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Research Article

# Prognosis after radical prostatectomy in men older than 75 years: long-term results from a single tertiary center

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ABSTRACT

**Background:** Despite longer lifespans, guidelines for prostate cancer treatment recommend surgery for those with over 10 years of life expectancy, potentially leaving older patients undertreated. This study examines the outcomes of radical prostatectomy (RP) in a large cohort of men older than 75 years.
**Materials and methods:** We retrospectively analyzed 636 patients from a pool of 4,500 RP cases at a single tertiary institution from 2004 to 2022. Patients younger than 75 years or with incomplete records were excluded. Baseline clinical variables, including PSA and biopsy grade group (GG), as well as post-operative pathology and oncological outcomes, were assessed. Achievement of continence based on no pads and ≤1 pad at last follow-up were evaluated.
**Results:** Mean age and PSA were 76.4 years and 15.3 ng/ml, respectively. At biopsy, GG1 and 2 were found in 18.1% and 31.5%, respectively, with 28.5% harboring GG4-5 tumors. After RP, 41.5% had GG upgrade compared to biopsy results, with 46.5% with ≥pT3 tumors. In a mean follow-up of 41.5 months, 82.3% were able to attain total continence of 0 pads, and 89.5% used ≤1 pads at the last follow-up. Overall and cancer-specific mortality was observed in 4.3% and 0.9%, respectively, and biochemical recurrence (BCR) occurred in 20.3% after a median of 154 months. At multivariate analysis, age was not a significant factor for BCR, whereas preoperative PSA, biopsy GG, margin positivity, and lymph node invasion were significant.
**Conclusion:** RP is feasible in men older than 75 years with decent oncological outcome, with absolute age insignificant within this age group. Risk of undertreatment should be acknowledged, and definite treatment must be considered.


## 1. Introduction

There is a clear worldwide shift toward older age in high-income populations, with worldwide expectancy now exceeding 72.5 years at 2020 and the nearby Japanese reaching the highest level at 84.4 years.[1] High-income countries, including South Korea, can expect an average of 80.9 years, and predictions estimate over 90 years of life expectancy at birth in advanced nations with good socioeconomic status and medical care. However, contemporary guidelines for prostate cancer management recommend that radical prostatectomy (RP) be considered for men with a life expectancy of over 10 years,[2–4] leaving older men with the risk of undertreatment despite potentially favorable outcome with definitive therapy. The concern for suboptimal treatment in geriatric men has been continuing since the early 2000s,[5] and with advances in surgical techniques allowing safer practice with minimized complications, there is a need for re-evaluation of benefits and outcomes of RP in older men. Therefore, this study retrospectively reviewed one of the largest cohorts of ≥75-year-old patients

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diagnosed with prostate cancer undergoing RP as primary treatment at a large-volume tertiary institution.

## 2. Materials and methods

A total of 636 patients were included in the final analysis after a retrospective review of 4,500 RP cases conducted at Seoul National University Bundang Hospital, South Korea, from 2004 to 2022, after approval by the institutional review board (IRB B-2108-705-105). Patients diagnosed before the age of 75 years or those with incomplete medical records as well as prior systemic treatment were excluded. Clinical variables including age, comorbidities, preoperative prostate volume, prostate-specific antigen (PSA), biopsy grade groups (GGs), number of previous biopsies, clinical stage, operative time, nerve-saving, and pathologic results after RP were assessed, as well as mortality and achievement of continence. Surgical methods of open, laparoscopic, and robotic were chosen at the individual surgeon's discretion. Robotic RP was performed with the da Vinci surgical system (Si, X, or Xi). Degree of nerve-saving was preoperatively and intraoperatively decided based on baseline voiding function, biopsy GG, clinical stage, and extent of extraprostatic invasion. Continuous variables are represented as mean ± standard deviation, and categorical variables as absolute number and percentage. All statistical analyses, including Student *t* tests for continuous variables, Pearson Chi-square tests for categorical variables, Kaplan-Meier curves for survival, and logistic regression analyses, were performed with SPSS package version 26.0 (Statistical Package for Social Sciences, Chicago, IL, USA). Statistical significance was given for 2-tailed $P$-value <0.05.

