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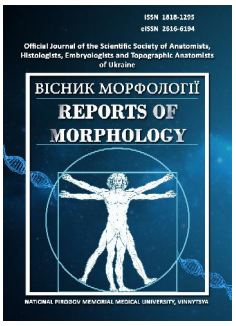

Discriminant models of the possibilities of occurrence and features of the course of benign nevi in men depending on the characteristics of dermatoscopic parameters

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Human skin is the first barrier to protect the body from external factors. Combinations of certain external and internal (genetically determined) factors can lead to cancer of this organ. One of such pathologies is nevi - still little studied disease. At the same time, modern medicine is interested in inventing mechanisms to predict their occurrence and course. The purpose of the study is to build and analyze discriminant models of the possibility of benign nevi in Ukrainian men depending on the characteristics of dermatoscopic parameters. Ukrainian men aged 22 to 35 years, patients with melanocyte benign simple nevi (n=34), melanocyte benign dysplastic nevi (n=27), melanocyte benign congenital nevi (n=14) and non-melanocyte benign nevi (n=17) get dermatoscopic examination. The possibility of benign nevi occurrence depending on the characteristics of dermatoscopic parameters was carried out using discriminant analysis in the licensed statistical package "Statistica 5.5". With the help of discriminant analysis, reliable models of the possibility of occurrence of benign nevi depending on the characteristics of dermatoscopic parameters are built. It was found that among patients with melanocyte benign simple, dysplastic, congenital and non-melanocyte benign nevi, a reliable interpretation of the obtained classification indicators is possible (discriminant function covers 70.7 % of cases; statistics Wilks' Lambda=0.185; p<0.001). The models include the general dermatoscopic index, the dermatoscopic criterion "Asymmetry" according to the ABCD system, the number of nevi on the body more than 1 cm and the dermatoscopic criterion "Color" according to the ABCD system. Moreover, the general dermatoscopic index and the dermatoscopic criterion "Asymmetry" according to the ABCD system make the greatest contribution to discrimination between Ukrainian men with benign nevi.

Keywords: *skin diseases, benign nevi, dermatoscopy, men, discriminant analysis.*

Introduction

The barrier function of the skin is to protect the human body from a variety of stimuli, namely: mechanical damage (in particular, through the damping function), physical factors (such as ultraviolet radiation), chemical factors, microorganisms, etc.

At the same time, performing such a "piece of work" makes the skin vulnerable to various pathologies. Each of the external factors ultimately acts as a kind of trigger that start a cascade of pathophysiological reactions. However, it should be understood that the activation of such mechanisms also requires an internal factor, which is mostly a genetic predisposition to the occurrence of a pathological condition.

An example of such pathology, in particular, is a nevus. Many studies show that this disease is a combination of exogenous and endogenous factors. Examination of 546 children with nevi revealed that 94.6 % of subjects had a phenotype of II, III categories, 66.7 % had brown eyes, 59.3 % had brown hair and 61.3 % had light skin. At the same time, a higher incidence of sunburn was associated with more nevi [2]. Another group of authors, who also worked with a sample of Spanish children with nevi, performed a multifactor analysis of external factors associated with the number of nevi. If in the group of 4-

year-olds only time spent in the sun was a statistically significant factor, in the group of 14-year-olds such factors were male gender, skin phototype, time spent on the beach and use of sunscreen on the beach [12].

The number of nevi on the human body, as well as their location is completely different. According to Italian scientists, 50 % of children have less than 10 nevi, 45 % have 10 to 30, and only 5 % have 30 to 50 [8]. At the same time, data from a sample of Spanish children showed that the average number of nevi is about 19 units [2].

Examination of more than 9,000 boys aged 18-20, ethnic Jordanians, revealed nevi in 642. Of these: 8.1 % noted their appearance in preschool age, 59.8 % at the age of 12-15 years. In 68.3 % of cases, nevi were observed on the upper torso and shoulders. Most of the representatives with nevi were from the northern regions of Jordan [9].

C. Patruno and co-authors [14] in a sample of 144 children found that the number of nevi is higher in boys than in girls ($p<0.05$), and the highest prevalence of nevi is observed on the torso and neck ($p<0.001$). As in previous studies, a correlation was found between the number of nevi and the time of insolation ($p<0.05$).

