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Research Article

Adverse pathology after radical prostatectomy: the prognostic role of cumulative cancer length >6-mm threshold in prostate cancer–positive biopsies

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ABSTRACT

Background: To investigate the role of Cumulative Cancer Length (CCL) and PCa positive core number (PCapcn) in random prostate biopsies as predictors of Adverse Pathology (AP) at definitive pathology.
Methods: We prospectively enrolled patients submitted to random ultrasound guided prostate biopsies for suspect PCa in our center since 2016. Inclusion criteria were PSA <20 ng/ml or >3 ng/ml and age<71 years. Data on CCL and Grade Group (GG) at biopsy and pathology after Radical Prostatectomy (RP) were collected. AP was defined as pT3 or higher TNM, Positive Surgical Margin (>2mm) or PCa Positive Lymph Node. ROC curve was used to establish an appropriate CCL and PCapcn thresholds that were then investigated as predictors of AP at definitive pathology.
Results: Among 882 eligible biopsies, 344 had PCa and underwent RP. Mean age was 64 years (SD 5). Mean PSA was 7.75 (SD: 3.66). At definitive pathology there were AP features in 196 (56.9%) RP. PCapcn and CCL were statistically significantly associated with AP (p<0.0001). At multivariate age-adjusted logistic regression only PCapcn had an OR of 1.513 (CI95% 1.140-2.007) p=0.004. Through ROC curve a CCL>6mm and PCapcn >3 thresholds for AP were established (Area: 0.769; p<0.0001 CI 95% 0.698-0.840 and Area: 0.767; p<0.0001 CI 95% 0.696-0.837). When considering CCL>6mm AP had OR 5.462 (CI 95% 2.717-10.978) p<0.0001 and PCapcn >3 had OR 7.127 (CI 95% 3.366-15.090) p<0.0001. In particular, for GG 1 and 2, CCL>6mm had OR 3.989 (CI 95% 1.839-8.652) p<0.0001, while PCapcn >3 had OR 5.541 (CI 95% 2.390-12.849) p<0.0001.
Conclusions: At present time, random prostate biopsies might carry useful information regarding tumor extension and aggressiveness. A CCL>6mm or PCapcn >3 might be associated with AP features, in particular for low and favorable intermediate risk PCa.

1. Introduction

In the era of multiparametric magnetic resonance imaging (mpMRI), target fusion biopsy plus systematic prostate biopsies is steadily becoming the new standard of care in prostate cancer (PCa) diagnosis, as PRECISION trial showed, thus substituting random ultrasound-guided prostate biopsy.[1,2] Random prostate biopsies still have a role as mpMRI can miss some clinically significant PCa that might be suitable for active treatment.[3]

However, at the present time, most PCa nomograms to predict disease extension and lymph node involvement are still mainly based on random prostate biopsies, so they usually evaluate PCa-positive core number to predict local disease extension, although mpMRI is increasingly having a role in local staging.[4–7] In this setting, as fusion biopsies are increasing, PCa-positive core number might become falsely high and overestimate local extension or

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lymph node involvement at radical prostatectomy (RP), so other ways to estimate tumor burden should be chosen in nomograms. In the past, other PCa biopsy features were investigated as predictors of definitive pathology with different outcomes.[8,9] Among the factors investigated, cumulative cancer length (CCL) may become a PCa-positive core number alternative in the era of mpMRI and fusion biopsies.[8]

The aim of our study is to investigate the role of CCL and PCa-positive core number in random ultrasound-guided prostate biopsies as predictors of adverse pathology (AP) at definitive pathology, in particular for low- and favorable intermediate-risk PCa.

2. Materials and methods

2.1. Ethics

The study obtained institutional review board approval. Study protocol conformed to the provision of the Declaration of Helsinki. We acquired a written informed consensus from every patient enrolled.

