INTRODUCTION
Prostate cancer is the second most frequently diagnosed cancer and the sixth leading cause of cancer death in men, accounting for 14% of the total new cancer cases and 6% of the total cancer deaths in men (GLOBOCAN 2008). The incidence of prostate cancer in China is lower than in Western countries. However, due to widespread use of serum prostate-specific antigen (PSA) testing and transrectal ultrasound (TRUS)-guided needle biopsy, an increasing number of patients with localized prostate cancer have been diagnosed every year in China (from 1.6 × 10^5 in 2002 to 4.3 × 10^5 in 2008).^2,3^

Radical prostatectomy (RP) is considered the standard of care for patients with localized prostate cancer. This was traditionally performed by open retropubic RP. During the last decade, minimally invasive surgery (laparoscopic and robot-assisted laparoscopic RP; LRP and RALP, respectively) has become popular worldwide. LRP has already become the gold standard for the treatment of localized prostate cancer in China. However, in Western countries, ~20% of patients who undergo RP have a positive surgical margin (PSM) in the final pathological analysis, which is associated with a higher risk of local recurrence and distant metastasis and may have a direct influence on survival and prognosis. The reported PSM rate in China is higher than that in Western countries. Therefore, it is crucial to find preoperative predictors for PSM that can contribute to optimizing surgical treatment of patients with prostate cancer.

In this study, we retrospectively examined 296 patients with prostate cancer who underwent LRP by a single experienced surgeon at our center, to define possible preoperative predictors of PSM.

PATIENTS AND METHODS
After diagnosis with TRUS-guided needle biopsy, 296 consecutive patients with prostate cancer received LRP by a single surgeon (GHQ) with experience of >200 cases between January 2011 and February
Preoperative predictors of PSM after LRP
R Yang et al

2015, at our center. Patients who had a previous transurethral resection of the prostate were excluded. All patients had magnetic resonance imaging (MRI) to assess whether extraprostatic extension (EPE) existed before surgery. Bone scan was used to rule out the metastatic bone disease. All patients had good physical performance and a long life expectancy. Informed consent was obtained from each patient after the surgeon reviewed the peer-reviewed data on cancer-specific survival, complication rates, expected convalescence period, and other alternative treatments (external beam radiotherapy or brachytherapy). All patients underwent at least 6 months of follow-up.

Systematic biopsies included 12 cores from separate regions, with six cores from each lobe. All biopsies were performed with an 18 gauge × 2 cm Tru-cut core biopsy needle (Bard, Tempa, AZ, USA) under TRUS guidance. The pathological evaluation focused on Gleason score, percentage of tumor per core, number of positive cores, perineural invasion (PNI), and tumor laterality. PNI was defined as the presence of prostate cancer tracking along or around a nerve within the perineural space.

Laparoscopic prostatectomy was performed under general anesthesia, using a transperitoneal approach described by Hasan and Gill. The procedure began with a wide inverted U-shaped incision along the peritoneum of the anterior abdominal wall to drop the bladder posteriorly and enter the Retzius space. The patient was dissected laterally on either side to expose and incise the endopelvic fascia. After ligating the dorsal venous complex, the bladder neck was transected precisely to identify the seminal vesicles and vas deferens, which were completely mobilized bilaterally. Denonvilliers’ fascia was incised to enter the prorectal space, and the lateral bladder pedicle controlled on each side. The neurovascular bundles were identified and precisely released using a combination of sharp cold cutting, Hem-o-lok clips, and the harmonic scalpel. The dorsal venous complex was transected, followed by apical dissection and urethral transection. Urethrovescical anastomosis was accomplished by a watertight, double-needle, running suture technique.

All specimens were formalin fixed, coated with India ink, weighed, and serial perpendicular sections were cut. The entire prostate was examined with 2–4 mm interval transactions in a plane perpendicular to the urethra; the apical and basal parts of the prostate were separately sectioned and examined in parallel slices. All specimens were evaluated by one experienced uropathologist and restaged according to the 2010 American Joint Committee on Cancer staging system. Surgical margins were reported as positive when cancer cells reached the inked outer surface of the gland.

