A COMPARISON BETWEEN RISK ASSESSMENT SCORES IN PROSTATE CANCER

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A COMPARISON BETWEEN RISK ASSESSMENT SCORES IN PROSTATE CANCER (Abstract): **Background and aim**: Prostate cancer remains a prevalent cause of malignancy in men worldwide, representing the fifth leading cause of death globally. Oncologic treatment and monitoring of these patients are conducted using multiple scores that assess the risk of biochemical recurrence, with the CAPRA score and D'Amico risk stratification scheme currently being the most widely used. The study aims to compare the prognostic classification of prostate cancer patients using two different scores, identifying similarities and differences that may arise. **Materials and methods:** This retrospective study evaluated both the D'Amico and CAPRA scores in 54 men diagnosed with non-metastatic prostate cancer at the Regional Institute of Oncology between 2017-2021. Transrectal ultrasound-guided biopsy was performed on all patients for diagnostic purposes. The Gleason system was used to grade biopsy cores, and the 8th Edition of AJCC Cancer Staging Manual was used to evaluate clinical stage. **Results:** Following the evaluation of patients with CAPRA scores, out of the total of 54 patients, 12.96% (n=7) had low risk, 42.59% (n=23) had intermediate risk, and 44.44% (n=24) had high risk. Applying the D'Amico score stratified patients into the following risk groups: 5 patients (9.26%) in the low-risk group, 9 patients (16.67%) in the intermediate-risk group, and 40 patients (74.07%) in the high-risk group. In our study, we observed that after overlapping the stratification of patients with the D'Amico and CAPRA scores, out of the seven patients classified as low risk according to the D'Amico stratification, two of them were considered intermediate risk. Furthermore, D'Amico's score considers that out of the 23 patients with intermediate scores, 69.57% (n=16) of them have a high risk. **Conclusions:** The D'Amico stratification tends to categorize patients into a less favorable prognostic group, necessitating a different management approach and active oncological monitoring. On the other hand, the CAPRA score, due to its multitude of composing criteria, individualizes each case, especially for patients classified in the low and intermediate risk groups, thus completing the D'Amico score. Therefore, it beneficial to utilize both scores in evaluating prostate cancer patients for an accurate prognostic assessment. **Keywords**: PROSTATE CANCER, CAPRA SCORE, D'AMICO RISK STRATIFICATION, BIOCHEMICAL RECURRENCE, PREDICTIVE MODELS.

INTRODUCTION

Prostate cancer represents the second most common malignancy in men worldwide, after lung cancer, being the fifth leading cause of death globally (1). The incidence of prostate cancer increases with age (2), and although only one in 350 men under the age of 50 will be diagnosed with this type of cancer (3), in men over 65 years old the incidence rate approaches 60% (4).

Treatment and monitoring of patients depend on the following clinic-pathological parameters found in many models for predicting recurrence after curative treatment: prostate-specific antigen (PSA) level, Gleason score, clinical tumor (cT) stage, various biopsy core characteristics (percentage of positive biopsies), or age (5). Prognostic scores, calculated based on these parameter values, are valuable tools in the oncological approach.

The trend in oncology is to optimize and refine these scores to provide the most accurate assessment of the patient's oncological status and, consequently, optimal therapeutic management. Currently, there are three widely used models (6) to stratify biochemical recurrence after radical prostatectomy: the D'Amico risk stratification scheme (7), the CAPRA score (8), and the Stephenson nomogram (9).

In an attempt to optimize disease progression prediction, in 1998, D'Amico *et al*. developed a combined modality staging system to stratify patients into three risk groups: low, intermediate, or high risk of biochemical recurrence after surgical and radio therapeutic treatment (7). In the D'Amico model, there are three variables categorized as follows: (i) prostate-specific antigen (PSA) levels ≤ 10, 10.1-20, and ≥ 20 ng/mL; (ii) clinical stage categories were cT1/2a, cT2b, and cT2c/T3 or higher; and (iii) biopsy Gleason score categorized as ≤ 6, 7, and ≥ 8.

