Clinical evaluation, PSA and preoperative Gleason score: an insufficient prognostic panel after radical prostatectomy

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Abstract

Introduction. Prostate cancer may express great variety in clinical behavior, from an indolent evolution to lethal disease. According to preoperative d'Amico criteria it is appreciated that patients with localized prostate cancer, PSA > 20 ng/ml, Gleason score of 8 to 10 are classified at high risk for recurrence of symptomatic or asymptomatic metastatic disease. The *Scandinavian Prostate Cancer Group 4* (SPCG-4) and *Prostate Intervention Versus Observation Trial* (PIVOT) trials generated new coordinates in the means of the right moment and treatment option in prostate cancer.
Objective. The aim of this study was to determine the number of patients restaged in the means of risk stratification after pathologic results from the radical prostatectomy specimen.
Materials and methods. 218 patients with prostate cancer were enrolled in a prospective study between June 2011 and January 2014, after obtaining the informed consent. All cases underwent open retropubic radical prostatectomy in our Center.
Results. Of the 29 pts staged preoperatively as cT1c, 21 were staged as pT2 postoperatively, the rest being staged as pT3. From the preoperative group staged cT2, after surgery and pathology, one case is staged pT1, 40 pts pT3, one case pT4 and only 48 pts staged pT2, the same as before surgery. For cT3 stage, 61 pts were actually pT3, representing 55,5% of the cT3 group, and 28% of the total number of pts in the study, as 36 pts were reassigned to other risk groups. Of the two cT4 cases, one was actually pT4 and one pT3.
Of the preoperative 2-6 Gleason group, 34,6% were reassigned to the intermediate risk group, and 4,8% were restaged as high risk. Of the initial intermediate risk group, 43 were actually intermediate risk, 17 pts were reassigned to low risk Gleason 2-6 group, and the remaining 11 were Gleason 8 and 9. Preoperatively high risk pts were restaged as follows: 17,3% reassigned to low risk group, 21,7% intermediate risk,the remaining 61 % maintaining in the high risk group.
Conclusions. For cT1c, 27,6% of the cases areoverstaged after pathology report, as for cT2 the proportion being even higher, of 45,5%, which explains the high risk of progression without surgical treatment for this stage. According to statistical data, cT3 stage isthen placed in an inferior risk group in 34% of cases. Regarding the number of initially overstaged patients (based upon cT), 16% of the study group are overstaged preoperatively, of which 33 pts fall in the cT3 stage, this being probably the result of insufficient information from the preoperative panel consisting of transrectal ultrasound, serum PSA, digital rectal examination and Gleason score from the biopsy specimens.

Key words: cancer, prostate, Gleason, panel, prostatectomy, risk, staging

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Introduction

Prostate cancer may express great variety in clinical behavior, from an indolent evolution to lethal disease. According to preoperative D'Amico criteria it is appreciated that patients with localized prostate cancer, PSA > 20 ng/ml, Gleason score of 8 to 10 are classified at high risk for recurrence of symptomatic or asymptomatic metastatic disease. According to the same classification, low risk prostate cancer is defined by cT1-T2a, PSA < 10 ng/ml, Gleason score less than 6, and intermediate risk group is cT2b-T2c, PSA 10 to 20 ng/ml, and a Gleason score of 7 [1].

For the low risk group, the results of two prospective randomized trials that compare radical retropubic prostatectomy and watchful waiting are available. *The Scandinavian Prostate Cancer Group 4* (SPCG-4) trial concluded that the overall survival is similar for the two groups, after 9 years of follow-up, but the data was limited to <65 years of age group. In *The Prostate Intervention Versus Observation Trial* (PIVOT) study, for the low risk group, radical prostatectomy did not significantly reduce the mortality [1]. In this risk group, clinically undetectable T1c tumors diagnosed trough prostatic biopsy represent the majority. Individually speaking, it is very difficult to differentiate a clinically insignificant tumor from a very aggressive one. Studies conducted so far showed that surgical treatment is the optimal solution, because pathology after surgery showed that 30% are restaged as locally advanced, only 11-16% being insignificant [2,3].

The cT2a subgroup should also undergo radical prostatectomy, current data showing that 33 to 55% will show progression in the absence of surgical treatment [4]. For this group, extended lymph node dissection (eLND) is not necessary, due to the fact that positive lymph nodes are found in maximum 5% of cases [5].