All patients received PSA detection and completed self-administered questionnaires concerning their voiding and sexual disorders at 1, 3, 6, 9, and 12 months and every 6 months thereafter postoperatively. Continence was defined as freedom from the use of any form of protection. Potency was defined as the ability to achieve vaginal penetration with or without phosphodiesterase type 5 inhibitors. Biochemical recurrence was defined as any detectable serum PSA (>0.2 ng ml⁻¹).

Continuous variables were reported as the median and range. The χ² test and Fisher’s exact test were used to evaluate the possible statistical correlation between the risk of PSM and several preoperative variables, including age, prostate volume, preoperative serum PSA level, biopsy Gleason score, maximal percentage of tumor per core, number of positive cores, PNI in biopsy, biopsy tumor laterality, and EPE. The correlation between PNI, Gleason score, and number of positive cores and capsular invasion was evaluated with the χ² test. Multivariate logistic regression analysis was performed step-wise to estimate the relative importance of the variables in predicting the risk of PSM. SPSS 17.0 statistical software (IBM SPSS, Chicago, IL, USA) was used to analyze the data. Kaplan–Meier curves and log-rank test by GraphPad Prism 6.0 (GraphPad Software, San Diego, CA, USA) were used to compare the risk of developing biochemical recurrence. P < 0.05 was considered statistically significant.

RESULTS
The clinical and biopsy characteristics of 296 patients treated with LRP are listed in Table 1. The median age of patients was 70 years (range: 51–80 years), median prebiopsy PSA value was 12.6 ng ml⁻¹, and the median prostate volume was 32 ml (range: 10.9–123 ml). Median biopsy Gleason score was 7 (range: 6–10). The median maximum percentage tumor per core was 60% (range: 5%–100%). PNI was present in 85 patients (28.7%). The number of patients with a bilateral tumor finding in biopsy was 150 (50.7%). EPE on MRI was noted in 116 patients (39.2%).

In the final pathological evaluation, 191 patients had pT2 disease, 101 had pT3 disease, and four had pT4 disease. PSM was present in 86 patients (29.1%). PSM rate in patients with pT2, pT3, and pT4 disease was 34/191 (17.8%), 48/101 (47.5%), and 4/4 (100%), respectively. The most common location of PSM was in the apex (54/296 [18.2%]). The PSM rate circumferentially and at the base was 21/296 (7.1%) and 27/296 (9.1%), respectively.

Table 2 shows the characteristics of PSM based on preoperative clinical and biopsy features. No association was observed in the univariable analysis between PSM and age (P = 0.565), PSA (P = 0.197), EPE on MRI (P = 0.295), and maximum percentage cancer per core (P = 0.213). Other parameters (prostate size, biopsy Gleason score, number of positive cores, biopsy PNI, and biopsy tumor laterality) were all significant risk factors of PSM using univariate analysis. Although 52.7% of biopsy-diagnosed unilateral disease was confirmed as bilateral disease in the final pathological report (P < 0.001) (Table 3), biopsy-determined tumor laterality was still a meaningful predictor of PSM (P < 0.001). Multivariate analysis is reported in Table 4. Among the five meaningful factors, Gleason score (odds ratio [OR] = 2.286, 95% confidence interval [95% CI] = 1.431–3.653, P = 0.001), PNI (OR = 4.961, 95% CI = 2.656–9.270, P < 0.001), number of positive cores (OR = 4.403, 95% CI = 1.878–10.325, P = 0.001) in biopsy specimens were predictors of PSM after LRP. In contrast, the volume of prostate gland showed a protective effect against PSM (OR = 0.572, 95% CI = 0.346–0.945, P = 0.029). Table 5 shows the three predictive factors (Gleason score, PNI, and number of positive cores) in biopsy specimens significantly increased the possibility of capsular invasion in the final pathological results (P < 0.05).

