REVIEW

Prostate Volume is A Predictor of Gleason Score Upgrading after Radical Prostatectomy in Low-Risk Prostate Cancer: A Systematic Review and Meta-analysis

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Purpose: The prediction of Gleason score (GS) upgrading in patients diagnosed with low-risk prostate cancer is particularly important when opting for active surveillance (AS). Thus, we aimed to explore the association between prostate volume and GS upgrading after radical prostatectomy in low-risk prostate cancer through a meta-analysis.

Methods: Multiple databases (Web of Science, MEDLINE, Embase, Scopus, and the Cochrane Library) were searched for eligible studies regarding this issue and reporting sufficient data up to May 2023. Specific search terms such as prostate cancer, radical prostatectomy, and prostate volume were used in our search strategy. Multivariable-adjusted odds ratios (ORs) and associated 95% confidence intervals (CIs) were calculated using random effects models according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses statement.

Results: Twenty studies comprising 14,823 patients who underwent radical prostatectomy matched our eligibility criteria. Moreover, GS upgrading between biopsy and surgical pathological specimens occurs in 32.2% (4,771) of cases. The results showed that smaller prostate volume is significantly associated with GS upgrading in patients with low-risk prostate cancer (OR = 1.08, 95% CI = 1.05–1.11; $P < 0.001$; I-square [I2] = 89.8%) from biopsy to radical prostatectomy after adjusting for confounding factors. Moreover, the results of our subgroup analyses revealed that smaller prostate volume remained a substantial risk factor of GS upgrading in the studies designed as retrospective cohorts and case-control studies performed in America, Italy, Turkey, and China. The findings are robust as indicated by sensitivity and meta-regression analyses.

Conclusion: Smaller prostate volume predicts clinically substantial GS upgrading in patients diagnosed with low-risk prostate cancer after radical prostatectomy. The intriguing findings might be helpful when management options other than surgery are selected based on the inability to recognise the true pathological GS of patients for AS. Further studies focus on risk-stratification and treatment planning for patients with low-grade prostate cancer are still needed to verify our results.

Keywords: prostate volume; gleason score; radical prostatectomy; systematic review; meta-analysis

INTRODUCTION

Patients diagnosed as prostate cancer are risk-stratified according to clinical stage, prostate specific antigen (PSA) and Gleason score (GS)[1]. These pre-treatment parameters are used by urologists to determine risk and provide treatment options for patients. Of these parameters, the GS of the biopsy is an important decision-making factor, as it is usually the most relevant to disease outcome. Therefore, GS plays an important role in predicting prostate cancer risk. Patients diagnosed with prostate cancer are treated by watchful waiting, active surveillance (AS), surgery, radiation and hormonal therapy according to different risk stratification. AS is regarded as the primary treatment for low-risk prostate cancer[2–4]. Tumours present in the core of the needle do not adequately reflect tumours present in the prostate, which is usually considered the most important cause of tumour degeneration. However, any error in the GS assay may lead to inappropriate monitoring of biologically aggressive tumours or the selection of treatment regimens with low cure rates[5]. Moreover, recent research has focused on the inappropriate application of AS based on the recommendation of inaccurate GS obtained from the initial prostate biopsy specimen [6]. There is a difference in GS after biopsy and radical prostatectomy, which has been reported[7]. Interestingly, biopsy GS has a remarkable upgrading rate after radical prostatectomy, which is associated with poorer outcomes[7]. Numerous efforts have been made to determine the preoperative risk factors for predicting GS upgrading. PSA, age and the number of biopsy cores are independent predictors of GS upgrading after radical prostatectomy[8–10]. However, whether prostate volume could also be a reliable predictor for GS upgrading after radical prostatectomy in low-risk prostate cancer is a debated issue.

The association between prostate volume and GS upgrading after radical prostatectomy remains contentious [11–13]. For example, Davies et al.[11] suggested that 31% of clinically low-risk prostate cancer are upgraded after radical prostatectomy at final pathology, whereas Corcoran et al.[12] and Lee et al.[13] reported negative results. Considering that most of the original studies were based on single-centre databases and limited population, we

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Table 1. Characteristics of the included studies

