

**“LUCIAN BLAGA” UNIVERSITY OF SIBIU**

**DOCTORAL SCHOOL IN MEDICINE**

**DOCTORAL FIELD –MEDICINE**

**SUMMARY OF THE PhD THESIS**

**CORRELATIONS BETWEEN ULTRASOUND-BASED  
PROSTATE DIMENSIONS, PSA AND NOCTURIA IN  
BENIGN PROSTATIC HYPERPLASIA**

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## **GENERAL PART:**

### **1) Introduction**

My focus on benign prostatic hyperplasia (BPH) in the doctoral study is due to the numerous case studies with increased incidence in patients over 50 years old thereof, the major impact it has on the quality of life. It is a chronic, progressive condition with multiple implications both medically and socially and financially.

The investigations required to identify the presence of this condition, in addition to the clinical diagnosis, are: ultrasound, PSA (prostate-specific antigen). These investigations can be completed with: urography with contrast substance, computed tomography (CT), nuclear magnetic resonance (MRI) and prostate puncture-biopsy.

### **2) Rationale of the theme**

The theoretical part includes several subchapters that present, in addition to the anatomy and embryological development of the prostate, recent notions about the physiology and pathophysiology of the gland. I insisted on the role of androgen receptors in BPH, on the role of the complement system, on the role of B and T lymphocytes and, last but not least on the P53 gene mutation that may have a significant role in promoting hyperplasia in prostate cells.

Also, the current means of diagnosis are presented, insisting on the clinical parameters, both the objective ones (prostate volume, urinary flow and post-micturition residue) and the subjective ones (frequency, intermittency, urgency, tension, nocturia, weak urinary stream and the feeling of incomplete bladder emptying). I dedicated a separate chapter to PSA (prostate-specific antigen), which has been used in clinical practice since 1988 and which revolutionized the clinical practice of urology. Although it has become the most valuable tumour marker widely used in prostate cancer screening, the volume and age of the prostate have been shown to be contributing factors to PSA growth in BPH as well. PSA also increases in prostatitis and prostate trauma. Two large studies, which included a large number of patients, the European one - ERSPC (European Randomized Study of Screening for Prostate Cancer) and the American one - PLCO (Prostate-Lung-Colorectal-Ovarian Cancer Screening Trial) have different results in terms of mortality in patients with PSA screening. The American study does not find a decrease in mortality, while the European one claims a decrease in specific mortality by 20%.

## **PERSONAL CONTRIBUTION**

### **Aimed research objectives:**

#### **A - The main objective**

#### **B - Secondary objective**

### **A) CORRELATIONS BETWEEN ULTRASOUND-BASED PROSTATE DIMENSIONS, PSA AND NOCTURIA IN BENIGN PROSTATIC HYPERPLASIA**

#### **1) The aim of the research**

Benign prostatic hyperplasia is a common condition of the male sex, which mainly affects men over 50 years old; it is a chronic, progressive disease, characterized by symptoms of the lower urinary tract, an increase in the size of the prostate and a decrease in urinary flow.

Due to the increasing frequency of elderly patients, along with the increase in life expectancy worldwide, it has multiple implications both from a social and financial point of view.

My aim was to see which prostate ultrasound-based diameter is most correlated with nocturia, what are the correlations in our geographic area between gland volume, nocturia, and PSA. I also made comparisons with other studies.

#### **2) Materials and methods**

In order to complete this study, a number of 204 patients from Southern Transylvania were qualified by applying the inclusions criteria, the great majority being from Sibiu County, of whom, during the study years (2018-2022), 7 cases were excluded from the study due to the diagnosis of ADK-P, thus leaving 197 cases in the study.

All patients gave their consent to participate in the study, under the protection of anonymity.

The age of the patients was between 40 and 90 years.

#### **Study inclusions criteria:**

Patients who presented to the urology department with prostatic symptomatology and who underwent suprapubic abdominal ultrasound and blood tests (PSA). They were also asked to complete a questionnaire corresponding to the IPSS score in the presence of the medical staff, focusing on the presence of nocturia. Only patients with nocturia were included in the study.

