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Impact of family history of prostate cancer on disease progression for prostatic cancer patients undergoing active surveillance: A systematic review and meta-analysis

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Purpose: To evaluate how a family history of prostate cancer influences the progression of the disease in individuals with prostate cancer undergoing active surveillance.

Materials and Methods: We conducted a thorough literature search in PubMed/MEDLINE, Embase, and Cochrane Library up to June 2023. This systematic review was registered in PROSPERO (CRD42023441853). The study evaluated the effects of family history of prostate cancer (intervention) on disease progression (outcome) in prostate cancer patients undergoing active surveillance (population) and compared them to those without a family history (comparators). For time to disease progression outcomes, the extracted data were synthesized using the inverse variance method on the log hazard ratios scale.

Results: A total of eight studies were incorporated into this systematic review and meta-analysis. The combined hazard ratio for unadjusted disease progression was 1.06 (95% confidential interval [CI] 0.66–1.69; p=0.82). The combined hazard ratio for adjusted disease progression was 1.31 (95% CI 1.16–1.48; p<0.0001). All the enlisted studies demonstrated high quality based on the Newcastle–Ottawa scale. The certainty of evidence for univariate and multivariate analysis of disease progression was very low and low, respectively. Publication bias for all studies was not significant.

Conclusions: For individuals with prostate cancer opting for active surveillance, a family history of prostate cancer may serve as an independent risk factor associated with an elevated risk of disease progression. Clinicians should be counseled about the increased risk of disease progression in patients with a family history of prostate cancer undergoing active surveillance.

Keywords: Active surveillance; Disease progression; Hereditary prostate cancer; Meta-analysis; Prostate neoplasms

INTRODUCTION

According to multiple clinical guidelines, utilizing active surveillance (AS) is advised as a viable choice for individuals with low-grade cases of prostate cancer (PC) [1-3]. While screening based on prostate-specific antigen (PSA) and implementing aggressive treatment have proven effective in decreasing PC mortality, the high rates of overtreating in-

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dolent tumors remain a significant concern [4]. AS, which is designed to delay or avoid treatment, has become the primary management strategy for men with favorable-risk disease [5]. However, there is a possibility that a patient may miss the window for a curative treatment, leading to disease progression or metastasis [6]. Considerable research studies have been devoted to identifying risk factors that can determine the eligibility of individuals for AS and predict patients who may experience more rapid progression [4].

Having a family history (FH) of PC is a widely recognized risk element for PC development, representing a complex mix of genetic and environmental factors [7,8]. Individuals with a FH of PC face an elevated risk for both earlier disease detection and the presence of locally advanced stages [9]. A recent study conducted across multiple centers revealed that men with a first-degree FH of PC, referred for prostate biopsy, exhibited a 1.77 times more likely to have clinically significant PC (i.e., Gleason score ≥3+4) than men without a FH [10]. Despite the well-established status of FH of PC as a risk factor for PC development, very little efforts have been directed toward determining whether those are suitable candidates for AS [6].

To date, there has been a lack of systematic reviews and meta-analyses investigating the impacts of a FH of PC on the progression of the disease in patients opting for AS. There is only one systematic review on this subject, concluding that having a FH of PC does not appear to elevate the risk of a patient developing more aggressive forms of the disease [11]. Consequently, it suggested that FH may not serve as a decisive factor in determining eligibility for AS. However, since the publication of that review, multiple studies have been conducted, and recent research findings have presented conflicting results [12,13].

Clinicians persist in encountering difficulties when precisely identifying suitable candidates for AS and determining the optimal monitoring strategy [14]. Although a FH of PC is a very important factor in accurately selecting candidates for AS, there is little evidence of the impact of FH in PC on disease progression.

Hence, the aim of this systematic review and meta-analysis is to integrate current findings for assessing the impact of FH of PC on disease progression for patients with PC undergoing AS.

MATERIALS AND METHODS

This study was pre-registered with the PROSPERO database (CRD42023441853). Instead of a formal ethics committee, the principles of the Helsinki Declaration were followed.

1. Literature search

We performed a comprehensive search of the literature up to June 2023, utilizing databases such as PubMed/MEDLINE, Embase, and Cochrane Library. This study included publications written in English without restrictions on the study design. To minimize publication bias, we excluded conference abstracts from our search. Utilizing MeSH (Medical Subject Headings), Emtree, and relevant keywords, we performed a comprehensive search using terms such as "prostate cancer," "active surveillance," and "family history". The specific search terms used can be found in the Supplementary Material. Applying the predetermined inclusion and exclusion criteria, JJ and DKK, the two authors, individually assessed the titles and abstracts of the initial search findings. In case of discordance, a third assessor, KSC was instructed to facilitate consensus.