First author year	Study design	Country (duration)	Sample size (No. upgrading, %)	Definition of Gleason score change (from bGS to pGS)	Surgical procedures, n	Biopsy methods	Mean PV, mL	Mean age, years	Mean PSA, ng/mL	Confounding factors
Chung MS. 2013 (18)	Case-control	Korea (2006-2011)	247 (87, 35.2%)	≤ 6 to ≥ 3+4	Open retropubic RP: 58; robot-assisted RP: 189	TRUS biopsy	NA	61.7	9.4	Age, BMI, PSA, PSA density, presence of hypoechoic lesion on TRUS and clinical stage
Corcoran NM. 2012 (12)	Case-control	Australia (2006-2011)	684 (261, 38.2%)	≤ 6 to ≥ 7	RP	TRUS biopsy	41.2	61	6.3	Age, PSA and clinical stage
Davies JD. 2011 (11)	Case-control (2000-2008)	America	1251 (387, 31%)	≤ 6 to ≥ 7	Open retropubic RP: 433; robot-assisted RP: 818	TRUS biopsy	45	59.7	5	Age, PSA, BMI, race, clinical stage, year of surgery, pathological processing method and interval from biopsy to surgery
Dong F. 2008 (19)	Case-control (1999-2007)	America	268 (134, 50%)	≤ 6 to ≥ 7	RP	TRUS biopsy	58.5	60	5.09	Age, date of surgery, clinical stage, preoperative PSA, surgical prostate weight, total number of biopsy cores and indicators of tumor volume, that is percent of biopsy length with cancer, number of cores positive for cancer and maximum percent of cancer in any core
Freedland SJ. 2005 (20)	Case-control	America (1988-2003)	1602 (434, 27.1%)	≤ 6 to ≥ 7	RP	TRUS biopsy	44	62.5	9.3	Age, race, BMI, height, pathologic Gleason sum, year of surgery and presurgery PSA concentration
Gershman B. 2013 (21)	Case-control	America (2001-2010)	1836 (543, 29.6%)	≤ 6 to ≥ 3+4	RP	TRUS biopsy	46.7	59.2	5.62	Age, prostate size, PSA, and race on risk of Gleason score upgrading
Hwang I. 2015 (22)	Case-control	Korea (2008-2012)	324 (154, 47.5%)	≤ 6 to ≥ 7	RP	TRUS biopsy	34.63	67.34	6.01	Age, digital rectal exam, BMI, PSA, PSA density and clinical stage
Jeon HG. 2017 (23)	Retrospective cohort	Korea (2006-2015)	854 (484, 56.7%)	≤ 6 to ≥ 4+3	RP	TRUS biopsy	35.6	64.1	5.05	Age, PSA, prostate volume and number of positive biopsy cores
Kassouf W. 2007 (24)	Case-control	America (1997-2004)	247 (122, 49.4%)	≤ 6 to ≥ 7	RP	TRUS biopsy	37	61	5.5	Age, PSA, clinical stage, biopsy and prostatectomy GS and pathological stage
Kim KH. 2013 (25)	Case-control	Korea (2005-2011)	451 (194, 43%)	≤ 6 to ≥ 7	RP	TRUS biopsy	38.1	64	8.79	Age, PSA, and clinical stage
Lee F. 2013 (13)	Case-control	America (NA)	1348 (443, 33%)	≤ 6 to ≥ 7	RP	TRUS biopsy	NA	NA	NA	Age, PSA, GS, total number of biopsy cores and number of positive cores
Lellig E. 2015 (26)	Case-control	Germany (2004-2007)	308 (118, 38.3%)	≤ 6 to ≥ 7	RP	TRUS biopsy	50	60	NA	Age, PSA, PSA density, GS and positive cores
Leyh-Bannurah SR. 2017 (27)	Retrospective cohort	Germany (2010-2015)	1338 (187, 14%)	≤ 6 to ≥ 7	RP	TRUS biopsy	42	62	5.8	Age, PSA, prostate volume and percentage of positive biopsy cores
Porcaro AB. 2017 (28)	Case-control	Italy (2013-2016)	24 (13, 54.2%)	≤ 6 to ≥ 7	RP	TRUS biopsy	37.7	69.5	6.8	Age, BMI, PSA, PSA density, biopsy positive cores, digital rectal exam and clinical tumour staging
Ngo TC. 2012 (29)	Case-control (2000-2010)	America	1259 (398, 30.7%)	≤ 6 to ≥ 7	RP	TRUS biopsy	40	65	5.8	Age, PSA, race and family history of prostate cancer
Sarici H. 2014 (30) (2007-2013)	Case-control	Turkey	321 (131, 40.8%)	≤ 6 to ≥ 7	RP	TRUS biopsy	45	65.27	10.07	Age, preoperative PSA, prostate volume, number of cores positive for cancer, maximum percent of cancer in any core and time since surgery
Tilki D. 2011 (31)	Case-control	Germany (2004-2007)	684 (203, 29.7%)	≤ 6 to ≥ 7	RP	TRUS biopsy	40	64.3	7.04	Age, BMI and PSA density
Turley RS. 2008 (32)	Case-control	America (1995-2006)	586 (138, 24%)	≤ 6 to ≥ 7	RP	TRUS biopsy	37.3	57.8	5.4	Age, race, BMI, pretreatment PSA, clinical stage, percent of cores involved with cancer, total cores biopsied, year of surgery surgical center and biopsy Gleason score
Vora A. 2013 (33) (2005-2012)	Case-control	America	959 (288, 30%)	≤ 6 to ≥ 7	RP	TRUS biopsy	49.3	67	6.4	Age, clinical stage, serum PSA value, Gleason biopsy score and percent cores positive for cancer
Xu N. 2018 (34) (2015-2016)	Case-control	China	229 (52, 22.7%)	≤ 6 to ≥ 7	RP	TRUS biopsy	39.9	66	15.5	Age, PSA, PSA density, biopsy GS and clinical stage

