3b (15)	6.1 ± 1.5	0.2 ng/mL	23.6 months	EPD, PSM, SVI
4.	Russo et al. 2014	Open or laparoscopic RP	T2a (48) T2b (17) T2c (66) T3a (9) T3b (3)	NR	0.2 ng/mL	46 months	BCR, Unfavourable Disease
5.	Suekane et al. 2007	RP	N+ (9)	NR	0.2 ng/mL	64 months	BCR, EPD, PSM, SVI
6.	Mortensen et al. 2009	RP	NR	NR	NR	NR	NCD
7.	Oikawa et al. 2020	RP	T2a (102) T2b (31) T2c (253)	NR	NR	85.7 months	BCR
8.	Grossfeld et al. 2002	RP	NR	NR	0.2 ng/mL	39.6 months	BCR
9.	Otsuka et al. 2018	RP or RARP	T2 (60) T3 (132) T4 (6)	5–6: 2 (1) 7: 91 (46) 8–10: 105 (53)	0.2 ng/mL	36 months	BCR
10.	San Fransisco et al. 2004	RP	T2 (434) T3 (37) N+ (5)	5–6: 311 (65.3) 7(3+4): 101 (21.2) 7(4+3): 33 (6.9) 8-9: 31 (6.5)	0.3 ng/mL	49 months	BCR
11.	Lotan et al. 2004	RP	T2 (407) T3a (168) T3b (55) N+ (32)	4-6: 245 (40%) 7: 300 (50%) 8-10: 60 (10%)	0.2 ng/mL	43.7 months	BCR, EPD, SVI

RP: Radical Prostatectomy; RARP: Robotic-assisted Radical Prostatectomy; GS: Gleason Score; PSA: Prostate-specific Antigen; BCR: Biochemical Recurrence; EPD: Extra Prostatic Disease; SVI: Seminal Vesicle Invasion; PSM: Positive Surgical Margin; NR: Not-recorded

Table 4. Risk of bias of the included studies according to the Newcastle-Ottawa Scale (NOS).

Included Studies	Selection				Comparability		Outcome		Total Score
Antunes et al. 2005	*	*	*		*	*		*	6
Freedland et al. 2003	*	*	*	*	*	*		*	7
Memis et al. 2011	*		*		*	*	*	*	6
Russo et al. 2014	*	*	*		*	*	*	*	7
Suekane et al. 2007	*	*	*	*	*	*		*	7
Mortensen et al. 2009	*	*	*	*	*	*			7
Oikawa et al. 2020	*	*	*	*	*	*		*	7
Grossfeld et al. 2002	*	*	*	*	*	*		*	7
Otsuka et al. 2018	*		*		*	*	*	*	6
San Fransisco et al. 2004	*	*	*	*	*	*		*	7
Lotan et al. 2004	*	*	*	*	*	*		*	7

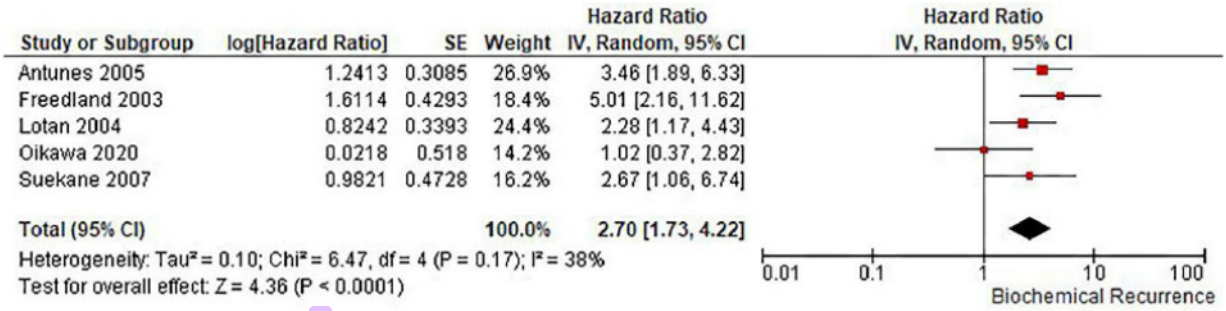

Figure 2. Pooled hazard ratio of the percentage of positive biopsy cores in predicting biochemical recurrence after radical prostatectomy.