2. Trial inclusion criteria and exclusion criteria

Adhering to the PICOS (population, intervention, comparator, outcome, and study design) approach, and following the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines [15], a systematic review and meta-analysis were conducted in this study. The current investigation assessed the impact of a FH of PC (intervention) on the progression of disease (outcome) among patients undergoing AS for PC (population), comparing it to PC patients without a FH (comparators).

We excluded the following cases from our analysis: (1) reviews, correspondence, editorials, conference abstracts, and case reports; (2) studies where outcome data extraction was not feasible; (3) studies investigating the impact of other factors on outcome; and (4) studies that did not report the relevant outcome.

The occurrence of disease progression in patients with PC under AS was the primary endpoint of this study. The secondary outcome was adverse pathological outcomes among the patients who progressed on AS and were treated with radical prostatectomy (RP). Adverse pathology on operation was defined as either upstaging from final biopsy prior to RP, extraprostatic extension, seminal vesicle invasion or lymph node involvement.

3. Data extraction

Two reviewers (JJ and DKK) independently extracted information using a predefined template, which encompassed the subsequent details: author(s) and year of study, geographical location, study structure, duration of follow-up, sample size, definitions of disease progression, outcome results inclusive of event counts, hazard ratios [HRs], odds

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ratios [ORs], 95% confidence intervals [CIs], and p-values, and potential conflicts of interest.

4. Study quality assessments and quality of evidence

The quality of the methodology and risk associated with the studies included were assessed using the Newcastle–Ottawa scale (NOS), a toll that evaluates three main domains: selection, comparability, and outcomes [16]. The assessors considered specific criteria within each domain, including selection bias (four items), comparability bias (one item), and outcomes bias (three items). A single study could receive a maximum of 9 stars, with 6 or more stars were signifying high quality and indicating less risk of bias.

The GRADE (Grading of Recommendations, Assessments, Developments, and Evaluation) approach was employed for evaluating the certainty of evidence [17]. This evaluation encompassed the methodology, precision and inconsistency of results, indirectness, and publication bias. Based on these considerations, the certainty of evidence was classified into four levels: high, moderate, low, and very low. Additionally, GRADEpro software (https://gradepro.org) was utilized to produce the summary of findings table.

5. Statistical analysis

HRs, ORs, and corresponding 95% CIs were extracted from the included studies for assessing the outcomes, with a specific focus on disease progression and adverse pathology on RP. In cases where studies solely presented Kaplan–Meier log-ranks, Wilcoxon p-values, or disease progression rates, we applied Tierney's methods to calculate HR and 95% CI values [18]. For time-to-event outcomes, the extracted data were synthesized using the inverse variance method on the log HR scale.

To evaluate the extent of heterogeneity among the studies, the Cochrane Q test and the I^2 statistic were utilized. A p-value of less than 0.05 from the Cochrane Q test and an I^2 value exceeding 50% were considered indicative of substantial heterogeneity [19]. Conducting sensitivity analysis involved systematically excluding the included studies and assessing the coherence of the results. To accommodate heterogeneity, we applied a random-effects model utilizing the DerSimonian and Laird methods [20]. Funnel plots were employed to examine publication bias, and the presence of symmetry in the funnel plot indicated an absence of publication bias.

All statistical analyses were conducted using Review Manager v.5.3 (The Nordic Cochrane Center, The Cochrane Collaboration, 2008). Two-sided p-values were reported, and statistical significance was defined as $p<0.05$.

RESULTS

1. Systematic review process

The systematic review's procedure was concisely depicted in the PRISMA flow diagram (Fig. 1). A collective of 231 research works were recognized through the initial exploration, with 46 coming from PubMed, 182 from Embase, and 3 from Cochrane Library, respectively. Within this pool, 48 studies were eliminated due to duplication. The titles and abstracts of remaining 183 papers underwent evaluation based on the predefined criteria for inclusion and exclusion, resulting in the exclusion of 172 studies. A thorough examination of the full text of the remaining 11 papers was conducted to determine their eligibility for inclusion in this research. Ultimately, a total of eight studies were included in the final analysis, comprising seven initially chosen studies and one additionally identified through manual search. Comprehensive attributes of the studies included in the selected research were outlined in Table 1 [6,12,13,21-25]. Out of these, one employed a prospective design, whereas the remaining studies adopted a retrospective approach. The primary focus of all studies was to explore the influence of FH on disease progression in patients with PC undergoing AS. The study of Leni et al. [13] set their primary outcome as grade reclassification, defined as grade group (GG) ≥2 at subsequent biopsies. And considering that patients with GG ≥2 at subsequent biopsies included GG ≥3 at follow-up biopsies and the definition of progression of other studies, the authors used the results of patients with GG ≥2 at subsequent biopsies.

