Striated Muscle in the Prostatic Apex: Does the Amount in Radical Prostatectomy Specimens Predict Postprostatectomy Urinary Incontinence?

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OBJECTIVE To investigate whether the amount of striated muscle (SM) removed with the apical aspect of the prostate at prostatectomy can be predictive of postprostatectomy urinary incontinence (UI).

METHODS The records of 61 consecutive patients seen in follow-up after prostatectomy were reviewed. Complete clinical data were collected. Two uropathologists reviewed the hematoxylin and eosin sections of the apical margin to semiquantitatively assess the amount of SM according to the following scheme: 0 = no SM, 1 = 1%-10% SM (of total tissue), 2 = 11%-30% SM, and 3 = >30% SM. Continence status was determined based on the last clinical visit, with UI considered as any reported leakage.

RESULTS Patients had a median age of 62 years at surgery (interquartile range, 58-66 years) and had a median follow-up after surgery of 100 weeks (interquartile range, 50-176 weeks). Both prostate weight and SM score ($P = .045$ for both) were statistically significant predictors of incontinence on multivariate analysis. The odds of a patient with an average SM score of ≥ 2 being incontinent was 11.7 times that of a patient with an average score of <2. Using an SM score of ≥ 2 had a specificity of 98% and a sensitivity of 19% for detecting incontinence in patients after radical prostatectomy.

CONCLUSION The amount of SM seen in the pathology specimen after radical prostatectomy has a significant effect on postoperative UI. UROLOGY 83: 888–892, 2014. © 2014 Elsevier Inc.

In men, prostate cancer is the most commonly diagnosed cancer and the second most common cause of death from cancer in the United States.[1] Over the past decade, the annual incidence of prostate cancer has decreased by almost 20%. Despite this, radical prostatectomy (RP) rates in the United States have increased dramatically over this period,[2,3] almost doubling from 2004 to 2010.[4] Urinary incontinence (UI) and erectile dysfunction are the two most significant long-term adverse effects after RP,[5] with 4%-31% of men having UI 12 months after RP.[6] As UI can significantly harm quality of life, it is important to determine and optimize potential risk factors.

After RP, the external urethral sphincter (EUS), or rhabdosphincter, is considered to be the most important anatomically in sustaining continence.[7-12] As such, careful apical dissection of the prostate during RP has been emphasized to preserve the overlapping striated muscle (SM) of the EUS.[10,12-18] Whether the amount of SM removed by RP is associated with UI is not clear. Assuming that the amount of SM represents the amount of rhabdosphincter removed with the apex during RP, we assessed whether the amount of SM in apical margin sections was predictive of UI.

MATERIAL AND METHODS

The study cohort comprised 61 consecutive patients seen in follow-up after undergoing RP at Princess Margaret Hospital in Toronto, Canada. Two uropathologists (A.E. and T.V.D.K.) devised a visual inspection method for assessing the amount of SM in apical margin sections from each prostatectomy

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Figure 1. Apical margin with minimal striated muscle (SM score = 1). Arrow indicates region of SM. SM, striated muscle.

specimen. At our institution, the apical margin was identified by placing a probe in the prostatic urethra. A 3-4 mm cone of tissue around the urethra at the apex (Supplementary Fig. 1) was amputated and divided into left and right halves. Each half was serially sectioned perpendicularly, typically resulting in 3 wedges of tissue from each half. These wedges were then embedded on the edge in 2 separate paraffin blocks corresponding to the left and right halves of the apical margin. Standard 5-μm hematoxylin and eosin sections from each half were reviewed to assess the amount of SM, which was expressed as the percentage of total apical margin surface area occupied by SM (percent SM). The following semiquantitative scoring system was used: (Supplementary Figs. 1, 2) 0 = no visible SM, 1 = 1%-10% of apical margin surface area occupied by SM, 2 = 11%-30%, and 3 = >30% (Figs. 1, 2). The tissue in each half was scored for percent SM, and the results were averaged to generate an overall SM score for each specimen. One pathologist (A.E.) scored all the apical margin slides in the cohort, and the other pathologist (T.V.D.K.) rereviewed randomly selected slides to ensure the robustness of the scoring system.

Complete clinical data, including age at surgery, surgeon, approach (open vs minimally invasive), nerve-sparing status, pathologic stage and grade, prostate weight based on the pathology report, positive surgical margins, salvage radiotherapy, and length of follow-up, were collected. No patient was incontinent before the surgery. Continence status was determined based on the last clinical visit, with UI considered as any reported leakage.