The number of nevi is quite volatile. A survey of 90 Puerto Rican children found that 85 % had nevi at the time of the examination. A re-examination a year later revealed new nevi in 62 % of people. The average increase in the number of nevi was 1.8 ($p<0.001$) [20].

However, why is there such an increased interest in the study of nevi? Nevi are often associated with the risk of melanoma. In particular, to a greater extent this risk is associated with the number of nevi on the human body. Particular attention is paid to the presence of congenital, giant or atypical nevi. Although, according to scientists, the mechanism of melanoma is dominated by exogenous components [4]. The annual rate of conversion of a single nevus to is estimated at 0.0005 % or less for patients in the age group less than 40 years [17]. At the same time for a choroidal nevus this indicator makes from 2 to 3 % depending on a race [10].

In addition, we should not forget about the decline in quality of life and deterioration of psycho-emotional state in people with nevi, especially when it comes to congenital nevi of large size or localization in exposed areas of the body [11].

Given the above information, for the needs of practical medicine there is a need to find and study the interdependencies that will predict the risk of benign nevi. The most promising in terms of simplicity and cheapness of data are dermatoscopic indicators, the justification of the use of which can be achieved only by conducting an experimental study, followed by adequate and complete statistical processing of the results.

The purpose of the study is to build and analyze discriminant models of the possibility of benign nevi occurrence in Ukrainian men depending on the characteristics of dermatoscopic parameters.

Materials and methods

On the basis of the Military Medical Clinical Center of the Central Region and the Department of Dermatology and Venereal Diseases with a course of postgraduate education National Pirogov Memorial Medical University, Vinnytsya, Ukrainian men (aged 22 to 35 years) with melanocyte benign simple nevi (n=34), melanocyte benign dysplastic nevi (n=27), melanocyte benign congenital nevi (n=14) and non-melanocyte benign nevi (n=17) were performed clinical-laboratory and pathohistological examinations. The diagnosis of nevi was established according to a two-stage algorithm for the classification of pigmented tumors, which was adopted at the First World Congress of Dermatoscopy (Rome, 2001) [15].

Committee on Bioethics of National Pirogov Memorial Medical University, Vinnytsya (protocol № 10 From 26.11.2020) found that the studies do not contradict the basic bioethical standards of the Declaration of Helsinki, the Council of Europe Convention on Human Rights and Biomedicine (1977), the relevant WHO regulations and laws of Ukraine.

All patients were determined the number of nevi on the body, the number of nevi on the body up to 0.6 cm, the number of nevi on the body up to 1.0 cm, the number of nevi on the body more than 1.0 cm and the number of nevi on the hands more than 0.2 cm.

The dermatoscopic index was calculated according to the so-called "ABCD rule of dermatoscopy":

"A" - Asymmetry. To determine this indicator, the studied neoplasm was visually divided along two asymmetrically favorable lines; in the presence of asymmetry on two axes the index 2 was appropriated;

"B" - Border sharpness. To assess this feature, the tumor was visually divided into eight equal parts, each fate, which has a clear limit, was assigned an index of 1;

"C" - Color. There are 6 dermatoscopic colors (light brown, dark brown, black, gray-blue, white, red). Each color present in the area of the tumor was assigned an index of 1;

"D" - Dermoscopic structures. The dermatoscopic picture distinguished the following structural elements: "pigment network", "stripes" ("radial radiance", "pseudopods"), "points", "granules", "unstructured areas", "blue-white veil", "regression structures", "vascular structures" (areas of milky red color, microvessels are visualized). Each element in the presence of it in the tumor was assigned an index of 1.

The total dermatoscopic index is calculated by the formula "A" + "B" + "C" + "D", where the constant coefficients A=1.3; B=0.1; C=0.5; D=0.5. At the general dermatoscopic index from 4.75 to 5.45 the new growth is regarded as a dysplastic nevus, and at values above 5.45 the preliminary diagnosis of a melanoma of skin is exposed.

The possibility of benign nevi occurrence depending on the characteristics of dermatoscopic parameters was carried out using discriminant analysis in the licensed statistical package "Statistica 5.5".

Results

Taking into account dermatoscopic parameters between men with benign nevi, the discriminant function covers 85.3 % of men with melanocyte simple nevi, 70.4 % of men with melanocyte dysplastic nevi, 21.4 % of men with melanocyte congenital nevi and 82.4 % of men with non-melanocyte nevi. In general, the model in patients with melanocyte simple, dysplastic, congenital and non-melanocyte benign nevi of men is correct in 70.7 % of cases (Table 1).