**Study exclusions criteria:**

- patients with prostate adenocarcinoma
- patients with hormonal treatment
- patients with lower urinary tract infections
- patients with recent 5-alpha-reductase inhibitor treatments
- patients with previous interventions on the prostate

The ultrasound was performed transabdominally, suprapubically, with a full bladder, through a frontal and a sagittal scan and not transrectally. We measured the antero-posterior (height), cranio-caudal (length) and transverse (width) diameters and then calculated the volume of the prostate. Depending on the data obtained, we made correlations between prostate dimensions, volume, clinical symptoms and PSA. We also took into account the patient's symptoms (especially nocturia) and the International Prostate Symptom Score – IPSS, as well as aspects related to the patient's quality of life - QOL -, after all, the medical target being that of ensuring a longevity as little as possible plagued by the unpleasant moments of prostate conditions.

One criterion taken into account is the **environment** from which the patients come.

Of the study group, 68.5%, respectively 129 people are from the urban environment and 34.5%, respectively 68 people from the rural environment. We made correlations between the environment of the patients, the degrees of the IPSS score and the volume of the prostate.

Among the 68 patients from the rural area, 19 fall into grade III of the IPSS score, 49 in grade II and none in grade I. Among the patients from the urban environment, 34 fall into degree III of the IPSS score, 7 into degree II and 17 into degree I

It is noticed, that the addressability of rural patients is lower than that of urban patients. They present when the urinary symptomatology is very disturbing, probably due to the lower educational level, low accessibility, negligence, movement-related difficulties. Another criterion taken into account is **the age of the patients**, knowing that the prevalence of BPH increases with age, advanced age being a risk factor for the clinical onset of the disease and its progression. Among the 197 people studied, between 40 and 94 years old, the vast majority of patients who present themselves to the urologist for symptoms associated with the prostate are over 60 years old, the age group with the highest addressability being the age group of 60-69 years old (44.67%). It is worth noting that patients under 50 also see a doctor for prostate conditions, certainly in a much lower percentage than the rest of the patient categories, as well as patients over 70, although we would expect a much higher percentage. Elderly patients probably get used to the symptoms and do not come to the consultation until complications arise.

Case incidence **correlated with nocturia.**

Taking into account the frequency of nocturia we concluded that:

- 56 patients urinated once a night (28.42%)
- 66 patients twice a night (33.50%)
- 43 patients three times a night (21.82%)
- 16 patients four times a night (8.12%)
- 16 patients 5 or more times per night (8.12%)

If we correlated nocturia with prostate volume, by decades of age, we observed that the frequency of nocturia increases with the increase in prostate volume, but nocturia does not correlate positively with age.

Regarding the ultrasound DIMENSIONS of the prostate, we performed the measurements on two ultrasound machines in two different medical units. Studying the specialized literature, we saw that there were no differences when comparing the results of prostate diameters on different ultrasounds, but there are small differences when performed by different doctors, especially regarding the antero-posterior diameter.

In this study we found the following:

The **TRANSVERSAL DIAMETER** is found below 40 mm in 45 patients (22.83%), between 40 and 60 mm in 137 patients (69.54%) and above 60 mm in 15 patients (7.6%).

Starting from the normal ultrasound dimensions of the prostate - 40/30/25 mm - we notice that the prostate grows due to the transverse diameter in most cases by 10-20 mm.

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From the statistical study, it is the least correlated with clinical symptoms, namely nocturia.

**CRANIO-CAUDAL DIAMETER** is below 30 mm in 23 patients (11.67%), between 30 and 50 mm in 148 patients (75.12%) and above 50 mm in 26 patients (13.2%).

The cranio-caudal diameter in over 75% of patients is between 30 and 50 mm.

Cranio-caudal diameter is most statistically correlated with nocturia and quality of life. According to this study, the cranio-caudal diameter is the best predictor of the clinical evolution of the condition.

**ANTERO-POSTERIOR DIAMETER** was below 30 mm in 31 patients (15.73%), between 30 and 50 mm in 14 patients (68.01%) and above 50 mm in 32 patients (16.24%).