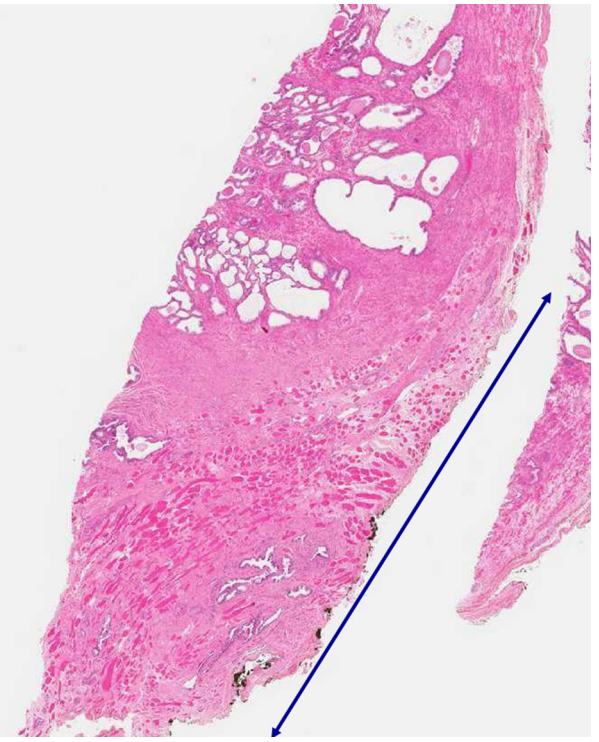

Figure 2. Apical margin with significant striated muscle (SM score = 3). Arrow indicates region of SM. SM, striated muscle.

A bivariate analysis was done to assess differences between continent and incontinent patients, with Student *t* test and chi-square test performed for continuous and categorical variables, respectively. Because of the size of the study, an SM score of ≥2 was chosen for analysis to compare patients with more significant amounts of SM removed (>10%) with those with a lesser amount of SM removed (≤10%). Variables with a *P* value <.50 were then included into a multivariate logistic regression model. Crude and adjusted odds ratios were reported for the final model. Sensitivity, specificity, positive and negative predictive values, and a positive likelihood ratio were calculated using an SM score of ≥2 as a cutoff. *P* values <.05 were considered significant. RStudio, v0.97.332 (RStudio, Boston, MA), was used for analysis.

The Research Ethics Board at the University Health Network, Toronto, Ontario, Canada, approved our study protocol.

RESULTS

The median age at surgery for the 61 patients included in the study was 62 years (interquartile range, 58-66 years). Twenty-one patients (34.4%) reported UI at last follow-up, with a median follow-up of 100 weeks (interquartile range, 50-176 weeks). Fifty-six patients (91.8%) had an average SM score <2, and 5 patients (8.2%) had an average SM score of ≥2. On bivariate analysis, only prostate weight was significantly different ($P = .025$), with incontinent men having a mean weight of 52.5 g compared with 44.0 g in continent men (Table 1). The SM score approached significance with a *P* value of .081. The operating surgeon was not predictive of incontinence ($P = .576$) or SM score ($P = .900$). Age, nerve-sparing status, prostate weight, length of follow-up, and SM

Table 1. Bivariate analysis between continent and incontinent men after radical prostatectomy

Variable	Continent		Incontinent		*P* Value
	Mean or Count	SD or %	Mean or Count	SD or %	
Age (y)					.430
≤60	17	73.9%	6	26.1%	
>60	23	60.5%	15	39.5%	
Approach					.669
Open	31	63.3%	18	36.7%	
Laparoscopic/ robotic	9	75.0%	3	25.0%	
Nerve sparing					.353
Bilateral/ unilateral	34	69.4%	15	30.6%	
None	6	50.0%	6	50.0%	
Prostate weight (g)	44.0	11.78	52.5	17.02	.025
SM score					.081
<2.0	39	69.6%	17	30.4%	
≥2.0	1	20.0%	4	80.0%	
Extracapsular extension					.746
Yes	14	60.9%	9	39.1%	
No	26	68.4%	12	31.6%	
Gleason grade					.545
6	14	73.7%	5	26.3%	
≥7	26	61.9%	16	38.1%	
PSM					.939
Yes	4	57.1%	3	42.9%	
No	36	66.7%	18	33.3%	
Salvage radiotherapy					.694
Yes	3	50.0%	3	50.0%	
No	37	67.3%	18	32.7%	
Follow-up (wk)	112.4	80.75	130.7	79.39	.401

PSM, positive surgical margin; SD, standard deviation; SM, striated muscle.

score were included in a multivariate logistic regression model to predict incontinence (Table 2). Both prostate weight and SM score ($P = .045$ for both) were statistically significant in the multivariate model. The odds of a patient with an average SM score of ≥2 being incontinent was 11.7 times that of a patient with an average score of <2.