2. Disease progression

1) Unadjusted disease progression

Four studies were incorporated into the examination of unadjusted disease progression. The combined HR was 1.06 (95% CI 0.66–1.69; p=0.82), as depicted in Fig. 2A. The assessment of heterogeneity using Cochran Q statistics revealed no significant diversity among the studies (p=0.14), with an I^2 value of 46%.

2) Adjusted disease progression

Five studies were incorporated into the analysis, and their results were combined to calculate the HR. The synthesized HR for adjusted disease progression was 1.31 (95% CI 1.16–1.48; p<0.0001), as depicted in Fig. 2B. The assessment of heterogeneity using Cochran Q statistics revealed no substantial diversity among the studies (p=0.33), with an I^2

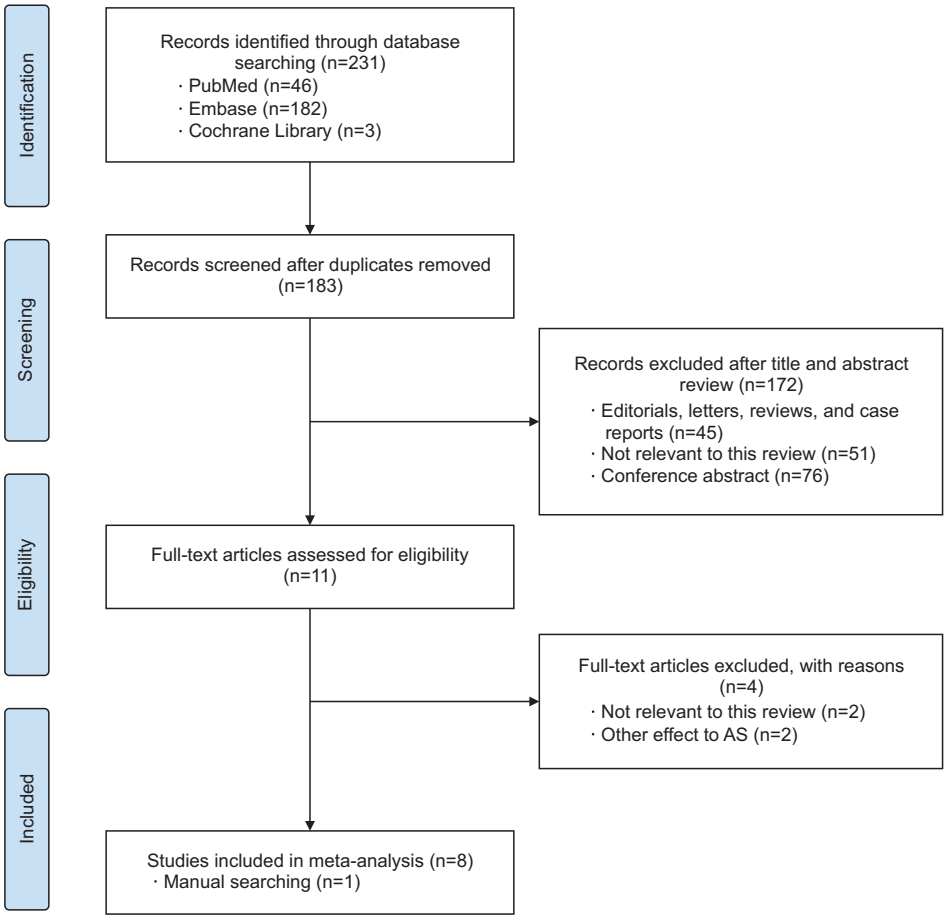

Fig. 1. Flowchart of the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analysis). AS, active surveillance.

value of 13%.

3) Adverse pathology on RP

Two studies were included in the analysis, and their results were pooled to calculate the OR. The pooled OR for adverse pathology on RP was 1.21 (95% CI 0.85–1.73; p=0.28), as shown in Fig. 2C. The assessment of heterogeneity using Cochran Q statistics indicated no significant heterogeneity between the studies (p=0.59), with an I^2 value of 0%.

