

Models predicting muscle-invasive and locally advanced upper tract urothelial cancer incorporating diffusion-weighted MRI

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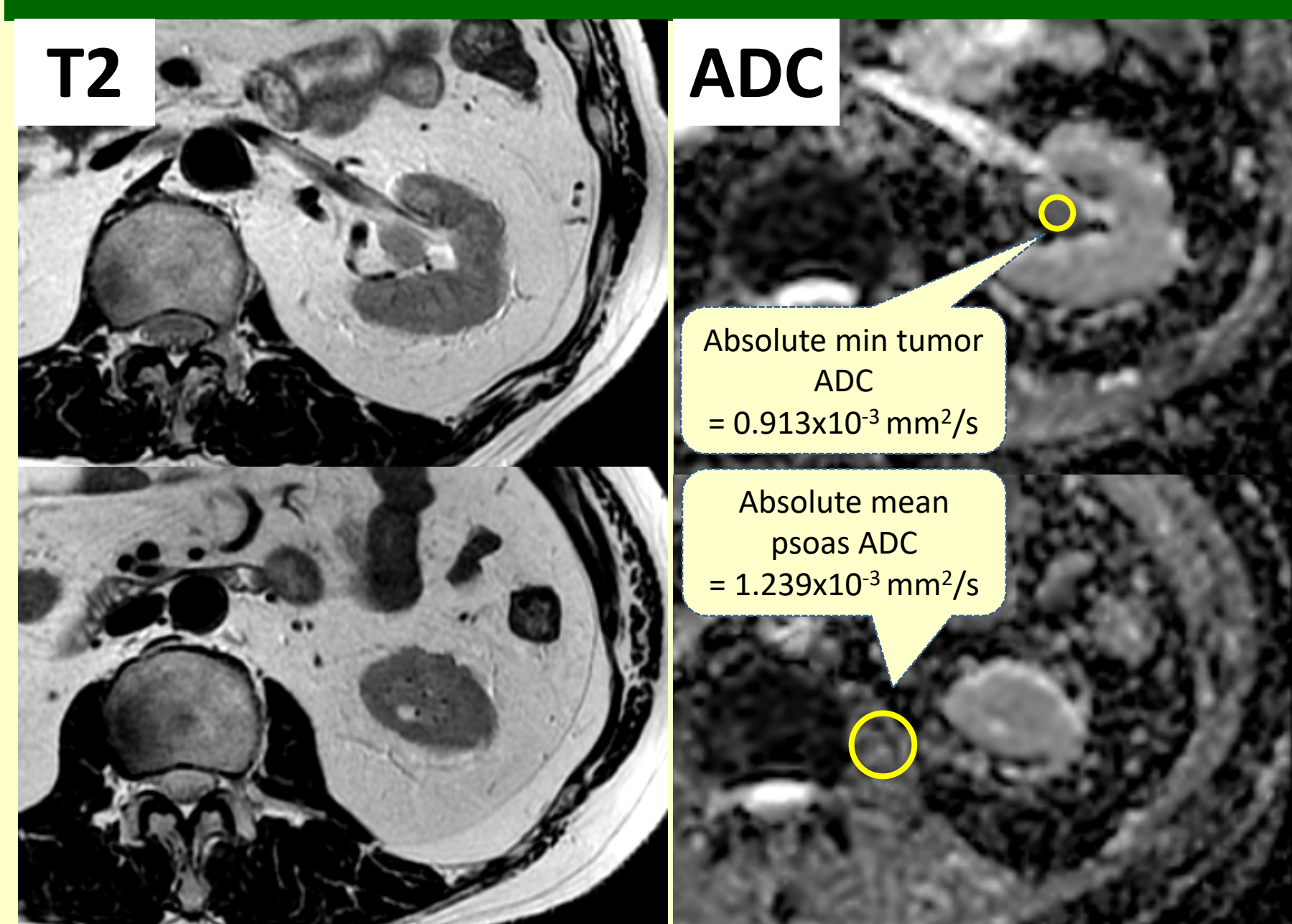
Introduction