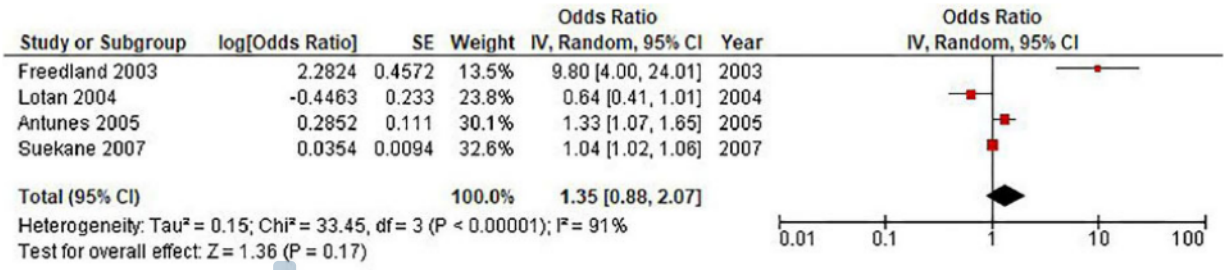

Figure 3. Pooled odds ratio of the percentage of positive biopsy cores in predicting extra prostatic disease.

shown in table 1. Out of the obtained studies, 75 duplicates were removed. Primary screening resulted in sixteen articles, which were further evaluated for eligibility. A total of eleven studies were included for qualitative synthesis and five studies for meta-analysis. A summary of this systematic screening process is shown in the PRISMA flowchart (Figure 1).

Study characteristics

A total of 5971 patients from eleven relevant studies were included in the analysis. The study characteristics and profiles after treatment are displayed in table 2 and 3. The included studies used different PSA cut-offs for defining BCR, ranging from 0.2-0.4 ng/mL. The median follow-up ranged from 23.6-85.7 months in PCa patients with the cT1-T3 disease. Adverse pathology was also evaluated including seminal vesicle invasion, extra-prostatic disease, and positive surgical margin.

Risk of bias

We assessed the risk of bias using Newcastle-Ottawa Scale (NOS). There were three studies with moderate risk and eight studies with low risk of bias. A resume of the tool can be seen in table 4. All studies included in this systematic review and meta-analysis are non-randomized studies, thus, there is a possibility of selection bias. Studies by Memis et al. and Otsuka et al. has lower NOS score than other included studies since there was no description of the derivation of the non-exposed cohort.[6,12]

PPBC in predicting BCR

A total of five studies reported BCR in PCa patients after RP. The pooled hazard ratio was 2.77 (95% CI: 1.97, 3.9; $p < 0.00001$). The forest plot in figure 2 shows that the

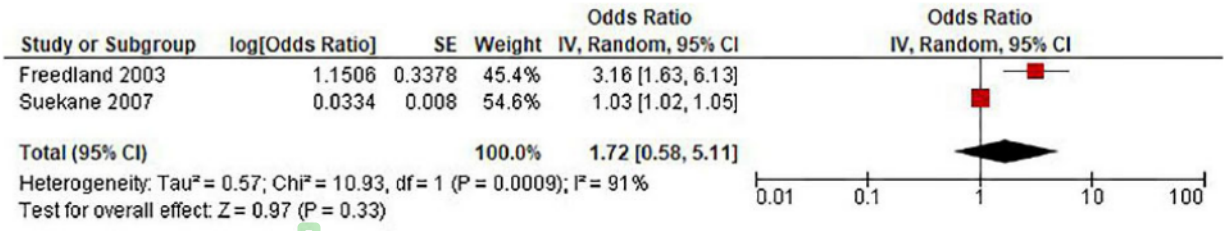

Figure 4. Pooled odds ratio of the percentage of positive biopsy cores in predicting positive surgical margin.

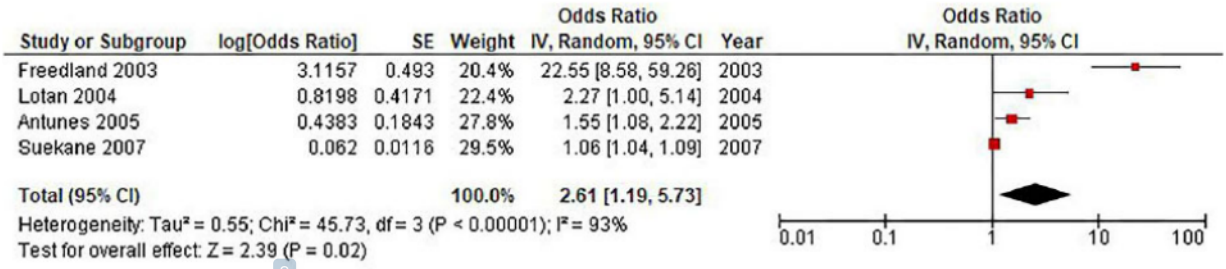

Figure 5. Pooled odds ratio of the percentage of positive biopsy cores in predicting seminal vesicle invasion.

included studies had low heterogeneity (heterogeneity p = 0.17, I^2 = 38%), and thus, the fixed-effect model was chosen for the analysis.