3. Quality assessment and qualitative risk of bias

The quality assessment results using the NOS were presented in Table 2 [6,12,13,21-25]. All the included studies were rated as high quality, with a score of 7 stars or higher.

We summarized the findings using the GRADE approach to assess the certainty of evidence for unadjusted and adjusted outcomes (Table 3). The certainty of evidence for both were assessed as very low and low, respectively.

To assess publication bias for both the outcomes, funnel plots were used. The symmetry observed in the funnel plots for the outcomes indicates the absence of noteworthy publication bias (Fig. 3).

Conducting a sensitivity analysis involved systematically excluding individual studies to evaluate their influence on the overall results. The findings remained largely consistent after excluding any particular study, underscoring the statistical robustness and reliability of our results.

DISCUSSION

The present study investigated currently available data to access the impact of FH of PC on disease progression in PC patients undergoing AS. We found that FH of PC may be a significant risk factor for disease progression in PC patients undergoing AS. The level of confidence in our study findings was assessed utilizing the GRADE approach. The confidence in the evidence was very low and low for unadjusted and adjusted outcomes, respectively.

AS emerged as a result of a paradigm shift in response to concerns of overdiagnosis and consequently high rates of overtreatment [26]. AS is a conservative treatment strategy in which patients with low-risk PC are monitored (i.e., PSA levels, periodic imaging, and repeat biopsies) until when progression to clinically significant disease requires intervention [4,26]. The eligibility criteria for AS vary widely among institutions and guidelines, involving several key variables

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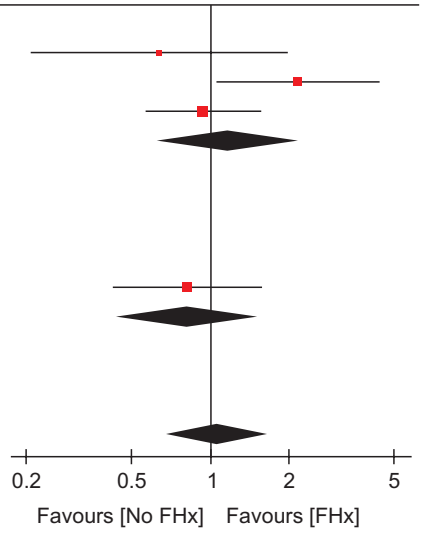
Table 1. Characteristics of studies included in this meta-analysis

Study	Country	Design of study	Period of follow-up (y)	Definition of progression	AS protocol	No. of AS without FH	No. of AS with FH	Conflict of interest
Goh et al. [21] (2013)	United Kingdom	Retrospective	5.6 (range, 0.3–9.1)	1. >50% of cores involved 2. Any increase in primary GS on repeat biopsy 3. Increase in composite GS of ≥8 on repeat biopsy	1. Histologically confirmed prostate cancer 2. Stage T1/2a, N0, M0 3. GS 3+3 4. PSA level of <15 ng/mL with cancer present in <50% of the total number of biopsy cores 5. Gleason 3+4 was only allowed if patients were aged >65 years.	350	73	NA
Iremashvili et al. [22] (2012)	United States	Retrospective	2.9 (IQR, 1.0–4.0)	1. High grade cancer 2. More than 2 positive cores on surveillance biopsy 3. Greater than 20% involvement of any core on surveillance biopsy	1. Biopsy Gleason sum less than 7 2. 2 or fewer positive biopsy cores, 20% or less tumor in any core 3. Clinical stage T1–T2a	205	44	NA
Jibara et al. [12] (2022)	United States	Retrospective	3.7 (IQR, 1.8–6.7)	1. Any upgrading from GG on biopsy	NA	2,413	764	NA
Leni et al. [13] (2023)	Italy	Retrospective	54 mo (IQR, 29–84 mo)	1. GG ≥2 at follow-up biopsies 2. GG ≥3 at follow-up biopsies	1. GG 1 (GS 3+3) 2. Irrespective of the number of positive cores 3. PSA ≤20 ng/mL 4. Clinical stage ≤T2a	537	119	None
San Francisco et al. [23] (2011)	Chile	Prospective	2.4	1. 3 or more positive cores 2. Increased grade (Gleason score 7 or greater) 3. More than 50% of any core involved with cancer	1. Clinically localized disease (T1c–T2c) 2. GS 6 or less with no pattern 4 3. Less than 3 cores positive for cancer 4. No more than 50% of cancer in any core	NA	NA	NA
Schneider et al. [24] (2023)	United States	Retrospective	6.3	1. Biopsy progression either grade (GG1 to ≥GG2 or GG2 to ≥GG3) 2. Volume (≤50% cores positive and ≤50% maximum core involvement on diagnostic biopsy, progressing to either >50% cores positive or >50% maximum core involvement)	1. cT1–T2a 2. GG 1 (and select low-volume GG2) disease with ≤50% positive cores 3. PSA <10 ng/mL	555	300	NA
Selkirk et al. [6] (2015)	United States	Prospective	20 mo	1. A surveillance biopsy with GS ≥7 2. Increase in the number of positive cores (≥4) 3. Increase in percentage involvement of any positive core to ≥50%	1. Clinical stage ≤T2a 2. GS ≤6 3. ≤3 cores positive 4. Maximum involvement of any core <50% 5. Tumor volume ≤5% of total biopsy volume	199	81	None
Shelton et al. [25] (2019)	United States	Retrospective	3.35 (range, 0.53–4.83)	1. Any increase in Gleason score 2. Increase in disease volume to ≥3 cores based on repeat biopsy.	NA	435	113	NA