Table 1: Characteristics of 296 patients undergoing laparoscopic radical prostatectomy

| Variable | Value |
|----------|-------|
| Age, median (range) (year) | 70 (51–80) |
| Prostate volume, median (range) (ml) | 32 (10.9–123) |
| PSA, median (range) (ng ml⁻¹) | 12.6 (2.9–180) |
| Biopsy Gleason score, median (range) | 7 (6–10) |
| Maximum percentage of tumor per core, median (range) (%) | 60 (5–100) |
| Number of positive cores, median (range) | 4 (1–12) |
| Biopsy perineural invasion number, n (%) | 85 (28.7) |
| Biopsy bilateral tumor, n (%) | 150 (50.7) |
| Extra-prostatic extension on MRI, n (%) | 116 (39.2) |
| Pathologic stage, n (%) |        |
| pT2 | 191 (64.5) |
| pT3 | 101 (34.1) |
| pT4 | 4 (1.4) |

PSA: prostatic-specific antigen; MRI: magnetic resonance imaging
Table 2: Univariate analysis of clinical and biopsy features for predicting PSM

| Variable       | Number of patients (%) | Surgical margin situation (%) | P*       |
|----------------|------------------------|-------------------------------|----------|
|                | Positive | Negative | Positive | Negative |
| Patients       | 296          | 86 (29.1) | 210 (70.9) |          |
| Age (year)     | <65        | 68 (23.0) | 23 (26.7) | 45 (21.4) | 0.565 |
|                | 65–75      | 173 (58.4) | 49 (57.0) | 124 (59.1) |          |
|                | >75        | 55 (18.6) | 14 (16.3) | 41 (19.5) |          |
| Prostate volume (ml) | <30                | 138 (46.6) | 50 (58.1) | 88 (41.9) | 0.026 |
|                | 30–60      | 127 (42.9) | 31 (36.0) | 96 (45.7) |          |
|                | >60        | 31 (10.5) | 5 (5.8) | 26 (12.4) |          |
| PSA (ng ml⁻¹)          | <10        | 90 (30.4) | 23 (26.7) | 67 (31.9) | 0.197 |
|                | 10–20      | 143 (48.3) | 39 (45.3) | 104 (49.5) |          |
|                | >20        | 63 (21.3) | 24 (27.9) | 39 (18.6) |          |
| Biopsy Gleason score | ≤6 (low)   | 100 (33.8) | 13 (15.1) | 87 (41.4) | <0.001 |
|                | 7 (moderate)| 118 (39.9) | 38 (44.2) | 80 (38.1) |          |
|                | >8 (high)  | 78 (26.3) | 35 (40.7) | 43 (20.5) |          |
| Number of positive cores | ≤3        | 123 (41.6) | 17 (19.8) | 106 (50.5) | <0.001 |
|                | >3         | 173 (58.4) | 69 (80.2) | 104 (49.5) |          |
| Maximum tumor per core (%) | ≤25      | 61 (20.6) | 18 (20.9) | 43 (20.5) | 0.213 |
|                | 25–50      | 75 (25.3) | 16 (18.6) | 59 (28.1) |          |
|                | >50        | 160 (54.1) | 52 (60.5) | 108 (51.4) |          |
| Biopsy perineural invasion | Absent     | 211 (71.3) | 36 (41.9) | 175 (83.3) | <0.001 |
|                | Present    | 85 (28.7) | 50 (58.1) | 35 (16.7) |          |
| Biopsy tumor laterality | Unilateral | 146 (49.3) | 25 (29.1) | 121 (57.6) | <0.001 |
|                | Bilateral  | 150 (50.7) | 61 (70.9) | 89 (42.4) |          |
| Extra-prostatic extension on MRI | Absent     | 180 (60.8) | 48 (55.8) | 132 (62.9) | 0.295 |
|                | Present    | 116 (39.2) | 38 (44.2) | 78 (37.1) |          |

*Chi-square test and Fisher’s exact test, comparing between negative and positive surgical margin situation. P < 0.05 was considered significant. PSA: prostatic-specific antigen; MRI: magnetic resonance imaging.