2.2. Population

The study inclusion criteria were age lower than 71 years and a prostate specific antigen (PSA) at biopsy time lower than 20 ng/ml and higher than 3 ng/ml. Patients were enrolled since November 2016. Patients in active surveillance or with a previous diagnosis of PCa were excluded. All patients underwent ultrasound-guided systematic prostate biopsy. We collected data on bioptic core number, Gleason score, and Grade Group (GG). To standardize biopsy and make the study results more reproducible in everyday practice, the CCL for each biopsy was calculated and investigated. CCL consisted in the sum of the linear cancer extension of all cores. In addition, the CCL/core ratio was calculated. Only patients who underwent RP were selected. PSA density was calculated via estimating prostate volume by transrectal ultrasound during biopsy.

Patients were classified into low- and favorable intermediate- and unfavorable intermediate- and high-risk groups according to D'Amico risk classification, PSA, and GG at biopsy and after RP. At biopsy, low- and favorable intermediate-risk patients were defined as GG 1 or 2 and any PSA, unfavorable intermediate-risk patients were defined as GG 3 with any PSA, and high-risk patients were defined as GG 4 and 5 with any PSA. At RP, low- and favorable intermediate-risk patients were defined as GG 1 or 2, excluding pT3 or higher, unfavorable intermediate-risk patients were defined as GG 3 excluding pT3 or higher, and high-risk patients were defined as any GG 4 or 5 or any pT3 or higher. As a special subgroup, at biopsy, we defined true low-risk patients with PSA <10ng/ml and GG 1.

A clinical staging was performed for every patient according to the risk class: abdominal ultrasound for low- and favorable intermediate-risk patients and computer tomography and bone scintigraphy for unfavorable intermediate- and high-risk patients.

AP was defined as T3 or higher TNM (tumor nodes metastasis) staging system, positive surgical margin (>2mm), or PCa-positive lymph node at definitive pathology. The patients were subsequently divided into two groups according to presence or absence of AP features.

2.3. Statistical analysis

Appropriate descriptive statistical analysis was performed for each variable. The Student t test and Chi-square test were used to find statistically significant variables between groups. Statistically significant variables were then investigated as predictors of AP with logistic regression. The receiving operator characteristic (ROC)

Table 1
Patient characteristics.

Patient characteristics (n = 344)		
PSA (ng/ml)		7.75 (3.66)
PSA density		0.32 (0.20)
Core number		15 (2)
PCa-positive core number		4 (3)
Positive core number (% on total core number)		27.7 (21.1)
Age (years)		64 (5)
DRE	No	76 (22.1%)
	Suspect	152 (44.2%)
	Positive	116 (33.7%)
Risk class at biopsy	Low risk and favorable intermediate	249 (72.3%)
	Unfavorable intermediate	59 (17.2%)
	High risk	36 (10.5%)
Risk class subgroup at biopsy	True low risk	78 (22.7%)
Grade Group at biopsy	1	117 (34.0%)
	2	132 (38.4%)
	3	59 (17.2%)
	4	24 (6.9%)
	5	12 (3.5%)
Risk class at RP	Low risk and favorable intermediate	110 (32.0%)
	Unfavorable intermediate	50 (14.5%)
	High risk	184 (53.5%)
Grade Group at RP	1	71 (20.6%)
	2	128 (37.2%)
	3	87 (25.3%)
	4	36 (10.5%)
	5	22 (6.4%)
Adverse pathology	Total	196 (56.9%)
	pT3 or higher	180 (91.8%)
	Positive surgical margins >2mm	33 (16.8%)
	pN+	30 (15.31%)
Family history of PCa		60 (17.4%)

PSA, prostate specific antigen; DRE, digital rectal examination; PCa, prostate cancer; RP, radical prostatectomy.
All continuous variables are expressed as mean (standard deviation). Categorical variables are expressed as n (%).

Table 2
Comparison between patients with or without adverse pathology features.

