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Correlation between corneal thickness and optic disc morphology in normal tension glaucoma using modern technical analysis

LAURENŢIU COMAN[1)], MONICA COSTESCU[2)], MIHAIL ALECU[2)], OANA ANDREIA COMAN[3)]

[1)]*Department of Physiology, Faculty of Medicine, "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania*

[2)]*Department of Dermatology and Venereology, "Dr. Victor Babeş" Clinical Hospital of Infectious and Tropical Diseases, Bucharest, Romania*

[3)]*Department of Pharmacology, Faculty of Medicine, "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania*

Abstract

The purpose of this study was to evaluate the relationship between central corneal thickness (CCT) and optic disc morphology in normal tension glaucoma (NTG). Patients with NTG underwent eye examination, optic disc imaging with Heildelberg Retina Tomograph II (HRT II) and ultrasound corneal pachymetry. The morphological parameters of the optic discs were used to classify the eyes into four groups: generalized enlargement (GE) type, myopic glaucomatous (MY) type, focal ischemic (FI) type and senile sclerotic (SS) type. A correlation between CCT and optic disc morphology obtained by HRT II was calculated. Multiple comparison and *post hoc* tests were performed in order to determine the significance of the differences between the four groups. The strongest correlation was between CCT and the parameters of optic disc imaging obtained at HRT II in the GE type of optic disc.

***Keywords*:** corneal thickness, normal tension glaucoma, optic disc morphology.

Introduction

Glaucoma is characterized by optic nerve fiber atrophy that causes a decrease in vision. Although an elevated intraocular pressure (IOP) is generally recognized as a major risk factor for glaucoma, it is well known that some patients with normal IOP still show a progression of the glaucomatous changes even to blindness [1, 2]. This clinical situation is named normal tension glaucoma. Normal tension glaucoma has no fundamental difference from primary (chronic) open angle glaucoma (POAG), except that the etiological or pathogenic process is accelerated at low level of IOP values [3]. Without an abnormally high IOP, frequently NTG is discovered because of abnormal disc optic appearance [4]. The Heidelberg Retina Tomograph II (HRT II) represents the latest device of confocal laser ophthalmoscopy to the examination of the optic disc [5]. This instrument acquires three-dimensional images of the optic nerve head and posterior pole with the possibility to calculate the size of the optic disc, the contour and shape of the optic disc, neuroretinal rim, optic cup, measurements of the peri-papillary retina and nerve fiber layer. Also, this instrument includes a software capable of providing an automated analysis clinically based [6].

On the other hand, one of the risk factors that have been shown to be powerful predictor of glaucomatous development is CCT [7, 8]. The mechanism for this relationship has been hypothesized to be related to the connection between corneal thickness and the overall inherent structural and elastic properties of the eye, which may determine its vulnerability to glaucoma [9]. Many reports have shown that thinner than average corneas may underestimate the true IOP whereas thicker than average corneas may overestimate the true IOP. This effect has been found in the order of 1 mmHg correction for every 25 µm deviation from a CCT of 550 µm. Nevertheless, this factor alone would not appear sufficient to explain the markedly increased susceptibility to glaucoma found in those with thinner corneas.

Also, the cornea and optic disc both fill scleral "gates" of the eye and due to the continuity of the cornea, sclera and optic disc lamina, CCT may represent a factor that reflects the biomechanics of the optic nerve head (ONH). Many researches shown that the biomechanics of the corneo-scleral shell affect cellular deformation of the ONH [10, 11]. These factors may relate more significantly to the risk of developing normal tension glaucoma. It seems reasonable that there should be a relationship between the CCT and biomechanical properties of the cornea and those of the sclera and ONH. We may consider the possibility that CCT may be extrapolated to topographic characteristics and parameters of the optic disc itself. While this relationship has been examined in glaucomatous eyes with ocular hypertension, there is little information on the relationship between CCT and NTG.

