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MRI factors to predict urinary incontinence after retropubic/ laparoscopic radical prostatectomy

Antonio Tienza¹ · Mateo Hevia¹ · Alberto Benito² · Juan I. Pascual¹ · Juan Javier Zudaire¹ · Jose Enrique Robles¹

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Abstract

Purpose Prostate cancer can be treated by radical prostatectomy (RP) and provoke a troublesome side effect: urinary incontinence (UI). We propose a verification of the usefulness of MRI and an identification of which structures are involved in UI after RP.

Methods Between September 2002 and December 2011, 550 patients underwent RP. We performed MRI to evaluate extraprostatic disease before surgery. To evaluate patient status, we measured the following structures: length (LP), width (WP), height (HP) and volume (PV) of the prostate, membranous urethral length (MUL), urethral wall thickness (UWT), levator ani muscle (LAM) and obturator internus muscle (OIM) thickness, ratio of levator ani muscle/ prostate volume (LAM/PV), volume of the urethra (VU). UI was defined according to ICS definition as the complaint of any involuntary leakage of urine and evaluated 1 year after surgery. Analyses were performed by mean comparisons, univariate and multivariate logistic regression with a 1000-resample bootstrapping.

Results Means of measurements were: LP 4.46 cm, WP 5.15 cm, HP 3.9 cm, PV 49.3 cc; LAM 0.51 cm, OIM 1.46 cm; MUL 1.43 cm, UWT 1.38 cm; and LAM/PV 0.013 cm/cc, VU 2.33 cc. One hundred and twenty-two (22.2 %) patients complained of urine leakage. Univariate obtained differences in PV, OIM, MUL, and UWT. After adjusting by confounders, multivariate analysis showed:

Antonio Tienza atienza@unav.es

MUL: [OR 0.134; CI 95 % (0.022–0.493); *P* 0.006]; PV: [OR 1.016; CI 95 % (1.004–1.029); *P* 0.005]; UWT: [OR 6.03; CI 95 % (1.068–44.1); *P* 0.033].

Conclusions MRI is a useful tool to predict UI after RP. The MUL and PV are well-identified structures that are involved in UI. Our study shows that UWT also influences UI.

Keywords Radical prostatectomy \cdot Urinary incontinence \cdot Magnetic resonance imaging \cdot Prostate cancer

Introduction

Prostate cancer (PCa) is the most common solid neoplasm in Europe [1]. In the last years, in most cases, the number of diagnosed patients requiring radical treatment has increased. Some doubt might arise in patients seeking surgery. The two greatest sources of doubt are: erectile dysfunction, which presents before surgery in many cases, and urinary incontinence (UI), which is the chief post-surgical issue. Together, these conditions lead patients to choose radiation therapy instead of radical prostatectomy (RP), but we must not forget that the main goal is to be cured.

UI is a troublesome side effect that implies to loss quality of life [2] and may affect 4–31 % of patients who received surgery, as Ficarra et al. [3] reported. An approach that every patient and physician can adopt is the possibility of determining who may be at risk of becoming incontinent. Some factors, such as age or nerve-sparing technique, have been well identified, but others, such as the body mass index (BMI), Gleason score or stage, are still being discussed [2, 3]. Meanwhile, an issue that is often requested but relatively rarely reported is previous UI status. We

¹ Department of Urology, Clinica Universidad de Navarra, Pio XII, 36, 31008 Pamplona, Spain

² Department of Radiology, Clinica Universidad de Navarra, Pio XII, 36, 31008 Pamplona, Spain

can assess this status according to the function when the patients disclose this condition on an interview or questionnaires and by the structure, if pelvic floor structures are analysed. The pelvic floor can be evaluated by physical examination, ultrasound or magnetic resonance imaging (MRI) [4], which is the optimal test to identify soft tissue.

In cases where an MRI has been performed to evaluate extraprostatic diseases of PCa, we propose a verification of the usefulness of MRI and an identification of which structures are involved in UI after RP.

