MP 53-09

New algorithm APhiGT for prostate cancer staging

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1. Background

The accuracy of prostate cancer (PC) clinical staging prior to radical treatment is an actual problem. The aim of our study was to develop a new mathematical algorithm for PC staging based on a set of laboratory and clinical data.

2. Methods

The design of our study has been conducted in accordance with the principles of the Declaration of Helsinki of World Medical Association. During 2008-2015, 337 PC patients who underwent radical prostatectomy (RPE) were included in the retrospective study. The average age of the patients was 62,7 ± 0,4 years. All patients were characterized by TNM and pTNM (Table 1), and by Gleason grading before and after RPE (Table 2).

Table 1. Patients' characteristics (TNM staging)

TNM/pTNM	pT_2N0 N (%)	pT_3N0 N (%)	$pT_{2-3}N+$ N (%)	∑ N
T_{1-2}	190 (56%)	68 (20%)	15 (5%)	273
T_3	16 (5%)	20 (6%)	28 (8%)	64
Sum ∑ (N)	206	88	43	

Table 2. Patients' characteristics (Gleason grading)

Gleason score before/ after prostatectomy	<7 after N (%)	≥7 after N (%)	∑ N
< 7 before	141 (42%)	65 (19%)	206
≥ 7 before	11 (3%)	120 (36%)	131
Sum ∑ (N)	152	185	

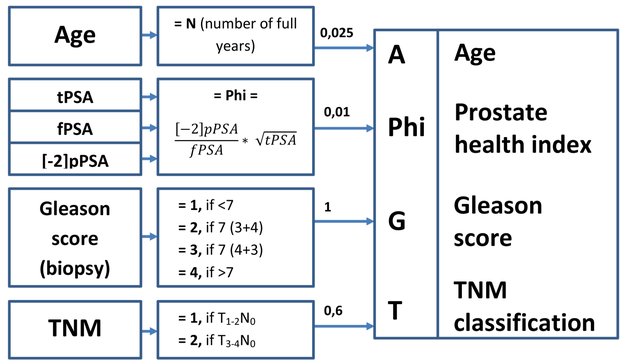
Based on pTNM and morphological Gleason (p Gleason) grading PC were divided into indolent (pT2 and Gleason <7, n=124) and aggressive (pT3 and/or Gleason ≥7, n=213).

Serum levels of total prostate-specific antigen (tPSA, < 30.0 ng/ml), free PSA (fPSA), [-2]pPSA were measured on Beckman Coulter Access 2 Analyzer using Hybritech calibration, with calculation of Prostate health index (Phi).

2. Methods (continued)

The algorithm APhiGT was developed by using logistic regression method (Figure 1).

Figure 1. Plan of multiparameter algorithm APhiGT



APhiGT is calculated by the formula:

APhiGT = 0,025 * A + 0,01 * Phi + G + 0,6 * T

Analysis was performed for tPSA, Phi and APhiGT with sensitivity, specificity and AUC calculation.

3. Results

ROC-analysis showed the advantage of the APhiGT algorithm in front of Phi and tPSA in the binary separation of patients into pTNM and p Gleason risk groups (Table 3), as well as in the separation of clinical insignificant (indolent) and significant (aggressive) PC (Table 4) in general tPSA range ≤ 30 ng/ml, and in narrow target tPSA range 2,5-10,0 ng/ml (Figure 2).

For the APhiGT algorithm, decisive rules have been developed. With APhiGT <3,4, we can predict pT2 and p Gleason <7. With APhiGT >5,0 – pT3 and/or p Gleason ≥7. Interval APhiGT 3,4-5,0 is a gray zone, the probability of aggressive PC increases with elevation of APhiGT.