Patients and Methods

The patients attending the glaucoma service underwent a complete ophthalmic examination in order to assess their eligibility, and 64 patients were enrolled. The inclusion criterion was: IOP examination (IOP<21 mmHg) measured on two consecutive occasions separated by an interval of at least two days, a glaucomatous visual field, glaucomatous optic disc changes (optic disc imaging with

HRT II) and ultrasound corneal pachymetry. Exclusion criteria were applied, prior ocular surgery and low quality HRT images (standard deviation of the mean topographic image more than 40 μm). Different features of the optic disc morphology are calculated from the measurements and used to characterize the morphology of the optic disc.

Because of the reliability of the HRT II, we believed that objective determinations of the morphology of the optic disc obtained by HRT II can be used to classify the optic discs into different morphological types. The design was a clinic-based retrospective study (Figure 1).

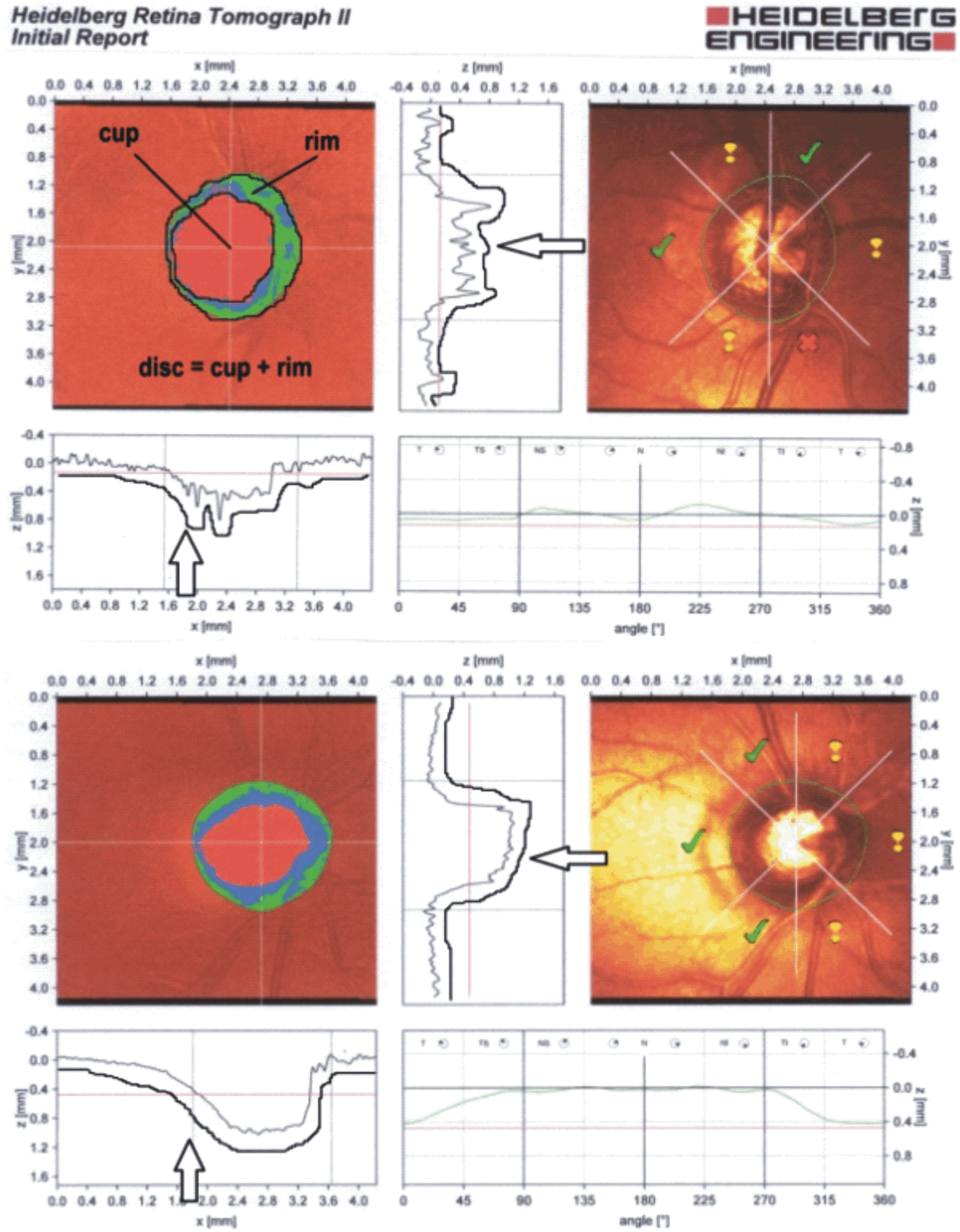

Figure 1 – ***Optic disc morphological parameters determined by HRT II.***

In Figure 1, we can see how the advances incorporated in HRT II permit the scanning of the optic disc. The software automatically aligns and averages the images to obtain a matrix of mean height measurements. The result produces the reflectance image and the topography image. After image processing is complete, the software displays both of these images. The reflectance image (on the right) is a false-color image that appears similar to a photograph of the optic disc. The topographic image (on the left), in contrast to the reflectance, relays information concerning