- Accurate prediction of pathologically muscle-invasive (MI, $\geq pT2$) and locally advanced disease (LAD, $\geq pT3$ or $pN+$) is crucial for selecting candidates of regional lymph node dissection and neoadjuvant chemotherapy among non-metastatic UTUC patients.
- However, cT staging with standard CT/MRI is often inconsistent with pT stage and understaging is common.
- Apparent diffusion coefficient values (ADC), measured on diffusion-weighted MRI, reflect invasive potential of bladder urothelial cancer [Kobayashi, Koga *et al. Eur Radiol* 2011, *J MRI* 2014].
- We developed algorithms predicting $\geq pT2$ and $\geq pT3$ incorporating ADC in UTUC patients.

Methods

- Of the 71 patients, 16 (23%) were diagnosed with $\geq cT3$ on CT/MRI. Pathological examination of NU revealed MI and LAD in 38 (54%) and 33 (46%), respectively (Table 1).
- ADC were significantly lower in MI ($P = 0.04$) and LAD ($P = 0.03$) than their less invasive counterparts (both $P < 0.001$, Fig 2).
- Independent predictors of MI were ADC < 0.87 (the best cutoff: OR 75, $P < 0.001$), hydronephrosis (OR 7.2, $P = 0.006$) and positive VUC (OR 7.8, $P = 0.011$ while those of LAD were ADC < 0.87 (OR 128, $P < 0.001$), hydronephrosis (OR 11, $P < 0.001$) and $\geq cT3$ (OR 9.9, $P = 0.03$) (Table 2).
- Based on these results, we developed scoring models predicting MI and LAD (total score 0~4), of which AUCs of the ROC curves were 0.91 and 0.92, respectively (Fig 3).

Figure 1. Measurement of standardized tumor ADC



Standardized tumor ADC
= minimal tumor ADC /
mean psoas ADC

A 74-year-old male with left renal pelvic tumor of $< cT3$. He had no hydronephrosis with positive VUC. His standardized tumor ADC was 0.737. Pathological T stage was T2.

Results

- Subjects included 71 pathologically confirmed UTUC patients who took MRI/CT within 1M before nephroureterectomy (NU) between April 2013 and December 2019.
- ADC of tumor and the psoas muscle were measured on ADC maps and standardized tumor ADC was used to overcome the incompatibility between different MRI protocols [Nishizawa *et al., Clin Imaging* 2017] (Fig.1).
- Best cutoffs of ADC were determined by partition analysis. Multivariable logistic regression analysis was used to develop models predicting MI and LAD. Parameters examined included age, sex, tumor location, tumor diameter, voided urine cytology (VUC), cT stage, hydronephrosis, and ADC.

Table 1. Demographics of 71 UTUC patients

Variables	N (%)					
	Total	$\geq pT2$	$< pT2$	P value	$\geq pT3$ or $pN+$	$< pT3$
Age*	74 (36-87)	75 (60-84)	74 (36-87)	0.24	77 (60-84)	74 (36-87)
Sex				1.00		
Female	20 (28)	11 (29)	9 (27)		11 (34)	9 (23)
Male	51 (72)	27 (71)	24 (73)		21 (66)	30 (77)
Tumor location				0.13		
Renal pelvis	30 (42)	14 (37)	16 (48)		11 (34)	19 (49)
Ureter	34 (48)	22 (58)	12 (36)		19 (59)	15 (38)
Both	7 (10)	2 (5)	5 (15)		2 (6)	5 (13)
cT stage				0.02		0.001
$\geq cT3$	16 (23)	13 (34)	3 (9)		13 (41)	3 (8)
$< cT3$	55 (77)	25 (66)	30 (91)		19 (59)	36 (92)
Tumor diameter* (mm)	32 (4-300)	32 (5-300)	33 (4-70)	0.59	34 (10-300)	30 (4-70)
Hydronephrosis				0.02		<0.001
Yes	39 (55)	26 (68)	13 (39)		25 (78)	14 (36)
No	32 (45)	12 (32)	20 (61)		7 (22)	25 (64)
Voided urine cytology				0.03		0.22
Positive	25 (35)	18 (47)	7 (21)		14 (44)	11 (28)
Negative	46 (65)	20 (53)	26 (79)		18 (56)	28 (72)
Standardized tumor ADC				<0.001		<0.001
< 0.87	46 (65)	36 (95)	10 (30)		31 (97)	15 (38)
≥ 0.87	25 (35)	2 (5)	23 (70)		1 (3)	24 (62)