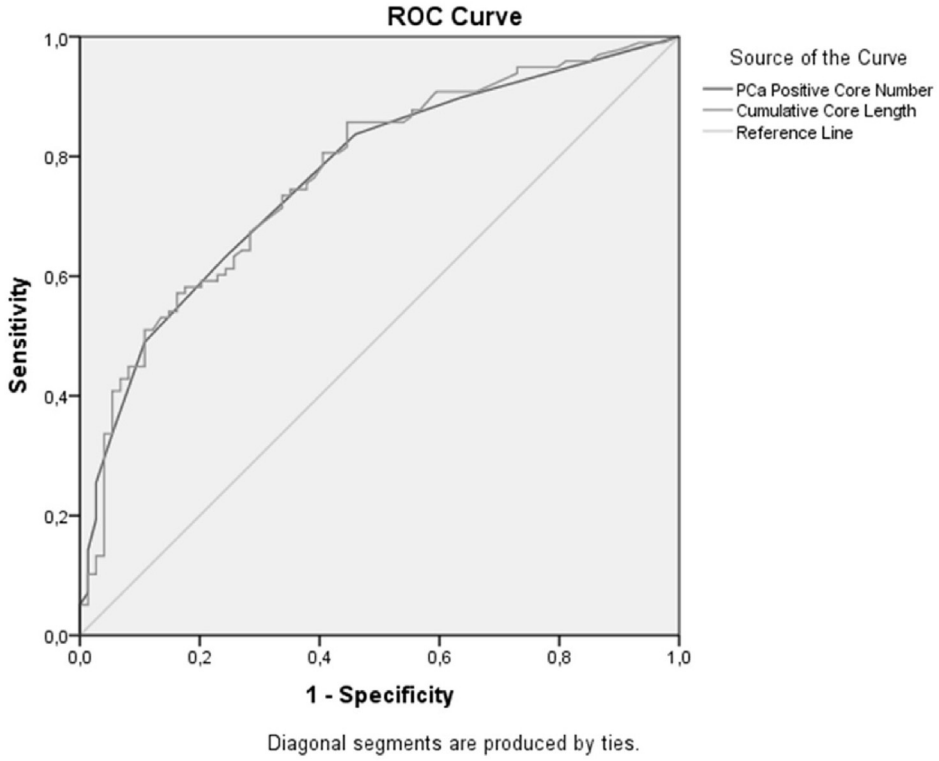
		Adverse pathology		*P*
		No (n = 148)	Yes (n = 196)	
Age (years)		63 (5)	64 (5)	0.802
Core number		15 (2)	15 (2)	0.533
PCa-positive core number		3 (2)	5 (3)	<0.0001
CCL (mm)		7.18 (9.37)	19.83 (18.09)	<0.0001
CCL/core (mm)		2.43 (1.55)	3.61 (2.23)	<0.0001
PSA at biopsy (ng/ml)		7.37 (3.52)	8.03 (3.74)	0.181
PSA density (ng/ml/cc)		0.25 (0.19)	0.33 (0.24)	0.299
DRE	Negative	38 (25.7%)	38 (19.4%)	0.147
	Suspect	73 (49.3%)	79 (40.3%)	
	Positive	37 (25.0%)	79 (40.3%)	
GG at biopsy	1	81 (54.7%)	36 (18.4%)	<0.0001
	2	48 (32.4%)	84 (42.9%)	
	3	17 (11.5%)	42 (21.4%)	
	4	2 (1.4%)	22 (11.2%)	
	5	0 (0.0%)	12 (6.1%)	
GG at RP	1	59 (39.9%)	12 (6.1%)	<0.0001
	2	62 (41.9%)	66 (33.7%)	
	3	26 (17.6%)	61 (31.1%)	
	4	1 (0.6%)	35 (17.9%)	
	5	0 (0.0%)	22 (11.2%)	
Biopsy risk class	True low	68 (45.9%)	26 (13.3%)	<0.0001
	Low and FI	133 (89.9%)	116 (59.1%)	
	UI	14 (9.5%)	45 (23.0%)	
	High	1 (0.6%)	35 (17.9%)	
RP risk class	Low and FI	109 (73.7%)	1 (0.5%)	<0.0001
	UI	38 (25.7%)	12 (6.1%)	
	High	1 (0.6%)	183 (93.4%)	

PSA, prostate specific antigen; CCL, cumulative cancer length; DRE, digital rectal examination; FI, favorable intermediate; GG, Grade Group; PCa, prostate cancer; RP, radical prostatectomy; UI, unfavorable intermediate.
All continuous variables are expressed as mean (standard deviation). Categorical variables are expressed as n (%).