PPBC in predicting extra prostatic disease

Figure 3 shows the pooled estimated effect size of PPBC in predicting extra prostatic disease. The forest plot from the combined analysis of the four studies indicated high heterogeneity (heterogeneity $p < 0.00001$, I^2 = 91%). Therefore, the random-effect model was selected for analysis. The meta-analysis revealed that there was no significant result of PPBC in predicting EPD (OR 1.35, 95% CI: 0.88, 2.07; p = 0.17).

PPBC in predicting positive surgical margin

Two studies reported positive surgical margins in PCa patients after RP. The pooled odds ratio was 1.72 (95% CI: 0.58, 5.11; p = 0.33), as shown in figure 4. The forest plot in figure 4 shows that the included studies had high heterogeneity (heterogeneity p = 0.0009, I^2 = 91%), and thus, the random-effect model was chosen.

PPBC in predicting seminal vesicle invasion

A total of four studies reported seminal vesicle invasion in PCa patients undergoing RP. The pooled OR was 2.61 (95% CI: 1.19, 5.73; p = 0.02). The random-effect model was used for the analysis since it has high heterogeneity (heterogeneity $p < 0.00001$, I^2 = 93%), which is shown in figure 5.

DISCUSSION

This is the first SRMA evaluating the role of the PPBC in predicting BCR and adverse pathology in PCa patients after RP. Our study included eleven articles evaluating the role of PPBC in predicting at least one outcome of interest. Our main finding showed that a higher PPBC is significantly associated with a higher risk of BCR and seminal vesicle invasion after the patients underwent RP.

A Study by Otsuka et al. reported that after 46 months of follow-up, PCa patients with PPBC > 50% would have 2.86 times higher risk of developing BCR after RP.[6] BCR may developed in up to 44% of patients with the mean follow-up 64 months after RP.[22] Selected pathological aspects, including percentage of Gleason grade 4/5, preoperative biopsy cores, and PSA density, have been shown to predict the risk of BCR after RP.[22] Similarly, Lotan et al. found that the number of positive biopsies and PPBC were associated with the risk of BCR, seminal vesicle invasion, extracapsular extension, regional lymph nodes metastases, perineural and lymphovascular invasion, and positive surgical margin status in patients undergoing RP.[30]

Antunes et al. reported more than 500 patients undergoing RP and bilateral pelvic lymphadenectomy where patients with a lower PPBC had a lower mean of preoperative PSA level than the one with higher PPBC. The PPBC < 25% was also associated with clinical stage T1c, while majority of patients with PPBC > 25% had T2 or T3. In multivariate analysis, the authors found that the serum PSA level cannot accurately predict the risk of extra-prostatic disease, although PPBC was an independent predictor of seminal vesicle involvement and extra-prostatic extension.[11]

Multivariate analysis from San Francisco et al. showed that the patients with PPBC higher than 28% would have 3.62 times higher risk of developing BCR with a median follow-up of 49 months after RP.[31] In a different paper, Freedland et al. also concluded that the PPBC independently predicted BCR and adverse pathology including seminal vesicle invasion, positive surgical margin status, and extra-prostatic extension following RP. The cutoff points for PPBC were less than 34%, 34% to 50%, and more than 50% provided significant risk stratification for BCR between them.[32]

Not only after RP, a study by Kestin et al. showed that PPBC is also a

powerful predictor of biochemical and clinical outcomes for PCa treated with radiotherapy. It suggested that PPBC should be considered as a primary factor in risk group stratification for PCa.[33] However, Zapatero et al. analyzing PCa patients undergoing radiotherapy revealed no significant association between high PPBC and clinical, pathological, and treatment factors. This could be due to the small sample size and number of events.[34]

A retrospective study from Memis et al. supported that PPBC from the dominant side of the prostate may become a parameter for predicting adverse pathology, particularly in terms of non-organ-confined disease and biochemical failure after RRP.[12] A study by Grossfeld et al. analyzing 938 patients with intermediate and high-risk PCa reported that a higher PPBC was associated with lower 5-years disease-free survival (DFS).[35]