the height of the surface contour of the optic disc and retina. The cross-sectional height of the retinal surface in relation to the reflectance and topographic images are shown in the two graphs below (along the Y-axis) and to the right (along the Y-axis) of the reflectance image. Black arrows show the contour line that is parallel with the line of height measurements. These lines are different each over and help to classify the eyes into four groups: generalized enlargement (GE) type, myopic glaucomatous (MY) type, focal ischemic (FI) type and senile sclerotic (SS) type.

Pearson's correlation coefficients were calculated to asses the associations between CCT and the optic disc morphological parameters. Analysis of variance for continuous data (ANOVA) was used to determine the significance of the differences in the four groups.

Patients with NTG underwent ultrasound corneal pachymetry (Figure 2).

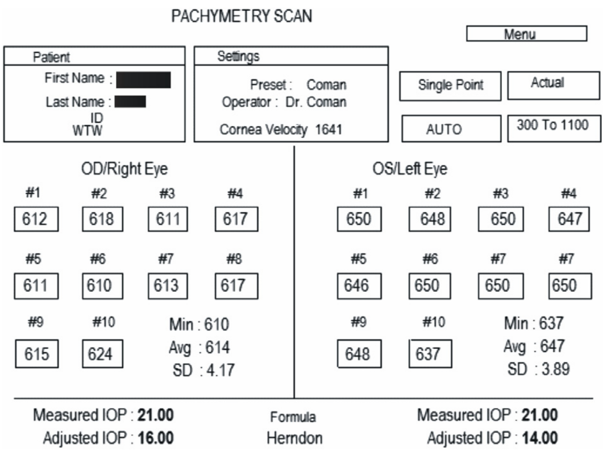

Figure 2 – ***Model of corneal pachymetry. The pachymetry scan results at the same patient, at both eyes, shows that adjusted IOP is with 5 units less at the right eye and with 7 units less at the left eye, versus measured IOP, because of a thicker cornea. The patients with thinner cornea have adjusted IOP values bigger than measured IOP values. IOP: Intraocular pressure.***

The circadian fluctuations in CCT were small and did not seem to interfere with the circadian intraocular pressure assess. Patients were divided into a thin CCT group (<530 μm) and a thick CCT group (>530 μm). The mean CCT for all NTG patients was 513.75 μm (SD±14.38 μm) but with a statistically significant change of CCT values with every optic disc type group (Figure 3).