Table 3
Comparison between presence or absence of adverse pathology in different prostate cancer risk classes and multinomial logistic regression to search for adverse pathology predictors in different prostate cancer risk classes.

Adverse pathology features according to PCa-positive core number and CCL			*P*	Multivariate analysis Odds ratio (95% confidence interval)	*P*
	No	Yes			
All cases (n = 344), no (n = 148), yes (n = 196)					
Age (years)	63 (5)	64 (5)	0.802	1.081 (1.006–1.163)	**0.034**
PSA (ng/ml)	7.37 (3.52)	8.03 (3.74)	0.181	1.050 (0.958-1.150)	0.295
PCa-positive core number	3 (2)	5 (3)	**<0.0001**	1.513 (1.140-2.007)	**0.004**
CCL (mm)	7.18 (9.37)	19.83 (18.09)	**<0.0001**	1.027 (0.977-1.080)	0.296
CCL/core (mm)	2.43 (1.55)	3.61 (2.23)	**<0.0001**	1.540 (1.018-2.331)	**0.041**
True low risk (n = 94), no = 68, yes = 26					
Age (years)	62 (5)	63 (5)	0.813	1.046 (0.882-1.242)	0.603
PSA (ng/ml)	6.02 (2.06)	6.76 (1.72)	0.258	1.185 (0.785-1.789)	0.420
PCa-positive core number	2 (1)	4 (2)	**<0.0001**	2.369 (1.085-5.175)	**0.030**
CCL (mm)	2.80 (2.67)	9.43 (10.7)	**<0.001**	1.031 (0.806-1.318)	0.810
CCL/core (mm)	1.40 (0.77)	1.94 (1.50)	0.160	1.910 (0.509-7.175)	0.338
Low risk and FI (n = 249), no = 133, yes = 116					
Age (years)	63 (5)	64 (5)	0.291	1.081 (0.993-1.176)	0.071
PSA (ng/ml)	7.44 (3.64)	7.75 (3.73)	0.644	1.028 (0.925-1.143)	0.607
PCa-positive core number	2 (2)	4 (2)	**<0.0001**	1.629 (1.140-2.326)	**0.007**
CCL (mm)	6.04 (7.96)	12.67 (11.78)	**<0.0001**	1.009 (0.940-1.083)	0.806
CCL/core (mm)	2.24 (1.47)	2.92 (1.74)	**0.030**	1.620 (0.970-2.706)	0.065
UI risk (n = 59), no = 14, yes = 45					
Age (years)	62 (6)	63 (6)	0.692	1.097 (0.923-1.303)	0.295
PSA (ng/ml)	6.17 (1.54)	7.84 (3.81)	0.243	1.166 (0.860-1.579)	0.322
PCa-positive core number	4 (3)	7 (3)	**0.041**	1.409 (0.806-2.461)	0.228
CCL (mm)	16.35 (15.39)	30.88 (17.19)	**0.046**	1.017 (0.926-1.116)	0.728
CCL/core (mm)	3.81 (1.69)	4.71 (2.27)	0.347	1.761 (0.603-5.139)	0.300
High risk (n = 36), no = 1, yes = 35					
Age (years)	59	65 (3)	0.063	NA	
PSA (ng/ml)	6.36	9.22 (3.80)	0.475	NA	
PCa-positive core number	3	6 (4)	0.425	NA	
CCL (mm)	8.00	29.81 (25.1)	0.411	NA	
CCL/core (mm)	2.70	4.55 (2.81)	0.531	NA	

PSA, prostate specific antigen; CCL, cumulative cancer length; FI, favorable intermediate; PCa, prostate cancer; UI, unfavorable intermediate.
All continuous variables are expressed as mean (standard deviation). The Student t test was used for univariate analysis. Multinomial logistic regression was used for multivariate analysis, and it is expressed as odds ratio (95% confidence interval).