Overall perioperative complication rate was 10.5%. Minor complications (Clavien grades 1 and 2) occurred in 7.8% of patients. Complications that required intervention (Clavien grade 3a and 3b) occurred in 2.7% of patients. After at least 6 months of follow-up (median: 22 months, range: 6–48 months), the continence rate was 91.6%, and the potency rate in previously potent patients who underwent nerve-sparing surgery was 34.6%. Thirty-six patients were excluded for further analysis of biochemical recurrence owing to loss to follow-up or taking adjuvant therapies. Three-year biochemical recurrence-free survival (RFS) in this study was 72.2% (Figure 1a). RFS curves were significantly different between the patients with and without PSM (3-year RFS: 53.6% [PSM⁺] vs 81.5% [PSM⁻], log-rank test: P < 0.001) (Figure 1b).

**DISCUSSION**

PSM status after RP is a well-established prognostic factor of prostate cancer, which is associated with increased biochemical failure and local disease recurrence, as well as the need for secondary treatment. Swindle et al.10 studied 1389 patients treated with RP from 1983 to 2000, and found that PSM was an independent predictor of 10-year tumor progression-free probability. Paulson et al.11 reported that PSM was associated with decreased overall survival. Our study also showed that the 3-year RFS in the PSM⁺ subgroup was significantly higher than that in the PSM⁻ group. Owing to refinements in surgical technique and a downward stage migration during the PSA era, there was a decreasing tendency in PSM rate in Western countries recently. Williams et al.12 studied 4247 men diagnosed with prostate cancer who all underwent RP and found that PSM rate decreased from 21.3% in 2004 to 16.6% in 2006. However, the PSM rates of LRP reported in China were still higher than those in Western countries. There are several possible explanations for this phenomenon. To begin with, LRP was popularized much later in China than in Western countries. Rodriguez et al.13 were of the opinion that there was a significant decrease in PSM rate after finishing 200 LRP operations. Therefore, to reduce the effect of the learning curve, the first 200 cases were excluded from the present study. Moreover, many patients were not diagnosed at an early stage because of the poor awareness of the general public of prostate cancer screening in China. In this study, 35.5% of patients had EPE in the final pathological evaluation. Therefore, defining accurate predictors of PSM preoperatively will help us to reduce the PSM rate after RP.

A Gleason score is given to prostate cancer based on its microscopic appearance. A higher Gleason score suggests high tumor aggression.
and worse prognosis. When compared with matched surgical specimen grades, biopsy Gleason score grading has a significant rate of downgrading, ranging from 27% to 57%. This discordance is related to the fact that prostate cancer is multifocal, with a heterogeneous population of tumor cells. Although biopsy lacks accuracy in predicting Gleason score in final pathology, Watson et al. found that patients with PSM tend to have greater biopsy Gleason scores than those with negative margins. Our study found that the PSM rate was 13.0%, 32.2%, and 44.8% in patients with a Gleason score of ≤6, 7, and ≥8, respectively. Gleason score in biopsy was shown to be a significant predictor of PSM in LRP. Our further analysis showed that patients with higher biopsy Gleason scores had more possibility of capsule invasion, which could interpret the difference of PSM rates above.

The number of positive cores, maximum percentage tumor per core, and tumor laterality can indirectly reflect tumor size. Our univariate analysis indicated that the number of positive cores and tumor laterality were significantly associated with PSM after LRP. Heidenreich et al. reported that <50% positive biopsy cores was a significant predictor of organ-confined prostate cancer with negative surgical margins. Tuliao et al. showed that the number of preoperative positive biopsy cores is a predictor of PSM after robot-assisted RP, especially in small prostates, which agrees with our study. As for tumor laterality, Bulbul et al. reported that a unilateral positive biopsy does not predict unilateral disease and does not reflect the exact volume of the tumor. Our data also confirmed this, so it could not be used as a predictor of tumor distribution or PSM.