Although the new biopsy protocols raised the number of biopsy cores to 12, this did not lead to an increase in prostate cancer detection. Extended biopsy results and freePSA levels can lead to anticipation of clinically insignificant cancers [2,3].

In the intermediate risk group, for the <65 years of age subgroup, overall survival was similar in both radical prostatectomy and watchful waiting arms. The same trial shows that in order to prevent a prostate cancer death, the number needed to treat is 15 for all age groups, 7 cancers belonging to the <65 years of age group [6,7].

Radical prostatectomy is the standard surgical treatment for intermediate risk group, with a life expectancy of >10 years, as for selected subgroups, watchful waiting could be a viable option [8].cT2b cases will progress in 5 years in about 70% without surgical treatment, thus making radical prostatectomy a gold standard treatment option [9]. For this group, extensive lymph node dissection is mandatory, as the positive lymph node proportion is above 5%, whereas limited lymph node dissection will miss 50% of the positive lymph nodes [5].

Advanced prostate cancer (T3a) stands for over 40% of diagnosed prostate cancers in older statistics [10]. Many randomized prospective trials compared radiotherapy and hormonal therapy. The combination of the two showed a clear survival benefit. No study showed their superiority to radical prostatectomy[11,12]. The interest for performing radical prostatectomy in high risk patients is rising lately, although the opinions are still conflicting. A good argument for radical prostatectomy is the fact that 12-27% of the patients are clinically over staged to high risk group. This percent of patients belong to the intermediate risk group, for which the gold standard therapy is radical prostatectomy, the progression free interval being the same [13].

Opposed to previously discussed, data showed that 33 to 66% of patients with radical prostatectomy will have positive surgical margins and 7 to 49% of lymph nodes will be positive on pathology report, therefor 56 to 78% of these patients will need hormonal or salvage radiotherapy [14,15]. For these case, the overall survival (OS) and cancer specific survival (CSS) at 5, 10 and 15 years are very good, being clearly superior to radiotherapy alone and similar to combined radio and hormonal therapy [16].

In the high risk Gleason 8-10 group, the localized tumor incidence is 23-31%, the prognostic after radical prostatectomy being similar for the entire group. Furthermore it seems that more than one third of the patients with a Gleason score of 8-10 on biopsy results have actually a Gleason score of 7 or less, the prognostic for this group being also good. Important parameters for the indication for radical prostatectomy are the serum PSA level and the cancer positive percent of the biopsy fragment [17]. For the high risk group, with a PSA level over 20 ng/ml, d'Amico et al. found biochemical relapse of more than 50% at 5 years. The conclusions of this study overlap the majority of contemporary data, showing a cancer specific survival of 90% at 10 years and 85% at 15 years [18]. Obviously, the combination of a PSA >20 ng/ml, Gleason score >8 and

cT3a stage modify drastically the biochemical recurrence and overall survival parameters. Data shows that the initial step in the management of this subgroup of prostate cancer might be aggressive therapy – radical prostatectomy. Positive lymph nodes in this cases is 5-40%, thus making extensive lymph node dissection a standard of care [15].

Objective

The aim of this study was to determine the number of patients restaged in the means of risk stratification after pathologic results from the radical prostatectomy specimen.

1. Study design and methodology

Study group and inclusion criteria.

A number of 218 patients were enrolled in a prospective manner from June 2011 – January 2014, after the inclusion and exclusion criteria below were met.

Table 1

	Inclusion criteria
1.	Informed consent was obtained from every patient.
2.	The patient was diagnosed with prostate cancer.
3.	The patient was evaluated biochemically and imagistic, and staged in a localized or local advanced stage.
4.	Patient is asymptomatic or minimally symptomatic.
5.	ECOG score 0 or 1.
6.	The patient did not receive neo adjuvant radiotherapy.
7.	The patient is fit for general anesthesia and surgery
8.	The life expectancy is > 10 years.
9.	Patient age under 85 years.
10.	A minimum of 4 weeks after prostate biopsy and a minimum of 6 months after TURP.
	Exclusion criteria
1.	Neo adjuvant therapy, cytotoxic therapy, external or internal radiotherapy.
2.	Severe illness, infection or other important morbidities.
3.	Known or suspect for cerebral metastases.
4.	Patient diagnosed in a late, metastatic stage.
5.	Patient unfit for anesthesia and surgery.
6.	Other neoplasia in the past 5 years.
7.	5 alpha reductase inhibitors or steroids in recent medical history.
8.	Major surgery in the previous 2 months.
9.	Neurologic or psychiatric illness.
10.	Clinical significant cardiologic diseases, including myocardial infarction, stable or unstable angina, cardiac failure NYHA III-IV, ventricular arrhythmia, stage II atrio-ventricular blockade, high risk hypertension.
11.	The patient is enrolled in a clinical trial.
12.	Vulnerable group patients that depend upon hospitals or medical teams, or patients that cannot provide an informed consent.