PSA, prostate-specific antigen; PV, prostate volume; bGS, biopsy Gleason score; pGS, prostatectomy Gleason score; NA, not available; RP, radical prostatectomy; BMI, body mass index; GS, Gleason score; TRUS, Transrectal Ultrasonography.

Table 2. Results of subgroup analyses.

Overall results	Studies, N	Participants,N	OR (95% CI)	p value	p of heterogeneity	I^2 (%)
	20	14,823	1.08 (1.05–1.11)	< 0.001	< 0.001	89.8
Study design						
Case-control	18	12,631	1.13 (1.09–1.18)	< 0.001	< 0.001	90.2
retrospective cohort	2	2,192	1.03 (1.00–1.06)	0.025	0.027	79.6
Country						
Korea	4	1,876	1.05 (0.99–1.11)	0.099	< 0.001	83.1
America	9	9,356	1.18 (1.10–1.26)	< 0.001	< 0.001	91.3
Germany	3	2,330	1.57 (0.90–2.76)	0.115	< 0.001	87.8
Australia	1	684	1.00 (0.98–1.11)	1.000	NA	NA
Italy	1	24	1.25 (1.10–1.42)	0.001	NA	NA
Turkey	1	321	5.67 (2.35–13.65)	< 0.001	NA	NA
China	1	229	1.43 (1.24–1.65)	< 0.001	NA	NA

CI, confidence interval; OR, Odds Ratio; NA, not applicable.

conducted a systematic review and meta-analysis of all clinical trials to further explore the association between prostate volume and GS upgrading after radical prostatectomy in low-risk prostate cancer.

MATERIALS AND METHODS

The systematic review and meta-analysis of original studies were conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guideline[14]. Moreover, a completed PRISMA 2009 checklist was applied to describe the methodology of our study. Thus, no ethical approval and patient consent are required.

Literature search

The Web of Science, MEDLINE, Embase, Scopus, and the Cochrane Library databases were searched for eligible studies until May 2023. The studies investigated the association between prostate volume and GS upgrading after radical prostatectomy in low-risk prostate cancer. No restrictions in language, publication type, or region was applied in the database search. The following combination of medical subject headings (MeSH) and non-MeSH search terms were used in our search strategy: ("prostatic neoplasms" OR "prostate cancer") AND ("radical prostatectomy") AND ("prostate volume" OR "prostate size") AND ("upgrad*" OR "downgrad*"). We also manually searched the reference lists from previous reviews and other relevant articles to identify additional reports of interest. Any discrepancy was resolved through consensus with the coinvestigators.

Inclusion and exclusion criteria

In the initial study selection, two investigators independently screened the titles and abstracts of the articles to identify ineligible reports and note the reasons for exclusion. Potentially eligible studies were subjected to a full-text review. Moreover, the relevance of the studies were confirmed after the study selection process. Studies were included if they met the following eligibility criteria: (1) original studies regarding the association between prostate volume and GS upgrading after radical prostatectomy (i.e. retropubic radical prostatectomy, robot-assisted radical prostatectomy or pure laparoscopic radical prostatectomy) in low-risk prostate cancer; (2) studies reporting the risk estimate (i.e. OR, hazard ratio [HR] and relative risk) with associated 95% CIs; otherwise, sufficient raw data for calculation should be provided if no risk estimates with associated 95% CIs were reported; and (3) observational studies (i.e. retrospective or prospective cohort, case-control or cross–sectional study) published as original articles. Prostate volume was measured using a 7.5 MHZ biplane endorectal transducer (type 8808, B-K Medical, Herlev, Denmark) before prostate biopsy or radical prostatectomy. Prostate volume was determined using the ellipsoid formula with the length, height and width of the total prostate obtained by TRUS (Transrectal Ultrasound). Smaller prostate was defined as prostate volume less than 40 ml according to the included studies. Low-risk prostate cancer is defined as PSA < 10ng/ml, GS score $\leq$ 6, and clinical stage T1 to T2a. We defined upgrading as GS 7 or more based on the pathological result of post-prostatectomy specimen amongst patients with low-risk prostate cancer. In case of duplicate publications, only the most recent or the higher-quality study was retained. Moreover, case reports, letters, reviews and meeting abstracts were excluded. Disagreements were resolved by consensus amongst coinvestigators.