PNI is a potential histopathological marker in the prostate needle-biopsy specimen, defined as the tracking of carcinoma around nerves. PNI on needle biopsy may signal an increased likelihood of EPE at the time of prostatectomy. Lee et al. found that biopsy PNI was associated with a significantly higher risk of PSM and pathological stage T3 disease. D’Amico et al. reported that PNI in biopsy was an independent prognostic factor for prostate cancer recurrence. PNI found in preoperative biopsies, has also been found to be a predictor of metastasis and prostate cancer death in patients treated with dose-escalated radiotherapy. PNI was confirmed as a predictor of PSM after LRP in our study, and with the highest OR value (4.961). Therefore, patients with PNI in biopsy should be paid more attention when doing LRP.

The size of the prostate is associated with oncological outcome. The larger amount of benign tissues in large glands decreases the chances of tumor exposure, whereas tumor in small prostates has a higher possibility of exposure during dissection. Thus, large glands are associated with more difficult procedures but better oncological results. In contrast, small glands are associated with easier surgery but less ideal oncological results. Labanaris et al. reported that men with smaller prostates had larger tumor volumes, were less organ confined, had more EPE, and experienced more biochemical recurrence. Sooriakumaran et al. found that small prostate volume had a higher rate of PSM in patients undergoing RP. The results of multivariate analysis in our study also showed that prostate size was a protective factor against PSM (OR < 1).

PSA has been used as a criterion for consideration for prostate biopsy. In addition to diagnosing prostate cancer, preoperative PSA value may be related to PSM. Shefla et al. reported that patients with a PSA value >10 ng ml⁻¹ were more likely to have PSM. Liss et al. demonstrated that with preoperative PSA >10 ng ml⁻¹, the risk of PSM increased nearly 8 times. In our study, there was no significant difference in PSM rate among three subgroups according to PSA values. This might have been attributed to some factors affecting the PSA level: some patients underwent irregular endocrine therapy in other hospitals; some patients may have had prostatitis; some patients experienced long-term indwelling catheterization before biopsy; and PSA detection was not standardized in hospitals from where some patients were referred. Although there was no significant difference, the PSA rate in the subgroup with PSA >20 ng ml⁻¹ was 38.1%, which was higher than in the other two subgroups (25.6% in PSA <10 ng ml⁻¹ and 27.3% in PSA 10–20 ng ml⁻¹). Therefore, we agree that for patients with preoperative PSA >20 ng ml⁻¹, PSA should still be fully considered. PSA density is a more significant predictor and cut-off value in terms of PSM compared with PSA. We will include this parameter in our future study.

The overall PSM rate in this study was higher than that of Western countries. A large proportion of our patients had PNI, a high Gleason score, a large number of positive cores in biopsy specimens, and/or high serum PSA, and may have been expected to have more advanced disease. This is reflected in the fact that 35.5% of our patients were found to have T3 or T4 disease. Stratifying patients by pathological stage, the PSM rate in patients with pT2 disease (17.8%) was comparable to the outcomes of studies from Western countries, while the PSM rate in patients with capsule invasion was as high as 49.5%. Therefore, the reason for the high PSM rate in this cohort was largely related to the high proportion of locally advanced disease. The median prostate volume in this study was also smaller than those in the series of Western countries. It is recognized that the relative volume of cancer to prostate volume is higher in small prostates. It may also have partially contributed to the high PSM rate here.

CONCLUSION
This study suggests patients with PNI, a high Gleason score, and a large number of positive cores in biopsy specimens tend to have EPE in the final pathological evaluation. These three factors are all predictors of PSM after LRP. In contrast, the volume of the prostate gland is a protective factor against PSM.

AUTHOR CONTRIBUTIONS
RY, KC, and TH collected the data, performed the statistical analysis, and drafted the manuscript. YFZ, HBL, and LFX carried out the statistical analysis, performed the statistical analysis, and drafted the manuscript. GTZ, XGL, and HQG conducted the patient care and follow-up. HQG and XGL conceived the study, and participated in its design and coordination, and helped to draft the manuscript. All authors read and approved the final manuscript.