## 3. Results

### 3.1. Baseline characteristics

Preoperative baseline characteristics are outlined in Table 1. Included patients were mean 76.4 years old with comorbidities of diabetes mellitus and hypertension identified in 24.5% and 56.6% of all patients, respectively, and a mean body mass index of 24.1 ± 2.9 kg/m$^2$. Mean PSA and prostate volume was 15.3 ± 22.9 ng/ml and 39.2 ± 16.8 ml, respectively. The calculated PSA density was 0.44 ± 0.69. At biopsy, low-intermediate risk GG1 and 2 was identified in 18.1% and 31.5% of all patients, respectively, with intermediate-high-risk biopsy GG identified in over 50%. To note, 20.3% and 8.2% of cases had GG4 and 5, respectively, and underwent radical surgery based on otherwise good functional status. In total, 68 patients (10.7%) had negative previous biopsy, and the rest were identified *de novo*. High clinical stage over T3 was suspected in 31.3%.

**Table 1**
Preoperative clinical characteristics

| Variables | Mean ± SD or n (%) |
|---|---|
| Age, years | 76.4 ± 1.6 |
| Body mass index, kg/m$^2$ | 24.1 ± 2.9 |
| Diabetes mellitus, n | 156 (24.5) |
| Hypertension, n | 360 (56.6) |
| Prostate volume, ml | 39.2 ± 16.8 |
| PSA, ng/ml | 15.3 ± 22.9 |
| PSA density, ng/ml/ml | 0.44 ± 0.69 |
| Biopsy grade group | |
| 1 | 115 (18.1) |
| 2 | 200 (31.5) |
| 3 | 138 (21.8) |
| 4 | 129 (20.3) |
| 5 | 52 (8.2) |
| Previous biopsy, n | 1.1 ± 0.5 |
| 1 | 565 (89.3) |
| ≥2 | 68 (10.7) |
| Clinical ≥T3, n | 199 (31.3) |

Data are presented as mean ± SD and n (%).
PSA, prostate-specific antigen; SD, standard deviation.

### 3.2. Operative characteristics

Robotic RP was performed in the majority of patients (89.0%), with 10.8% undergoing open and 0.2% laparoscopic surgery (Table 2). The mean operative time was 155.6 ± 49.9 minutes. The estimated blood loss was 213.9 ± 388.2 ml, with intraoperative or postoperative transfusion done in 4.7%. Nerve-saving was performed in 64.7%. In a comparative analysis between robotic and open RP, the difference in total operation time was not significant (154.7 ± 49.8 min vs. 161.1 ± 46.7 min, $P = 0.311$). However, estimated blood loss (136.1 ± 107.4 ml in robotic vs. 735.9 ± 890.9 ml in open RP, $P < 0.001$) and transfusion rates (0.5% in robotic vs. 37.7% in open RP, $P < 0.001$) were significantly better with the robotic

**Table 2**
Univariate and multivariate regression analysis for pGG ≥ 3 and pGG ≥ 4

| Variables | Mean ± SD or n (%) |
|---|---|
| Operation type, n | |
| Open RP | 69 (10.8) |
| Robotic RP | 566 (89.0) |
| Laparoscopic RP | 1 (0.2) |
| Operation time, min | 155.6 ± 49.9 |
| Estimated blood loss, ml | 213.9 ± 388.2 |
| Transfusion rate, n | 30 (4.7) |
| Nerve saving, n | 291 (64.7) |

Data are presented as mean ± SD and n (%).
RP, radical prostatectomy; SD, standard deviation.