Among men with benign nevi, the discriminant variables are the general dermatoscopic index (IND), the dermatoscopic criterion "Asymetry" according to the ABCD system (AS), the number of nevi on the body more than 1 cm (BOL_10) and the dermatoscopic criterion "Color" according to the ABCD system (COL) (Table 2). Among the above indicators, the general dermatoscopic index and the dermatoscopic criterion "Asymmetry" have the largest contribution to discrimination between groups of patients with benign nevi by men. The set of all dermatoscopic variables has a pronounced (Wilks' Lambda=0.185; F(12.23)=16.75; p<0.001) discrimination between groups of patients with benign nevi men (see Table 2).

Table 1. Matrix of percentages of coverage of discriminant function for patients with benign nevi men depending on features of dermatoscopic indicators.

Classification Matrix (nabil-gr.sta)					
Rows: Observed classifications					
Columns: Predicted classifications					
	Percent Correct	G_1:2 p=0.3696	G_2:3 p=0.2935	G_3:4 p=0.1522	G_4:5 p=0.1848
G_1:2	85.3	29	3	0	2
G_2:3	70.4	8	19	0	0
G_3:4	21.4	5	4	3	2
G_4:5	82.4	3	0	0	14
Total	70.7	45	26	3	18

Notes: here and in the following tables, 1:2 - men with melanocyte simple nevi; 2:3 - men with melanocyte dysplastic nevi; 3:4 - men with melanocyte congenital nevi; 4:5 - men with non-melanocyte nevi.

Table 2. Summary of the analysis of discriminant function between men with benign nevi depending on the characteristics of dermatoscopic parameters.

Discriminant Function Analysis Summary (nabil-gr.sta)						
Step 4, N of vars in model: 4; Grouping: DZ_1 (4 grps)						
Wilks' Lambda: 0.185 approx. F (12.23)=16.75 p<0,0000						
	Wilks' Lambda	Partial Lambda	F-remove-3.850	p-level	Toler.	(R-Sqr.)
IND	0.266	0.695	12.41	0.0000	0.087	0.913
AS	0.263	0.703	11.98	0.0000	0.171	0.829
BOL_10	0.233	0.792	7.436	0.0002	0.972	0.028
COL	0.203	0.910	2.787	0.0456	0.234	0.766

Notes: here and in the following tables, Wilks' Lambda - statistics of Wilkes lambda; $F_{(12.23)}$=16.75 - critical ($_{12.23}$) and received (16.75) the value of the Fisher test; p - p-level related to the total value Wilks' Lambda; Partial Lambda - Wilkes statistics lambda single contribution of variable to discrimination between populations; F-remove - the standard F-test is related to the corresponding one Partial Lambda; p-level - p-level related to the corresponding F-remove; Toler. - tolerance values for each variable.

Table 3. Indicators of classification of discriminant variable patients with benign nevi men depending on features of dermatoscopic indicators.

Classification Functions; grouping: DZ_1 (nabil-gr.sta)				
	G_1:2 p=0.3696	G_2:3 p=0.2935	G_3:4 p=0.1522	G_4:5 p=0.1848
IND	6.848	8.087	3.302	1.305
AS	-6.930	-5.784	-2.293	-1.334
BOL_10	-0.005	0.273	0.047	0.033
COL	-3.041	-5.017	0.902	-0.938
Constant	-7.644	-12.31	-5.937	-1.888

For patients with benign nevi men, classification indicators (Df) were determined, by means of which it is possible to classify patients into different groups of benign nevi (Table 3).

Below in the form of equations the definition of indicators of classification where assignment to men of patients with melanocytic simple nevi is possible at value Df close to 7.644 is given; to men patients with melanocyte dysplastic nevi - at a Df value close to 12.31; to men patients with melanocyte congenital nevi - at a Df value close to 5.937; to men with non-melanocyte nevi - with a Df value close to 1.888:

Df (*for men with melanocyte simple nevi*) = IND x 6.848 - AS x 6.930 - BOL_10 x 0.005 - COL x 3.041 - 7.644;

Df (*for men with melanocyte dysplastic nevi*) = IND x 8.087 - AS x 5.784 + BOL_10 x 0.273 - COL x 5.017 -12.31;

Df (*for men with melanocyte congenital nevi*) = IND x 3.302 - AS x 2.293 + BOL_10 x 0.047 + COL x 0.902 - 5.937;

Df (*for men with non-melanocyte nevi*) = IND x 1.305 - AS x 1.334 + BOL_10 x 0.033 - COL x 0.938 - 1.888.