3. Results (continued)

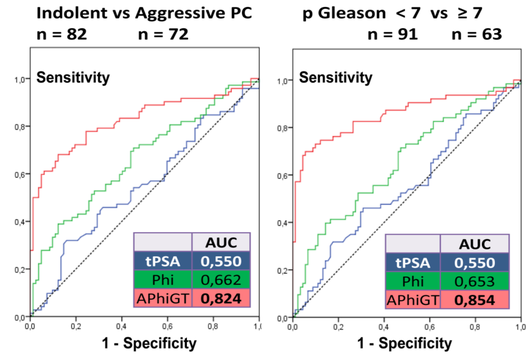
Table 3. Results of ROC-analysis for comparison of clinical groups (tPSA range ≤ 30 ng/ml)

	AUC (area under ROC curve)	
Parameter	p Gleason < 7 vs ≥ 7	pT2 vs pT3
tPSA	0,653	0,752
Phi	0,672	0,767
APhiGT	0,862	0,800

Table 4. Results of ROC-analysis for comparison of PC aggressiveness

	AUC (area under ROC curve)	
	Indolent (I) vs Aggressive (A) PC	
tPSA range	≤ 30 ng/ml	2,5-10,0 ng/ml
N	124 I vs 213 A	76 I vs 67 A
tPSA	0,703	0,577
Phi	0,73	0,675
APhiGT	0,872	0,817

Figure 2. ROC-Curves for comparison of PC aggressiveness and Gleason score (tPSA range 2,5-10,0 ng/ml).



3. Results (continued)

pGl	N	tPSA	Phi	APhiGT
< 7	152	10,1 ± 0,5 (8,2)*	61,7 ± 2,4 (58,2)	3,87 ± 0,04 (3,77)
P		***0,004***	***0,001***	***< 0,001***
7 (3+4)	93	12,7 ± 0,7 (10,7)	76,0 ± 3,6 (71,2)	4,64 ± 0,09 (4,52)
P		***0,049***	***0,014***	***< 0,001***
7 (4+3)	54	15,4 ± 1,2 (13,9)	96,8 ± 7,5 (87,7)	5,77 ± 0,14 (5,88)
P		*0,337*	*0,637*	***< 0,001***
> 7	31	17,3 ± 1,6 (15,5)	102,7 ± 9,9 (90,6)	6,69 ± 0,21 (6,77)

*Mean ± SE (Median)

pT	N	tPSA	Phi	APhiGT
pT2a-b	16	8,7 ± 1,0 (7,6)*	58,3 ± 8,9 (52,4)	4,21 ± 0,28 (3,62)
P		*0,269*	*0,834*	*0,972*
pT2c	191	9,8 ± 0,4 (8,3)	60,2 ± 1,9 (58,2)	4,20 ± 0,07 (3,86)
P		***<0,001***	***< 0,001***	***< 0,001***
pT3a	66	15,5 ± 1,0 (13,2)	92,2 ± 5,8 (83,5)	5,15 ± 0,16 (4,75)
P		*0,170*	*0,101*	***0,0045***
pT3b	64	17,6 ± 1,0 (16,9)	106,7 ± 6,7 (100)	5,79 ± 0,16 (5,75)

*Mean ± SE (Median)

I/A*	N	tPSA	Phi	APhiGT
pT2N0, pG < 7	124	9,1 ± 0,5 (7,8)**	55,9 ± 2,4 (52,0)	3,77 ± 0,04 (3,69)
P		***0,039***	***0,009***	***< 0,001***
pT2N0, pG ≥ 7	82	10,8 ± 0,7 (9,9)	66,0 ± 3,0 (62,8)	4,83 ± 0,12 (4,66)
P		***<0,001***	***< 0,001***	*0,057*
pT3N0	88	15,6 ± 0,8 (14,8)	91,7 ± 3,8 (91,8)	5,17 ± 0,13 (4,99)
P		*0,095*	***0,043***	***< 0,001***
pN+	43	18,3 ± 1,5 (18,1)	114,8 ± 10,6 (93)	6,08 ± 0,19 (6,15)

* Indolent (I) vs Aggressive (A) PC

**Mean ± SE (Median)

4. Conclusions

These results show the high diagnostic potential of APhiGT algoritm for prostate cancer staging before treatment.

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Poster presented at the AUA Annual Meeting, May 18–21, San Francisco, CA, USA