Discontinuation criteria for the patient is linked to concomitant medication or disease that may prohibit surgery.

All patients had an indication for radical retropubic prostatectomy. All surgical procedures were performed in the Center for Uronephrology and Renal Transplantation, Fundeni Clinical Institute, Bucharest by a team of two urologic surgeons, using a standard surgical technique performed in our department. The prostatectomy specimens were examined by two pathologists, the result being validated after 15 to 21 days. All imagistic investigations were performed in the Radiology and Clinical Imaging Department in our Center.

All patients signed the informed consent form before any study procedure. The study protocols and informed consent were analyzed and approved by the Institution's Ethical Committee.

2. Radical retropubic prostatectomy.

Radical prostatectomy consist of complete surgical excision of the prostate and seminal vesicles, together with the periprostatic fatty tissue, followed by uretro-vesical anastomosis. Retropubic extraperitoneal approach allows simultaneous access to the prostate and de lymphatic nodes, but has a high bleeding risk. Surgery is performed 6 to 8 weeks after the prostate biopsy or 12 weeks after TURP, in order to allow resolution of the local inflammatory changes and resorption of hematomas from previous maneuvers. The surgical procedure requires special surgical instruments, and

surgical outcomes depend largely on the surgeon's skill.

Results

1. Staging the prostatic biopsy specimens according to Gleason score.

For the 218 cases enrolled, mean Gleason score was 6,27, with a median of 6. Minimal Gleason score was 2, with a maximum of 9 and a standard deviation of 1,10. One has to notice the mean and median values in the low risk 2-6 and medium risk 7 area, for which radical prostatectomy is the standard indication. Also in the group there is a subgroup of high Gleason score that puts them in the high risk category, for which radical prostatectomy is the foundation for multimodal approach.

2. Preoperative TNM staging.

For TNM preoperative staging, to avoid study bias, because of non homogenous imagistic data regarding N and M, we only considered the T element. We considered 4 T categories: T1, T2, T3 and T4. 29 patients, accounting for 13,3% of the group were staged T1, 90 patients accounting for 41,3% were staged T2, 97 patient accounting 44,5% were evaluated as T3 and 3 patients representing 0,9% were staged T4.

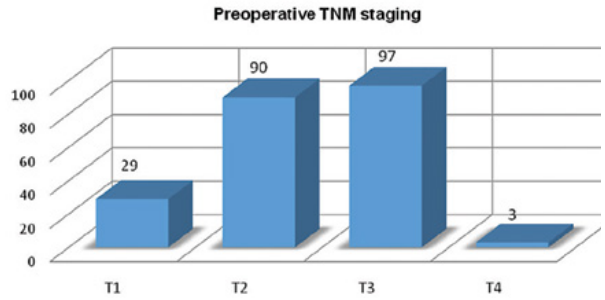


Fig. 1. Preoperative TNM staging.

3. Postoperative TNM staging.

For this staging parameter we considered 4 categories based on the pT element. The distribution resulted from processing data from the database, after prostatectomy specimens were processed. 2 cases were assigned as pT1, accounting for 0,9% and 101 specimens were staged pT2. This means that 47,2% turned out to be localized disease postoperative. 5 of the cases representing 2,3% were evaluated as pT4, the rest of 110 cases were staged as pT3.

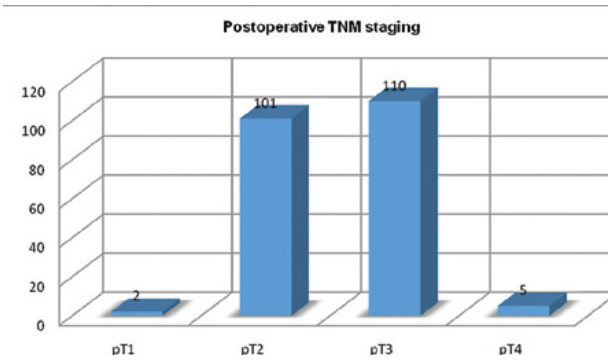


Fig. 2. Postoperative TNM staging.