From a statistical point of view, the antero-posterior diameter, is positively correlated with nocturia, but the correlation is not as strong as for the cranio-caudal diameter, but it is greater than for the transverse diameter.



**Prostate volume** is considered the greatest risk factor associated with BPH progression, as men with a prostate volume of 30 ml or greater are 3-4 times more likely to develop complications, such as acute urinary retention.

We calculated prostate volume using the formula: antero-posterior diameter x cranio-caudal diameter x transverse diameter x 0.523. In approximately 43% of patients, the volume was between 30 and 50 cm<sup>3</sup> and in approximately 30%, it was over 60 cm<sup>3</sup>.

In patients in this study, with a prostate volume of over 70 cm<sup>3</sup>, the frequency of nocturia is over 3 times, reaching up to seven times per night.

With a prostate volume of 50 to 69 cm<sup>3</sup>, the frequency of nocturia is between two and five nocturnal urinations, with the most frequent being three times.

At a prostate volume between 30 and 49 cm<sup>3</sup>, nocturia is between once and four times per night with a predominance of two. At volumes below 30 cm<sup>3</sup>, nocturia occurs once or twice per night

In conclusion, we can say that the frequency of nocturia generally increases with increasing prostate volume, but we cannot estimate prostate volume based on clinical symptoms alone because there are cases in which with a large prostate volume, the frequency of urination is reduced and vice versa, or when there is a small volume, the frequency is increased. The explanation may be the uneven increase in prostate volume, mainly due to the median lobe, and then nocturia is more frequent, or mainly due to the lateral lobes, and then nocturia sets in later and the frequency of urination is lower.

### **Correlation between PSA value, age and number of patients**

Another criterion taken into consideration in the study was the PSA value.

Until now, the determination of serum PSA concentrations is considered a useful test for detecting an enlarged prostate in men in whom prostate cancer has been ruled out. It is a useful test, recommended for men over 50 years old, easy to perform, which aims to predict prostate volume in men with BPH, a very common male condition.

Normally, in healthy men, under physiological conditions, the PSA value is low. Only when the architecture of the prostate tissue is disturbed, PSA passes into the surrounding extracellular space and reaches the systemic circulation, always being a marker of a prostatic condition.

We tried to study PSA values over time, but this study was not conclusive due to fluctuating PSA values during periods of prostatic inflammation, LUTS (lower urinary tract syndrome) or specialty treatments (Dutasterida) that modify PSA values.

In this study, PSA values were as follows:

- 51 patients had values between 0-1ng/ml (25.88%);

- 32 patients between 1-2 ng/ml (16.24%);
- 46 patients between 2-3 ng/ml (23.35%)
- 28 patients between 3-4 ng/ml.(14.21%)
- 32 patients between 4 and 10 ng/ml (16.2%)
- 8 patients values above 10 ng/ml (4.06%)

Between PSA and:

- a) **Age** - we found a significant **positive correlation**;
- b) **Prostate volume** - we found **positive correlation**;
- c) **Ultrasound dimensions of the prostate** - we found **positive correlation** especially due to the antero-posterior and cranio-caudal diameter;
- d) **Nocturia** - we found **positive correlation**.

### 3) Statistical study

#### Data analysis

Central tendencies for continuous variables were presented as median and interquartile range (P25 - Percentile 25, P75 - Percentile 75). Spearman correlation coefficient was used to analyze correlations between prostate ultrasound dimensions and PSA, IPSS, QOL, nocturia, age. Cluster analysis was used to identify distinct groups of patients according to prostate ultrasound dimensions and nocturia level. Multivariate analysis, using decision trees (CART method), was used to determine the association between prostate ultrasound dimensions, PSA and IPSS grade. Scatter plots, boxplots, simple and grouped plots, decision trees were used for graphical representation. Data analysis was performed using the SPSS v.20 software package.