Data extraction and methodological quality assessment

Two investigators independently extracted important information from the included studies. Any discrepan-

Table 3. Results of meta-regression analyses.

Meta-regression			Number of obs = 20		
REML estimate of between-study variance			tau2 = 0.32		
% residual variation due to heterogeneity			I^2 = 91.20%		
Proportion of between-study variance explained			Adj R-squared = -14.10%		
Joint test for all covariates			Model F (2,17) = 0.37		
With Knapp-Hartung modification			Prob > F = 0.6949		
Log OR	**exp(b)**	**Std. Err.**	**t**	***P*>|t|**	**95% CI**
Country	0.9321729	0.0760266	-0.86	0.401	0.78–1.11
Study design	0.9133589	0.4429134	-0.19	0.854	0.33–2.54
_cons	1.378663	0.9128118	0.48	0.634	0.34–5.57

Table 3. CI, confidence interval; OR, Odds Ratio.

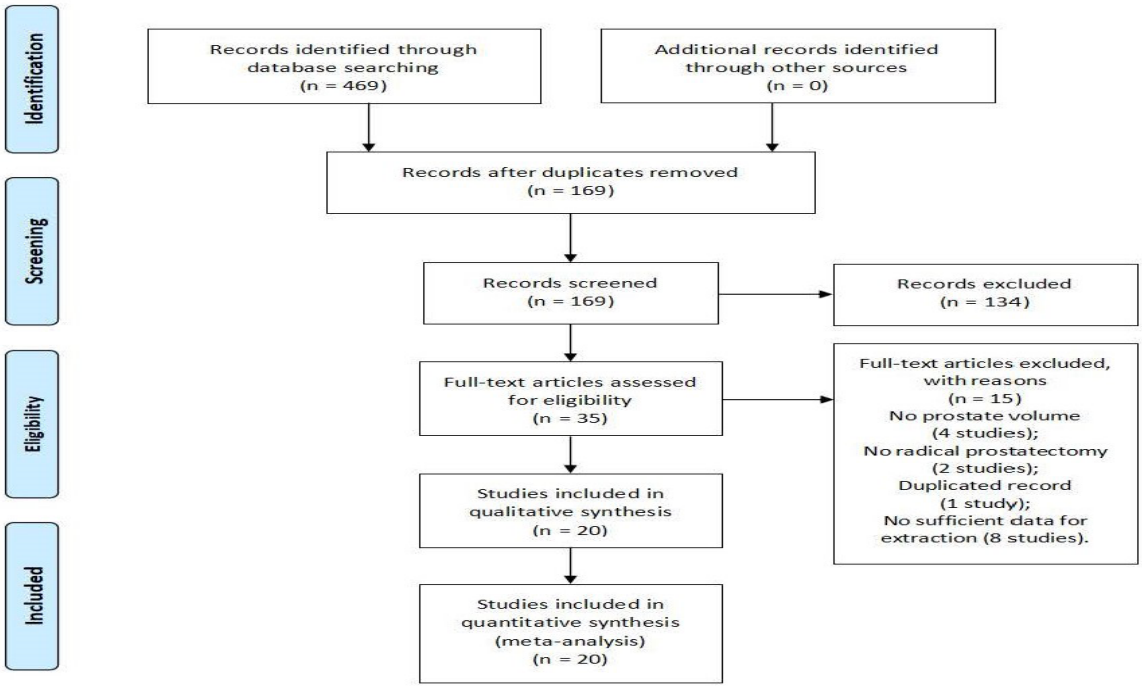

Figure 1. Flow diagram of literature searches according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement.

cy regarding data extraction was resolved by consensus with the coinvestigators. The following basic characteristics were extracted into a standardised Excel (Microsoft Corporation) file: first author, publication year, country, study design, duration of patient recruitment, sample size and number of upgrading cases, surgical procedure, biopsy method, definition of GS change, participant characteristics (i.e. mean age, prostate volume and PSA), risk estimates with associated 95% CIs and confounding factors. In addition, we contacted the primary authors to acquire missing data if eligible studies did not provide sufficient information.

