The Use of Pulse Wave Velocity in Predicting Pre-Eclampsia in High-Risk Women

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In this study, we evaluated the diagnostic utility of pulls wave velocity (PWV) alone or in combination with other diagnostic markers in predicting pre-eclampsia (PE) on high-risk women. Pregnant women at high risk for PE were recruited between 32 and 36 weeks of gestation period. This study is the first in Romanian and shows that PWV may be a potentially promising predictor of early-onset PE in women at high risk for PE. All these patients were treated and were instructed according to the ESC/ESH guidelines regarding hypertensive patients. Statistical analysis was performed using the Chi-square, a Mann-Whitney test, Pearson correlation, and linear regression tests.After we ran several test the main conclusions are that there is a positive correlation between the para-clinics data (creatinine, Esbach proteinuria) and the pulls wave velocity for aorta (PWVao). The risk for preeclampsia is increasing if the body mass index (BMI) of the patients is higher than the average value (BMI>26) or if the patient is a smoker.

Keywords: pulls pregnancy, pulls wave velocity, preeclampsia

The importance of evaluating the diagnostic utility of pulls wave velocity (PWV) alone or in combination with other diagnostic markers in predicting pre-eclampsia (PE) on high-risk women is crucial. Pregnant women at high risk for PE were included in our study, all of them were between 32 and 36 weeks of gestation period. This study is the first in Romanian and shows that PWV may be a potentially promising predictor of early-onset PE in women at high risk for PE. All these patients were treated and were instructed according to the ESC/ESH guidelines regarding hypertensive patients [1].

Preeclampsia is a condition that may affect 2-8% of the population of pregnant women [5, 6]. Preeclampsia is one of the primary causes of maternal morbidity and mortality. After the delivery, most pathological conditions related to PE improve immediately.

Arterial stiffness (AS) is an important change in the arterial aging process. Carotidfemoral PWV (cfPWV) is considered the *gold-standard* measurement of arterial stiffness. PWV can be determined at the following levels: large arteries, central, elastic type, represented by aortic cfPWV. In most studies, stiffness is assessed by cfPWV because it is best correlated with overall mortality and cardiovascular mortality [7].

Due to the assessments of endothelial function and cardiovascular risk using vessel hemodynamic measurements have improved, several non-invasive methods have been developed to evaluate AS of pregnant women with and without pre-eclampsia.

Experimental part

Material and methods

Study population

We have a follow up study, all our patients were being checked during 2 years. All 50 patients were hospitalized in Bega County Hospital. 50 % of the patients of this group were diagnosed with preeclampsia during pregnancy. As well, we have 25 pregnant women with no known hypertension or pregnancy complications, this is considered to be our *control group'*, included in the study during a regular prenatal checking at the obstetrics and gynecology clinic. For both groups we collected in our data base their age, pregnancy age (in month), the values of systolic BP (TAS) and diastolic BP (TAD), the Esbach proteinuria, the mean arterial pressure (PWV), the creatinine value and the hemoglobin value. As well, we calculated the body mass index (BMI) and we recorded if they are smokers. We made a parallel analysis: for the whole sample and for the two subgroups, who were separated by the criteria of preeclampsia present or absent.

Biochemical and hematological parameters

Biochemical tests were performed, biochemical auto analyzer with original kits and total leukocyte counts were measured by an automated hematology analyzer, in peripheral venous blood samples drawn after 12 h of overnight fasting. Absolute cell counts were also measured. We took the Esbach proteinuria test, the creatinine test.

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Statistical analysis

The data were analyzed using the SPSS_V17 software and the descriptive statistics were made using the Microsoft Excel software. We applied a Kolmogorov-Smirnov test in order to verify the type of the distribution in our variables. We obtained a p value, $p < 0.05$ so we don't have a normal distribution in our data. In order to see if there are any differences between the continuous variables in the two groups we applied a Mann -Whitney test was and a Chi-square test for the categorical variables. Also, we computed a risk analysis to see if smoking can be considered a risk factor for preeclampsia. The Pearson coefficient was used for analyzing the power of correlation between the numerical variables. We used a linear regression analysis to evaluate the relative importance of parameters. Statistical significance was defined as $p < 0.05$.

Results and discussions

We made a parallel descriptive statistics, for the whole sample (N=50), and for the two subgroups the preeclampsia group (N1=25), and the control group (N2=25). All the data are presented in table 1,2 and 3. Due to the fact that we observed that there are some differences between the two subgroups we applied a Mann - Whitney test to see if this differences between the group with patients having preeclampsia and the control group can be considered significant ($p<0.05$). We obtained significant differences for the blood pressure (TAS and TAD), BMI, creatinine and hemoglobin. In the group with preeclampsia we have significant higher values for blood pressure (TAS and TAD), BMI and for creatinine; the hemoglobin values are significantly lower than in the control group. All the p values are shown in table 4.