Materials and methods

Study population

Between September 2002 and December 2011, 586 patients underwent RP for clinically localized or locally advanced PCa. There were 36 (6 %) excluded patients without documented MRI scan, who had received treatment by salvage RP or who were lost to follow-up. According to the D'Amico risk categories, the patients were evaluated by prostate-specific antigen (PSA), digital rectal examination (DRE) and the biopsy Gleason score. A MRI of the pelvis was performed to evaluate the extent of PCa before surgery. RP was carried out via open retropubic RP (RRP) or laparoscopic RP (LRP) surgery.

Clinical data and variable definitions

Preoperative, surgical and pathological features were collected to define our series and to analyse the confounding factors. The preoperative variables were: age at surgery, BMI, DRE, PSA value, report of urgency or prior UI, biopsy Gleason score, D'Amico risk category (low, intermediate, high risk) and MRI scan result (normal, extraprostatic disease/seminal vesicle invasion). The surgical features were: type of approach (RRP/LRP), time of surgery and nerve-sparing technique (NST) (including unilateral or bilateral and extrafascial technique). The post-operative variables were: pathologic tumour stage (pT2 vs. pT3) and pathologic Gleason score, as reported by a urologic cancer specialist and certified pathologist. The previously described variables were used to adjust the influence of the MRI measurements on UI.

Patients' follow-up was performed after 3 and 6 months to evaluate the PSA control and 12 months to evaluate the urinary status [3]. We used the UI definition recommended by International Continence Society (ICS): the complaint of any involuntary leakage of urine to classify these patients as continent or incontinent [5].

A cross-sectional study was performed to interview all of the incontinent patients and to complete a valid and Spanish-translated questionnaire, the short form of the International Consultation on Incontinence Questionnaire (ICIQ-SF) [2]. The number of pads required was also collected.

MRI measurements and imaging

The examinations were performed with a 1.5-T scanner Siemens Magnetom[®] Aera or Symphony (Siemens AG, Germany). Patients were examined in the supine position. The imaging protocol included a transversal T1-weighted 2D gradient echo sequence. High-spatial-resolution T2-weighted TSE sequences were obtained in the axial, coronal and sagittal orientation with the following parameters: TR 4000–6000 (m s), TE 99–110 (m s), FoV (200–250) (mm), matrix size (256–320) (rectangular pixels), number of slices 30/45 [n], slice thickness 3 (mm), turbo-factor 20–25 and acquisition time (TA) 3:20/4:00 (min:s) [6].

Examinations were performed preoperatively by a board-certified radiologist and reported as normal (no evidence of tumour) or abnormal according to the TNM system cancer-suspicious area (T2a-c), presence of extraprostatic extension (T3a) and seminal vesicle involvement (T3b) [7]. Measurements of the pelvis were taken in a blind manner as described in Fig. 1. All data were collected in centimetres with two decimal places.



Fig. 1 MRI planning to perform measurements

The sagittal T2-weighted TSE sequences allowed for the length of the prostate (LP) and membranous urethral length (MUL) from the entry of the urethra into the penile bulb to the prostatic apex, to be measured, and part of the pelvic floor, levator ani muscle (LAM) thickness was measured from the axial T2-weighted TSE sequences at its wider slide. Similarly, we also measured the obturator internus muscle (OIM) thickness, because we believed that it could influence continence due to the relation of its fascia with the superior and inferior layers of the diaphragmatic part of the pelvic fascia. Coronal T2-weighted sequences were also used to measure LAM and OIM. The membranous urethra is a muscular organ that contains smooth muscle fibres in the shape of incomplete circles on the anterior and lateral faces [8]. Membranous urethra was measured before entering in the prostate and in its wider part, in axial sequences and defined as urethral wall thickness (UWT). Finally, the width (WP) and height (HP) of the prostate were also measured in this sequence. Prostate volume (PV) was calculated from the formula: height \times length \times width $\times \pi/6$ in centimetres [9]. The relationship between levator ani muscle/PV (LAM/PV) [10] and the assumed volume of the ure hra (VU) ($\pi \times$ half of UWT² × length) [11] was also computed.