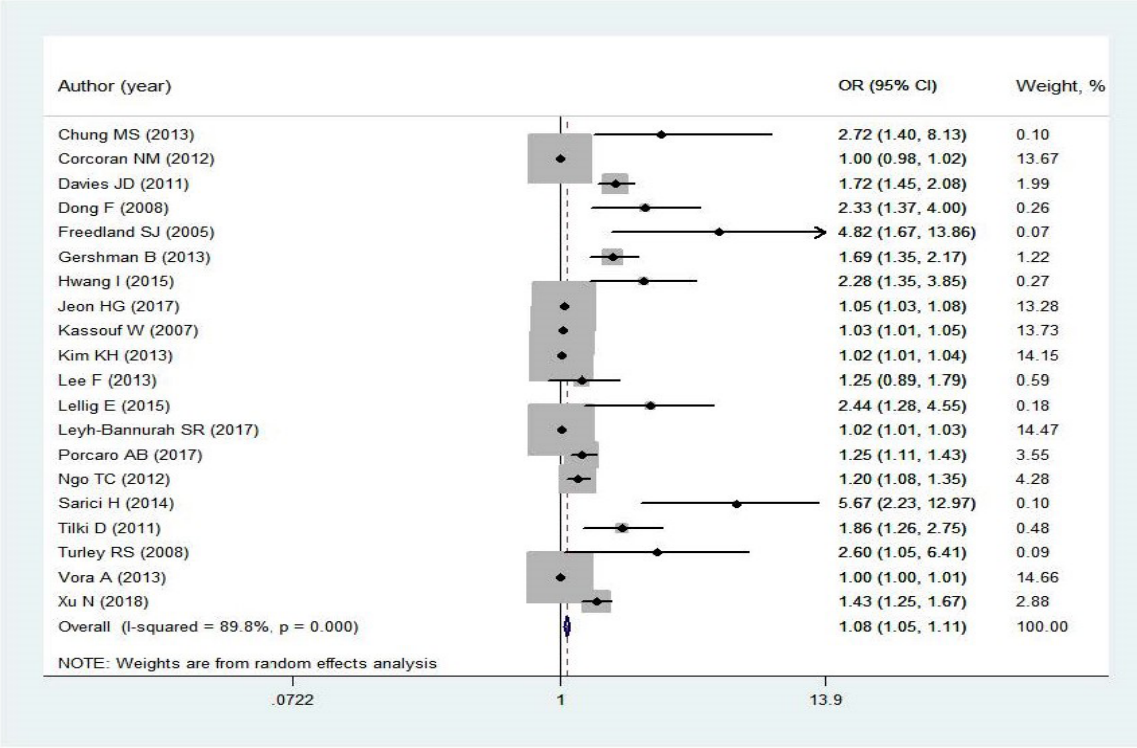

Figure 2. Meta-analysis on association between prostate volume and GS upgrading. CI, confidence interval, OR, Odds Ratio.