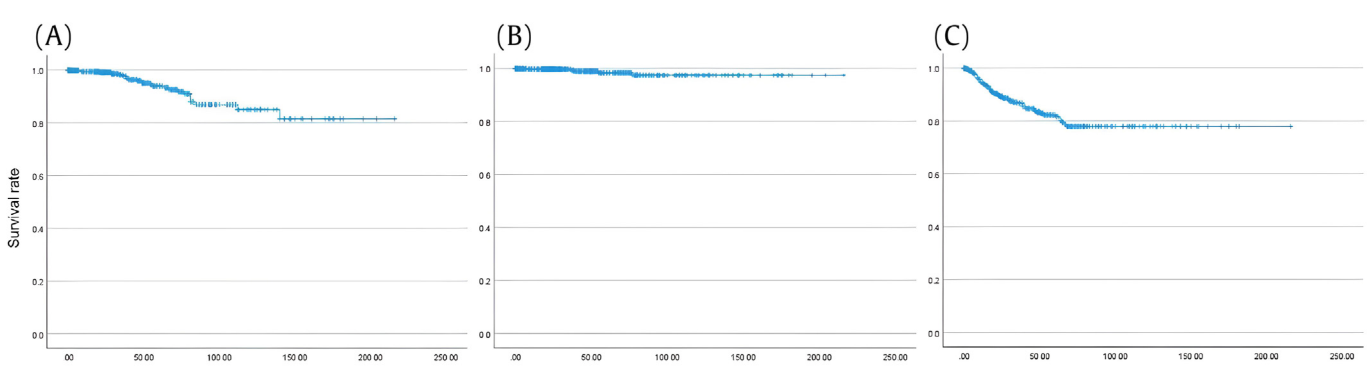


**Fig. 1.** Kaplan-Meier curves for (A) overall survival, (B) cancer-specific survival, and (C) biochemical recurrence-free survival.

**Table 3**
Pathologic and oncologic outcomes

| Variables | Mean ± SD or n (%) |
|---|---|
| RP volume, cc | 44.2 ± 16.6 |
| Tumor volume, cc | 8.2 ± 8.9 |
| RP grade group | |
| 1 | 17 (2.7) |
| 2 | 215 (34.0) |
| 3 | 234 (37.0) |
| 4 | 48 (7.6) |
| 5 | 118 (18.7) |
| Pathologic ≥T3, n | 294 (46.5) |
| Presence of node metastasis, n | 22 (5.5) |
| Positive LNs, n | 0.12 ± 0.66 |
| Margin positivity, n | 191 (30.2) |
| Seminal vesicle invasion, n | 130 (20.6) |
| Bladder neck invasion, n | 45 (7.1) |
| Angiolymphatic invasion, n | 166 (26.1) |
| Perineural invasion, n | 545 (86.2) |
| Pad-free status, n | 470 (82.3) |
| ≤1 pad status, n | 511 (89.5) |
| BCR, n | 129 (20.3) |
| Cancer-specific mortality, n | 6 (0.9) |
| Overall mortality, n | 27 (4.3) |

Data are presented as mean ± SD and n (%).
BMI, body mass index; PSA, prostate-specific antigen; PIRADS, Prostate Imaging-Reporting and Data System; SD, standard deviation.

approach. Also, more patients underwent nerve-sparing techniques with robotic surgery (71.3% vs. 27.3% in open, $P < 0.001$), likely due to the technical ease and visibility of neurovascular bundle structures.

### 3.3. Outcome after RP

Tumor volume at RP specimens showed a mean of 8.2 ± 8.9 cc (Table 3). GG at pathology was upgraded in 262 (41.5%) compared to biopsy results, with 2.7%, 34.0%, 37.0%, 7.6%, and 18.7% harboring GG1 to 5 tumors, respectively. Compared to 31.3% ≥cT3 suspected prior to surgery, pathologic staging showed 46.5% to have ≥pT3, with upstaging identified in 135 patients (21.4%). Node metastasis was found in 5.5%, with a mean of 0.12 ± 0.66 positive nodes. Positive margins were found in 30.2%, with similar rates regardless of operation method (31.9% of open and 30.2% of robotic RP, $P = 0.297$). Invasion to the seminal vesicles and bladder neck were identified in 20.6% and 7.1%, respectively. Angiolymphatic and perineural invasions were found in 26.1% and 86.2%.