Table 1

THE DESCRIPTIVE STATISTICS FOR THE WHOLE GROUP

Whole Sample (N=50)	Age	ESBACH Proteinuria	VG	Mother's TAS	Mother's TAD	BMI	PWVao [m/s]	Creatinine	Hemoglobin
Mean	29.68	0.44	34.06	128.12	74.14	26.24	5.40	0.82	11.24
Standard Error	0.90	0.06	0.19	1.73	1.71	0.29	0.11	0.03	0.13
Median	31	0.3	34	129	70.5	27	5.5	0.8	11.1
Mode	36	0.2	35	140	85	27	5.8	0.8	10.9
Standard Deviation	6.34	0.41	1.36	12.25	12.12	2.09	0.80	0.19	0.92
Sample Variance	40.18	0.16	1.85	150.03	146.82	4.35	0.65	0.04	0.85
Minimum	18	0.1	32	99	50	21	3.8	0.6	9.7
Maximum	42	1.8	36	150	100	31	7	1.3	12.9

Table 2

THE DESCRIPTIVE STATISTICS FOR THE GROUP WITH PREECLAMPSIA.

Sample 1 (N1=25)	Age	ESBACH Proteinuria	VG	Mother's TAS	Mother's TAD	BMI	PWVao [m/s]	Creatinine	Hemoglobin
Mean	30.88	0.52	33.92	135.88	80.04	27.72	5.54	0.91	10.80
Standard Error	1.18	0.09	0.31	1.67	2.55	0.24	0.14	0.04	0.17
Median	34	0.4	34	140	85	27	5.8	0.8	10.8
Mode	36	0.4	32	140	85	27	5.8	0.8	9.8
Standard Deviation	5.90	0.43	1.53	8.34	12.75	1.21	0.70	0.21	0.85
Sample Variance	34.78	0.18	2.33	69.53	162.54	1.46	0.49	0.04	0.72
Minimum	20	0.1	32	124	50	26	4.2	0.6	9.8
Maximum	37	1.8	36	150	100	31	7	1.3	12.8

Table 3

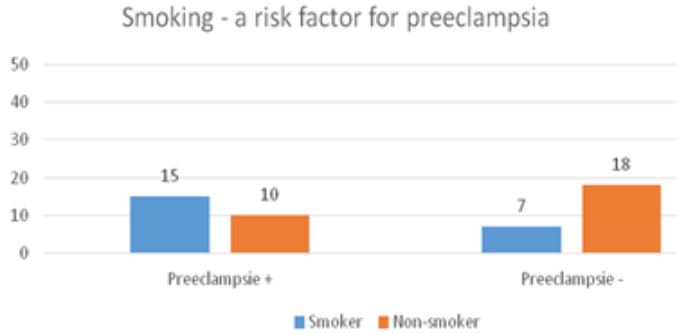
THE DESCRIPTIVE STATISTICS FOR THE CONTROL GROUP.

Sample 2 (N2=25)	Age	ESBACH Proteinuria	VG	Mother's TAS	Mother's TAD	BMI	PWVao [m/s]	Creatinine	Hemoglobin
Mean	28.48	0.36	34.20	120.36	68.24	24.76	5.27	0.73	11.68
Standard Error	1.33	0.07	0.24	2.11	1.61	0.34	0.18	0.02	0.15
Median	30	0.2	34	120	68	25	5.2	0.7	11.9
Mode	18	0.2	33	120	70	24	6.3	0.6	12.2
Standard Deviation	6.65	0.37	1.19	10.55	8.04	1.69	0.89	0.12	0.77
Sample Variance	44.26	0.14	1.42	111.32	64.69	2.86	0.79	0.01	0.60
Minimum	18	0.1	32	99	54	21	3.8	0.6	9.7
Maximum	42	1.8	36	132	87	28	7	1	12.9

Table 4

THE p-VALUES OBTAINED BY APPLYING THE MANN - WHITNEY TEST FOR THE NUMERICAL VARIABLES, IN ORDER TO COMPERE THE MEAN VALUES OF THE TWO GROUPS

Group 1 vs. Group 2	Age	ESBACH Proteinuria	VG	Mother's TAS	Mother's TAD	BMI	PWVao [m/s]	Creatinine	Hemoglobin
Asymp. Sig. (2-tailed)	.072	.075	.532	.000	.000	.000	.307	.002	.001