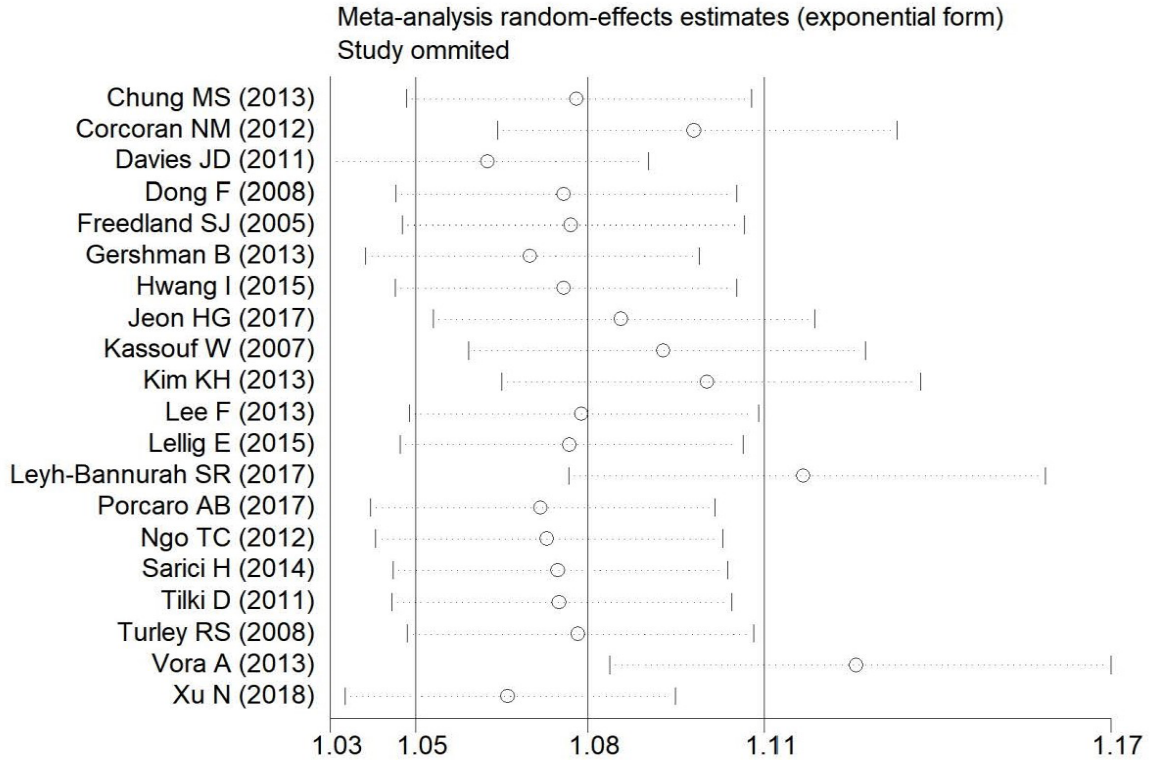

Figure 3. Results of sensitivity analyses.

The quality of the eligible studies was assessed by two investigators by utilising the Newcastle–Ottawa scale (NOS)[15], which consists of 10 items. Each item was assessed as "yes" or "no/unclear," which correspond to "1" and "0," respectively, based on the information extracted from the studies. The total score ranged from 0 to 10 and categorised as follows: a score of 8 to 10 was regarded as high quality, a score of 5 to 7 was regarded as moderate quality, and a score of 5 or below was considered low quality. Disagreements were also settled by discussion amongst coinvestigators.

Data synthesis and analysis

The total risk estimates of the studies were computed using ORs with associated 95% CIs through the STATA statistical software (version 15.0; serial number: 10699393; StataCorp Wyb) to appraise the predictive value of prostate volume in GS upgrading after radical prostatectomy. Forest plots depict the overall results and heterogeneity amongst studies. Furthermore, I^2 test was conducted to assess the effect of heterogeneity on the meta-analysis results. I^2 values of 0%, 25%, 50% and 75% represent no, low, moderate and high heterogeneity, respectively. Random effects model was applied when the heterogeneity is $I2 \geq 50\%$ according to the Cochrane review guidelines[16]; otherwise, a fixed effects model was utilised. Statistical significance was set at $P < 0.05$. Subgroup analyses stratified by country and study design were conducted to investigate the influence of various methodological considerations and patient characteristics on heterogeneity. Moreover, we conducted sensitivity analysis by individually omitting each study to assess the stability and consistency of the results. Meta-regression analysis was also carried out to explore the possible sources of heterogeneity in several variables, and the restricted maximum likelihood method was used for analysis. All of the analyses were based on the Cochran-Mantel-Haenszel Test. Finally, Egger's tests[17] were conducted to assess publication bias.

RESULTS

Study identification and selection

Initially, our search identified 469 records. Only 169 studies were retained after eliminating duplicates. Furthermore, 134 studies were excluded after title and abstract screening, and 35 articles were assessed via full-text review. Finally, 15 articles were excluded for the following reasons: four studies did not report prostate volume; two studies did not report radical prostatectomy; one study was repeated for the same population; eight studies had no sufficient data for extraction (as shown in **Figure 1**). Consequently, 20 observational studies[11–13, 18–34] comprising 14,823 patients who underwent radical prostatectomy were identified for the systematic review and meta-analysis in accordance with the eligibility criteria.

Study characteristics

The basic characteristics of the included studies are outlined in Table 1. Specifically, all of the included studies are retrospective studies (two are retrospective cohorts [23, 27] and eighteen are case-control studies [11–13, 18–22, 24–26, 28–34]) published between 2007 and 2017. The sample size ranged from 24 to 1836 patients. Moreover, GS upgrading between biopsy and surgical pathological specimens occurs in 32.2% (4,771) of the 14,823 cases. Amongst the included studies, nine were conducted in America[11,13,19–21, 24,29,32,33]; four were