AS, active surveillance; FH, family history; GS, Gleason score; PSA, prostate-specific antigen; NA, not applicable; IQR, interquartile range; GG, grade group.

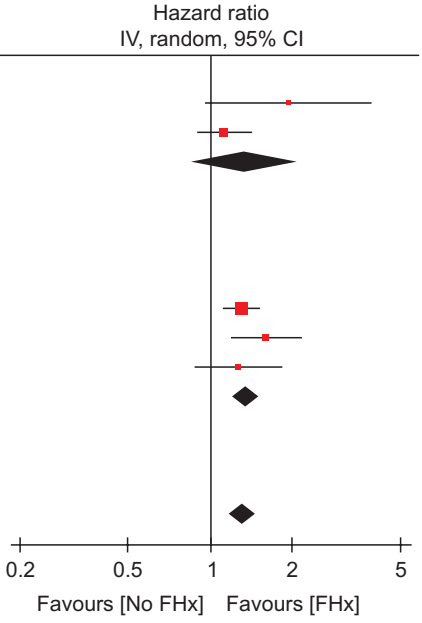
A Disease progression (unadjusted)

Study or subgroup	log [hazard ratio]	SE	Weight	Hazard ratio IV, random, 95% CI
>50% of cores involved or any increased GG				
Goh et al. [21] (2013)	-0.44629	0.569794	13.5%	0.64 [0.21, 1.96]
San Francisco et al. [23] (2011)	0.770108	0.36012	24.9%	2.16 [1.07, 4.38]
Selkirk et al. [6] (2015)	-0.06188	0.255197	34.4%	0.94 [0.57, 1.55]
Subtotal (95% CI)			72.7%	1.16 [0.60, 2.22]
Heterogeneity: Tau^2=0.19; Chi^2=4.75, df=2 (p=0.09); I^2=58%				
Test for overall effect: Z=0.43 (p=0.66)				
Others				
Iremashvili et al. [22] (2012)	-0.19845	0.330369	27.3%	0.82 [0.43, 1.57]
Subtotal (95% CI)			27.3%	0.82 [0.43, 1.57]
Heterogeneity: not applicable				
Test for overall effect: Z=0.60 (p=0.55)				
Total (95% CI)			100.0%	1.06 [0.66, 1.69]
Heterogeneity: Tau^2=0.10; Chi^2=5.51, df=3 (p=0.14); I^2=46%				
Test for overall effect: Z=0.23 (p=0.82)				
Test for subgroup differences: Chi^2=0.53, df=1 (p=0.46); I^2=0%				



B Disease progression (adjusted)