- A positive correlation was observed between PSA and ultrasound dimensions of the prostate: cranio-caudal diameter ( $r = 0.262$ ,  $p=0.000$ ), antero-posterior diameter ( $r = 0.256$ ,  $p=0.000$ ), transverse diameter ( $r = 0.176$ ,  $p=0.013$ ). Similarly, a significant positive correlation was observed between PSA and prostate volume ( $r = 0.299$ ,  $p=0.000$ ), respectively between PSA and age.
- A positive correlation was observed between IPSS and ultrasound dimensions of the prostate: cranio-caudal diameter ( $r = 0.438$ ,  $p=0.000$ ), antero-posterior diameter ( $r = 0.406$ ,  $p=0.000$ ), transverse diameter ( $r = 0.215$ ,  $p=0.002$ ). Similarly, a significant positive correlation was observed between IPSS and prostate volume ( $r = 0.450$ ,  $p=0.000$ ), respectively between IPSS and age.

The analysis of the mean values of ultrasound dimensions according to the IPSS grade confirms the results of the correlation analysis. Elevated values of these dimensions are observed with increasing IPSS grade.

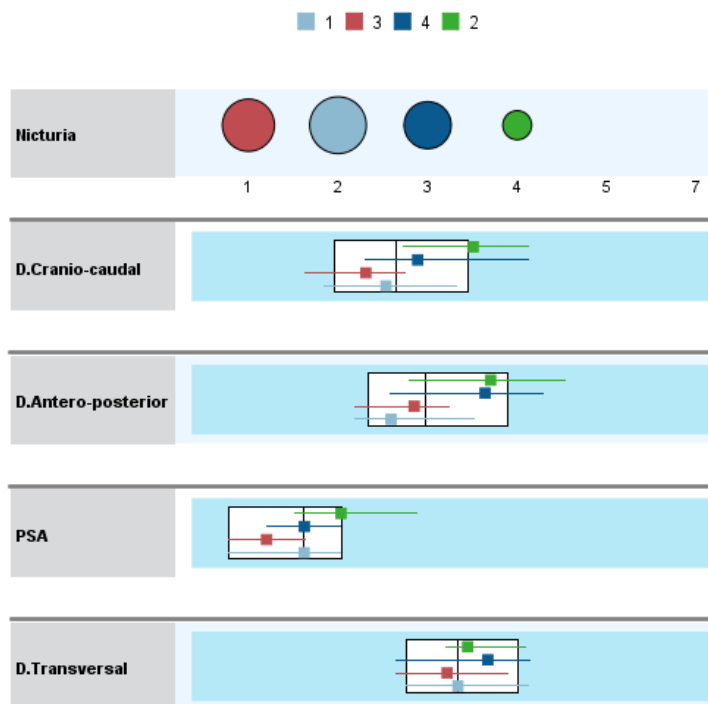
- A positive correlation was observed between QOL and ultrasound-based dimensions of the prostate: cranio-caudal diameter ( $r = 0.467$ ,  $p=0.000$ ), antero-posterior diameter ( $r = 0.425$ ,  $p=0.000$ ), transverse diameter ( $r = 0.209$ ,  $p=0.003$ ). Similarly, a significant positive correlation was observed between QOL and prostate volume ( $r = 0.475$ ,  $p=0.000$ ), respectively between IPSS and age ( $r = 0.343$ ,  $p=0.000$ ).
- A positive correlation was observed between nocturia and ultrasound dimensions of the prostate: cranio-caudal diameter ( $r = 0.404$ ,  $p=0.000$ ), antero-posterior diameter ( $r = 0.279$ ,  $p=0.000$ ), respectively a positive but statistically insignificant correlation with the transverse diameter ( $r = 0.128$ ,  $p=0.072$ ). A significant positive correlation was observed between nocturia and prostate volume ( $r = 0.352$ ,  $p=0.000$ ), and a very low correlation coefficient was observed between nocturia and age ( $r = 0.176$ ,  $p=0.013$ )
- Analyzing the mean values of the ultrasound dimensions of the prostate for each value of nocturia, an increase in nocturia is observed with an increase in cranio-caudal diameter ( $p=0.000$ ) and antero-posterior diameter ( $p=0.003$ ), respectively with advancing age ( $p=0.000$ ).
- Positive correlations were observed between PSA and IPSS score ( $r=0.366$ ,  $p=0.000$ ), QOL ( $r=0.365$ ,  $p=0.000$ ), nocturia ( $r=0.261$ ,  $p=0.000$ ). Also, IPSS score was positively correlated with QOL ( $r=0.696$ ,  $p=0.000$ ), nocturia ( $r=0.581$ ,  $p=0.000$ ). An increased (significant) value of the correlation coefficient was observed between QOL and nocturia ( $r=0.719$ ,  $p=0.000$ ), patients with higher values of nocturia having higher values of QOL, so the quality of life is low.