After a mean follow-up of 41.5 ± 40.1 months (median, 30.0 months), 82.3% of all men were able to achieve total continence with no pads at the last follow-up. In total, 89.5% showed continence with ≤1 pad used. All-cause mortality was observed in 27 (4.3%) of all patients, with a mean survival of 53.1 ± 31.8 months (Fig. 1). Only 6 (0.9%) men died due to prostate cancer–related causes. Post-RP biochemical recurrence (BCR) occurred in 20.3% after a median BCR-free survival of 154 months [95% confidence interval (CI), 116.4–191.6]. At univariate analysis for BCR, preoperative PSA [hazard ratio (HR), 1.026; 95% CI, 1.016–1.038; $P < 0.001$], biopsy GG (HR, 1.832; 95% CI, 1.543–2.176; $P < 0.001$), clinical ≥T3 (HR, 3.780; 95% CI, 2.530–5.646; $P < 0.001$), margin positivity (HR, 4.634; 95% CI, 3.085–6.959; $P < 0.001$), and lymph node invasion (HR, 5.124; 95% CI, 2.086–12.586; $P < 0.001$) showed statistical significance (Table 4). After multivariate analysis, PSA (HR, 1.010; 95% CI, 1.001–1.019; $P = 0.023$), biopsy GG (HR, 1.511; 95% CI, 1.203–1.897; $P < 0.001$), margin positivity (HR, 2.964; 95% CI, 1.784–4.924; $P < 0.001$), and lymph node invasion (HR, 2.678; 95% CI, 1.021–7.026; $P = 0.045$) were shown to be independent predictors of BCR. Absolute age or associated comorbidities were not significant.

## 4. Discussion

In order to reflect the continuously improving life expectancy both worldwide and domestically, a subcohort of ≥75-year-old men undergoing RP in a large-volume tertiary institution were retrospectively reviewed for case-series analysis. After a mean follow-up duration of 41.5 months, RP resulted in less than 1% of cancer-related deaths, with nearly 90% able to achieve continence after surgery. Pathologic analysis indicated that a large percentage (41.5%) had GG upgrade compared to prediction from biopsy, suggesting that these groups of patients may have a higher rate of underestimated tumors with potential poor prognosis if conservatively treated via active surveillance or watchful waiting. Our results indicate that if the patient is not contraindicated for surgery, RP may benefit survival, and that age itself is not significant for poor outcomes in these patients. As indicated from the regression analysis, men with initially high PSA (HR, 1.010) and biopsy GG (HR, 1.511) should be counseled for active therapy at biopsy, as they are likely to experience BCR even after RP. If positive margins or nodal metastasis are identified, adjuvant radiation or androgen deprivation therapy should be considered, as done in younger patients.

In our study, nearly 90% of all patients underwent robotic RP, resulting in a shorter estimated blood loss and transfusion that replicates the advantages of RP for minimizing trauma to the surrounding extraprostatic structures and handling of the major vessels including the dorsal venous complex.[6] The higher percentage may reflect the patient preference as well as that of the surgeon to perform the operation in a more safe and efficient manner to ensure complete removal of tumor as well as achievement of early continence in patients with old age who may otherwise easily suffer from voiding dysfunction in conventional open methods.

A recently reported assessment of treatment patterns for Korean men aged ≥75 years showed that RP is chosen as the primary treatment in 13.1% (114/873), following androgen-deprivation therapy (70.3%, 614/837).[7] Patients undergoing RP were more

**Table 4**
Univariate and multivariate logistic regression analysis for biochemical recurrence

| Variables | Univariate | | | Multivariate | | |
|---|---|---|---|---|---|---|
| | HR | 95% CI | P | HR | 95% CI | P |
| Age | 1.016 | 0.899–1.148 | 0.800 | 0.917 | 0.788–1.067 | 0.262 |
| Diabetes mellitus | 0.776 | 0.485–1.240 | 0.288 | | | |
| Hypertension | 1.126 | 0.761–1.667 | 0.553 | | | |
| PSA | 1.026 | 1.016–1.038 | <0.001 | 1.010 | 1.001–1.019 | 0.023 |
| Biopsy GG | 1.832 | 1.543–2.176 | <0.001 | 1.511 | 1.203–1.897 | <0.001 |
| Clinical ≥T3 | 3.780 | 2.530–5.646 | <0.001 | 1.673 | 0.987–2.836 | 0.056 |
| Margin positivity | 4.634 | 3.085–6.959 | <0.001 | 2.964 | 1.784–4.924 | <0.001 |
| Lymph node invasion | 5.124 | 2.086–12.586 | <0.001 | 2.678 | 1.021–7.026 | 0.045 |

HR, hazard ratio; CI, confidence interval; PSA, prostate-specific antigen; GG, grade group.

likely to have lower PSA and GG as well as a lower risk of nodal or organ metastasis (all $P < 0.001$). Good functional status [odds ratio (OR), 0.066] and younger age (OR, 0.066) were significant predictors of RP versus hormonal or radiation therapy, indicating that if the patient is fit for surgery, RP is preferred. This is supported by population-based analysis from the Korean healthcare database noting a notable two-fold increase in RP (22.4% to 45.4%) and decreasing proportions of hormonal therapy (60.3% to 45.4%),[8] suggesting that with evolving techniques, surgery is frequently performed and well-tolerated.