Statistical analyses

A Student's *t* test or the Mann–Whitney *U* test was carried out to compare each MRI measurement between continent and incontinent patients. Significant independent variables were included in the univariate logistic regression analyses. According to review publication data [3], all of the analyses were adjusted for confounding factors. Finally, we performed a multivariable regression with a 1000-resample bootstrapping technique to correct for overfit [12]. The levels of classification and prediction were measured by logistic regression classification table and the area under the receiver operating characteristic curve (ROC curve). All statistical analyses were carried out using the SPSS software package version 21.0 (IBM Corp, Somers, NY, USA). A confidence interval (CI) of 95 % was assumed, and a *P* value <0.05 was considered significant.

Results

Table 1 presents the characteristics of the 550 patients who were included in the analyses. The mean of age was 63.5 years, the mean BMI was 27.5 kg/m², urgency or prior UI was reported by 67 (12.2 %) patients, median of PSA was 7.1 ng/ml, RRP was provided to 378 (68 %) of patients, LRP was provided to 172 (32 %) patients, and average time of surgery was 179 min. (\pm 68) and NST was

Table 1 Patient clinical-pathological characteristics of the series

$\frac{1}{1}$	528 (05 8 0/.)
	528 (95.8 %)
Age (years)	62.5
Median	63
Benge	41 82
Range \mathbf{D}_{α} and \mathbf{D}_{α} (\mathbf{D}_{α} / \mathbf{D}_{α})	41-65
<24.0	162 (22 6 6)
<u><</u> 24.9	102 (22.0 %)
23-29.9	420 (38.3 %)
\geq 30	150 (18.9 %)
Digital rectal examination	500 ((7 0 g))
Normal	592 (67.9 %)
Abnormal	210 (24.1 %)
PSA (ng/ml)	
Mean	9.3
Median	7.1
Range	2.2–136
Biopsy Gleason score	
≤ 6	339 (66.3 %)
7	119 (23.3 %)
≥ 8	53 (10.4 %)
D'Amico risk categories	
Low risk	264 (48 %)
Intermediate risk	170 (30.9 %)
High risk	108 (19.6 %)
MRI result	
Normal	390 (73.9 %)
Extraprostatic disease/vesicle invasion	136 (25.7 %)
Surgery type	
Open (retropubic) RP	377 (71.4 %)
Laparoscopic RP	151 (28.6 %)
Time of surgery (min)	
Mean	179
Median	164
Range	65-453
Pathological stage	
T2	378 (71.9 %)
≥T3	148 (28.1 %)
Pathologic Gleason score	
<u>≤6</u>	281 (53.8 %)
7	139 (26.6 %)
>8	102 (19.5 %)

performed in 297 patients (54 %). There were 122 (22.2 %) patients classified as incontinent after 1 year of follow-up. In the cross-sectional study, 115 (20.9 %) patients were classified as incontinent according to the ICIQ-SF: the mean score was 10.9 (\pm 16.4), and the mean of pads/day was 1.7 (\pm 1.3). There were 23 patients (18 % of incontinent) who preferred not to use pads. Only one pad/day was

needed in 52 patients (9.4 % of the series), two pads in 21 (3.8 %) and more than three pads in 19 (3.4 %). A total of 24 patients with urgency or prior UI were incontinent after RP and were excluded from further analysis.

The mean (range) of the MRI measurements were for prostate measures: LP 4.46 (1.67–8.48) cm, WP 5.15 (2.38–7.97) cm, HP 3.9 (1.5–6.64) cm and PV 49.3 (5.3–196) cc; for muscle measures: LAM 0.51 (0.2–1.9) cm and OIM 1.46 (0.3–3.07) cm; for urethral measures: MUL 1.43 (0.67–3.43) cm and UWT 1.38(0.78–2.16) cm; and for relationship between measures: LAM/PV 0.013 cm/cc and VU 2.33 (0.75–7.42) cc.

A comparison of means was made for the continent and incontinent patients. Table 2 shows the mean (standard deviation) of each group and the p value of the test. PV, OIM, MUL and MUW were the variable significantly different between groups. The coronal sequence measurements of LAM and OIM are not shown due to a strong similarity with axial results.