### **Analysis of the relationship between nocturia, ultrasound-based dimensions of the prostate and PSA**

The use of cluster analysis provided an overview of the relationship between nocturia, prostate ultrasound dimensions and PSA. Four groups of patients can be observed [figure 1]. The group of patients with nocturia values of 1 (red) and 2 (light blue) have smaller dimensions compared to the groups of patients with nocturia values of 3 (dark blue) and 4 (green), respectively, as follows:

- cranio-caudal diameter: red group: 39.23, light blue group: 36.29 vs. dark blue group: 44.51, green group: 47.2
- antero-posterior diameter: red group: 38.69, light blue group: 37.82 vs. dark blue group: 43.53, green group: 44.53;
- transverse diameter: red group: 49.25, light blue group: 47.05 vs. dark blue group: 49.20, green group: 50.28

Also, much higher PSA values can be observed for the group with a nocturia value of 4 (green) compared to the other groups (median PSA value - green group: 4.53 vs. red: 2.95, light blue: 2.67, dark blue: 3.29)



*Figure 1: Analysis of the relationship between nocturia, prostate diameters and PSA*

**There is a positive correlation between nocturia and prostate volume. There is also a positive correlation between PSA and prostate volume.**

#### **4) Results and discussions**

Benign prostatic hyperplasia is a common male condition, which mainly affects men over 50 years of age. It is a chronic, progressive disease with multiple implications both medically and socially and financially.

It also concerns the medical world, especially urologists, due to the relationship between BPH and prostate adenocarcinoma. BPH contributes greatly to morbidity, affecting the quality of life of patients mainly due to nocturia, which leads to sleep disorders and nocturnal falls. Nocturia is actually the main reason why men see a doctor.

In this study, we took a sample of the population from southern Transylvania who presented to urology department with prostate disease, without taking into account comorbidities.

We correlated the ultrasound-based dimensions of the prostate, its volume, and clinical symptoms, especially nocturia, and found that BPH progresses with age and with increasing prostate volume.

Also, patients from rural areas present later for urological consultation, with more pronounced symptoms.

Regarding the correlation with age, the results obtained are similar to those obtained by Krimpen and Baltimore who, in the Longitudinal Study of Aging, suggest a prostate growth rate of 2 -2.5% per year in elderly men [1]

The ultrasound-based dimensions of the prostate are normally – 40/30/25 mm. In this study, the transverse diameter had values between 40 and 60 mm in 69.54% of patients, the cranio-caudal diameter between 30 and 50 mm in 75% of patients, and the antero-posterior diameter between 30 and 50 mm in 68% of patients. We can, therefore, conclude that in most cases the prostate diameters increase by 10-20 mm.

Of the three prostate diameters measured by ultrasound, the cranio-caudal diameter is most correlated with the increase in clinical symptoms, especially nocturia. This diameter also influences the IPSS score and quality of life the most.

Nocturia, on the other hand, was not positively correlated with age.

An increase in prostate volume leads to an increase in clinical symptoms, an increase in IPSS and a decrease in QOL. IPSS is used to assess LUTS.

Our results are also consistent with those obtained by Kim EH et al in “The use of 5-alpha reductase inhibitors in the treatment of PHB”, who concluded that men with prostate volumes over 30 ml have a 3-4 times greater increase in symptoms, with a 3-4 times greater incidence of complications, than men with prostates under 30 ml. [2]. O’Leary et al also concluded that there is a strong positive correlation between IPSS score, nocturia and benign prostatic hypertrophy and it is a convenient tool to assess quality of life and to map treatment strategies [3].