Russo et al. researched some predictive factors for low-risk PCa patients who became active surveillance candidates. Cancer involvement in positive cores less than 0.4 mm had a significantly better 3- and 5-year biochemical recurrence-free survival (BRFS).[36]

The fraction of PPBC could also provide additional prognostic value in addition to T-stage and Gleason scores, to independently predict extra-prostatic disease.[37] Oikawa et al. demonstrated that PPBC could anticipate preoperative covariates in patients with pT2 PCa and negative resection margin status after RP where the BRFS rate was significantly higher in patients with a positive biopsy core ≤ 20% than those with ≥ 21%.[38]

The clinical tumor, Gleason score, and PSA level are already stated in the recent EAU guidelines in predicting BCR.[39] Considering the usefulness of PPBC as mentioned above, we want to include it as a quantitative parameter to predict BCR. This present study indicates that PPBC is useful in predicting BCR and SVI risk after RP. This parameter should be reported in all prostate needle biopsy results before deciding the prompt treatment for localized PCa.

There were several limitations existed in this study. Some outcomes in this study had a significant heterogeneity due to differences in studies baseline characteristics such as clinical stage, the number of biopsy cores taken, and PSA cut-off for BCR. All studies included in this systematic review and meta-analysis are non-randomized studies, thus, there is a possibility of bias due to various confounding factors that can affect the final results. Some included studies used continuous variables and the others used dichotomous variables with PPBC cut-off. We only analyzed studies using continuous variables since three studies used different cut-offs.[12,22,36] However, all studies using cut-offs also showed that the group with high PPBC had higher risk of BCR.

Our findings highlighted the role of PPBC in predicting the risk of BCR and SVI in patients with prostate cancer after RP.

CONCLUSION

This SRMA found that a higher percentage of PPBC among PCa patients undergoing RP is associated with higher risk of BCR and SVI but not EPD and PSM.

CONFLICTS OF INTEREST

The authors declare that they have no conflict of interest.

FUNDING SOURCE

This work was supported by Program Beasiswa Dokter Spesialis of the Indonesian Endowment Fund for Education (LPDP) Scholarship, Ministry of Finance.

ETHICS COMMITTEE APPROVAL

This systematic review and meta-analysis do not require ethical approval.

AUTHOR CONTRIBUTION

- Ahmad Fathira Fitra (A.F.F.) is involved in the concept and project design, materials, literature search, data collection and/or processing, analysis and/or interpretation, writing the manuscript, and final approval of the version to be submitted.
- Niwanda Yogiswara (N.Y.) is involved in the materials, literature search, data collection and/or processing, analysis and/or interpretation, writing the manuscript, and final approval of the version to be submitted.
- Wahjoe Djatisoesanto (W.D.) is involved in the concept and project design, supervision, resources, materials, literature search, data collection and/or processing, analysis and/or interpretation, writing the manuscript, and final approval of the version to be submitted.
- Eric Chung (E.C.) is involved in the supervision, resources, materials, writing the manuscript, and final approval of the version to be submitted.
- Lukman Hakim (L.H.) is involved in the concept and project design, supervision, resources, materials, literature search, data collection and/or processing, analysis and/or interpretation, writing the manuscript, and final approval of the version to be submitted.

REGISTRATION OF RESEARCH STUDY

- Name of the registry: PROSPERO
- Unique Identifying number or registration ID: CRD42022337620
- Hyperlink to registration: https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=337620

REFERENCES

1. Mottet N, Bellmunt J, Bolla M, Briers E, Cumberbatch MG, De Santis M, et al. EAU-ESTRO-SIOG Guidelines on Prostate Cancer. Part 1: Screening, Diagnosis, and Local Treatment with Curative Intent. Eur Urol. 2017;71(4):618–29.
2. Penson DF. Urology Board ReviewLeslieS.W.: Urology Board Review. New York: McGraw Hill Medical2009. 521 pages. J Urol. 2010;183(6):2473.
3. Partin AW, Wein AJ, Kavoussi LR, Peters CA, Dmochowski RR. Campbell-Walsh-Wein Urology twelfth ed. Philadelphia: Elsevier Health Sciences; 2020.
4. Montaño JJ, Barceló A, Franch P, Galceran J, Ameijide A, Pons J, et al. Prostate Cancer Survival by Risk and Other Prognostic Factors in Mallorca, Spain. Int J Environ Res Public Health. 2021 Oct 24;18(21):11156.
5. Cui P-F, Cong X-F, Gao F, Yin J-X, Niu Z-R, Zhao S-C, et al. Prognostic factors for overall survival in prostate cancer patients with different site-specific visceral metastases: A study of 1358 patients. World J Clin cases. 2020;8(1):54–67.
6. Otsuka M, Kamasako T, Uemura T, Takeshita N, Shinozaki T, Kobayashi M, et al. Factors predicting biochemical recurrence after radical prostatectomy among patients with