Study or subgroup	log [hazard ratio]	SE	Weight	Hazard ratio IV, random, 95% CI
>50% of cores involved or any increased GG				
San Francisco et al. [23] (2011)	0.65752	0.35760167	3.1%	1.93 [0.96, 3.89]
Schneider et al. [24] (2023)	0.12221763	0.11633097	24.9%	1.13 [0.90, 1.42]
Subtotal (95% CI)			28.1%	1.33 [0.82, 2.15]
Heterogeneity: Tau^2=0.07; Chi^2=2.03, df=1 (p=0.15); I^2=51%				
Test for overall effect: Z=1.15 (p=0.25)				
Others				
Jibara et al. [12] (2022)	0.26236426	0.07850756	45.3%	1.30 [1.11, 1.52]
Leni et al. [13] (2023)	0.47	0.151	15.9%	1.60 [1.19, 2.15]
Shelton et al. [25] (2019)	0.23111172	0.18829045	10.7%	1.26 [0.87, 1.82]
Subtotal (95% CI)			71.9%	1.35 [1.18, 1.53]
Heterogeneity: Tau^2=0.00; Chi^2=1.63, df=2 (p=0.44); I^2=0%				
Test for overall effect: Z=4.55 (p<0.00001)				
Total (95% CI)			100.0%	1.31 [1.16, 1.48]
Heterogeneity: Tau^2=0.00; Chi^2=4.59, df=4 (p=0.33); I^2=13%				
Test for overall effect: Z=4.22 (p<0.0001)				
Test for subgroup differences: Chi^2=0.00, df=1 (p=0.95); I^2=0%				



C Adverse pathology on RP

Study or subgroup	log [odds ratio]	SE	Weight	Odds ratio IV, random, 95% CI
Jibara et al. [12] (2022)	0.131	0.2136	71.3%	1.14 [0.75, 1.73]
Leni et al. [13] (2023)	0.3485	0.3363	28.7%	1.42 [0.73, 2.74]
Total (95% CI)			100.0%	1.21 [0.85, 1.73]
Heterogeneity: Tau^2=0.00; Chi^2=0.30, df=1 (p=0.59); I^2=0%				
Test for overall effect: Z=1.07 (p=0.28)				

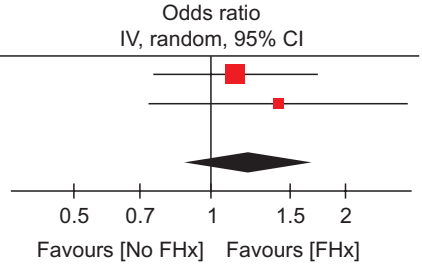


Fig. 2. Forest plots of outcomes (A) disease progression (unadjusted), (B) disease progression (adjusted), (C) adverse pathology on RP. SE, standard error; IV, inverse variance; CI, confidence interval; GG, grade group; FHx, family history; RP, radical prostatectomy.

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Table 2. Results of quality assessment by the Newcastle–Ottawa scale

Study	Selection 1	Selection 2	Selection 3	Selection 4	Comparability A	Comparability B	Outcome 1	Outcome 2	Outcome 3	Score
Goh et al. [21] (2013)	-	*	*	*	*	*	*	*	*	8
Iremashvili et al. [22] (2012)	-	*	*	*	*	*	*	*	*	8
Jibara et al. [12] (2022)	-	*	*	*	*	*	*	*	*	8
Leni et al. [13] (2023)	-	*	*	*	*	*	*	*	*	8
San Francisco et al. [23] (2011)	-	*	*	*	*	*	*	*	-	7
Schneider et al. [24] (2023)	-	*	*	*	*	*	*	*	*	8
Selkirk et al. [6] (2015)	-	*	*	*	*	*	*	*	*	8
Shelton et al. [25] (2019)	*	*	*	*	*	*	*	*	*	9

Table 3. GRADE (Grading of Recommendations, Assessments, Developments, and Evaluation) quality assessment of evidence of each comparison

No. of studies	Certainty assessment						Effect		Certainty	Importance
	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Relative (95% CI)	Absolute (95% CI)		
Unadjusted										
4	Observational studies	Not serious	Not serious	Not serious	Serious[a]	None	HR 1.06 (0.66 to 1.69)	1 fewer per 1,000 (2 fewer to 1 fewer)	●○○○ Very low	Critical
Adjusted										
5	Observational studies	Not serious	Not serious	Not serious	Not serious	None	HR 1.31 (1.16 to 1.48)	1 fewer per 1,000 (2 fewer to 1 fewer)	●●○○ Low	Critical
Adverse pathology on RP										
2	Observational studies	Not serious	Not serious	Not serious	Serious[a]	None	OR 1.21 (0.85 to 1.73)	1 fewer per 1,000 (2 fewer to 1 fewer)	●○○○ Very low	Critical

CI, confidence interval; HR, hazard ratio; RP, radical prostatectomy.
[a]:95% CI includes a HR of 1.0.