At the last clinic visit, 89.5% of all patients at our institution showed ≤1 pad used, with 82.3% achieving complete continence (0 pads), which is better or comparable to that described in previously published literature. A retrospective review of 5,624 patients from an Australian database has shown that men aged ≥75 years were more likely to have significantly decreased pad-free rates of 50% compared to 86% in men younger than 55 years.[9] Social continence of ≤1 pad/day was also worsened with age, decreasing from 98% to 85% in men aged <55 years and ≥55 years, respectively. On the other hand, Greco et al have reported a similarly high achievement of continence at 12 months in ≥70-year-old men compared to those aged <70 years, corroborating evidence from open retropubic RP.[10] Kundu et al, from their experience in 3,477 retropubic RP cases, showed that 93% were able to achieve continence overall, and while the rate of postoperative complications was significantly associated with older age ($P < 0.0001$), 86% of men older than 70 years were continent after RP, indicating that with proper technique, the age factor can be overcome.[11] A study on a large patient cohort consisting of 8,296 patients by Mandel et al further supports the relatively high rate of continence achieved in our study, as they reported 1-year continence of 86.5% in a subcohort of men older than 75 years with better outcome with nerve-sparing techniques and low tumor stage, although this patient population included only 166 (2.0%) men aged ≥75 years.[12] Earlier experience of robotic RP in 2010 indicated relatively lower rates of achieving continence, with only 59% probability of achieving continence at 1 year for our study population,[13] implicating that the implementation of modern nerve-saving techniques and advances in robotic surgery as well as surgeon dexterity may critically impact functional outcomes.

There is a lack of consensus on whether age at diagnosis is associated with poor pathology, due to the wide variance in cancer behavior.[14] Men diagnosed over 75 years old have been shown to have higher rates of Gleason 5 patterns compared to the majority diagnosed between 55 and 75 years old.[15] The results of our study replicate such findings, as our study population had over 25% GG4-5 and a high rate of GG upgrade and upstaging. Age is certainly a critical factor in the decision for definitive treatment, and many nomograms are developed for the prediction of life expectancy in men diagnosed with prostate cancer, with variable discriminatory performance.[16] The model developed by Walz et al utilizes age, Charlson comorbidity index, and type of treatment and reports a high level of discrimination (84.3%).[17] However, such models tend to be underused in real life, potentially leading to undertreatment in older men who may actually benefit from curative therapy. In our study, only 4.3% (27/636) of the included patients suffered from all-cause mortality after RP, with 6 (0.9%) men dying from prostate cancer–related causes. Even in those patients who died during follow-up, the mean survival duration was a reasonable 53.1 ± 31.8 months, suggesting that men seemingly unfit for surgery based on age alone should consider more active treatment. A recent study on mortality after RP indicates that, at least domestically, RP is well tolerated.[18] Our study also showed that absolute age at diagnosis was further unrelated to BCR, whereas high PSA and biopsy GG, margin positivity, and lymph node invasion were considered possible factors. These factors are in line with other studies not restricted to old age,[19,20] providing further evidence for equal treatment in older patients without restriction due to absolute age alone.

Our study is not without limitations. Due to its retrospective design over a relatively long period, we cannot exclude selection bias as well as survival and outcome benefits due to changes in surgical technique and clinical practice. The difference due to open and robotic RP may have had an influence in achieving continence, explaining the relatively higher rates compared to previous studies. Also, this cohort only assessed patients who received RP as definitive treatment and thus does not represent the outcome in ≥75-year-old patients diagnosed with prostate cancer who may have otherwise opted for radiation therapy. Also, as this was a case-series analysis, there is a lack of comparison to younger age groups, which was outside the scope of this particular article. However, to the best of our knowledge, our study included one of the largest populations of patients undergoing RP and provided evidence for RP with curative intent for this age group. Future prospective trials are needed to validate our results.

## 5. Conclusion

RP in ≥75-year-old men is a reasonable option, especially considering the high achievement of continence and good survival outcomes. Geriatric patients with high functional status eligible for surgery should be considered for RP with curative intent. Larger cohorts in clinical trials should be assessed to confirm our findings.