Jung JW considers that ultrasound estimation of prostate volume is important in choosing the best treatment option (current guidelines recommend the use of 5-alpha reductase inhibitors only for prostate volumes over 40 cm<sup>3</sup>) and in predicting disease symptoms and discusses several large studies, including the MTOPS study [4].

Raza I et al also concludes that prostate volume increases with age, as does the IPSS score. He says that prostate volume is of utmost importance because it helps surgeons choose the therapeutic approach - prostate with an enlarged middle lobe requires surgery, while that without an enlarged middle lobe can be treated with 5-alpha reductase inhibitors [5]. Kim J.M. et al also positively correlate prostate volume with symptomatology, but adds body mass index to the study. [6] Dai X et al investigated the association between BPH and urological cancer and concluded that BPH is associated with a decreased risk of prostate cancer and bladder cancer [7].

However, the PLCO study of 500 men did not find a strong correlation between prostate size and LUTS. Overland et al also reported a weak correlation between prostate volume and IPSS in Norwegian men. Bosch et al also reported a weak correlation between prostate volume and clinical symptoms [8,9]

Given that the conclusions of the studies are not uniform, it is likely that the statistical data depend on the geographical area, the sample taken in the study, and comorbidities. However, most studies show a positive correlation between clinical symptoms and prostate volume [10,11,12]

In our study, of the three ultrasound dimensions of the prostate, nocturia may be specifically correlated with the cranio-caudal diameter. However, we did not find studies with which we could make comparisons.

Another correlation is that between prostate volume, PSA, and age

PSA is considered normal at values below 1.4 ng/ml up to 40 years, below 2 ng/ml up to 50 years, below 3.1 ng/ml up to 60 years, below 4.1 ng/ml up to 70 years, and below 4.4 ng/ml over 70 years. It has been found that PSA increases from 60 years by approximately 0.04 ng/ml/year [13]

At a PSA value above 4 ng/ml, the positive predictive value is approximately 30%, which means that approximately one in three men with PSA above 4 ng/ml will be diagnosed with adenocarcinoma in the future at a prostate biopsy.

PSA is the most important tumor marker in the detection of prostate cancer, but at values between 4 and 10 ng/ml, in the so-called – gray area – this screening test for prostate cancer is not ideal. Other methods have been tried to be more conclusive - and here, we mention the calculation of prostate-specific antigen density - PSAD - which is the ratio between serum PSA concentration and prostate volume. There are studies (Aksoi Ylmaz et al) that concluded that PSAD is significantly higher in patients with adenocarcinoma than in those with benign prostatic hypertrophy. [14]

Our study focused on the increase in prostate volume in the absence of adenocarcinoma, in benign prostate disease and we found a positive, statistically significant correlation between: PSA, age and prostate volume. The data are similar to those in the literature, in which variations appear especially by ethnicity - for example, Japanese men have a smaller prostate than Europeans or Americans. Hochberg et al reported a correlation coefficient between PSA and prostate volume of 0.33-0.41 in a series of white patients. Studies on Japanese, South Koreans and Indians reported a significant positive correlation coefficient between PSA and prostate volume of 0.65, 0.1 and 0.7 [15] Moon DG in “The influence of prostate volume on the prostate specific antigen level”, says that prostate volume is an important factor that contributes to the increase in serum PSA levels in the absence of adenocarcinoma.

The use of PSA to predict prostate volume may be useful in highlighting clinical progression and in making therapeutic decisions for patients with BPH. Mosli et al, in a study of Saudi men, found that prostate volume and PSA are strongly correlated [16]. Roehrborn et al first evaluated PSA values as a predictor of prostate volume taking into consideration that serum PSA can be used in making therapeutic decisions. Mochtar et al reported that PSA thresholds of 2 and 2.5 ng/ml predict prostate volumes of 30 and 40 ml. Chung et al reported a correlation coefficient of 0.56 in Korean men. Other studies report

correlation coefficients of 0.37-0.6. Variations are large depending on ethnicity and especially on the methods used to measure PSA and prostate volume [17]

Stone BV et al, in “Prostate size, nocturia and digital rectal examination”, concluded that prostate-specific antigen levels were significantly correlated with prostate size measured by ultrasound [8]. Weber et al reached the same conclusion. Bohnen et al concluded that a serum PSA level greater than 1.5 ng/ml could be a cut-off value for a prostate volume greater than 30 cc. Other studies have also shown that the development of BPH is maximal in men with PSA greater than 1.5 and a prostate volume greater than 30 cc. [16]. Bagus I et al concluded that in Indonesian men, both prostate volume and PSA increased with age [15].