The obtained results of the χ^2 test indicate that, taking into account the established dermatoscopic parameters, a reliable interpretation of the obtained classification indicators between men with patients with all groups of benign nevi is possible (see Table 4).

Table 4. Test report χ^2 with removed consecutive roots in patients with benign nevi men, depending on the characteristics of dermatoscopic parameters.

Chi-Square Tests with Successive Roots Removed (nabil-gr.sta)						
	Eigen-value	Canonicl R	Wilks' Lambda	Chi-Sqr.	df	p-level
0	2.074	0.821	0.185	146.9	12	0.0000
1	0.577	0.605	0.568	49.17	6	0.0000
2	0.116	0.323	0.896	9.559	2	0.0084

Notes: Eigenvalue - root values for each discriminant function; Canonicl R - the canonical value of R for different roots; Chi-Sqr. - standard criterion χ^2 of successive roots; Df - number of degrees of freedom; p-level - p-level of the corresponding χ^2.

Discussion

Dermatoscopic method of research occupies a key place in the primary diagnosis and differential diagnosis of nevi. The most popular in terms of differential diagnosis is the exclusion of melanoma. Dermatoscopy allows to perform differential diagnosis 27 % more effectively than the usual examination with the naked eye [16]. However, it should be noted that the effectiveness of this method directly correlates with the experience of the dermatovenerologist who conducts the examination [21].

T. Alendar and H. Kittler [1] analyzed dermatoscopic studies to identify nevi most often associated with melanoma. Of the 357 cases of melanoma, the occurrence of nevus was recorded in 8.7 % of cases. At the same time, in 11.8 % an unambiguous conclusion could not be made. Most melanoma formation occurred on the background of superficial or superficial-deep congenital nevus.

A group of researchers performed a dermatoscopic examination of 3823 atypical nevi in 541 individuals. Pathomorphological examination was subsequently performed for 264 samples taken during dermatoscopy. In 30.5 % the pathomorphological conclusion was melanoma [13].

Analysis of the results of dermatoscopy revealed signs that distinguish nevi from melanoma. The most characteristic criteria for melanoma were pattern asymmetry (OR, 4.9; 95 % CI, 4.1-5.8), contour asymmetry (OR, 3.2; 95 % CI, 2.7-3.7), disorganized pattern (OR, 3.3; 95 % CI, 2.9-3.7), pronounced disorder of architecture (OR, 6.6; 95 % CI, 5.6-7.8) ($p<0.001$). Also as criteria it is possible to apply absence of vessels (ICC, 0,46; 95 % CI, 0,42-0,51), dark brown color (ICC, 0,40; 95 % CI, 0,35-0,44), vessels with a coma (ICC, 0.44; 95% CI, 0.40-0.49) ($p<0.001$). In total, the ABCD rule had the highest specificity (59.4 %) [3].

The effectiveness of the ABCD rule is also indicated by other studies [16].

A group of researchers led by Di Cesare A. [5] found features of the dermatoscopic picture for blue nevus. For the study, 95 cases of blue nevus and 190 melanoma and basal cell carcinoma were selected for comparison. In all 95 cases of dermatoscopy of the blue nevus, the phenomenon of homogeneous pigmentation was observed, in 84.2 % there was a homogeneous pattern (blue, black or brown) or a mixture of two colors (blue and black, brown or blue). 15.8 % had combinations of more than 2 colors. In 49.5 %, pigmentation was observed against the background of the absence of a pigment network, and in 50.5 % local dermatoscopic patterns were detected.

Patients with more than 100 nevi are 7 times more likely to develop melanoma than individuals with fewer nevi (combined RR 6.89; 95 % CI, 4.63, 10.25). In general, people with more than 40 nevi also have a high chance of developing melanoma (combined RR 1.47; 95 % CI, 1.36, 1.59) and people with more than 15 nevi have a 5-fold higher risk of melanoma than persons without nevi (combined RR 4.82; 95 % CI, 3.05, 7.62) [16].