Extensive pT categories is represented in table 2 and fig. 3.

Table 2	**Postoperative TNM staging**			
Valid	Frequency	Percent	Valid percent	Cumulative percent
pT1cpN0pMx	2	0,9	0,9	0,9
pT2 apN0pMx	16	7,3	7,3	8,3
pT2bpN0pMx	13	6,0	6,0	14,2
pT2cpN0pMx	71	32,6	32,6	46,8
pT2cpN1pMx	1	0,5	0,5	47,2
pT3apN0pMx	54	24,8	24,8	72
pT3apN1pMx	5	2,3	2,3	74,3
pT3bpN0pMx	40	18,3	18,3	92,7
pT3bpN1pMx	11	5,0	5,0	97,7
pT4 pN0pMx	1	0,5	0,5	98,2
pT4pN1pMx	4	1,8	1,8	100,0
Total	218	100,0	100,0	

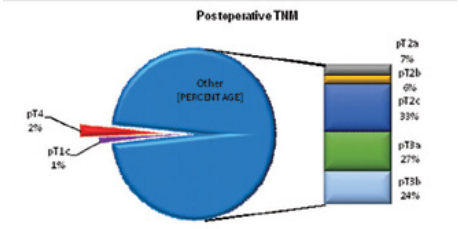


Fig. 3. Postoperative TNM.

4. Determining the proportion of patients that are restaged after pathology result in other risk group than the preoperative staging, with regard of T element and Gleason score

In order to establish correlations for this in order to fulfill objective, we first compared the distribution of the patients in the means of preoperative T staging with postoperative pT staging. This way, we tried to establish the niche group of patients, that donot fall in the same group as they were assigned preoperatively.

PreoperativeTNM * PostoperativeTNM Crosstabulation							
Table 3			Postoperative TNM staging				
			pT1	pT2	pT3	pT4	Total
Preoperative TNM Staging	T1(a,b,c)	Number	0	21	8	0	29
		% TNM preop	0%	72,4%	27,6%	0%	100%
		% TNM postop	0%	20,8%	7,3%	0%	13,3%
		% of Total	0%	9,6%	3,7%	0%	13,3%
	T2(a,b,c)	Number	1	48	40	1	90
		% TNM preop	1,1%	53,3%	44,4%	1,1%	100%
		% TNM postop	50,0%	47,5%	36,4%	20%	41,3%
		% of Total	0,5%	22,0%	18,3%	0,5%	41,3%
	T3(a,b)	Number	1	32	61	3	97
		% TNM preop	1,0%	33,0%	62,9%	3,1%	100%
		% TNM postop	50,0%	31,7%	55,5%	60%	44,5%
		% of Total	0,5%	14,7%	28,0%	1,4%	44,5%
	T4(a,b)	Number	0	0	1	1	2
		% TNM preop	0%	0%	50%	50%	100%
		% TNM postop	0%	0%	0,9%	20%	0,9%
		% of Total	0%	0%	0,5%	0,5%	0,9%
	Total	Number	2	101	110	5	218
		% TNM preop	0,9%	46,3%	50,5%	2,3%	100,0%
		% TNM postop	100%	100%	100%	100%	100%
		% of Total	0,9%	46,3%	50,5%	2,3%	100%

We see now that among the 29 patients evaluated preoperative as T1, 21 were restaged postoperative as pT2, accounting for 20,8% of the total number of patients clinically staged as T1 and 9,6% of the total number of patients in the study. The remaining 8 patients were staged as pT3, accounting for 27,6% of the initial cT1 group and 3,7% of the total number. This means that 100% of the initially cT1 patients were restaged in higher risk groups after pathology report.

From the cT2 group, with a,b and c subgroups, one case is staged as pT1, accounting for 1,1% of cT2 cases and 0,5% of the total number of patients. Also, 40 cases are restaged as pT3 representing 44,4% of the cT2 cases and 18,3% of the total number of patients. Only one case is restaged as pT4, and just 48 patients are staged postoperatively in the same group pT2 . from the 90 patients staged cT2, only 47,5% are actually pT2.

cT3 stage, with a or b subgroups stands for advanced disease, with uni or bilateral capsular invasion, with or without seminal vesicle involvement. Patient distribution was: 61 patients staged postoperatively as pT3, in the same risk group, accounting for 55,5% of the cT3 group and 28% of total patient number. 36 cases were restaged in other risk groups, representing 44,5% of the cT3 group and 16,6% of the total number. One case was restaged as pT1, 32 cases as pT2, acouning for 31,7% of cT3 and 14,7% of the total , and 3 cases were restaged as pT4.