clinical T3 prostate cancer. Jpn J Clin Oncol. 2018;48(8):760–4.
7. Joniau S, Hsu C-Y, Gontero P, Spahn M, Van Poppel H. Radical prostatectomy in very high-risk localized prostate cancer: Long-term outcomes and outcome predictors. Scand J Urol Nephrol. 2012;46(3):164–71.
8. Freedland SJ, Partin AW, Humphreys EB, Mangold LA, Walsh PC. Radical prostatectomy for clinical stage T3a disease. Cancer. 2007;109(7):1273–8.
9. Ward JF, Slezak JM, Blute ML, Bergstralh EJ, Zincke H. Radical prostatectomy for clinically advanced (cT3) prostate cancer since the advent of prostate-specific antigen testing: 15-year outcome. BJU Int. 2005;95(6):751–6.
10. Schreiber D, Rineer J, Sura S, Teper E, Nabhani T, Han P, et al. Radical prostatectomy for cT3-4 disease: an evaluation of the pathological outcomes and patterns of care for adjuvant radiation in a national cohort. BJU Int. 2010;108(3):360–5.
11. Antunes AA, Srougi M, Dall'oglio MF, Crippa A, Campagnari JC, Leite KRM. The percentage of positive biopsy cores as a predictor of disease recurrence in patients with prostate cancer treated with radical prostatectomy. BJU Int. 2005;96(9):1258–63.
12. Memis A, Ugurlu O, Ozden C, Oztekin CV, Aktas BK, Akdemir AO. The correlation among the percentage of positive biopsy cores from the dominant side of prostate, adverse pathology, and biochemical failure after radical prostatectomy. Kaohsiung J Med Sci. 2011;27(8):307–13.
13. Payne H. Management of locally advanced prostate cancer. Asian J Androl. 2009;11(1):81–7.
14. Bill-Axelson A, Holmberg L, Garmo H, Rider JR, Taari K, Busch C, et al. Radical prostatectomy or watchful waiting in early prostate cancer. N Engl J Med. 2014;370(10):932–42.
15. Peller PA, Young DC, Marmaduke DP, Marsh WL, Badalament RA. Sextant prostate biopsies. A histopathologic correlation with radical prostatectomy specimens. Cancer. 1995;75(2):530–8.
16. Wills ML, Sauvageot J, Partin AW, Gurganus R, Epstein JI. The ability of Sextant Biopsies to Predict Radical Prostatectomy Stage. Urology. 1998;51(5):759–64.
17. Zhou M, Hayasaka S, Taylor Jmg, Shah R, Proverbs-Singh T, Manley S, Et Al. Lack of Association of Prostate Carcinoma Nuclear Grading With Prostate Specific Antigen Recurrence After Radical Prostatectomy. J Urol. 2001;166(6):2193–7.
18. Wittschieber D, Köllermann J, Schlomm T, Sauter G, Erbersdobler A. Nuclear Grading Versus Gleason Grading in Small Samples Containing Prostate Cancer: A Tissue Microarray Study. Pathol & Oncol Res. 2010;16(4):479–84.
19. Tarján M, Tot T. Prediction of extracapsular extension of prostate cancer based on systematic core biopsies. Scand J Urol Nephrol. 2006;40(6):459–64.
20. Ravery V, Chastang C, Toublanc M, Boccon-Gibod L, Delmas V, Boccon-Gibod L. Percentage of Cancer on Biopsy Cores Accurately Predicts Extracapsular Extension and Biochemical Relapse after Radical Prostatectomy for T1–T2 Prostate Cancer. Eur Urol. 2000;37(4):449–55.
21. Furuya Y, Fuse H, Nagakawa O, Masai M. Preoperative parameters to predict tumor volume in Japanese patients with nonpalpable prostate cancer. Int J Clin Oncol. 2002;7(2):109–13.
22. Suekane S, Noguchi M, Nakashima O, Yamada S, Kojiro M, Matsuoka K. Percentages of positive cores, cancer length and Gleason grade 4/5 cancer in systematic sextant biopsy are all predictive of adverse pathology and biochemical failure after radical prostatectomy. Int J Urol. 2007;14(8):713–8.
23. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372:n71–n71.
24. Higgins J, Green S. Cochrane Handbook for Systematic Reviews of Interventions. John Wiley & Sons, Ltd; 2008.