The correlation between prostate volume, PSA and age has been the subject of several studies that found, as in our study, a positive correlation between the three elements [18,19,20,21]

There are studies that have tried to see if the ratio between free PSA and PSA complexed with alpha1-antichymotrypsin and total PSA would have a greater diagnostic utility than PSA. The results were not promising for Jung et al, while Brawer et al found that complexed PSA better differentiates adenoma from prostate cancer and could replace total and free PSA [22].

## 5) Conclusions

The results of the study show positive correlations between ultrasound dimensions of the prostate and PSA, nocturia and age.

Higher values of the correlation coefficients were observed in the case of cranio-caudal diameter. On the other hand, cranio-caudal diameter is identified as the first factor determining patient groups according to nocturia values and other ultrasound dimensions of the prostate, the group of patients with nocturia values over 4 having a median of 47 for cranio-caudal diameter (significantly higher than the other groups).

The statistical study shows a positive, statistically significant correlation between PSA and age and prostate volume. There is also a positive correlation between PSA and prostate ultrasound dimensions. PSA also has higher values in the group with high nocturia, at a higher IPSS score.

Analyzing the average prostate ultrasound dimensions for nocturia, a significant increase in nocturia is observed, especially with the cranio-caudal diameter, then with the antero-posterior diameter and an insignificant correlation with the transverse diameter. Nocturia has a positive, statistically significant correlation with prostate volume, but a low correlation coefficient with age.

BPH progresses with advancing age and with increasing prostate volume. It should be noted that we studied a random group of patients with different clinical histories.

Regarding the age of the patients, we can conclude that the most common age group affected is between 60-69 years (44.7%).

Most patients fall into grade II of the IPSS score, and the frequency of nocturia is 1-3 times per night, with only 16% of patients experiencing nocturia more than four times.

The frequency of nocturia generally increases with increasing prostate volume, but we cannot estimate prostate volume only based on clinical symptoms because there are cases in which with a large prostate volume the frequency of urination is reduced and vice versa, when with a small volume of the prostate, the frequency is increased.

Regarding the correlation between ultrasound dimensions of the prostate and PSA, this study found that both prostate volume and PSA value increase with age.

- Prostate volume predicted by age and PSA level show large individual variations.
- There is a significant correlation between PSA and ultrasound dimensions of the prostate and its volume, data that coincide with those in the specialized literature
- PSA value and prostate volume are used to highlight clinical progression and response to drug treatment in prostate diseases.
- The change in PSA values is also influenced by other factors (inflammation, infections, trauma, drug treatments - 5-alpha reductase inhibitors - finasteride and dutasteride) and not only by the increase in prostate size.
- At high PSA values (above 10 ng/dl), the frequency of ADK-P is increased – 57% in this study. At values lower than 4 ng/dl no patient with ADK-P was detected in this study

## **B) THE EFFECT OF ALPHA-BLOCKERS ON THE IRIS**

### **1) Introduction**

Another aspect that we discussed is the effect of alpha-blockers on the iris, the so-called Intraoperative Floppy Iris Syndrome (IFIS) or Floppy Iris Syndrome, which can occur during cataract surgery. It was discovered in 2005 and is of interest to both urologists and ophthalmologists. Tamsulosin, along with other alpha-blockers - doxazosin, alfuzosin, terazosin, silodosin – relaxes the smooth muscles of the prostate and bladder neck with a decrease in urinary frequency and an improvement in the quality of life of urological patients.[23]

There is evidence that blocking  $\alpha_1$  adrenergic receptors causes relaxation of the iris dilator muscle, with weak pupillary response.