Several years later, in 2005, the Cancer of the Prostate Risk Assessment (CAPRA) score was published (8). The CAPRA score is based on five variables categorized as follows: (i) PSA levels of ≤ 6, 6.1-10.0, 10.1-20.0, 20.1-30, or ≥ 30 ng/mL; (ii) clinical stage of cT1/2 or cT3; (iii) biopsy Gleason score of no Gleason pattern 4, secondary Gleason pattern 4/5, or primary Gleason pattern 4/5; (iv) age of <50 or ≥ 50 year, and (v) percentage of cancer in the biopsy <34% or ≥ 34%. This score was designed as a predictive stratification tool that could be easily calculated. Subsequently, the CAPRA score was upgraded to the post prostatectomy score (CAPRA-S) and Japanese primary androgen-deprivation therapy (J-CAPRA) (10).

Both the D'Amico and the CAPRA score have been externally validated, and their ability to predict biochemical recurrence has been confirmed over time (11–14).

The aim of our study was to compare the prognostic classification of prostate cancer patients using both the D'Amico score and the CAPRA score to identify similarities and differences that may arise. The analysis of these similarities and differences may lead the oncologist to use one of these two scores in daily practice, considering that it provides beneficial risk stratification for patient monitoring.

MATERIALS AND METHODS

The study population consisted of 54 men diagnosed with prostate cancer (without distant metastases) at the Regional Institute of Oncology between January 1st, 2017, and December 31st, 2021. All patients underwent multicore transrectal ultrasound-guided biopsy for diagnosis. Biopsy cores were graded according to the Gleason system (15). PSA values were measured before digital rectal examination or biopsy. Clinical stage was assigned by the attending urologist / oncologist follow-

ing the American Joint Committee on Cancer TNM guidelines (16, 17). The variables we tracked were: (i) patient age, (ii) PSA value, (iii) Gleason score, (iv) TNM staging and (v) percentage of cancer in the biopsy. All patients were evaluated using both the D'Amico and CAPRA scores, and the results were compared.

RESULTS

The mean age of patients was 68.75 years (range: 48-84 years); one patient was under 50 years old (1.85%) and 53 were over 50 years old (98.15%). The median follow-up time among survivors in our patient cohort was 2 years Out of the 54 patients, 6 (11.11%) registered disease progression and 3(5.56%) have deceased.

In the study group, PSA values were as follows: < 6 ng/mL – 6 patients (11.11%), ≥ 6 – 10 ng/mL – 12 patients (22.22%), ≥ 10 – 20 ng/mL – 22 patients (40.74%), ≥ 20 – 30 ng/mL – 6 patients (11.11%), 8 patients (14.81%) > 30 ng/mL (tab. I).

TABLE I.

Comparison between the distribution of patients according to specific criteria in CAPRA and D'Amico scores

CAPRA score			D'Amico score		
Criteria		Cases # (%)	Criteria		Cases # (%)
Age	<50 y.o.	1 (1.85%)			
	>50 y.o.	53 (98.15%)			
PSA	< 6 ng/mL	6 (11,11%)	PSA	< 10 ng/mL	18 (33.33%)
	≥ 6-10 ng/mL	12 (22.22%)			
	≥ 10-20 ng/mL	22 (40.74%)		10-20 ng/mL	22 (40.74%)
	≥ 20 - 30 ng/mL	6 (11.11%)			
	> 30 ng/mL	8 (14.81%)		>20 ng/mL	14 (25.93%)
Gleason score	4 or 5 patterns	16 (29.63%)	Gleason score	≤ 6	16 (29.63%)
	4 or 5 secondary patterns	22 (40.74%)		7	26 (48.15%)
	4 or 5 primary patterns	16 (29.63%)		≥ 8	12 (22.22%)
Stage	cT1 or cT2	25 (46.30%)	Stage	cT1 – cT2a	5 (9.26%)
				cT2b	12 (22.22%)
	cT3a	29 (53.70%)		≥ cT2c	37 (68.52%)
Cancer in core biopsy	< 34%	16 (29.63%)			
	> 34%	38 (70.37%)			

- number; % - percentage

Gleason scores provided by the histopathological exam of prostate biopsy showed the subsequent distribution: 6 (3 + 3) in 16 patients (29.63%), 7 (3 + 4) in 21 patients (38.89%), 7 (4 + 3) in 5 patients (9.26%), 8 (4 + 4) in4 patients (7.41%), 8 (3 + 5) and 8 (5 + 3) – each in 1 patient (1.85%), 9 (4 + 5) and (5 + 4) – each in 3 patients (5.56%) (tab. I).