Regarding cT4 stage,in which radical prostatectomy is a part of a multimodal approach, the two cases were staged postoperatively one as pT3 and one as pT4. We can say that half of the cT4 cases are restaged in an inferior risk group.

The diagram showed in figure 5 reflects all above mentioned data.

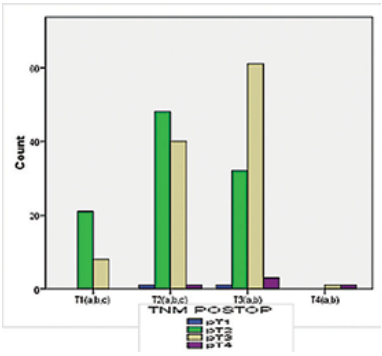


Fig. 4. Preoperative TNM diagram

The second coordinate is to compare patient distribution by the means of preoperative and postoperative Gleason score. Our objective was to identify the groups of patients that do not fall in the same risk group after examining the prostatectomy specimen.

According to D'Amico classification, there are 3 risk groups regarding Gleason score: low risk, with Gleason 2-6, intermediate risk with Gleason 7 and high risk with Gleason 8-10.

After examining the distribution of Gleason score pre and postoperatively for the low risk group, we noted the following:

- Patients initially scored Gleason 2 turned out to be 100% Gleason 4 postoperatively.
- The only Gleason 3 (2+1) score preoperatively belongs in fact to intermediate risk group, being actually a Gleason 7 after examining the prostatic specimen.

Preoperative Gleason score* Postoperative Gleason score Crosstabulation									
Table 4			Postoperative Gleason score						
			2	4	5	6	7	8	9	Total
Preoperative Gleason score	2	Number	0	1	0	0	0	0	0	1
		% preoperative Gleason score	0%	100%	0%	0%	0%	0%	0%	100%
		% postoperative Gleason score	0%	4,2%	0%	0%	0%	0%	0%	0,5%
		% of Total	0%	0,5%	0%	0%	0%	0%	0%	0,5%
	3	Number	0	0	1	0	1	0	0	1
		% preoperative Gleason score	0%	0%	100%	0%	100%	0%	0%	100%
		% postoperative Gleason score	0%	0 %	1,1%	,0%	1,1%	0%	0%	0,5%
		% of Total	0%	0%	0,5%	0%	0,5%	0%	0%	0,5%
	4	Number	0	6	2	5	2	1	0	14
		% preoperative Gleason score	0%	42,9%	14,3%	35,7%	14,3%	7,1%	0%	100%
		% postoperative Gleason score	0%	25%	2,2%	8,9%	2,2%	3,8%	0%	6,4%
		% of Total	0%	2,8%	0,9%	2,3%	0,9%	0,5%	0%	6,4%
	5	Number	1	3	8	8	8	0	0	25
		% preoperative Gleason score	4%	12%	32%	32%	32%	0%	0%	100%
		% postoperative Gleason score	50%	12,5%	8,8%	14,3%	8,8%	0%	0%	11,5%
		% of Total	0,5%	1,4%	3,7%	3,7%	3,7%	0%	0%	11,5%
	6	Number	0	9	32	31	32	4	1	83
		% preoperative Gleason score	0%	10,8%	38,6%	37,3%	38,6%	4,8%	1,2%	100%
		% postoperative Gleason score	0%	37,5%	35,2%	55,4%	35,2%	15,4%	20%	38,1%
		% of Total	0%	4,1%	14,7%	14,2%	14,7%	1,8%	0,5%	38,1%
	7	Number	1	4	43	9	43	9	2	71
		% preoperative Gleason score	1,4%	5,6%	60,6%	12,7%	60,6%	12,7%	2,8%	100%
		% postoperative Gleason score	50%	16,7%	47,3%	16,1%	47,3%	34,6%	40%	32,6%
		% of Total	0,5%	1,8%	19,7%	4,1%	19,7%	4,1%	0,9%	32,6%
	8	Number	0	1	4	3	4	12	1	21
		% preoperative Gleason score	0%	4,8%	19%	14,3%	19%	57,1%	4,8%	100%
		% postoperative Gleason score	0%	4,2%	4,4%	5,4%	4,4%	46,2%	20%	9,6%
		% of Total	0%	0,5%	1,8%	1,4%	1,8%	5,5%	0,5%	9,6%
	9	Number	0	0	1	0	1	0	1	2
		% preoperative Gleason score	0%	0%	50%	0%	50%	0%	50%	100%
		% postoperative Gleason score	0%	0%	1,1%	0%	1,1%	0%	20%	0,9%
		% of Total	0%	0%	0,5%	0%	0,5%	0%	0,5%	0,9%
	Total	Number	2	24	91	56	91	26	5	218
		% preoperative Gleason score	0,9%	11%	41,7%	25,7%	41,7%	11,9%	2,3%	100%
		% postoperative Gleason score	100%	100%	100%	100%	100%	100%	100%	100%
		% of Total	0,9%	11%	41,7%	25,7%	41,7%	11,9%	2,3%	100%