In the analysis of discriminant equations of patients with benign nevi of Ukrainian men depending on dermatoscopic indicators, we found that a reliable interpretation of the obtained classification indicators between patients with melanocyte benign simple, dysplastic, congenital and non-melanocyte benign nevi is possible (discriminant function covers 70.7% of cases; Wilks' Lambda=0.185; $p<0.001$). The discriminant models include the general dermatoscopic index, the dermatoscopic criterion "Asymmetry" according to the ABCD system, the number of nevi on the body more than 1 cm and the dermatoscopic criterion "Color" according to the ABCD system. Moreover, the greatest contribution to discrimination between men with benign nevi is made by the general dermatoscopic index and the dermatoscopic criterion "Asymmetry" according to the ABCD system.

It should be noted that the world scientific community has also achieved significant success in predicting the occurrence of oncopathology, in particular dermatooncopathology, through the use of anthropometric indicators, including height, weight, body mass index, body circumference, etc. [6, 7, 18, 19].

Given the above data, it is encouraging to apply different approaches to predicting the occurrence or course of a nevus, in particular both dermatoscopic and constitutional. This area of research can be considered in subsequent publications.

Conclusions

1. Reliable discriminant models developed on the basis of dermatoscopic indicators allow to predict with high probability the possibility of melanocyte benign simple, dysplastic, congenital and non-melanocyte benign nevi occurrence in Ukrainian men.

2. The composition of discriminant equations in patients with benign nevi Ukrainian men includes the general dermatoscopic index, dermatoscopic criteria "Asymmetry" and "Color" according to the ABCD system and the number of nevi on the body more than 1 cm.

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ДИСКРИМІНАНТНІ МОДЕЛІ МОЖЛИВОСТІ ВИНИКНЕННЯ ТА ОСОБЛИВОСТЕЙ ПЕРЕБІГУ ДОБРОЯКІСНИХ НЕВУСІВ У ЧОЛОВІКІВ ЗАЛЕЖНО ВІД ОСОБЛИВОСТЕЙ ДЕРМАТОСКОПІЧНИХ ПОКАЗНИКІВ

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Шкіра людини є найпершим бар'єром захисту організму від зовнішніх чинників. Комбінації дії певних зовнішніх та внутрішніх (генетично детермінованих) чинників можуть призводити до виникнення онкологічних захворювань даного органу. Однією з таких патологій є невуси - досі мало вивченого захворювання. В той же час сучасна медицина зацікавлена у винайденні механізмів передбачення їх виникнення та перебігу. Мета дослідження - побудувати та провести аналіз дискримінантних моделей можливості виникнення доброякісних невусів в українських чоловіків залежно від особливостей дерматоскопічних показників. Українським чоловікам віком від 22 до 35 років, хворим на меланоцитарні доброякісні прості невуси (n=34), меланоцітарні доброякісні диспластичні невуси (n=27), меланоцітарні доброякісні вроджені невуси (n=14) та немеланоцитарні доброякісні невуси (n=17) проведено дерматоскопічне обстеження. Можливість виникнення доброякісних невусів залежно від особливостей дерматоскопічних показників проведено за допомогою дискримінантного аналізу в ліцензійному статистичному пакеті "Statistica 5.5". За допомогою дискримінантного аналізу побудовані достовірні моделі можливості виникнення доброякісних невусів в залежності від особливостей дерматоскопічних показників. Встановлено, що між хворими на меланоцитарні доброякісні прості, диспластичні, вроджені та немеланоцитарні доброякісні невуси можлива достовірна інтерпретація отриманих показників класифікації (дискримінантна функція охоплює 70,7 % випадків; статистика Wilks' Lambda=0,185; p<0,001). До складу моделей входять загальний дерматоскопічний індекс, дерматоскопічний критерій "Asymmetry" по системі ABCD, кількість невусів на тілі більше 1 см та дерматоскопічний критерій "Color" по системі ABCD. Причому, загальний дерматоскопічний індекс і дерматоскопічний критерій "Asymmetry" по системі ABCD вносять найбільший внесок у дискримінацію між хворими на доброякісні невуси українськими чоловіками.

Ключові слова: *захворювання шкіри, доброякісні невуси, дерматоскопія, чоловіки, дискримінантний аналіз.*