The Association of Shorter Interval of Biopsy-Radical Prostatectomy and Surgical Difficulty

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Purpose: We discuss the safety and perioperative outcomes of a 2-week interval between prostate biopsy and laparoscopic radical prostatectomy (LRP).

Materials and Methods: We retrospectively reviewed the medical records of 182 patients with prostate cancer (PCa) who underwent transperitoneal LRP 2 weeks after prostate biopsy between 2012 and 2015. We evaluated the following perioperative outcomes: operative time, estimated blood loss (EBL), infection, conversion to open surgery, positive surgery margins (PSM), and complications. We also reviewed studies discussing a shorter interval between biopsy and LRP in peer-reviewed publications.

Results: The mean operative time and EBL were 100.2 min and 82.2 ml, respectively. There were no rectal injuries or conversions to open surgery, totally 19 (10.4%) patients experienced complications (Clavien-Dindo Grade I and II): fever occurred in six patients (3.3%), urinary leak in four (2.2%), incomplete paralytic ileus in four (2.2%), deep vein thrombosis in two (1.1%), and postoperative anemia in four. The average bedrest time after surgery was 2.5 days. PSM was detected in twenty-one patients (11.5%) . 167 patients (91.7%) recovered continence. Follow-up ranged from 13-37 months, the biochemical recurrence (BCR) rate was 10.4% (19/182).The seven peer-reviewed studies we reviewed that a shorter interval was safe and did not influence surgical outcomes.

Conclusion: Our study shows that a 2-week interval between biopsy and LRP is safe and does not negatively affect surgical outcomes.

Keywords: laproscopic radical prostateectomy;biospy;interval.

INTRODUCTION

Currently, all of prostate cancers (PCa) are diagnosed by transrectal ultrasound (TRUS)-guided prostatic biopsy. For localized prostate cancer, radical prostatectomy (RP) continues to be a commonly performed and effective treatment. Traditionally, urologists recommend an interval of ≥ 6–8 weeks after TRUS-guided prostatic needle biopsy before RP[(1)], because of the hypothesis that biopsy can results inflammatory response and bleeding that may take several weeks to subside .[(2)] However, studies have shown that a shorter interval of 4–6 weeks does not affect immediate operative outcomes such as operative time, estimated blood loss (EBL), and positive surgical margin (PSM) status[(3)]. Despite this finding, to our knowledge, rarely studies have evaluated the surgical difficulty and operative outcomes of LRP 2 weeks after prostatic biopsy. We retrospectively studied a series of patients who underwent LRP 2 weeks after prostate biopsy, and we aimed to examine whether a shorter interval of 2 weeks between biopsy and LRP was associated with surgical difficulty or operative efficacy.

MATERIALS AND METHODS

Study population

Following ethics committee approval and patient consent, we retrospectively reviewed 182 patients undergoing LRP between February 2012 and December 2015. All the patients underwent the biopsy and LRP in the university hospital. The inclusion criteria were T1, T2 and T3a prostate cancer without distant metastasis. The exclusion criteria included history of pelvic surgery, radiotherapy, having undergone hormonal therapy, fever and severe bleeding of rectum related to biopsy and repeated biopsy. The characteristic of patients and disease has been illustrated in **Table 1**.

Study design

All patients diagnosed with PCa basing on TRUS-guided biopsy (12+X) had a transperitoneal LRP by the same urologist. Prophylactic antibiotics was used half an hour before biopsy, and another dose of antibiotic was used 24 hours later. All patients did a pre-biopsy pelvic MRI to explore the infiltration of prostate capsule.

The preoperative PSA level, Gleason score, age, body mass index (BMI), operative time, EBL, transfusion rate, length of stay, stage and margin status, conversion

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Table 1. The patient characteristics, perioperative outcomes and complication rates.