Graph 1.The relation between patients with / without preeclampsia and smokers / non-smokers

Variables	Pearson coefficient r	Determination coefficient R^2	p- value
Association between PWVao [m/s] and age	r = 0.93	$R^2 = 0.86$	p < 0.001
Association between PWVao [m/s] and gestational period	r = 0.95	$R^2 = 0.89$	p < 0.001
Association between PWVao [m/s] and ESBACH Proteinuria	r = 0.91	$R^2 = 0.82$	p < 0.001

Table 5

THE ASSOCIATION BETWEEN THE PWVAO [m/s] VALUES AND THE AGE, GESTATIONAL AGE AND ESBACH PROTEINURIA VALUES

Further on we computed a risk analysis in order to see if we can find any associations between the habit of smoking and the presence of preeclampsia during pregnancy. [8].We have a follow up study so we calculated both the relative risk (RR) value and the odds ratio (OR) value and their 95% confidence interval. For the significance of the differences we applied a Chi square test. We obtained that smoking can be considered a risk factor for the appearance of preeclampsia during pregnancy ($p=0.04$, $RR=1.91$, $95\% \in (1.07, 3.38) = 3.86$, $95\% \in (1.18, 12.61)$ [9].This differences are plotted in Graph1.

Another main problem could be the fact that the patient may have cardiovascular diseases, thrombophilia kidney diseases, [10,11] and hepatic disease in her heredocolaterale antecedents. Some of our patients, who are registered at the Bega Hospital in the Obstetrics and Gynecologic section have in the family chronic kidney failure and their first degree relatives are going on a dialysis program [12].

In the last part of our study we tested to see if there is any association between the PWVao [m/s] values and the age of our patients, the gestational age and the ESBACH Proteinuria. In all three cases we obtained a positive, direct strong correlation ($r>0.75$), where r is the Pearson coefficient. From the regression model we obtained an extremely significant association in all three cases ($p<0.001$. All the data are presented in Table 5 and plotted in Graf. 2,3 and 4.

Conclusions

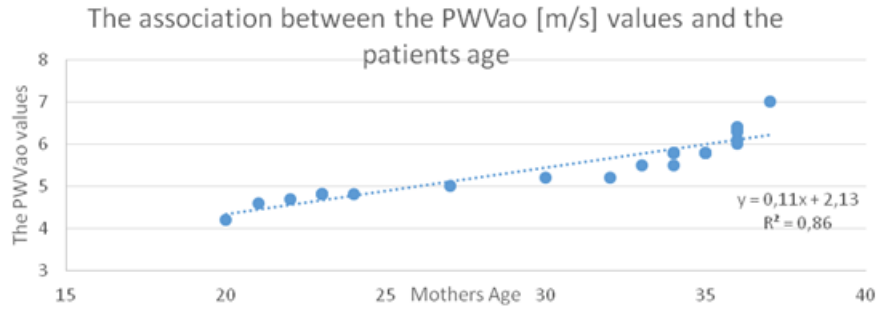
So, we can state that patients with a high risk of cardiovascular disease require on-going care. Adverse cardiovascular events occur more frequently in cases with AS and its hemodynamic consequences can be fatal for pregnant patients who are having also preeclampsia. Therefore, assessment of AS in cases of pre-eclampsia is important.

We obtained a positive association between the Esbach proteinuria and the pulls wave velocity for aorta ($r > 0.75$, $p < 0.001$), and as well an positive strong correlation between PWVao [m/s] and the patient age and gestational age (calculated in month) ($r>0.75$, $p < 0.001$).

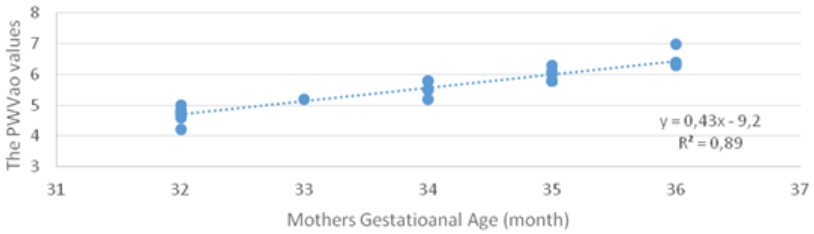
Another important aspect is the mother vices. We obtained that smoking can be considered a risk factor for the appearance of preeclampsia ($p=0.04$, $RR=1.91$, $95\% \in (1.07, 3.38) = 3.86$, $95\% \in (1.18, 12.61)$.