## **2) Materials and methods**

Regarding the effect of tamsulosin on the iris, 100 male patients out of 601 patients who underwent cataract surgery at the Oftatotal Clinic in Sibiu during one year (2022) were studied. The age of the patients enrolled in the study was between 60 and 89 years. Of the one hundred patients, only 24 took medications for BPH. Of these, 5 patients took prostamol, a phytotherapeutic preparation, which is an extract of *Serenoa repens*, and the remaining 19 took Tamsulosin (trade name Omnic, Fokusin, Tamsol), which is an alpha-blocker, most commonly used in the treatment of BPH.

## **3) Results**

All patients operated for cataract included in the study had been previously treated in the urology service for micturition disorders and benign prostatic hypertrophy.

We followed the changes that occurred preoperatively, intraoperatively and early postoperatively. All patients were operated on by the same surgeon and with topical anesthesia, by the phacoemulsification method with artificial lens implant in the capsular bag.

All patients had problems with the dilation of the pupil preoperatively. In 15 patients, moderate mydriasis was achieved intraoperatively by pharmacological dilation including intracameral administration of phenocaine and mechanical dilation or stripping. In four patients, the application of iris dilators was necessary. Due to the small pupil in two patients, the iris was caught in the phacoemulsification probe, and a small incomplete iris coloboma was formed. Sometimes, Descemet's roll occurred in four patients, after which the pupil remained in mydriasis and areflective. The visual acuity of the patients was satisfactory, between 0.9 -1 and 0.6. In two patients, a uveal reaction occurred, easily controlled by treatment with steroid anti-inflammatory drugs. There were no major complications such as retinal detachment or endophthalmitis.[24]

## **4) Discussions**

This topic is of much debate.

It appears that stopping Tamsulosin for a short period of time does not prevent IFIS occurrence, as the iris damage appears to be irreversible. One study also reported a drug-melanin interaction that causes iris dilator muscle atrophy and, consequently, IFIS. [25] IFIS, on the other hand, interferes with cataract surgery in some patients who develop floppy iris.

The pupil gradually becomes smaller as the procedure progresses. Even if the pupil is dilated before cataract surgery, it becomes miotic during the operation, and a pupil that is too small makes cataract removal particularly difficult. In a floppy iris, the pupil tends to protrude through the wound and dilation of the pupil may be difficult. [26]

## 5) Conclusions

Collaboration between ophthalmologists and urologists is necessary in cataract surgery intervention in patients treated with Tamsulosin, because both conditions (BPH and cataracts) occur at an older age.

### **C) PERSONAL CONTRIBUTIONS AND ELEMENTS OF ORIGINALITY OF THE THESIS**

This study is the first to be done in southern Transylvania both in terms of the correlation between ultrasound dimensions, PSA and nocturia, and in terms of the effect of alpha-blockers (Tamsulosin) on the iris.

The data obtained are generally consistent with those obtained in other studies, the results showing positive correlations between prostate volume, PSA and nocturia. If PSA and prostate volume have a positive, statistically significant correlation with nocturia, the correlation coefficient is very low between nocturia and age. What we did not find in other studies is the correlation that exists between cranio-caudal diameter and nocturia. This diameter is most closely related to the accentuation of clinical symptoms, especially nocturia, and quality of life. Of course, the study has limitations because it addressed a relatively small number of patients, only from a certain area of the country - Transylvania. We await other studies to confirm or refute our data.

Regarding the effect of Tamsulosin on the iris, we aimed to raise awareness among both urologists and ophthalmologists about the complications that may occur after prolonged use of alpha-blockers. If urologists are satisfied with the effect of the drug on the prostate, the same cannot be said about ophthalmologists, who, due to the effect on the iris, there may be complications during cataract surgery. The topic is relatively new and aims at raising an alarm signal about an adverse effect of the drug frequently used in urology.

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**LIST OF ABBREVIATIONS:**

HBP- benign prostatic hypertrophy

ADK-P- prostate adenocarcinoma

PSA- prostate-specific antigen