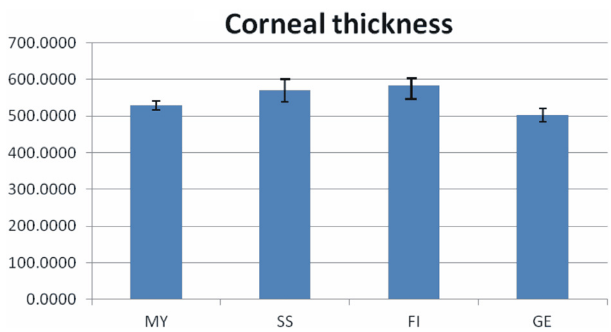

Figure 3 – ***Corneal thickness repartition with thinnest cornea in GE optic nerve type. GE: Generalized enlargement, FI: Focal ischemic, SS: Senile sclerotic, MY: Myopic glaucomatous.***

Sixty-four eyes were studied. Main outcome measures were: disc area, cup area, rim area, rim volume and corneal thickness. The morphological parameters of the optic discs were used to classify the eyes into four groups: GE type, MY type, FI type and SS type. A correlation between CCT and optic disc morphology obtained by HRT II was calculated. Eyes were classified as follows: 23 (35%) as MY type, 18 (28%) as GE type, 13 (22%) as SS type and 10 (15%) as FI type (Figure 4).

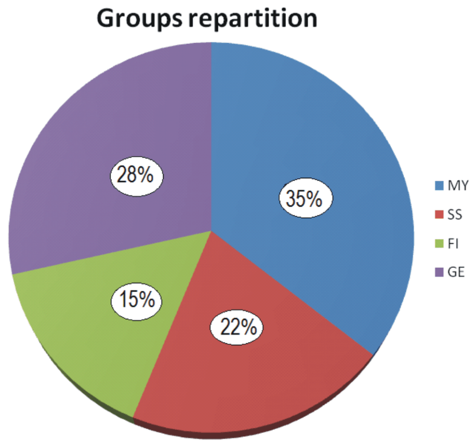

Figure 4 – ***Repartition of optic disc morphological groups after HRT II. GE: Generalized enlargement nerve optic type, FI: Focal ischemic nerve optic type, SS: Senile sclerotic nerve optic type, MY: Myopic glaucomatous nerve optic type.***

Results

In patients with the GE type, several parameters of the optic disc obtained by HRT II were significantly different from those in the other groups. They had a larger disc area, deeper cup depth, larger cup area and volume, and thinner rim area. The optic disc area of the patients with the MY type was smaller than GE type and this may be related with a higher prevalence of myopia (Figure 5).

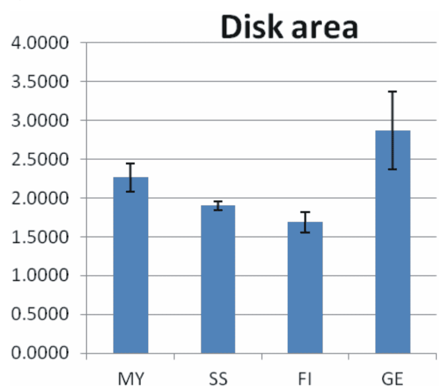

Figure 5 – ***The higher disc area is correlated with GE type of optic nerve. GE: Generalized enlargement, FI: Focal ischemic, SS: Senile sclerotic, MY: Myopic glaucomatous.***

The smallest rim volume we found in FI disc type while in MY and GE type was bigger (Figure 6).

In the patients with FI, none of the parameters were significantly correlated with CCT. This is reasonable because the damage on the optic disc is focal and the generalized parameters of HRT II are difficult to detect.

On the other hand, the damaged area of the optic disc and visual acuity should be closely correlated in this disc type compared to the other disc type.

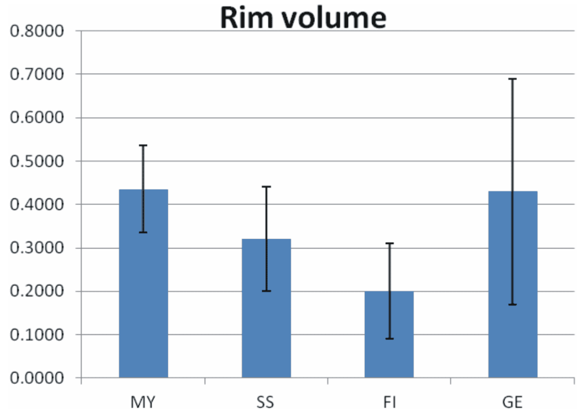

Figure 6 – ***The highest rim volume values are in GE and MY optic nerve types. GE: Generalized enlargement, FI: Focal ischemic, SS: Senile sclerotic, MY: Myopic glaucomatous.***

Association of the cup area with the other HRT parameters was assessed (Figure 7).