Table 2. Multivariable model predicting $\geq pT2$ and $\geq pT3$ or $pN+$ UTUC

Predictive factors	$\geq pT2$			$\geq pT3$ or $pN+$		
	OR	95% CI	P value	OR	95% CI	P value
ADC < 0.87	75	14-774	<0.001	128	15-4129	<0.001
Positive cytology	7.8	1.5-62	0.011			
Hydronephrosis	7.2	1.7-39	0.006	11	2.5-61	<0.001
$\geq cT3$				9.9	1.3-219	0.03

Conclusions

Muscle-invasive and locally advanced UTUC may be accurately predicted using our scoring models, which could help select candidates for lymph node dissection and neoadjuvant chemotherapy prior to NU.

Figure 2. Associations of ADC with $\geq pT2$ and $\geq pT3$ or $pN+$ UTUC

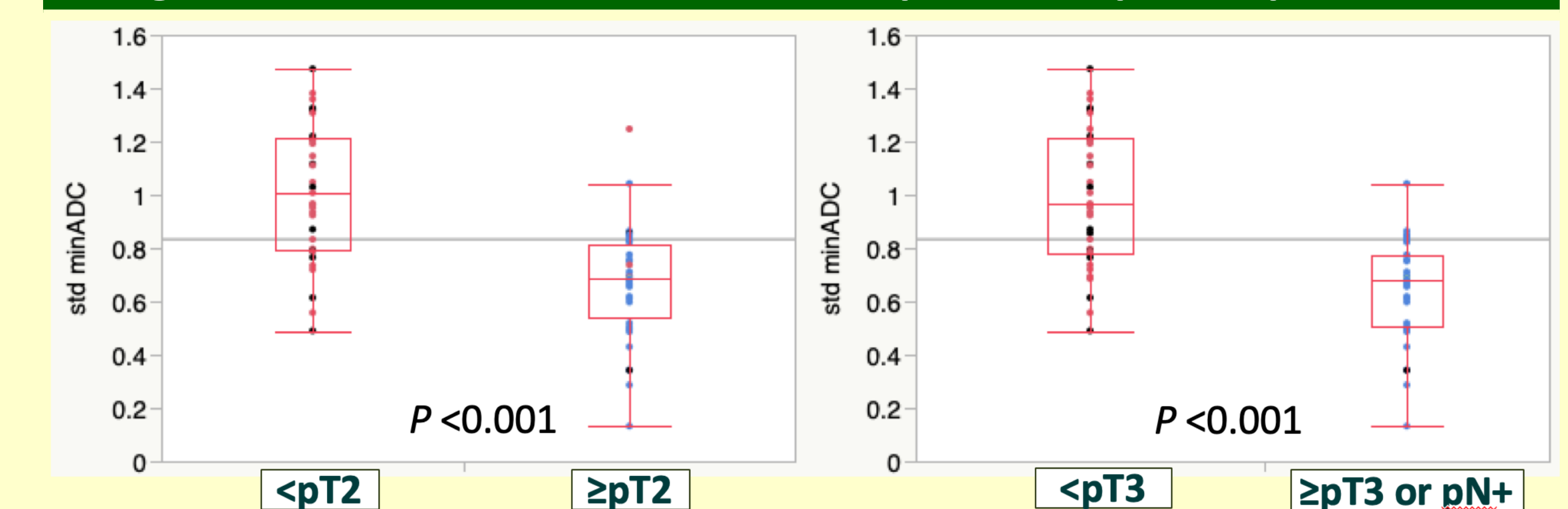
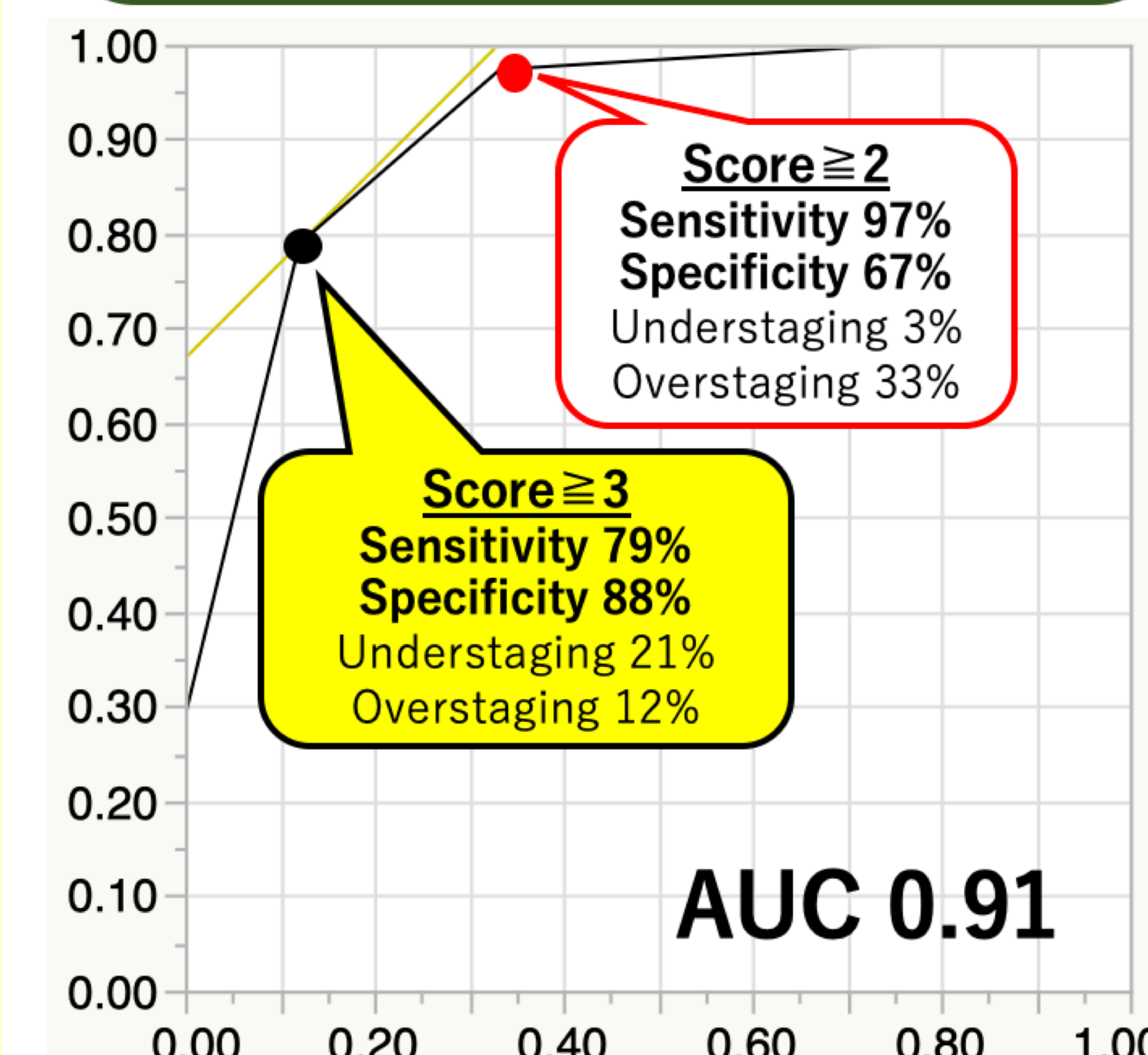