COMPETING INTERESTS
The authors declare no competing interests.

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REFERENCES

1. Jemal A, Bray F, Center MM, Ferlay J, Ward E, et al. Global cancer statistics. CA Cancer J Clin 2011; 61: 69–90.

2. Brawer MK. Prostate-specific antigen: current status. CA Cancer J Clin 1999; 49: 264–81.

3. Hodge KK, McNeal JE, Terris MK, Stamey TA. Random systematic versus directed ultrasound guided transrectal core biopsies of the prostate. J Urol 1989; 142: 71–4.

4. Gerber GS, Thisted RA, Scardino PT, Frohmuller HG, Schroeter FH, et al. Results of radical prostatectomy in men with clinically localized prostate cancer. JAMA 1996; 276: 615–9.

5. Tewari A, Sooki et al., Bloch DA, Seshadri-Kreuden U, Hiebert AE, et al. Positive surgical margin and perioperative complication rates of primary surgical treatments for prostate cancer: a systematic review and meta-analysis comparing retropubic, laparoscopic, and robotic prostatectomy. Eur Urol 2012; 62: 1–15.

6. Grossfeld GD, Chang JJ, Broering JM, Miller DP, Yu J, et al. Impact of positive surgical margins on prostate cancer recurrence and the use of secondary cancer treatment: data from the CaPSURE database. J Urol 2000; 163: 1171–7.

7. Vis AN, Schroer FH, van der Kwast TH. The actual value of the surgical margin status as a predictor of disease progression in men with early prostate cancer. Eur Urol 2006; 50: 258–65.

8. Kausik SJ, Blute ML, Sebo TJ, Leibovich BC, Bergstralh EJ, et al. Prognostic significance of positive surgical margins in patients with extraprostatic carcinoma after radical prostatectomy. Cancer 2002; 95: 1215–9.

9. Hasan WA, Gill IS. Laparoscopic radical prostatectomy: current status. BJU Int 2004; 94: 7–11.

10. Swindle P, Eastham JA, Ohori M, Kattan MW, Wheeler T, et al. Do margins matter? The prognostic significance of positive surgical margins in radical prostatectomy specimens. J Urol 2005; 174: 903–7.

11. Paulson DF, Moul JW, Walther PJ. Radical prostatectomy for clinical stage T1–2N0M0 prostate cancer: detailed pathological analysis and prognosis. BJU Int 2011; 107: 1734–40.

12. Rodriguez AR, Rachna K, Pow-Sang JM. Laparoscopic extraperitoneal radical prostatectomy: impact of the learning curve on perioperative outcomes and margin status. JSLS 2010; 14: 6–13.

13. Allsbrook WC Jr., Mangold KA, Johnson MH, Lane RB, Lane CG, et al. Interobserver reproducibility of Gleason grading of prostatic carcinoma: general pathologist. Hum Pathol 2001; 32: 81–8.

14. Watson RB, Civants F, Soloway MS. Positive surgical margins with radical prostatectomy: detailed pathological analysis and prognosis. Urology 1996; 48: 80–90.

15. Cupp MR, Bostwick DG, Myers RP, Desterling JE. The volume of prostate cancer in prostatectomy: impact of the learning curve on perioperative outcomes and margin status. J Urol 1995; 153: 1543–8.

16. Heidenreich A, Richter S, Thuer D, Pfister D. Prognostic parameters, complications, and oncologic and functional outcome of salvage radical prostatectomy for locally recurrent prostate cancer after 21st-century radiotherapy. Eur Urol 2010; 57: 437–43.

17. Tuliao PH, Koo KC, Komninos C, Chang CH, Choi YD, et al. Number of positive preoperative biopsy cores is a predictor of positive surgical margins (PSM) in small prostates after robot-assisted radical prostatectomy (RARP). BJU Int 2015; 116: 897–904.