- For the initial Gleason 4 group, after restaging the distribution was: 6 cases Gleason 4, accounting for 2,8%, 5 cases Gleason 6 representing 2,3%, 2 cases Gleason 7 accounting for 0,9% and one case Gleason 8 representing 0,5%. We can see now that 21,5% of the cases initially appreciated as Gleason 4 are in fact placed in the intermediate or high risk group postoperatively.
- Regarding the initial Gleason 5 group, one case was scored Gleason 2, accounting for 0,5% of the total

number of patients, 3 patients were revaluated as Gleason 4, representing 1,4% of total, 5 cases are the same Gleason accounting for 2,3% of total and 8 patients were revaluated as Gleason 6 and 7 respectively, accounting for 3,7% of the total number. We can see that 32% of the initially Gleason 5 group, actually are rescored and fall in the intermediate risk Gleason 7 group.

- In the initial Gleason 6 group the postoperative re scoring showed 9 case appreciated Gleason 4 accounting for 4,1% of total, 6 cases Gleason 5, representing 2,8%, 32 cases appreciated as intermediate risk accounting for 14,7% of total, 4 cases Gleason 8 and one case Gleason 9. For this group, we had 31 patients evaluated postoperatively as Gleason 6,accounting for 14,2% of total, and if we compare only to low risk group, 38,6% turned out to be Gleason 7 and therefore intermediate risk, and 5% high risk with Gleason score of 8 and 9.

In the preoperative intermediate risk group, after examining prostatic specimens, we find 43 cases of intermediate risk, accounting for 19,7% of total number and 71,1% of the total group, 17 cases representing 23,9% are rescored as Gleason 2-6 and restaged as low risk and the remaining 11 cases are evaluated Gleason 8 and 9 and pass in the high risk category.

The initially high risk group of Gleason 8 turns out to be high risk in 12 cases, with the same Gleason score, accounting for 5,5% of total cases and 57,1% of the high risk group, one case re scored Gleason 4, one re scored Gleason 9, 3 cases Gleason 6 and 4 cases Gleason 7. Therefore for this risk group, re scoring places 61,9% in the high risk group, 19% intermediate risk and 19,1% are appreciated as low risk. Among the 2 cases of initial Gleason score of 9, one is rescored and belongs to the intermediate risk group and the other remains Gleason 9 and in the high risk category.

Discussions

1. Evaluation of staging elements

Preoperative TNM staging is established by the amount of information gathered through

digital rectal examination of the prostate and serum PSA level, and only in selected cases superior information is offered by pelvic MRI investigation or bone scan.

The first level of evaluation is to establish whether the prostate cancer is confined to the prostate or has extracapsular invasion, which is critical for further therapeutic decision. According to Spigelman et al., digital rectal examination of the prostate usually understages the prostatic tumor, as less than 50% of pathological results from biopsies correlates with initial clinical examination [19]. This fact leads to the necessity for further imaging for cases where a conservative approach is decided, and existing data do not completely characterize the neoplasia.

A second important element is the total PSA level, which increases in advanced disease state. Partin A.W. et al. establish in 1990 the PSA specificity for the prostate and the absence of a correlation between clinical stage and PSA value [19]. Freeland et al. introduce in 2002 another critical element for preoperative T staging [20]. That element is the length and percent of neoplasic involvement of the biopsy core, and also the number of positive cores. In 2003, Queen D.I. stated that this parameters are predictive for extracapsular invasion, positive surgical margins and lymph node involvement, while trying to establish one of the first nomograms, in order to be able to predict post prostatectomy prognostic using preoperative evaluation of certain parameters [21].