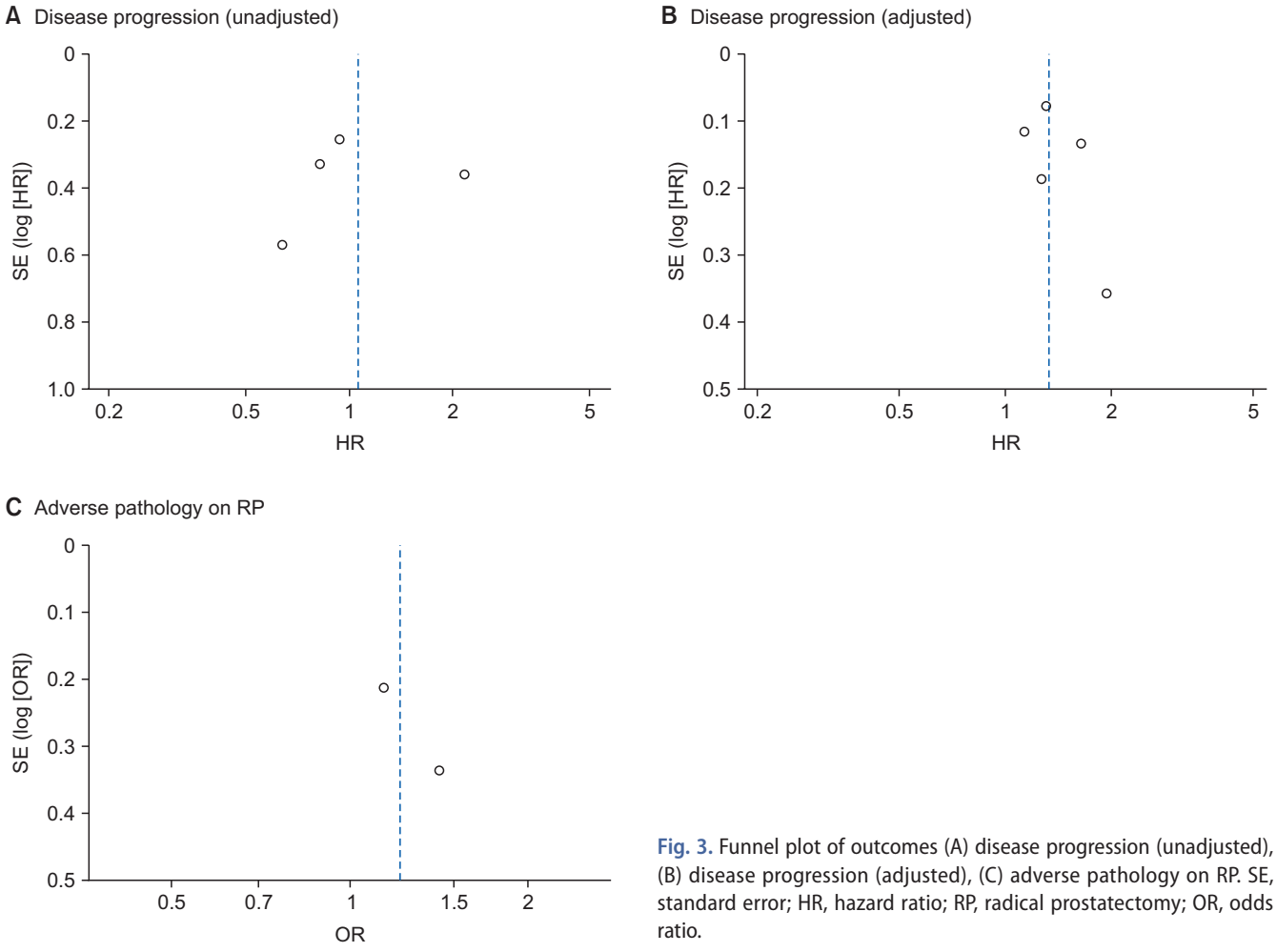

Fig. 3. Funnel plot of outcomes (A) disease progression (unadjusted), (B) disease progression (adjusted), (C) adverse pathology on RP. SE, standard error; HR, hazard ratio; RP, radical prostatectomy; OR, odds ratio.

such as PSA parameters, biopsy Gleason grade, and clinical stage [5,27]. Typical definitions for risk progression in AS encompass biochemical (such as PSA level or rate of change), histologic (such as Gleason grade or expansion of biopsy core involvement), stage (as determined by digital rectal exam or imaging studies), and therapeutic (shifting towards surgery, radiation, or other therapies) [4]. In the present study, all the included studies evaluated histologic progression in PC patients undergoing AC. We found that a FH of PC may be a significant risk factor for disease progression in PC patients undergoing AC.