Area Under the Curve

Test Result Variable(s)	Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
PCa Positive Core Number	0.767	0.036	0.000	0.696	0.837
CCL	0.769	0.036	0.000	0.698	0.840

Legend: PCa=Prostate Cancer; CCL=Cumulative Cancer Length

a. Under the nonparametric assumption

b. Null hypothesis: true area = 0.5

Figure 1. Receiver operating characteristic curve shows cumulative core length and prostate cancer–positive core number. ROC, receiver operating characteristic.

curve was used to establish an appropriate PCa-positive core number and CCL threshold, and then, they were independently investigated as predictors of AP at biopsy through univariate analysis and multivariate logistic regression. We focused in particular in true low-risk subgroup and low- and favorable intermediate-risk PCa. Statistical significance was set at p-value <0.05, and confidence interval (CI), at 95%. Analysis was performed using SPSS version 20.0 (SPSS Inc, Chicago, IL, USA).

3. Results

A total of 882 patients were eligible according to the study criteria and were included. Among them, 344 patients had PCa and underwent subsequent RP, and thus, they were considered for analysis. Patient characteristics and groups are listed in Table 1.

AP was reported in 196 (56.9%) patients. The patients were divided into two groups according to the presence or absence of AP features and then subdivided into the predefined risk groups. Their characteristics are reported in Table 2.

There was a statically significant difference ($p < 0.0001$) between PCa-positive core number and thus CCL in all groups, whereas in unfavorable intermediate- ($p = 0.04$) and high-risk groups, that was not statistically significant. However, on multivariate analysis, CCL lost its significance. The results are reported in Table 3. PCa-positive core number was a statistically significant predictor of AP in all cases and in both true low-risk and low- and favorable intermediate-risk groups, with an odds ratio (OR) of 1.513 (95% CI = 1.140–2.007), $p = 0.004$; OR of 2.369 (95% CI = 1.085–5.175), $p = 0.030$; and OR of 1.629 (95% CI = 1.140–2.326), $p = 0.007$, respectively.

Furthermore, we observed that the CCL/core ratio was a predictor of AP at RP in any case, with an OR of 1.540 (95% CI = 1.018–2.331), $p = 0.041$. However, when analysis was extended to risk groups, it failed to be a significant predictor of AP in all of them. The results are further listed in Table 3.

Table 4
Comparison between presence of or absence of adverse pathology in different prostate cancer risk classes and multinomial logistic regression considering 3 prostate cancer–positive core thresholds or cumulative core length >6-mm threshold.

Adverse pathology features according to 3 PCa-positive core thresholds			*P*	Multivariate analysis	*P*
	No	Yes			
All cases (n = 344), no (n = 148), yes (n = 196)					
Age (years)	63 (5)	64 (5)	0.802	1.080 (1.008–1.157)	**0.028**
3 PCa-positive core	67 (45.3%)	163 (83.2%)	**<0.0001**	7.127 (3.366-15.090)	**<0.0001**
All cases (n = 344), no (n = 148), yes (n = 196)					
Age (years)	62 (5)	63 (5)	0.813	1.006 (0.845-1.197)	0.949
3 PCa-positive core	15 (22.1%)	17 (65.4%)	**0.011**	6.362 (1.305-31.017)	**0.022**
Low risk and FI (n = 249), no = 133, yes = 116					
Age (years)	63 (5)	64 (5)	0.291	1.077 (0.993-1.168)	0.074
3 PCa-positive core	56 (42.1%)	90 (77.6%)	**<0.0001**	5.541 (2.390-12.849)	**<0.0001**
Adverse pathology features according to CCL >6-mm threshold			*P*	Multivariate analysis	*P*
	No	Yes			
All cases (n = 344), no (n = 148), yes (n = 196)					
Age (years)	63 (5)	64 (5)	0.802	1.050 (0.983-1.121)	0.144
CCL>6mm	67 (45.3%)	159 (81.1%)	**<0.0001**	5.462 (2.717-10.978)	**<0.0001**
True low risk (n = 94), no = 68, yes = 26					
Age (years)	62 (5)	63 (5)	0.813	0.955 (0.809-1.127)	0.588
CCL>6mm	10 (14.7%)	15 (57.7%)	**0.009**	6.484 (1.403-29.966)	**0.017**
Low risk and FI (n = 249), no = 133, yes = 116					
Age (years)	63 (5)	64 (5)	0.291	1.046 (0.969-1.130)	0.251
CCL>6mm	53 (39.8%)	83 (71.6%)	**<0.0001**	3.989 (1.839-8.652)	**<0.0001**