Partin et al. reach the conclusion that a combination of preoperative PSA, digital rectal examination and Gleason score on biopsy specimens is more efficient than any of the abovementioned taken separately [22]. In 2011, Eifler et al. publish an "upgrade" of the Partin nomogram, after studying these parameters onpatients enrolled in their study between 2006 and 2011 [23].

For preoperative TNM staging, in order to avoid study bias, because of non homogenous imagistic data regarding N and M, we only considered the T element. We considered 4 T categories: T1, T2, T3 and T4. 29 patients, accounting for 13,3% of the group were staged T1, 90 patients accounting for 41,3% were staged T2. This means that 54,6% of the cases were staged based upon rectal examination, PSA level and ultrasound, and an incorrect classification in 7,4% if regarded to postoperative classification. 97 patients accounting for 44,5% of total were evaluated and staged as T3, while 3 patients were assigned to T4, meaning a 7,4% of incorrect preoperative classification for advanced disease.

After collecting and processing data after obtaining pathology report of prostatectomy specimens, we found 2 cases for pT1 stage accounting for 0,9%, 101 specimens were evaluated and staged as pT2, 5 cases were pT4 representing 2,3% and the rest of 101 cases were staged pT3. From the 29 patients staged initially as pT1, 72,4% are staged pT2 while 27,6% are in

advanced stage. Our result is similar to the results of a study by Elgamal A.A. and van Poppel H.P., who find on a 100 cases group a clinical substaging of cT1 to pT3 of 30% [24].

Among the patients initially staged cT2, 40 cases turn out to be pT3, accounting for 18,3% of total and pT4 in 1,1%. These data may explain the 35 to 70% risk of progression in 5 years in the absence of radical prostatectomy.

First Graversen et al. in 1990, and then Walz J. and Bill Axelson in 2007 and 2011 publish data that show the critical importance of surgical radical treatment, and also point out a risk of progression for T2b and T2c of over 70% at 5 years [25,26,27].

For T3 stage, with a and b sub stages, the patient distribution was: 61 cases were in the same risk group postoperatively, accounting for 55,5% of the cT3 group, and 28% of total number, 33 cases are staged in a lower risk group, accounting for 34% of cT3 group and 16,6% of total number of patients.

In 2005, Ward et al. point a 13 to 27% clinical overstage for T3, that lead to increasing surgical interest for T3 stage [28].

2. Analyse of the number of cases restaged in a different risk group after pathology report, with regard to T element and Gleason score.

Clinical undetectable cT1c tumors, diagnosed through prostate biopsy for elevated PSA became prevalent. For this group, the key is to determine which are the aggressive tumors. The vast majority of papers show that they are frequently significant, in up to 30%. The major challenge is their discovery, as after pathology report they go in the high risk group [29].

For the studied population, among the 29 patients initially evaluated T1c, 21 were then re staged pT2, accounting for 72,4% of the group and 9,6% of total number in study. The remaining 8 patients were staged as pT3, representing 27,6% of clinically evaluated T1c cases and 3,7% of the total number. This means that all of the cases initially staged T1c were actually in a higher risk group, which is congruent with current literature.

For T2 cancers, the prognostic is good in the disease is really organ confined. For patients with clinically palpable tumors or detected on imaging studies, according to the vast majority of data, the 5 years progression rate is up to 70%, in the absence of treatment. For the intermediate risk group from the T element point of view, post pathology staging places the patient in the high risk group in about 40% of cases [30]. From the cT2 group, 40 patients are re staged as pT3, accounting for 44,4 % of T2 group. We see that only 48 cases are staged as pT2, and one cas as pT4 after pathology report. Of the 90 patients staged initially cT2, only 45,5% belong to high risk group, again data consisting with the majority of studies.

T3 stage is defined by capsular invasion uni or bilaterally. In the past, this stage accounted for about 40% of newly diagnosed prostate cancers. Although nowadays this percent dropped in a dramatic fashion, management of this stage is still a challenge for the clinician. Surgical treatment was initially discouraged, because of the important risk of positive margins, lymph node invasion or late recurrence [31]. A few randomized trials compared the efficiency of radiotherapy and hormonal therapy, demonstrating superior efficiency for the combination of the two, but no study proved their superiority to surgical treatment [32].