Using an SM score of ≥2 had a specificity of 0.98 (95% confidence interval [CI], 0.87-1.00) and a sensitivity of 0.19 (95% CI, 0.05-0.42) for detecting incontinence in patients after RP. This suggests that patients with an average SM score of ≥2 after surgery have a 98% chance of incontinence. The positive predictive value was 0.80 (95% CI, 0.28-0.99), and the negative predictive value was 0.70 (95% CI, 0.56-0.81). Positive likelihood ratio for the average SM score was 7.62.

COMMENT

The EUS, or rhabdosphincter, is considered the most important structure anatomically in maintaining continence after RP.[7-12] The EUS extends from the prostatic apex to the proximal bulbar urethra, with its SM fibers extending over the ventral aspect of the prostate in a horseshoe or omega-like shape.[8,10,12,19,20] As initially demonstrated by Oelrich,[21] at puberty, the growth of the prostate accelerates, leading to incorporation of the overlying SM of the EUS. Specifically at the prostatic apex, the fibers of the EUS both partly overlap the prostate and are contained within it.[22,23] Elbadawi et al[24] showed that the adult male urethral rhabdosphincter is an integral component of the prostate at its anterolateral aspects. They also demonstrated that the apical aspect of the prostate contains mixed slow- and fast-twitch striated myofibers, suggesting a dual mechanism of maintaining continence during bladder filling and preventing stress incontinence. The importance of the EUS after RP was noted by Strasser et al,[9] who used 3-dimensional transrectal ultrasound to demonstrate that the contractility of the remaining rhabdosphincter after prostate surgery was associated with postoperative urinary stress incontinence.

To our knowledge, this is the first study to investigate an association between the amount of SM removed during RP and incontinence. We found that men with an average SM score of ≥2 (SM occupying >10% of apical margin) were 11.7 times more likely on multivariate analysis to be incontinent than those with a score <2. This further emphasizes the importance of the EUS in maintaining continence after RP and provides a possible method of predicting future incontinence in the immediate postoperative period. On multivariate analysis, the only other factor predictive of incontinence in this population was prostate weight, which has been reported in previous studies.[6] The nerve-sparing technique was not found to be associated with improved continence in our study ($P = .188$). In a recent meta-analysis, Ficarra et al[6] reported that age, body mass index, comorbidity index, lower urinary tract symptoms, and prostate volume were the most relevant preoperative factors predictive of UI after robotic-assisted RP. Because of the retrospective nature of the study, we were unable to assess body mass index or lower urinary tract symptoms. It should also be noted that most patients in this study underwent open RP, with only 20% having laparoscopic or robotic-assisted RP. Complementing our study, Von Bodman et al[25] recently reported that both urethral length and urethral volume as measured on prostate magnetic resonance imaging were significantly associated with recovery of continence after RP.

Our results lead further credence to the importance of preserving the EUS at apical dissection during RP, as has been suggested by Wallner et al and others.[7,10,12,18] As demonstrated by Lee et al,[15] this remains difficult as the prostatic apex can overlap the urethral sphincter in up to 85% of patients. They also found that the shape of the prostatic apex overlapping the membranous urethra on magnetic resonance imaging was predictive of postoperative incontinence after RP. Identifying the exact border of the EUS overlapping the prostate intraoperatively is the main difficulty for the surgeon.[10] As well, preserving the urethral sphincter during apical dissection of the prostate must be balanced with

Table 2. Multivariate logistic regression for variables associated with incontinence in men after radical prostatectomy