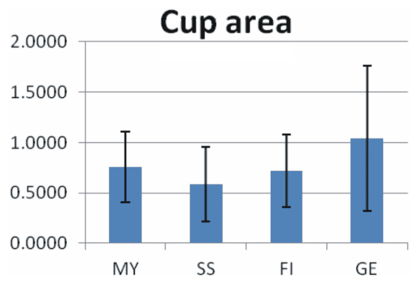

Figure 7 – ***The highest cup area is in GE and MY optic nerve types while the smallest is in SS and FI optic nerve types. GE: Generalized enlargement, FI: Focal ischemic, SS: Senile sclerotic, MY: Myopic glaucomatous.***

A significantly shallower mean and maximum cup depth was found in patients with the SS type than in the other disc group. The average of this group was older than the other groups and they have the best prognosis while this parameter was worse in the GE type group.

We hypothesized that the correlation coefficients between the optic disc parameters and the values of CCT will be higher when the parameters of the different types of optic disc morphology are individually assessed. Therefore, the CCT has a negative correlation but a mild association with disc area parameter of optic disk in GE type group (Figure 8).

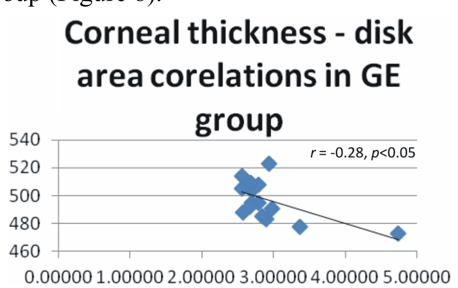

Figure 8 – ***CCT has a negative correlation but a mild association with disc area in GE optic nerve type. CCT: Central corneal thickness, GE: Generalized enlargement.***

The SPSS Statistics version 13.0 software was used to generate Pearson's correlations coefficients. The significance level was set at $p<0.05$. The correlation between CCT and cup area parameter is negative but significant in GE type group (Figure 9).

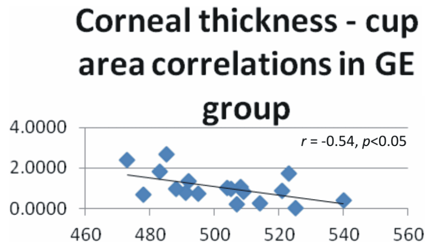

Figure 9 – ***CCT has a negative but significant correlation with cup area in GE optic nerve type. The CCT and cup area values (blue points) demonstrate that is a correlation between them and this correlation was significant in GE group only. CCT: Central corneal thickness, GE: Generalized enlargement.***

The correlation between CCT and rim volume is positive but with a mild association. The thicker is cornea the bigger is the rim volume (Figure 10).

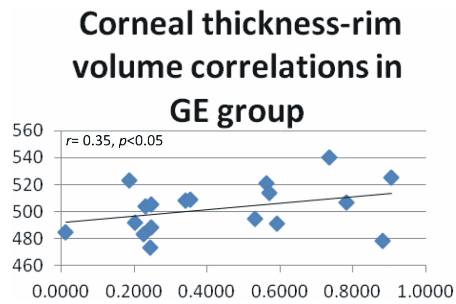

Figure 10 – ***CCT has a positive correlation but mild association with rim volume in GE optic nerve type. The CCT and rim volume values repartition (blue points) demonstrate that the thicker is cornea the bigger is the rim volume. CCT: Central corneal thickness, GE: Generalized enlargement.***