A univariate logistic regression analysis was performed with each variable. The results were: PV: [OR 1.013; CI 95 % (1.002–1.025); *P* value 0.018]; OIM: [OR 0.54; CI 95 % (0.352–0.830); *P* value 0.005]; MUL: [OR 0.17; CI 95 % (0.057–0.544); *P* value 0.003] and UWT: [OR 4.9; CI 95 % (1.18–20.3); *P* value 0.029].

Before performing the multivariable logistic regression, an analysis of possible confounding factors was performed. The factors analysed against the MRI measures were age, BMI, PSA, DRE, MRI scan result, biopsy Gleason score, D'Amico risk category, type of approach (RRP/LRP), NST, pathologic tumour stage and pathologic Gleason score [3]. No significant association was found between patient factors except for age. An interaction between OIM and age was found with a *P* value of 0.022 and a Pearson correlation coefficient of 0.204 (negative correlation; *P* value = 0.000).

Table 3 shows the multivariable logistic regression analysis with CI 95 % after adjustment by a 1000-resample

Table 2 Comparison of measurements by group

Variable	Continent	Incontinent	P value
LP	4.4 (±0.89)	4.5 (±1.01)	0.227
WP	5.1 (±0.69)	5.1 (±0.83)	0.989
HP	3.8 (±0.69)	3.9 (±0.83)	0.329
PV	53 (±21)	59 (±30)	0.027
LAM	1.2 (±0.23)	1.2 (±0.26)	0.868
OIM	1.8 (±0.22)	1.71 (±0.37)	0.019
MUL	1.45 (±0.32)	1.36 (±0.29)	0.007
UWT	1.36 (±0.21)	1.44 (±0.25)	0.020
LAM/PV	0.0131 (±0.008)	0.0137 (±0.012)	0.652
VU	2.28 (±0.79)	2.49 (±1.16)	0.163

Bold values indicate statistical significance (P < 0.05)

Table 3 Multivariate logistic regression analyses

Variable	OR	CI 95 %	P value	Bootstrapping adjusted CI 95 %	P value
MUL	0.134	0.032-0.563	0.006	0.022-0.493	0.006
PV	1.016	1.004-1.029	0.012	1.004-1.029	0.005
UWT	6.03	1.224-29.6	0.027	1.068-44.1	0.033
OIM			0.918		



Fig. 2 ROC curve

bootstrapping technique, which retained MUL, PV and UWT. The model shows a goodness of fit of 77 % and an area under the curve of 71.4 % (Fig. 2). In accordance with the data presented, a cut-off point with the greatest differences was computed: patients with a PV larger than 50 cc, a MUL shorter than 1.43 cm and a urethral wall thicker than 1.4 cm are at increased risk of become incontinent after RP. These results imply an increased risk of 1.6 % per cc of prostate (which means 16 % each 10 cc), 7 % per 5 mm of MUL and 600 % per millimetre of additional ure-thra thickness.

Discussion

UI is one of the greatest problems following RP. The search to avoid this side effect has led to several studies and surgical techniques. UI usually affects between 4 and 31 % of patients receiving surgery [3]; in our study, 122 (22.2 %) patients were classified as incontinent and 92 (16.7 %)

patients used one pad/day or more. The wide range in rates is because of the definition used and method of data collection [13, 14]. We choose the ICS definition of incontinence which tends to be the strictest. Other authors prefer to use a definition based on pad/day which is more permissive, or based on the 1-h pad test which could be less applicable and subject to bias. The only point in common is that, to date, there is not consensus [14]. We did not exclude all patients with urgency or prior UI (67 patients), only those that developed UI after RP (24 patients). As Schwartz et al. [15] and Prabhu et al. [16] commented, RP could also be helpful in patients with LUTS. Thus, our opinion is that those 45 patients who were not excluded benefited from surgery.