The classification/setting of patients in clinical stages revealed: 5 patients (9.26%) in cT1-cT2a, 12 patients (22.22%) in cT2b, 8 patients (14.81%) in cT2c and 29 patients (53.70%) in cT3a (tab. I).

According to the results of the histopathological exam, the percentage of positive cores in prostate biopsy was < 34% in 16 patients (28.63%) and >34% in 38 patients (70.37%) (tab. I).

Based on the evaluated clinical and

pathological parameters, the application of the D'Amico score led to the following patient stratification: 5 patients (9.26%) in the low-risk group, 9 patients (16.67%) in the intermediate-risk group, and 40 patients (74.07%) in the high-risk group. Similarly, following the assessment of patients using the CAPRA score, out of the total of 54 patients, 7 (12.96%) had low risk, 23 (42.59%) had intermediate risk, and 24 (44.44%) had high risk (tab. II).

Interestingly, upon evaluating the same patients using the D'Amico score, out of the 7 patients classified as low risk according to CAPRA score, two of them (28.57%) were considered intermediate risk. Furthermore, the D'Amico score indicated that out of the 23 patients classified as intermediate risk, 16 of them (69.57%) were categorized as high risk. Regarding patients classified as high risk according to the D'Amico classification, all 24 corresponded to the high-risk category in the CAPRA classification (tab. III).

TABLE II.

Distribution of patients in risk groups according to CAPRA and D'Amico scores

CAPRA score			D'Amico score		
Risk	**Score**	**Cases # (%)**	**Risk**	**Score**	**Cases # (%)**
Low	1	3 (5.56%)	low	3	5 (9.26%)
	2	4 (7.41%)			
Intermediate	3	5 (9.26%)	intermediate	4	2 (3.7%)
	4	6 (11.11%)		5	3 (5.56%)
	5	12 (22.22%)		6	4 (7.41%)
High	6	8 (14.81%)	high	5	2 (3.7%)
	7	4 (7.41%)		6	9 (16.67%)
	8	4 (7.41%)		7	14 (25.93%)
	9	3 (5.56%)		8	11 (20.37%)
	10	5 (9.26%)		9	4 (7.41%)

- number; % - percentage

TABLE III.

Differences in distribution of patients in risk groups according to CAPRA and D'Amico scores

CAPRA score		Correspondence to D'Amico score	
Risk group	**# (%)**	**Risk group**	**# (%)**
Low	7 (12.96%)	Low	5 (9.26%)
		Intermediate	2 (3.7%)
Intermediate	23 (42.59%)	Intermediate	7 (12.96%)
		High	16 (29.63%)
High	24 (44.44%)	High	24 (44.44%)

- number; % - percentage

Regarding patient survival, the 3 patients who deceased were categorized in the high-risk group in both the D'Amico score and the CAPRA score (tab. IV). Furthermore, concerning survival without progression, out of the 6 patients who experienced tumor recurrence over a 2-year follow-up period, the CAPRA score classified 2 patients in the intermediate-risk group and 4 in the high-risk group.

On the other hand, the D'Amico score categorized 5 patients in the high-risk group and 1 in the intermediate-risk group (tab. V).

TABLE IV.

Correlation between risk groups in CAPRA and D'Amico scores and overall survival

Overall survival – CAPRA and D'Amico scores				
RISK GROUP	Survival	Death	Survival	Death
	# (%)	# (%)	# (%)	# (%)
	CAPRA SCORE		d'AMICO SCORE	
Low	7 (100%)	0 (0.0%)	5 (100%)	0 (0.0%)
Intermediate	23 (100%)	0 (0.0%)	9 (100%)	0 (0.0%)
High	21 (87.5%)	3 (12.5%)	37 (92.5%)	3 (7.5%)

- number; % - percentage

TABLE V.