Variable	Unadjusted OR	95% CI		*P* Value	Adjusted OR	95% CI		*P* value
		Lower	Upper			Lower	Upper	
Age (y)								
≤60	1.00				1.00			
>60	1.85	0.59	5.75	.289	1.48	0.40	5.40	.555
Score								
<2.0	1.00				1.00			
≥2.0	9.18	0.95	88.30	.055	11.70	1.05	130.15	.045
Nerve sparing								
Bilateral/unilateral	0.44	0.12	1.59	.212	0.36	0.08	1.64	.188
None	1.00				1.00			
Prostate weight	1.05	1.00	1.09	.035	1.05	1.00	1.10	.045
Follow-up (wk)	1.00	0.10	1.01	.395	1.00	0.99	1.01	.581

CI, confidence interval; OR, odds ratio.

minimizing positive surgical margins.[16] Positive surgical margins are most commonly found at the prostatic apex after robotic-assisted RP, occurring in approximately 5% of cases.[26] Seven of 61 patients in our series were found to have a positive surgical margin, including only 1 patient with an SM score of ≥2. This patient, also having extracapsular extension, was incontinent after RP, suggesting that a more conservative apical dissection was not an option.

Walsh recognized the importance of the EUS at apical dissection in his anatomic approach to the radical retropubic prostatectomy. Other authors have since proposed modifications to the RP in an effort to conserve the EUS. Notably, Rocco et al[27] proposed a technique to restore the rhabdosphincter after RP by a posterior musculofascial reconstruction, which has been shown to improve the early return of continence within the first 30 days after RP.

Limitations of this study could arise from its retrospective nature, small sample size of 61 patients, and the method used to assess the amount of apical SM removed during each prostatectomy. The small sample size of our study contributed to the wide CIs that were observed. We also used a "no leak" definition of UI that was physician reported. There is variability in the literature regarding the measurement of continence after RP, with some studies using a "no pad" definition.[26] Using a validated questionnaire would have allowed us to measure the severity of UI in each patient and correlated it to the SM score. No patients in our study had surgical treatment for their incontinence at the time of analysis, but this is a possible outcome for patients with severe UI. Nam et al[28] reported that 5% of patients who undergo RP are expected to be treated with surgery for UI during a 15-year period. Limitations associated with our method of scoring percent SM include the potential for interspecimen variability in the shape and size of the cone of tissue defined as the apical margin. In addition, the percent SM was assessed by semiquantitative visual inspection to provide an estimate of the amount of rhabdosphincter removed with each specimen. Examination of additional sections from the apical aspect of the prostate along with an image analysis–based quantitation method may have provided more precise percent SM scores. During the slide review phase of this study, it was the experience of the study pathologists that the greatest amount of SM in each prostatectomy specimen was found in the 3-4 mm cone of tissue defined as the apical margin. As such, our analysis was restricted to apical margin sections only. We did attempt to use image analysis to score the percent SM; however, this approach was abandoned in favor of simple visual inspection because of poor specificity for the detection of SM. A particular challenge, despite considerable effort to resolve the problem, was the inability of the image analysis software to distinguish congested blood vessels and corpora amylacea from SM.

Our study had a higher number of patients reporting UI (34.4%) than typically reported in the literature. This is likely a result of the sample size of our study and the fact that they were not identified prospectively at the time of surgery but in follow-up. We would expect the percentage of patients reporting UI to regress to the mean with a larger sample size.

Most patients in our study were assessed after open RP. A recent meta-analysis found a better 12-month urinary continence recovery after robotic-assisted RP compared with open RP.[6] It is possible that robotic-assisted RP could provide better anatomic visualization of the prostate on apical dissection and lead to less SM being resected.

In our study, an SM score of ≥2 had a specificity of 98% and a sensitivity of 19% for detecting incontinence in patients after RP. Although there may be limitations associated with our method of determining SM score, it is easily performed and reproducible provided that apical margin sections are submitted in a standard manner.[29] Although further research is required in a larger prospective patient population to confirm our findings, pathologists could eventually consider including an SM score as part of routine reporting for RP specimens. Such information in the immediate postoperative period could be valuable to patients in terms of managing expectations regarding future complications.

CONCLUSIONS

Our study found a significant association between the amount of SM found in the apical aspect of the prostate on RP and future UI. This could potentially be used to predict future UI in the immediate postoperative period. In the future, prospective studies using a validated questionnaire and larger sample size are needed to further investigate this relationship.

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APPENDIX

Supplementary Data

Supplementary data associated with this article can be found in the online version at http://dx.doi.org/10.1016/j.urology.2013.12.055.