25. Greene DR. Editorial Comment on: Systematic Assessment of the Ability of the Number and Percentage of Positive Biopsy Cores to Predict Pathologic Stage and Biochemical Recurrence after Radical Prostatectomy. Eur Urol. 2007;52(3):744–5.
26. Wells GA, Shea B, O'Connell D, Peterson J, Welch V, Losos M, Tugwell P. Newcastle-Ottawa quality assessment scale, Ottawa Hospital Research Institute, (OHRI). (2014). Available from: https://doi.org/10.2307/632432.
27. Case BG. Risks Interpreting Odds. J Am Acad Child & Adolesc Psychiatry. 2013;52(3):319-324.
28. Greenland S, Senn SJ, Rothman KJ, Carlin JB, Poole C, Goodman SN, et al. Statistical tests, P values, confidence intervals, and power: a guide to misinterpretations. Eur J Epidemiol. 2016/05/21. 2016;31(4):337–50.
29. DerSimonian R, Laird N. Meta-analysis in clinical trials. Control Clin Trials. 1986;7(3):177–88.
30. Lotan Y, Shariat SF, Khoddami SM, Saboorian H, Koeneman KS, Cadeddu JA, et al. The Percent Of Biopsy Cores Positive For Cancer Is A Predictor Of Advanced Pathological Stage And Poor Clinical Outcomes In Patients Treated With Radical Prostatectomy. J Urol. 2004;171(6 Part 1):2209–14.
31. San Francisco IF, Regan MM, Olumi AF, Dewolf WC. Percent of Cores Positive for Cancer Is A Better Preoperative Predictor Oof Cancer Recurrence After Radical Prostatectomy Than Prostate Specific Antigen. J Urol. 2004;171(4):1492–9.
32. Freedland SJ, Aronson WJ, Terris MK, Kane CJ, Amling CL, Dorey F, et al. Percent of Prostate Needle Biopsy Cores With Cancer is Significant Independent Predictor of Prostate Specific Antigen Recurrence Following Radical Prostatectomy: Results From SEARCH Database. J Urol. 2003;169(6):2136–41.
33. Kestin LL, Goldstein NS, Vicini FA, Martinez AA. Percentage of Positive Biopsy Cores as Predictor of Clinical Outcome in Prostate Cancer Treated With Radiotherapy. J Urol. 2002;168(5):1994–9.
34. Zapatero A, Adrados M, Torres L, Talaya MS, Cruz Conde A, Martin de Vidales C, et al. Positive prostate biopsy following radiotherapy can predict metastasis-free survival in localized prostate cancer. Reports Pract Oncol Radiother J Gt Cancer Cent Pozn Polish Soc Radiat Oncol. 2019. 2020;25(1):55–9.
35. Grossfeld GD, Latini DM, Lubeck DP, Broering JM, Li Y-P, Mehta SS, et al. Predicting disease recurrence in intermediate and high-risk patients undergoing radical prostatectomy using percent positive biopsies: results from CaPSURE. Urology. 2002;59(4):560–5.
36. Russo GI, Cimino S, Castelli T, Favilla V, Urzì D, Veroux M, et al. Percentage of cancer involvement in positive cores can predict unfavorable disease in men with low-risk prostate cancer but eligible for the prostate cancer international: Active surveillance criteria. Urol Oncol Semin Orig Investig. 2014;32(3):291–6.
37. Mortensen MM, Mortensen PS, Borre M. Percentage of tumour-positive biopsy cores: An independent predictor of extraprostatic disease. Scand J Urol Nephrol. 2009;43(2):109–13
38. ikawa M, Tanaka T, Narita T, Noro D, Iwamura H, Tobisawa Y, et al. Impact of the Proportion of Biopsy Positive Core in Predicting Biochemical Recurrence in Patients with Pathological Pt2 and Negative Resection Margin Status after Radical Prostatectomy. Pathol & Oncol Res. 2020;26(4):2115–21.
39. Morote J, Comas I, Planas J. Re: Nicolas Mottet, Joaquim Bellmunt, Erik Briers, et al. EAU-ESTRO-ESUR-SIOG Guidelines on Prostate Cancer. European Association of Urology. Eur Urol. 2018;73(5):e134–5.

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