It is generally understood that a FH of PC is associated with early development of PC and worse oncologic outcomes after RP [8-10]. The risk of PC was increased by 50% to 200% in patients with a FH, and the prevalence of familial disease is 5% to 30% [28,29]. Males with a first-degree FH of PC have a 2 or 3-times greater likelihood of developing PC; having a brother with PC imparts a marginally elevated risk compared to having a father with PC [8,30,31]. The risk of PCa is impacted by the quantity of impacted relatives, proximity of the relative (i.e., first degree vs second degree) [10], the family member's age at diagnosis and age at death from PCa, high-grade illness, and other cancers (e.g., breast or ovarian) [32]. A recent systematic review and meta-analysis indicated that having a first-degree relative with breast cancer is linked with a 1.2-fold heightened risk of PCa [33]. Twin studies have shown that PCa exhibits greater genetic heritability than other common cancers, with a heritability estimated at 58% [34,35]. In addition, men with a FH of PC are more likely to have germline variants that are associated with aggressive PC [36].

Nevertheless, there are divergent findings regarding the influence of FH on survival outcomes in PC. A systematic review and meta-analysis conducted in 2021 indicated that FH of PC did not elevate the likelihood of biochemical recurrence or cancer-specific death in individuals with localized PC [37]. The authors attributed this inconsistency to PSA screening, which potentially increases the likelihood of early detection and timely management for patients with a FH of PC.

The fact that no disparities existed in oncologic results between individuals with a FH of PC and those without was

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considered as a rationale for not including FH of PC in the exclusion criteria for AS, provided they met other eligibility criteria [38,39]. However, since those two studies retrospectively searched for candidate of AS among patients with relatively favorable risk who were treated with RP, they overlooked the duration from the beginning to the end of AS, which is very crucial considering the objective of AS is to avoid overtreatment. The present study found that FH of PC may potentially act as a standalone factor contributing to disease progression of PC in patients undergoing AS.

This investigation marked the inaugural systematic review and meta-analysis examining the impact of FH of PC on patients undergoing AS; however, it has two limitations. First, there was inconsistency in the definition of disease progression among the included studies. Nevertheless, the histologic definition of disease progression was used in all the studies included in this study. Second, eligibility criteria for AS varied among the reviewed studies. However, despite this drawback, a noteworthy strength of this study lies in being the initial systematic review and meta-analysis that explored the effects of FH of PC on disease progression in patients undergoing AS. To the best of our knowledge, there has been only one systematic review, without meta-analysis, of six studies, which suggested that FH of PC should not be employed as an absolute exclusion criterion for AS [11]. Nevertheless, this investigation conducted a meta-analysis by integrating outcomes from eight studies and presented the results suggesting that FH of PC could act as an independent risk factor for disease progression in PC patients undergoing AS. Our study is poised to provide valuable insights for clinicians deliberating the use of AS as a treatment for PC patients with a FH of PC.

CONCLUSIONS

FH of PC may be an independent risk factor for disease progression in PC patients undergoing AS. However, these results do not suggest that AS should not be performed in PC patients with a FH of PC unconditionally. Clinicians should be counseled about the higher risk of disease progression when PC patients with FH are included in an AS. Further studies are necessary to explore the fundamental genetic factors that increase the risk of disease progression in PC patients undergoing AS.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

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None.

AUTHORS' CONTRIBUTIONS

Research conception and design: Do Kyung Kim and Kang Su Cho. Data acquisition: Jinhyung Jeon, Jae Heon Kim, and Jee Soo Ha. Statistical analysis: Do Kyung Kim, Jinhyung Jeon, and Jee Soo Ha. Data analysis and interpretation: Jae Heon Kim and Won Jae Yang. Drafting of the manuscript: Jinhyung Jeon and Won Jae Yang. Critical revision of the manuscript for scientific and factual content: Jinhyung Jeon and Do Kyung Kim. Administrative, technical, or material support: Do Kyung Kim, Jinhyung Jeon, and Jee Soo Ha. Supervision: Kang Su Cho. Approval of the final manuscript: all authors.

SUPPLEMENTARY MATERIAL

Supplementary material can be found via https://doi.org/10.4111/icu.20240053.

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