Characteristics[a]	N=182
Age(y)	68.5 ± 7.1
BMI(kg/m^2)	24.2 ± 1.7
PSA(ng/ml)	18.5 ± 6.7
Gleason score	
≤ 6	56
= 7	65
≥ 8	61
Operative time (mins)	100.3 ± 27.5
EBL(ml)	82.2 ± 20.2
Rectal injury	None
Transfusion	None
Conversion to open	None
Postoperative complications(n)	
Urinary leak	4
Pelvic hematoma	0
Fever(≥38.5℃)	6
Postoperative anemia	4
Deep vein thrombosis	2
Incomplete paralytic ileus	3
Length of bed rest(d)	2.5
Positive surgery margin(%)	11.5
Pathologic stage(n)	
≤ T2a	35
T2b	47
T2c-T3a	100
recovered continence(%)	91.7
BCR(%)	10.4

[a]Data are presented as mean ± SD or number (percent)

to open surgery, rectal injury, incontinence, biochemical recurrence (BCR) were analyzed. To evaluate the safety and effectiveness of short interval between biopsy and LRP.

Surgical technique

All the patients underwent LRP 2 weeks after biopsy. All procedures were performed through a five-port transperitoneal approach. The pelvic peritoneum was incised followed by the vesicle, which was dissected along the vas deferens. The perirectal fatty tissue was then entered. Dissection was performed between the rectum and the posterior aspect of Denonvilliers' fascia to avoid rectal injury. Fat tissue around the prostate was removed after detaching the bladder, followed by incising the endopelvic fascia to free the prostate and the muscles of pelvic wall. Bladder neck incision, ligation of the dorsal venous complex, apical dissection, posterior reconstruction, and urethro-bladder anastomosis were performed with continuous suture. Bladder neck suspension to the dorsal venous complex (DVC) was performed to improve continence. Obturator triangle lymph node dissection was performed in moderate and high-risk PCa patients.

Outcome assessment

Anal function exercises three times each day began on the day of urethral catheter removal and continued until recovery of continence or 6 months postoperatively. Postoperative continence was defined as being urinary pad-free. Patients were followed-up at 2, 4, 6 and 8 weeks postoperatively and every 3 months thereafter. PSA level and questions regarding the daily use of urinary pads were assessed at each visit. BCR was defined as two consecutive increases in PSA of > 0.2 ng/ml. The classification of complications was evaluated by the Clavien-Dindo Grade as described in previous literature[4].

We reviewed the literatures which compared the safety and effectiveness of LRP according to the interval between of biopsy and LRP.

Statistical analysis was performed using analysis of variance and t-tests with statistical significance set at $p < 0.05$.

RESULT

Table 1 shows patients' demographic data and tumour characteristics. All patients included in the study had pathologic stage T1c–T3a N0M0 PCa.

Median operative time and EBL were 100.3 ± 27.5 mins and 82.2 ± 20.2 ml, respectively. There were no conversions to open surgery, and no patients experienced rectal injury. Overall, 19 (10.4%) patients experienced postoperative Clavien-Dindo Grade I and II complications, including fever > 38.5°C in 6 patients (3.3%) who recovered with antibiotic therapy. Four patients (2.2%) suffered urinary leakage consisting of urine outflow from the peritoneal drainage tube postoperatively, with the volume of urine leakage ranging from 300–1100 ml per day. All affected patients recovered in 6 days postoperatively with conservative treatment and without additional surgery. Four patients (2.2%) suffered incomplete paralytic ileus and recovered in 4-6 days postoperatively with total parenteral nutrition. Deep vein thrombosis occurred in two patients (1.1%), and four patients developed unexplained anemia without active bleeding and pelvic hematoma. The average number of days of postoperative bed rest was 2.5 days, and PSM was detected in twenty-one patients (11.5%) . No Clavien-Dindo Grade III to V complications occurred. 142 patients (78%) regained continence within 6 weeks postoperatively, and 167 patients (91.7%) regained continence 6 months postoperatively without requiring urine pads. Follow-up ranged from 13–37 months, the BCR rate was 10.4% (19/182), and the mean time to BCR was 24.3 months (**Table 1**).

In our literature review[3,5-10], one study of a shorter interval between biopsy and LRP reported a slight increase in perioperative complications. The results from all of other studies that we reviewed showed that performing radical prostatectomy 2–6 weeks after biopsy did not adversely influence surgical difficulty or perioperative efficacy.