## Conflicts of interest

All authors have no conflict of interest to declare.

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## References

1. Cambois E, Duthé G, Meslé F. *Global Trends in Life Expectancy and Healthy Life Expectancy*. Oxford University Press; 2023.
2. Network, N.C.C.. *Prostate Cancer* (Version 3.2022) 2022.
3. EAU. *EAU Guidelines. Edn. presented at the EAU Annual Congress Amsterdam 2022*. Arnhem, The Netherlands: EAU Guidelines Office; 2022.
4. Chin HW, Kim J, Rasp G, Hristov B. Prostate cancer in seniors: Part 1: Epidemiology, pathology, and screening. Fed Pract 2015;32:41S.
5. Schwartz KL, Alibhai SM, Tomlinson G, Naglie G, Krahn MD. Continued undertreatment of older men with localized prostate cancer. Urology 2003;62:860.
6. Perera S, Fernando N, O'Brien J, Murphy D, Lawrentschuk N. Robotic-assisted radical prostatectomy: learning curves and outcomes from an Australian perspective. Prostate Int 2023;11:51.
7. Park DJ, Kang HW, Kwon SY, Seo YJ, Lee KS, Kim BH, et al. Current treatment patterns within 1 year after prostate cancer diagnosis in Korean patients over 75 years old: a retrospective multicenter study. Prostate Int 2023;11:34.
8. Park J, Suh B, Shin DW, Hong JH, Ahn H. Changing patterns of primary treatment in Korean men with prostate cancer over 10 years: a nationwide population based study. Cancer Res Treat 2016;48:899.
9. Gondoputro W, Thompson J, Evans M, Bolton D, Frydenberg M, Murphy DG, et al. How does age affect urinary continence following robot-assisted radical prostatectomy? A prospective multi-institutional study using independently collected, validated questionnaires. J Urol 2022;207:1048.
10. Greco KA, Meeks JJ, Wu S, Nadler RB. Robot-assisted radical prostatectomy in men aged > or =70 years. BJU Int 2009;104:1492.
11. Kundu SD, Roehl KA, Eggener SE, Antenor JA, Han M, Catalona WJ. Potency, continence and complications in 3,477 consecutive radical retropubic prostatectomies. J Urol 2004;172:2227.
12. Mandel P, Graefen M, Michl U, Huland H, Tilki D. The effect of age on functional outcomes after radical prostatectomy. Urol Oncol 2015;33:203 e11.

13. Shikanov S, Desai V, Razmaria A, Zagaja GP, Shalhav AL. Robotic radical prostatectomy for elderly patients: probability of achieving continence and potency 1 year after surgery. J Urol 2010;183:1803.
14. Delongchamps NB, Wang CY, Chandan V, Jones RF, Threatte G, Jumbelic M, et al. Pathological characteristics of prostate cancer in elderly men. J Urol 2009;182:927.
15. Ji G, Huang C, Song G, Xiong G, Fang D, Wang H, et al. Are the pathological characteristics of prostate cancer more aggressive or more indolent depending upon the patient age? Biomed Res Int 2017;20171438027.
16. Panaiyadiyan S, Kumar R. Prostate cancer nomograms and their application in Asian men: a review. Prostate Int 2023.
17. Walz J, Gallina A, Saad F, Montorsi F, Perrotte P, Shariat SF, et al. A nomogram predicting 10-year life expectancy in candidates for radical prostatectomy or radiotherapy for prostate cancer. J Clin Oncol 2007;25:3576.
18. Pak S, You D, Jeong IG, Lee DE, Kim SH, Joung JY, et al. Cause of mortality after radical prostatectomy and the impact of comorbidity in men with prostate cancer: a multi-institutional study in Korea. Cancer Res Treat 2020;52:1242.
19. Lee W, Lim B, Kyung YS, Kim CS. Impact of positive surgical margin on biochemical recurrence in localized prostate cancer. Prostate Int 2021;9:151.
20. Hong SK, Song SH, Kim HJ, Lee HS, Nam JH, Lee SB. Temporal changes of PIRADS scoring by radiologists and correlation to radical prostatectomy pathological outcomes. Prostate Int 2022;10:188.