As part of the extraprostatic disease evaluation, we performed a MRI. This allowed us to use the sequences to identify which structures could have an influence on UI. Our study is not novel and is based on others such as Myers et al. [17] and Mikuma et al. [4] who reported the anatomy of the pelvic floor by MRI in 1998 but focused on coronal sequences. Coakley et al. [18] in 2002 reported that a longer membranous urethra is associated with a more rapid return to continence, as did Paparel [19], Hakimi [20] and Dubbelman [21]. But Song [10] and Von Bodman [11] found as predictive factor the ratio of levator ani muscle to the PV and urethra, respectively, to be predictive factors. Jeong et al. [22] developed a nomogram including MUL and PV and also reported that patients with a moderately large-sized dorsal vascular complex (2.3-2.8 cm2) regained their continence significantly sooner than those with a small-sized dorsal vascular complex [23]. An analysis from the CaPSURE database showed that PV is a predictor of recovery from UI, and a volume greater than 50 cc led to lower rates of continence 1 year after surgery [24]. The growth of the prostate is because of hyperplasia of the glandular and stromal cells from the transitional zone, which leads to subsequent changes in the bladder [5, 25]. The possible mechanism of influence is a differential prior status, men with larger prostates may be more likely to have a voiding dysfunction related to benign prostate hyperplasia, and surgery may be easier in small prostates, as a better nerve-sparing technique and longer membranous urethra could be performed.

In 2012, Lim et al. [26]. reported the association of the shape of the prostatic apex with continence which agrees with Lee et al. 2006 [27]. The depth of the urethrovesical junction seems also to be related to UI, as Haga et al. previously reported [28]. Conversely, Ozkaptan et al. did not find a pelvic bone dimension associated with recovery from UI, but they found PV related to the transfusion rate [29]. MRI could be useful to predict UI by itself or can be added to other tools such as urethral pressure profilometry [21]. As we can see, there are several studies that have used

MRI, but a review to gain consensus about what to measure is necessary.

Our data showed that MUL, UWT and PV were associated with continence, adjusted for other factors. It should be noted that the CIs of MUL and PV are fairly narrow, while UWT has a high odds ratio and wider CI. The latter could be explained by the range and distribution of values in a single series. Our results are consistent with Coakley [18] and Paparel [19] in a 14-mm mean membranous urethra; meanwhile, Lim et al. [26] reported a mean of 10.4 mm. The OIM also has an influence on UI. Although this muscle is not strictly part of the pelvic floor, we thought that might have an influence due to the relationship with the pelvic fascia. It has not been reported before, and we found a small relationship with age. The ratio of the levator ani muscle to PV did not show an influence in our study, nor did the urethral volume, as previously reported by Von Bodman et al. [11]. As Dubbelman et al. [21] reported, the urethral sphincter could be measured as MUL by MRI: our definition of UWT matched with the width of the sphincter. We are unsure why UWT had an influence on UI; perhaps, this influence is due to a hypertrophy of the urethral striated muscle, but we found no reports of this in the literature and thus do not know the underlying mechanism.

We have identified that a group of patients with a PV greater than 50 cc, consistent with Milhoua findings [30], a membranous urethra shorter than 1.43 cm and a urethral wall more than 1.4 cm are at greater risk to suffer UI. The categorization of the continuous variables and patients groups should be read with caution. We believe that it is better to report each unit of increase that draw conclusions for a single individual. This group of patients is at more risk, but we should weigh each particular case and not determine a general RP treatment or say that they will definitely become incontinent.

The next step to consider in UI studies is the changes in the pelvic floor anatomy after RP. Sohn et al. [31] performed a study with thirteen patients showing that puborectalis muscle thickness and bladder neck position could play an important role in continence recovery, but due to the small number of patients, no solid conclusion can be formulated.

A few limitations need to be considered in our study. The study design (retrospective and cross-sectional) limits the evidence obtained. To assess the preoperative urinary status, it would be more appropriate to use validated questionnaires: we only retrospectively collected patients who reported prior urgency or UI. The UI definition used here is the strictest definition and covers a wide range of patients; this definition could be widely discussed. However, the issue of which UI definition should be is still unresolved. An MRI is indicated in intermediate- or high-risk patients, but not in low-risk patients, and should be performed to evaluate the factors reported, thereby compromising the feasibility of other studies.

In conclusion, MRI is a useful tool to predict UI after RP. The MUL and PV are well-identified structures that are involved in UI. Our study shows that UWT also influences UI.

Conflict of interest The authors declare no conflict of interest.

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