Discussion

Morphological evaluation of the optic disc and corneal thickness in NTG has been made. Only one study of central corneal thickness with thickness of the lamina cribrosa in human cadavers did not allow for conclusive results due to histological artifacts in preservation techniques and sectioning [12, 13]. Therefore, we undertook this study to evaluate a possible link between CCT and optic disc morphological parameters. The examination of the optic disc in glaucoma is unique in many aspects because provides the opportunity to directly observe the effects of progressive neurodegeneration of the optic nerve on a microscopic scale [14, 15]. Over the years, more objective and quantitative measurements of the optic nerve topography have been developed. Long times, the direct ophthalmoscope that describe optic disc structure have been sought. However, detection of progressive glaucomatous change in the optic disc using this method is extremely difficult due to poor reproducibility and high inter- and intra-observer variability. Other optic disc investigation method is photography by monocular and stereophotographic techniques. This non-quantitative method requires subjective physician interpretation and is time-consuming. Over the last time, more objective ocular techniques have been developed to provide high accurate and reproducible quantitative measurements of the contour of the optic disc. These efforts has resulted in the development of confocal scanning laser ophthalmoscopy, which obtains high-resolution 3D images, both perpendicular (X-axis, Y-axis) to optic axis and along the optic axis (Z-axis). This technique provides rapid, non-invasive, non-contact imaging of the ocular fundus.

After excluding eyes with prior intraocular surgeries and low-quality HRT images, we found a significant negative correlation between CCT and optic disc area, a negative but significant correlation between CCT and cup area and a positive but with mild association between CCT and rim volume, all this in patients with NTG and GE morphological type of optic disc.

CCT is inversely correlated to optic disc area, the most important parameter of the optic disc. Although thicker corneas have been recognized to cause slight over-estimation of true intraocular pressure (IOP), they may also indicate the presence of a substantially smaller, and thus more robust, optic nerve head (FI or SS morphological type of optic disc). Patients with thinner corneas, which slightly underestimate the true IOP may also have larger and more deformable optic disc (GE and MY morphological type of optic disc).

The cornea and optic disc both fill the two sclera "holes" of the eye so we may consider the possibility that CCT may be extrapolated to the characteristics of the optic disc itself, including disc area and deformability, factors that may relate significantly to the risk of developping glaucoma [16–18]. Optic disc size and morphology influences the susceptibility of axonal damage in glaucoma [19]. The axonal damage is associated with the higher lamina cribrosa pore-to-disc area ratio and thinner connective tissue support in this region [20]. Laplace's Law dictates that the deformability of a disc with smaller radius is less that of one with larger radius.

Because our findings indicate that CCT inversely correlated with optic disc area, CCT may also be correlated with the optic nerve's predisposition to damage. Eyes with thinner and more deformable corneas may have larger and more deformable optic discs, making them more susceptible to glaucomatous damage. Therefore, the more significant and real implication of thinner corneas may be as a marker for more deformable optic discs, whereas increased corneal thickness may simply indicate more rigid, resistant globes including optic disc laminae.

Conclusions

The strongest correlation was between CCT and the parameters of optic disc imaging obtained at HRT II in the GE type of optic disc. CCT is inversely correlated to optic disc area. The thicker cornea indicates the presence of a substantially smaller, and thus more robust, optic nerve head while thinner cornea may have larger and more deformable optic disc. HRT II is valuable for determining the morphological characteristics of the optic disc and there are low to moderate significant correlations between the parameters of HRT II and CCT in all patients with NTG. HRT II measurements would be more useful when they are applied to the different optic disc types. CCT can influence NTG management in a clinical context. It helps attribute risk and hence aids patient management decisions.

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Corresponding author

Laurenţiu Coman, MD, PhD, Department of Physiology, "Carol Davila" University of Medicine and Pharmacy, 8 Eroilor Sanitari Avenue, 050474 Bucharest, Romania; Phone +40722–859 772, e-mail: laurentiucmn@yahoo.com

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