Correlation between risk groups in CAPRA and D'Amico scores and progression free survival

Progression free survival – CAPRA and D'Amico scores				
RISK GROUP	Recurrence absent	Recurrence present	Recurrence absent	Recurrence present
	# (%)	# (%)	# (%)	# (%)
	CAPRA SCORE		D'Amico	
Low	7 (100%)	0 (0.0%)	5 (100%)	0 (0.0%)
Intermediate	21 (91.3%)	2 (8.7%)	8 (88.9%)	1 (11.1%)
High	20 (83.3%)	4 (16.7%)	35 (87.5%)	5 (12.5%)

- number; % - percentage

DISCUSSION

Over time, several studies have demonstrated that the risk of biochemical recurrence after prostate cancer treatment is heterogeneous and depends on factors such as PSA level, clinical stage of the disease, biopsy Gleason score, and characteristics of the core biopsy variables (7–9, 18). Due to this heterogeneity, different authors have proposed various risk classification schemes to quantify the individual rate of biochemical recurrence more accurately after prostate cancer treatment (7–9, 18). In this context, the D'Amico (7) and CAPRA (8) models are the most widely used prediction tools for tumor recurrence risk. However, there have been relatively few studies directly comparing these two stratification models (6, 19).

Among these, the most important are those by Lughezzani *et al.* (19), which directly compare the CAPRA score with the D'Amico risk stratification scheme, and that of Boehm *et al*., which compares the ability of the scores to predict cancer-specific mortality in a large European cohort of patients (6). The study of Lughezzani *et al.* included 1,976 prostate cancer patients treated by open radical prostatectomy. The conclusion was that the CAPRA score outperformed the other scoring models when calibration and decision curve analysis were used as benchmarks (19). Interestingly, they observed that the predictions of the D'Amico model showed limited ability to distinguish high rates of biochemical recurrence in patients. On the other hand, the CAPRA model could discriminate between a much wider varieties of biochemical recurrence risks and showed

the greatest benefit in predicting biochemical recurrence at 3 and 5 years, being the best tool in the cohort (19).

Another study that aimed to identify the most informative prediction tool for cancer-specific mortality was conducted by Boehm *et al.* (6). On a cohort of 2,485 prostate cancer patients who underwent radical prostatectomy, the investigators analyzed three preoperative models (D'Amico, CAPRA, and Stephenson), comparing their ability to predict 10-year cancer-specific mortality. For the 10-year prediction, the CAPRA score showed the highest net benefit. In contrast, the D'Amico model showed underestimation of cancer-specific mortality (6).

In our study we observed that after overlapping the evaluation of patients with the D'Amico and CAPRA scores, out of the 7 patients classified as low risk according to the D'Amico stratification, 2 of them were considered intermediate risk. Furthermore, the D'Amico score categorized 16 (69.57%) out of the 23 patients classified as intermediate risk as high risk. As a result of the overlapping of the two scores, we noticed that the D'Amico risk stratification scheme tends to place patients in a higher risk group.

In our practice as oncologists, we commonly utilize the NCCN (National Comprehensive Cancer Network) guidelines (20), which employ risk prognostic groups ranging from very low to very high (6 groups), as well as the D'Amico classification, for prognostic scoring in prostate cancer. The CAPRA score tends to be more commonly used by urologists, primarily as a prognostic score for patients undergoing surgical intervention for curative purposes. Currently, there is a trend towards a less invasive therapeutic approach, specifically radiotherapy as a method of curative treatment, which is increasingly preferred by patients. As our study results have also shown, the D'Amico stratification tends to categorize patients into a less favorable prognostic group, necessitating a different management approach and active oncological monitoring. On the other hand, the CAPRA score, due to its multitude of composing criteria, individualizes each case, especially for patients classified in the low and intermediate risk groups, thus completing the D'Amico score.

CONCLUSIONS

The assessment of the risk of recurrence should be done on an individual basis, considering the specific characteristics of each patient. The CAPRA score tends to be more comprehensive due to the complexity of the criteria it encompasses, including age (which is absent in the D'Amico score calculation), better stratification of PSA values, and especially the Gleason score, considering each Gleason pattern separately and implicitly each ISUP (International Society of Urological Pathology) prognostic grading group. Therefore, we find it beneficial to utilize both scores in evaluating prostate cancer patients for an accurate prognostic assessment. However, individualization is crucial; placing a patient in a higher prognostic group may benefit them by allowing the application of all necessary therapeutic measures. At the same time, overtreatment should be avoided as much as possible to preserve the patient's quality of life.

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