Figure 3. Scoring models predicting $\geq pT2$ and $\geq pT3$ or $pN+$ UTUC

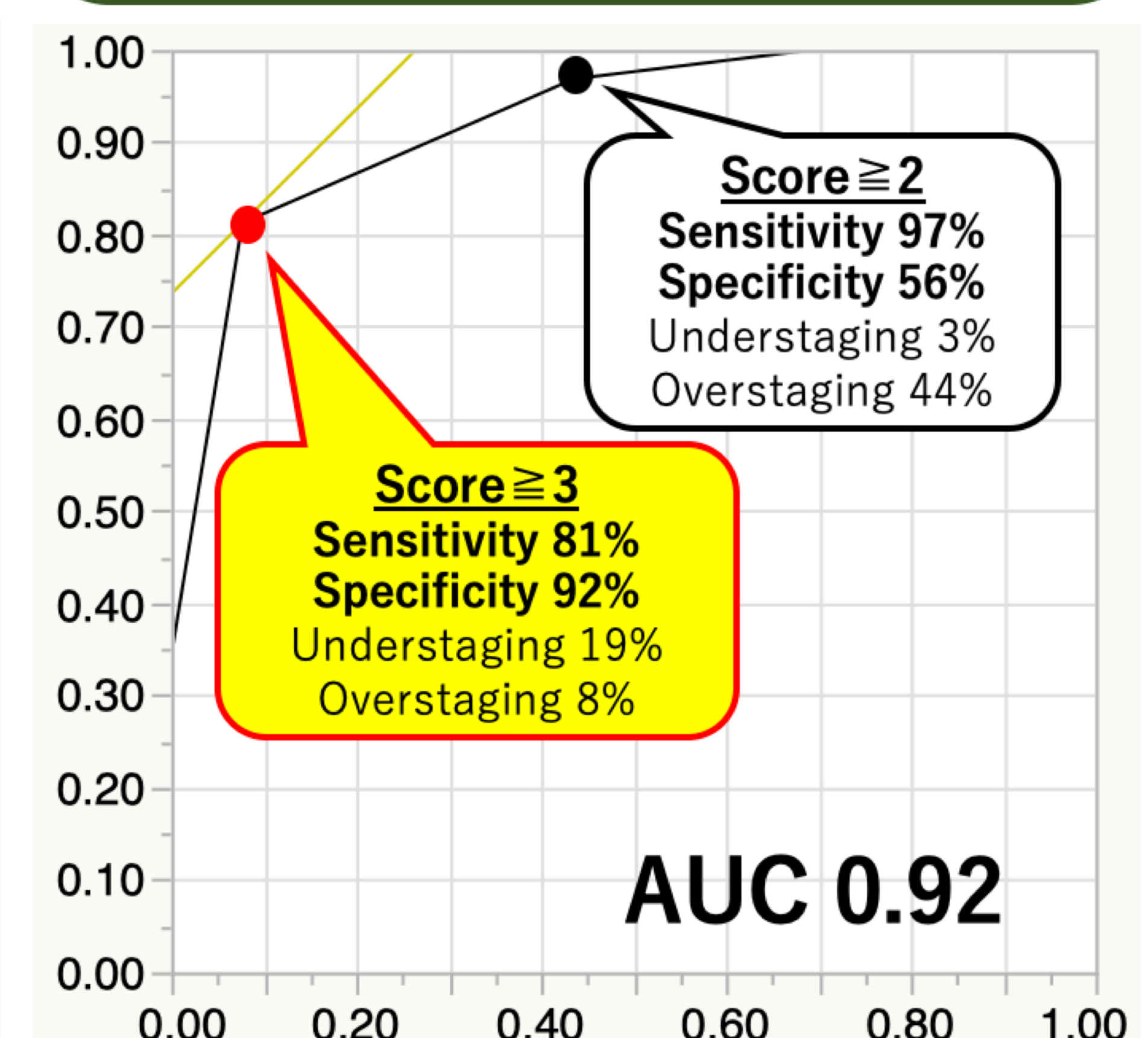
Model for Muscle Invasion

ADC < 0.87 +2
Hydronephrosis +1
Positive VUC +1



Model for LAD

ADC < 0.87 +2
Hydronephrosis +1
 $\geq cT3$ +1



Candidate selection	Preferable cutoff score*	Reason for the cutoff
Regional LND	≥ 2	Less understaging
Neoadjuvant chemo	≥ 3	Less overstaging

*Applicable to both models.