CCL, cumulative cancer length; FI, favorable intermediate; PCa, prostate cancer.
All continuous variables are expressed as mean (standard deviation). Categorical variables are expressed as n (% of the column number). The Student t test and Chi-square test were used for univariate analysis. Multinomial logistic regression was used for multivariate analysis and is expressed as odds ratio (95% confidence interval).

By the use of the ROC curve, we established an adequate area under the curve CCL and PCa-positive core number cutoff to better discriminate patients suspected of AP feature; in detail, a 6-mm threshold (area: 0.769; $p < 0.0001$, 95% CI = 0.698–0.840) was established for CCL and a 3 positive core threshold (area: 0.767; $p < 0.0001$, 95% CI = 0.696–0.837) for PCa-positive core number. The ROC curve is shown in Fig. 1. All patients were then reassigned according to the new categorization, in particular, in the true low-risk subgroup and low-risk and favorable intermediate-risk group, and each threshold was investigated separately through age-adjusted multivariate logistic regression, thus establishing that both >3 PCa-positive core and CCL>6mm were associated with an increased risk in AP, as reported in Table 4. In detail, for all patients, CCL>6mm had an OR of 5.462 (95% CI = 2.717–10.978), $p < 0.0001$. For the low- and favorable intermediate-risk groups, CCL>6mm had an OR of 3.989 (95% CI = 1.839–8.652), $p < 0.0001$, whereas the true low-risk group had an OR of 6.484 (95% CI = 1.403–29.966), $p = 0.017$. In addition, >3 PCa-positive core had an OR of 7.127 (95% CI = 3.366–15.090), $p < 0.0001$, in all cases, whereas for the low- and favorable intermediate-risk group, the OR was 6.362 (95% CI = 1.305–31.017), $p = 0.022$, and in the true low-risk group, the OR was 6.484 (95% CI = 1.403–29.966), $p = 0.017$.

Information regarding clinical staging is listed in Table 5.

4. Discussion

As technology is greatly improving our diagnostic ability to avoid overtreatment for not clinically significant PCa, we still have to update our current predictive tools to determine lymph node involvement, extraprostatic disease, and tumor aggressiveness. In

Table 5
Clinical and pathological PCa staging according to the risk class.

Risk class		cTNM, n (%)		pTNM, n (%)	
PCa risk class	Low and favorable intermediate risk (n = 249)	cT2aNx	147 (59.0%)	pT2a Nx	77 (30.9%)
				pT2b Nx	82 (32.9%)
				pT2c Nx	1 (0.4%)
		cT2bNx	102 (41.0%)	pT3a Nx	88 (35.4%)
				pT3b Nx	1 (0.4%)
	Unfavorable intermediate risk (n = 59)	cT2a N0 M0	36 (61.0%)	pT2b N0	1 (1.7%)
				pT2c N0	1 (1.7%)
				pT3a N0	30 (50.8%)
		cT2b N0 M0	23 (39.0%)	pT3b N0	15 (25.4%)
				pT3a N1	4 (6.8%)
				pT3b N1	8 (13.6%)
	High risk (n = 36)	cT2a N0 M0	7 (19.4%)	pT2c N0	2 (5.5%)
		cT2b N0 M0	5 (13.9%)	pT3a N0	5 (13.9%)
				pT3a N1	4 (11.1%)
		cT2c N0 M0	24 (66.7%)	pT3b N0	11 (30.6%)
				pT3b N1	14 (38.9%)

PCa, prostate cancer; TNM, tumor nodes metastasis.

fact, fusion target biopsies might lead to an exaggeratedly high number of PCa-positive core, mostly performed at the suspected area, thus making those tools inaccurate and leading to development of new tools.[7,10]