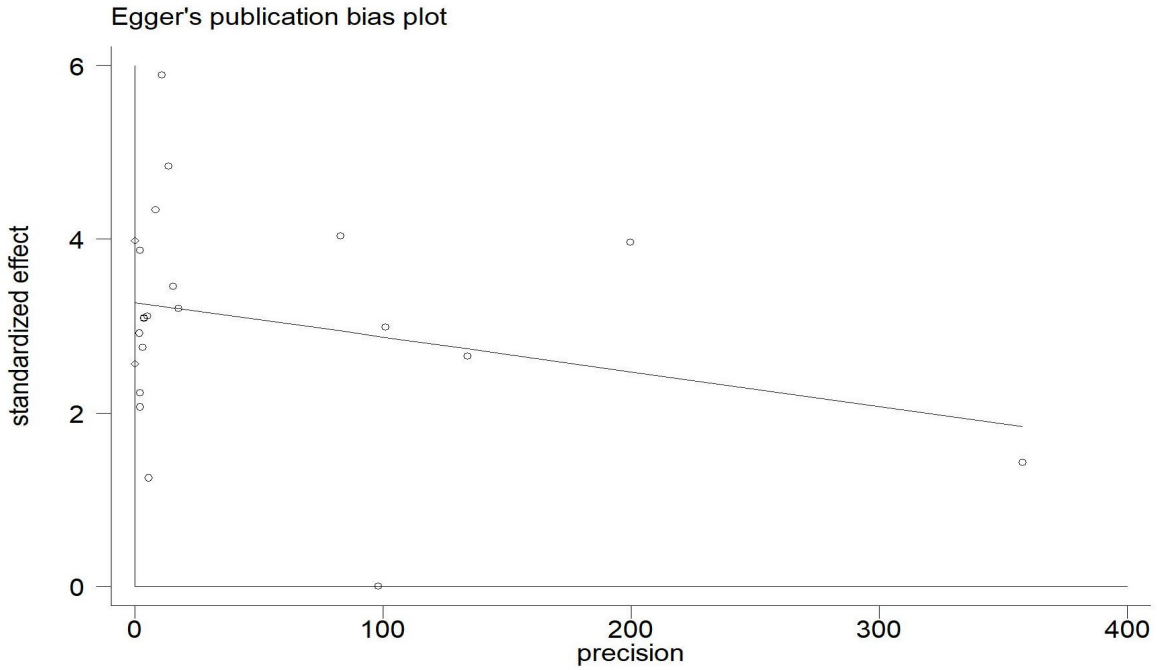

Figure 4. Results of the Egger's test.

conducted in Korea[18,22,23,25]; three were conducted in Germany[26,27,31]; and one study each was conducted in China[34], Turkey[17], Australia[12] and Italy[28]. Only two studies[11,18] clearly stated the use of two surgical methods (open retropubic and robot-assisted radical prostatectomy). All patients of the included studies received transrectal ultrasound-guided prostate biopsy. In addition, the mean prostate volume ranged from 34.63 mL to 58.5 mL. All studies were published in English[11–13, 18–34]. Note that all the included studies reported risk estimates adjusted for confounding factors.

Methodological quality assessment

The methodological quality of the included studies was assessed according to NOS. Twelve studies[11,19–25, 27–30] obtained nine or ten points and were regarded as high quality, seven studies[12,18,26,31–34] acquired seven or eight points and were regarded as moderate quality, and the remaining one study[13] scored five and was considered of low quality.

Association of prostate volume and GS upgrading

Twenty studies[11–13,18–34] provided sufficient data regarding the association between prostate volume and GS upgrading after radical prostatectomy in patients diagnosed with low-risk prostate cancer. The results showed that smaller prostate volume is significantly associated with a significantly increased risk of GS upgrading in patients with low-risk prostate cancer (OR = 1.08, 95% CI = 1.05–1.11; $P < 0.001$; $I^2 = 89.8\%$) from biopsy to radical prostatectomy after adjusting confounding factors. However, substantial heterogeneity was observed. Thus, a random effects model was applied for pooled analysis, and the results are shown in Figure 2. Moreover, the results of our subgroup analyses revealed that smaller prostate volume remained a substantial risk factor of GS upgrading when stratifying studies by different countries except for the studies performed in Korea, Australia and Germany (as shown in **Table 2**). Furthermore, prostate volume is an independent predictor in the case-control studies (OR = 1.13, 95% CI = 1.09–1.18; $P < 0.001$; I2 = 90.2%) and retrospective cohorts (OR = 1.03, 95% CI = 1.00–1.06; $P = 0.025$; $I^2 = 79.6\%$) when stratified by different study designs (as shown in **Table 2**).

Sensitivity analysis revealed that the stability of the results exhibited no remarkable change by omitting each study individually (**Figure 3**). We also conducted a meta-regression analysis to further explore the significant heterogeneity amongst studies, and the results demonstrated that none of the covariates (country, $P = 0.401$; study design, $P = 0.854$) resulted in heterogeneity amongst the included studies. Thus, the adjusted R-squared values of −14.1% indicated that the regressors only slightly contributed to the explanation of the response variables (as shown in **Table 3**). Finally, according to the results of Egger's test, no publication bias was observed by inspection of the formal statistical tests (Egger's test, $P = 0.239$; **Figure 4**).