18. Bulbul MA, El-Hout Y, Haddad M, Taiwi A, Houijai A, et al. Pathological correlation between needle biopsy and radical prostatectomy specimen in patients with localized prostate cancer. Can Urol Assoc J 2007; 1: 264–6.

19. Bastacky SI, Walsh PC, Epstein JJ. Relationship between perineural tumor invasion on needle biopsy and radical prostatectomy capsular penetration in clinical stage B adenocarcinoma of the prostate. Am J Surg Pathol 1993; 17: 336–41.

20. Potter SR, Partin AW. The significance of perineural invasion found on needle biopsy of the prostate: implications for definitive therapy. Rev Urol 2000; 2: 87–90.

21. Lee HY, Roberts R, Shah RB, Wjoji K, Wei JT, et al. Perineural invasion is a marker for pathologically advanced disease in localized prostate cancer. Int J Radiat Oncol Biol Phys 2007; 68: 1059–64.

22. D’Amico AV, Wu Y, Chen MH, Nash M, Renshaw AA, et al. Perineural invasion as a predictor of biochemical outcome following radical prostatectomy for select men with clinically localized prostate cancer. J Urol 2001; 165: 126–9.

23. Fung FY, Qian Y, Stenmark MH, Halverson S, Blas K, et al. Perineural invasion predicts increased recurrence, metastasis, and death from prostate cancer following treatment with dose-escalated radiation therapy. Int J Radiat Oncol Biol Phys 2011; 81: e361–7.

24. Koutidis N, Mourey E, Champigneulle J, Margi P, Corman L. Robot-assisted or pure laparoscopic nerve-sparing radical prostatectomy: what is the optimal procedure for the surgical margins? A single center experience. Int J Urol 2012; 19: 1076–81.

25. Pirozzi PM, Kimmann MD, Wessnitzer MS, Benson MC, McKiernan JM, et al. Prostate volume and pathologic prostate cancer outcomes after radical prostatectomy. Urology 2007; 70: 696–701.

26. Frota R, Turna B, Santos BM, Lin YC, Gill IS, et al. The effect of prostate weight on the outcomes of laparoscopic radical prostatectomy. BJU Int 2008; 101: 589–93.

27. Newton MR, Phillips S, Chang SS, Clark PE, Cookson MS, et al. Smaller prostate size predicts high grade prostate cancer at final pathology. J Urol 2010; 184: 930–7.

28. Labarans AP, Zugen W, JHTH. Robot-assisted radical prostatectomy in patients with a pathologic prostate specimen weight ≥ 100 grams versus ≤ 50 grams: surgical, oncologic and short-term functional outcomes. Urol Int 2013; 90: 24–30.

29. Sooki et al., Bloch DA, Seshadri-Kreuden U, Hiebert AE, et al. Positive surgical margins with radical prostatectomy: a contemporary analysis of risk factors. BJU Int 2008; 102: 603–8.

30. Zheng XY, Xie LP, Wang YY, Ding W, Yang K, et al. The use of prostate specific antigen (PSA) density in detecting prostate cancer in Chinese men with PSA levels of 4–10 ng/mL. J Cancer Res Clin Oncol 2008; 134: 1207–10.

31. Shafro SW, Opek C, Soloway MS. Update on bladder neck preservation during radical retropubic prostatectomy: impact on pathologic outcome, anastomotic strictures, and continence. Urology 1998; 51: 73–8.

32. Liss M, Osann K, Orrstein D. Positive surgical margins during robotic radical prostatectomy: a contemporary analysis of risk factors. BJU Int 2008; 102: 603–8.

33. Chang JS, Choi H, Chang YS, Kim JB, Oh MM, et al. Prostate-specific antigen density as a powerful predictor of extracapsular extension and positive surgical margin in radical prostatectomy patients with prostate-specific antigen levels of less than 10 ng/mL. Korean J Urol 2011; 52: 809–14.

34. Di Benedetto A, Soares R, Doyee Z, Bult S, McGregor RG, et al. Laparoscopic radical prostatectomy for high-risk prostate cancer. BJU Int 2015; 115: 780–6.