CCL was already studied as a predictor of definitive pathology features, with different and variable outcomes. In fact, in a recent article, Audenet et al[9] failed to find any predictor in biopsy features for low-risk PCa; in particular, they evaluated CCL, but their criteria for AP were different as they excluded extraprostatic disease extension differently from us. In their study, however, when they applied extraprostatic disease extension, the results were found to be concordant with ours, with 50% of APs. The different AP criteria were applied considering the biochemical recurrence risk, which in their study was not related to extraprostatic disease extension, but only to seminal vesicle invasion or lymph node invasion or upgrade to GG higher than or equal to 3.[9] The reason for their categorization was that in low-risk PCa, GG 1 has an important effect on reduction of biochemical recurrence risk, as reported by Imnadze et al,[11] independently from considered AP features. However, Chen et al[12] reported that a low CCL in prostate biopsies was related to clinically insignificant PCa, thus sustaining our hypothesis that a CCL threshold could also be associated with AP features in true low-risk patients. In our study, a CCL of >6mm was found to be a good predictor of AP not only in the true low-risk group but also in the low- and favorable intermediate- and in unfavorable intermediate-risk PCa, thus making our results valuable to predict AP features potentially linked to biochemical recurrence after radical treatment of PCa also in these patients.

In 2012, Briganti et al[5] updated their nomogram for predicting PCa lymph node involvement, considering the percentage of cores with PCa instead of the number of positive cores, while with the introduction of mpMRI by Gandaglia et al,[10] it was later updated with mpMRI tumor features and fusion target plus systematic biopsy outcomes to increase its accuracy. This necessity to overcome the actual limits of the existing nomograms led to an increased attention on other biopsy features. In fact, Simopoulos et al[13] recently found an association between maximum cancer core length in fusion target biopsies, cancer volume, and pathological stage, in particular, with a similar threshold, from 6mm and higher, with a higher predictive value with a higher threshold. Their study, however, is limited to only target biopsies, thus excluding this relationship for systematic biopsies. In our findings, this relationship is found also for systematic biopsies, thus implying that the combination of CCL in both fusion target biopsies and systematic biopsies may overcome the current limitation in nomograms that combine results from target plus systematic biopsies.

Komai et al[14] evaluated the ratio between CCL and core numbers, thus finding that a CCL/core ratio of <0.20 mm was associated with clinically insignificant PCa defined as International society of urological pathology (ISUP) 1, cT2a, and PSA<20ng/ml. This relationship might also confirm our findings, thus confirming that biopsy features might provide useful information regarding definitive pathology. In fact, we found that the CCL/core ratio was a significant predictor of AP in all cases: the higher the ratio, the higher the chances to have AP, while in the study by Komai et al,[14] the lower the ratio, the higher the chances of having clinically insignificant PCa. Nevertheless, we failed to find a relationship between the CCL/core ratio and AP in low-risk PCa, but with the limitation that we did not check with a threshold. In addition, we just demonstrated that independently from the CCL/core ratio, the higher the CCL, the higher the risk of AP and thus of clinically significant PCa, associated with a higher biochemical recurrence rate.[14,15]

Furthermore, our threshold is not established arbitrarily, but is calculated using a ROC curve, which demonstrated also a similar outcome for the number of PCa-positive cores, the previous standard in PCa risk calculation.

The rationale between the direct correlation between CCL and AP might be that the more the tumor is extended, as reported with CCL, the bigger the tumor mass and thus the higher the risk of extracapsular or lymph node extension or positive surgical margins.

Our study has limitations; in fact, patients were prospectively enrolled, but they did not have a previous mpMRI, thus reducing accuracy and causing many patients with no clinically significant PCa to be found positive and reducing our possibilities to transfer our results in a fusion target plus systematic biopsy setting. Patients were all Caucasians, so results are obviously impaired and should also be tested with other races to be confirmed.

In our study, we evaluated an alternative way to predict local tumor extension related to CCL, instead of PCa-positive cores, thus finding a promising alternative in a random biopsy setting.

Declaration of Competing Interest

The authors have nothing to disclose.

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