One of the limits of the studies regarding the results of radical prostatectomy for cT3 stage might be the early initiation of neo-adjuvant treatment. The evidence is building up that surgical treatment for these patients is a reality [28-32]. Over staging is relatively frequent, accounting for 13 to 27% of cases. The outcome of radical prostatectomy for this group in terms of prognostic is similar to the intermediate risk group [31,32]. On the other hand, the majority of studies showed a 33 to 66% rate of positive surgical margins, and 7,9 to 49% positive lymph nodes. This is the reason for the need for adjuvant treatment for 56 to 78% of the patients with initial surgical treatment, according to Ward J.F. and Hsu C.Y., in two of the most extensive papers published in this matter. The key issue remains the selection of the patients for surgical treatment, the role of nomograms comprising Gleason score, preoperative PSA, clinical and imagistic data being of crucial importance [33].

Radical prostatectomy for T3 stage requires certain surgical experience and skill, in order to keep morbidity, functional and oncological outcomes in acceptable limits [43]. Recent data showed the absence of recurrent disease at 5 and 10 years for 45-62% of cases, respectively 43-51%, in selected cases the percent going to 90-99% at 5 years and 85-92% at 10 years. Regardless of the type or moment of neo-adjuvant treatment, current data shows that real clinical stage is the main element for prognostic [35].

T3 stage had the following distribution: 61 patients were staged in the same group, accounting for 62,9% of the cT3 group, and 28% of total number, 32 being staged in the intermediate risk group, representing

33% of cT3 group, 1% in the low risk group and 3,1% in the high risk group. There are 34% of overstaged cT3 cases, which is greater than 13-27% s in current literature, a possible explanation for this difference being insufficient high performance imaging information, knowing that both clinical examination and transrectal ultrasound have a 60% sensitivity.

A paper published in 2006 by Johnstone P.A. et al. showed that for a group of 72 cases of prostatectomy for cT4 stage, overall survival was superior to radiotherapy or hormonal therapy, and similar to the simultaneous combination of the two [36].

Gontero et al. demonstrates the equivalence of results for prostatectomy for cT4N0-N1M1a stage and organ confined disease stage, in terms of general morbidity. Differences were noted in term of the need for transfusion, operative time and the incidence of lymphocele. Cancer specific survival after 7 years was 90,2% for the group with extracapsular extension and 99,3% for the organ confined disease group [37].

In another study on a group of 51 patients staged as cT3b and cT4, Joniau demonstrates a postoperative over staging rate of over one third, 7,8% representing confound disease and 29,4% minor invasion in the prostatic capsule – T3a. These patients received only surgical treatment. 35,3% did not receive adjuvant therapy and 21,6% being free of treatment after a follow up of 108 months. The overall survival was 73-88% al 5 years and 71% at 10 years [38].

Regarding preoperative cT4 stage group, for which prostatectomy may be a part of a multimodal approach, the two cases were staged pT3 and pT4. The insufficient number of cT4 cases do not allow for statistical comparison with data in current literature.

Conclusions

1. Postoperative T element, was misclassified in 14,8% comparing to preoperative staging with the aid of digital rectal examination, ultrasound and PSA level.
2. Of the 29 cases clinically staged cT1c,27,6% are re staged in higher stage, in cT2 stage the proportion being 45,5%, which explains the high risk for progression in the absence of surgical treatment for this group.
3. Data shows that 34% of cT3 is re staged to inferior risk groups, similar data being found in many current data, which rejuvenated surgical interest for treatment for this stage.
4. Of the 29 patients staged cT1c, 8 cases accounting for 27,6% were re staged in high risk group, fact that is again similar to other contemporary data.
5. By combining the T element, Gleason score and PSA we found 92 cases that belong to low and intermediate risk groups that have a real indication for radical prostatectomy.
6. Of the 90 of cT2 patients, only 45,5% truly belong to high and very high risk group.
7. For cT3 group there is a 34% of over staging, which exceeds the 13-27% from other groups. An explanation for this significant difference might be the insufficiency of high performance imaging, as both transrectal ultrasound and clinical examination have up to 60% sensitivity.
8. Another important conclusion in that approximatively 40% of cases are under evaluated as low risk, where for the intermediate risk group 15,4% belong to high risk group, where for thehigh risk group biochemical relapse is over 50% at 5 years.
9. Regarding over staged patients from the T element point of view, 35 cases accounting for 16% of total group are over staged preoperatively. We note that 33 of these cases belong to cT3 (34% of evaluated cases), this result owing probably to insufficient data provided by transrectal ultrasound, PSA level and low sensitivity of rectal examination.

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