DISCUSSION

PCa is a major cause of mortality among men worldwide. It is generally considered a relatively slow-progressing malignancy. However, most patients with malignant tumors suffer serious mental anxiety and usually hope to receive treatment as soon as possible. Imaging studies such as those using magnetic resonance imaging (MRI) after prostate biopsy found that haematoma persisted up to 21 days post-biopsy in 81% of patients, was still present in 49% of patients 28 days later, and in some patients, persisted to 4.5 months post-biopsy[11-13]. Post-biopsy haematoma is located within the prostate rather than outside of the prostatic capsule, and does not interfere with assessing the prostatic extracapsule using MRI[14]. Post-biopsy prostate haematoma also does not adversely influence intraoperative dissection of the prostate and seminal vesicle. Inflammatory adhesions are another factor considered to interfere with surgery due to shorter biopsy-to-surgery intervals. Resolution of acute inflammation is followed by tissue proliferation and remodeling. The acute inflammatory

response usually lasts 24-48 hours but may persist for up to 2 weeks in some patients. Tissue remodeling with collagen scar formation begins 3–4 weeks after tissue injury and is followed by resolution of acute inflammation[15,16]. In our surgery experience, there were no significant inflammatory adhesions of extracapsule of prostate with an interval of 2 weeks between biopsy and LRP. However, pelvic surgery history resulted in adhesions of periprostate. So, the patients had suffered transurethral resection of prostate previously were excluded[17].

We found no haematoma or inflammatory adhesions in the periprostatic tissue or seminal vesicle intraoperatively in our cohort. Also, bleeding related to the biopsy was located in prostate and seminal vesicle. These findings were consistent with White et al's report [11] .

In this study, we report a new treatment model for PCa, and performed 182 cases of LRP within 2 weeks after biopsy, excluding patients in whom the prostatic capsule was invaded by carcinoma on MRI. Our results showed that operative difficulty and complications were not affected by the shorter interval, consistent with other studies[18,19]. In our opinion, bleeding during LRP mainly results from the dissection of DVC and prostate ligament, rather than from dissection of the seminal vesicle and prostatic capsule. As is known, prostatic volume is not a factor in EBL[20], therefore, LRP for localized PCa using a shorter interval between biopsy and LRP does not increase EBL.

Another important keypoint in LRP is PSM based on histopathology. The rate of PSM reported in the literature is 9-38.8% for localized PCa[19], and the independent predictor of PSM is clinical stage rather than surgical technique or biopsy-to-LRP interval[5,21].

Follow-up ranged from 13-37 months, the BCR rate was 10.4%, and the mean time to BCR was 24.3 months, in our study. The shorter interval in our centre did not increase PSM or BCR rate.

The shorter interval in our study did not increase difficulty dissecting the urethra and DVC. In each LRP surgery performed in our centre, we suspend the bladder neck to the DVC followed by urethral-bladder anastomosis to promote continence. Combined with anal function exercises, the incontinence rate 6 months postoperatively was relatively lower in our patient series (8%). In our cohort we excluded the T3b PCa because of the high-risk PCa result in high rate of incontinence[22].

In our literature review, most studies described an interval of 4–6 weeks. Only one study reported a serious of 31 cases undergoing a < 2-week interval, and the authors reported this interval was feasible and safe in robotic assisted laparoscopic prostatectomy (RALP) [10]. The results of our review also revealed that performing LRP 4–6 weeks after prostate biopsy compared to within 2 weeks does not adversely influence surgical difficulty and perioperative outcomes. Park[5] reported longer operative time and larger EBL in longer interval(> 4 weeks) in open surgery($P < 0.05$). However there was no significant differences in laparoscopic surgery($P > 0.05$)[5] . Conversely, George[6] did not recommend early RALP after biopsy because of a greater risk of complications.

To our knowledge, our study evaluated the safety and effectiveness of a 2-week interval between prostatic biopsy and LRP; however, there are several limitations in our study. Firstly, the relatively small sample size and a long-term follow-up are required for improved statistical power. Second, we did not compare the mortality and operative outcomes with more than 2 weeks intervals between biopsy and surgery.

CONCLUSIONS

LRP at 2 weeks after prostatic biopsy does not appear to be more technically difficult, increase PSM, or affect urinary continence. Our data provide reassurance to urologists and patients choosing LRP with a relatively shorter interval after biopsy. Using a 2-week interval shortens the waiting time from diagnosis to treatment.

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CONFLICT OF INTEREST

The authors report no conflict of interest.

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