DISCUSSION

Main findings

We conducted a systematic review and meta-analysis of the predictive value of prostate volume in GS upgrading after radical prostatectomy in patients diagnosed with low-risk prostate cancer. According to the results, smaller prostate volume is an independent predictor for GS upgrading in patients with low-risk prostate cancer from biopsy to radical prostatectomy. Notably, sensitivity analysis revealed that the stability of the results had no remarkable change by omitting each study individually, although the meta-regression could not identify the potential factors that may affect the level of heterogeneity between studies. No publication bias was observed according to the results of Egger's test and funnel plot. We observed that two studies shared negative results

amongst the included studies[12,13]. Corcoran et al.[12] conducted a case-control study that comprise 684 patients who underwent radical prostatectomy with matched diagnostic biopsies. Amongst all patients with GS 6 prostate cancer preoperatively, 261 (67.4%) were upgraded to GS 7 or higher in the final pathology. The results of multivariable analysis suggested that prostate cancer is not a significant predictor of GS upgrading (HR = 1, 95% CI = 0.98–1.02; $P = 0.78$). Moreover, Lee et al.[13] also performed a case-control study that include 1,348 men who underwent radical prostatectomy. Their study indicated that smaller prostate volume is not associated with GS upgrading compared with higher prostate volume. The overall results showed no remarkable changes when we discarded these studies from the meta-analysis; therefore, the statistical results validate the reliability and rationality of the meta-analysis.

Implications for clinical practice

Urology surgeons and radiation oncologists need to identify the clinical predictors of GS upgrading after radical prostatectomy and screen out higher-risk patients, who need further clinical decisions for AS. Several previous studies reported that the independent predictors of GS upgrading in patients diagnosed with low-risk prostate cancer include the higher proportion of positive cores and non-white race[35,36]. The association between prostate volume and risk of GS upgrading is perhaps interesting, as it can reflect the basic prostate biology in smaller glands. Earlier, Uzzo et al.[37] conducted a study that investigated the sampling artifact and detection bias in larger prostate size. Moreover, another research performed by Kulkarni et al.[38] demonstrated that sampling artifact in larger prostate size may lead to GS upgrading in the prevention trial. However, more recent clinical studies on the effect of prostate volume on GS upgrading have reported reverse results, that is, a smaller prostate volume is more likely to be upgraded after adjusting confounding factors[25–29]. Furthermore, the potential mechanisms were explored in several researches. Men with larger prostates tend to have elevated PSA levels driven by BPH (Benign Prostatic Hyperplasia), and thus they may undergo prostate biopsy earlier than other patients, leading to an early cancer diagnosis, when well-differentiated prostate cancer is more likely to occur[20,32,39]. Some studies reported that PSA rise is often not detected early in small prostate volumes. Other studies indicated that smaller prostate volume may be a sign of low androgen activity and the cancers produced in this environment may have inherently more aggressive biological characteristics[20,40]. Nevertheless, future studies regarding this topic should be performed to explore the exact mechanisms behind this phenomenon, which may have clinical implications for risk stratification and treatment options for patients with low-risk prostate cancer.

In general, the meta-analysis exhibited several crucial strengths. Firstly, the present meta-analysis is the first to explore the association between prostate volume and GS upgrading after radical prostatectomy in patients diagnosed with low-risk prostate cancer, and subgroup analyses were conducted by different countries and study designs to determine whether these variables influence the level of heterogeneity according to the PRISMA guidelines. Secondly, multivariable-adjusted risk estimates were applied to minimise confounding factors that may influence the overall results. Finally, the results of the meta-regression and sensitivity analyses validated the reliability and rationality of our study. However, few limitations about the meta-analysis should be noted. Firstly, almost all of the included studies have a case-control design, which might have disadvantages regarding potential missing data and risk of bias. Secondly, inevitable reasons, such as non-extractable data and unavailable full text, might lead to incomplete retrieval. Thirdly, substantial heterogeneity was observed; therefore, the risk of introducing potentially remarkable heterogeneity was imminent even though meta-regression was performed. Unfortunately, we were unable to implement the analysis of different ages, BMI, and time to definitive treatment, because adequate data regarding these issues were not available in the primary literature. Thus, we expect that future studies will focus more on additional risk factors to facilitate the clinical management of patients with prostate cancer. Finally, our understanding of the association between prostate volume and GS upgrading in different surgical procedures and biopsy methods remains insufficient, because these important information were not sufficiently reported in the included studies. Therefore, further high-quality studies are still needed to improve the predictive power of the potential risk factors.

CONCLUSIONS

In conclusion, smaller prostate volume is an independent predictor for GS upgrading in patients diagnosed with low-risk prostate cancer after radical prostatectomy. Our findings might be useful for a more accurate risk stratification and optimal therapy selection in patients with prostate cancer, especially those opting for AS. Nevertheless, further studies are still needed to verify our results and focus on other important risk factors to improve the management of patients with prostate cancer.

CONFLICT OF INTEREST

All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest or non-financial interest in the subject matter or materials discussed in this manuscript.

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