Graph 3: The association between the PWVao [m/s] values and the gestational age values

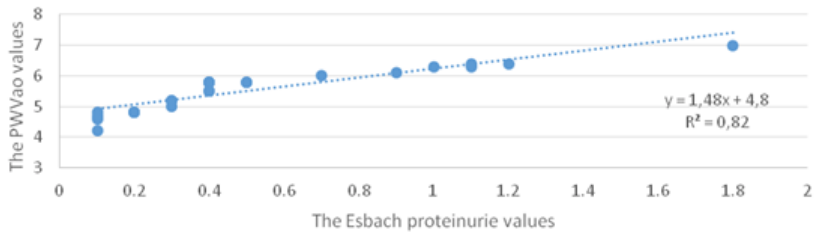
Graph 4: The association between the PWVao [m/s] values and ESBACH Proteinuria values



Graph. 2. The association between the PWVao [m/s] values and the age values



Graph 3. The association between the PWVao [m/s] values and the gestational age values



Graph 4. The association between the PWVao [m/s] values and ESBACH Proteinuria values

References

1.IURCIUC, S., CIMPEAN, A.M., MITU, F., HEREDEA, R., IURCIUC, M., Vascular aging and subclinical atherosclerosis: why such a never ending and challenging story in cardiology?, Clinical Interventions In Aging, Vol.12, pag 1339-1345, DOI: 10.2147/CIA.S141265 Published: 2017

2.IURCIUC, M., AVRAM, C., IURCIUC, S., FRANCULESCU, C., VLAD, A., MANCAS, S., Comprehensive rehabilitation programs may improve some of the ambulatory blood pressure parameter. Proceedings of the 17th European Congress of Physical and Rehabilitation Medicine. Minerva Medica. 2010:253–255.

3. IURCIUC, S., AVRAM, C., TURI, V., et al. Physical training, hemodynamic parameters and arterial stiffness: friends or foes of the hypertensive patient? In Vivo. 2016;30(4):521–528.

4.IURCIUC, M., AVRAM, C., IURCIUC, S., et al. Exercise training and vascular compliance. J Romanian Sports Med. 2007;10:563–568

5.GHULMIYYAH, L., SIBAI, B., Maternal mortality from preeclampsia/ eclampsia. Semin Perinatol 2012;36:56–9.

6.STEEGERS, E.A., von DADELSZEN, P., DUVEKOT, J.J., PIJNENBORG, R., Pre-eclampsia. Lancet 2010;376:631–44.

7.PANNIER, B., GUERIN, A.P., MARCHAIS, S.J., MICHEL, E., GERARD, M.L., Stiffness of capacitive and conduit arteries. Hypertension. 2005;45:592–596.

8.PETRE, I., BERNAD, E., CRAINA, M.,CITU, C.,BOLINTINEANU, S., POP, E., STOIAN,D., SIPOS,S., LUNGEANU, D.,FURAU, C., FURAU, G.,PANTEA, S., IONITA,I., - Determining markers PlGF, sFlt1 and the ratio sFlt1/PlGF - prognostic tool in patiente with preeclampsia, Rev Chim. (Bucharest), **67**, no. 11, 2016, p. 2365

9.BONTE, D.C.,BOGLUT, A.,DUTA, C.,PETRE**,** I., BERNAD, E.,VLAD DALIBORCA,C., IACOB,R.E., DIMA,M., IACOB,D., The Harmful Effects of Smoking during Pregnancy and Correlating Lead and Selenium Levels in Mothers and Premature Fetuses, Re. Chim. (Bucharest), **67**, no. 1, 2016, p. 116

10.MILULESCU,A.,DORNEANU, F., IACOB, D., STOIAN, D.,PETRE,I., CHIRIA, V.D., MARGAN, R., IONITA,I., MARTI,D., MOLERIU,L.C., Procalcitonina - Diagnostic Marker in Neonatal Sepsis, Mat. Plast., **54**, no. 4, 2017

11.MLADIN-MICOARA N.C., LUNGEANU D., MORARIU S.I., CIACLI C.A., MOLERIU,L.C., STELEA L., PETRE, I., IONITA,I., CALAMAR POPOVICI, D., PUSCHITA M., Biomarkers in Diagnosing Preeclampsia and their Correlation with Blood Pressure, publicat la Rev. Chim. (Bucharest), **68**, no. 10, 2017, p. 2449

PANTEA S., LUCHIAN G., CORINA PANTEA, F. LAZAR, D. BORDOS, M. PAPURICA , CARMEN BALASA-GURAGATA, S. NICOARA, ANCA MATES, The placement of Tenckhoff peritoneal dialysis catheter by laparoscopic approach, Chirurgia, Vol 103, Issue:6

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