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Pigmented Lesions Assessment in the Routine Dermatooncologist and Oncologist Practice

Оценка пигмента в рутинной практике дерматоонколога и онкохирурга

Abstract

Introduction. The incidence of melanoma tends to rise. Over the past two decades, the absolute annual rates of newly diagnosed cases of melanoma in the Republic of Belarus have increased by 2.5 times. Risk factors for melanoma commonly include fair skin phototypes, male sex, high numbers of melanocytic nevi, dysplastic nevi, immunosuppression, personal or family history of melanoma, and exposure to ultraviolet (UV) radiation.

Melanoma is a unique type of neoplasia – it can be diagnosed through visual examination in the early stages. Traditionally, pigment lesions are examined using the ABCD+E rule. Introduced in 1985, it has made sizeable progress in the verification of melanoma. However, with the emergence of new methods in the late 1980s and early 1990s (epiluminescence microscopy, dermoscopy) it became evident that the ABCD+E rule is not as effective for early diagnosis of melanoma. As a result, some countries (Australia, New Zealand, Germany, Netherlands, UK) have introduced risk-assessment tools that take into account personal medical history, as well as clinical and dermoscopic analysis of pigment lesions in their national skin cancer screening programs.

Today, the ABCD+E rule is essentially the only tool to verify melanoma used in clinics in the Republic of Belarus. The high relevance of the problem requires a new national screening program for melanoma and non-melanoma skin cancers in the near future.

The aim of the study was to assess the effectiveness of the ABCD+E rule in the early diagnosis of pigmented skin lesions.

Materials and methods. This is a study of a group of patients (854) with pigmented skin lesions (nevi and suspicious of melanoma) based at the outpatient surgery department. The study is direct, diagnostic, observational, retrospective, longitudinal, and single-centered. Statistical processing of the results was carried out using the Statistica 10.0 application package.

Results. There was no significant difference in the sum of the criteria (SC) of the ABCD+E rule in the study groups. Visual clinical evaluation of local status at the initial admission was subjective. Comparing groups with morphologically confirmed melanomas (85) and “melanomas” who later turned out to be non-melanomas (67), the rule showed its inconsistency in half of the cases. Furthermore, SC in the cases with pigmented lesions that initially were assessed as nevi and later turned out to be cutaneous melanoma (17) was 2 times significantly lower. The most specific criteria were A (asymmetry) and B (irregular border) – 96% and 67%, respectively. Nevertheless, their sensitivity was assessed as low (for A – extremely low, 8%). Criteria C (color) and D (diameter) had low indicators of both sensitivity and specificity. The sensitivity of criteria E (evolving) was the

highest – 62%, but its specificity of 33% cannot be considered sufficient. No correlation was found between the thickness of the melanoma and the sum of criteria for the ABCD+E rule.

Conclusion. Even the maximum score of the ABCD+E rule cannot be reliable evidence that the doctor is dealing with melanoma, and vice versa, a low score does not guarantee the absence of a malignant neoplasm. Initial dermatooncological examination requires a mandatory assessment of the individual relative risk factors of developing skin melanoma and a dermoscopic examination of the pigment lesions.

Keywords: cutaneous melanoma, ABCD+E rule.

Резюме

Введение. Повсеместно заболеваемость меланомой имеет тенденцию к росту. За последние две декады абсолютные показатели ежегодной регистрации вновь выявленных случаев меланомы в Республике Беларусь увеличились в 2,5 раза. К факторам риска для меланомы принято относить: светлые фототипы кожи, мужской пол, наличие большого количества меланоцитарных и диспластических невусов, иммуносупрессию, персональную или семейную историю меланомы, а также воздействие ультрафиолетового (УФ) излучения.

Меланома является уникальным видом неоплазий – ее можно обнаружить при визуальном осмотре на ранних стадиях. Классическая оценка пигмента на приеме подразумевает использование правила ABCD+E. Предложенное в 1985 г., оно позволило добиться определенных успехов в верификации меланомы. Однако с появлением новых методик визуализации в конце 1980-х – начале 1990-х гг. (эпилюминисцентная микроскопия, дермоскопия) стало очевидным, что возможности правила ABCD+E в ранней диагностике меланомы ограничены. В результате некоторые страны (Австралия, Новая Зеландия, Германия, Нидерланды, Великобритания) в свои национальные программы скрининга рака кожи стали внедрять механизм оценки рисков, учитывающий анамнез, клинику и дермоскопический анализ пигмента.

В Республике Беларусь на современном этапе правило ABCD+E по сути является единственным инструментом верификации меланомы в профильных клиниках. Высокая актуальность проблемы требует разработки в ближайшем будущем стратегии национальной программы скрининга меланомы и немеланомных раков кожи.

Цель. Оценка эффективности использования в клинической практике правила ABCD+E в ранней диагностике пигментных новообразований кожи профильными специалистами.

Материалы и методы. Исследование выполнено в группе пациентов (854) с пигментными новообразованиями кожи (невоидные и подозрительные на меланому) на базе амбулаторного отделения малоинвазивной хирургии в формате прямого, диагностического, обсервационного, ретроспективного, продольного, одноцентрового. Статистическая обработка результатов проведена с использованием пакета прикладных программ Statistica 10.0.

Результаты и обсуждение. Достоверной разницы суммарного показателя правила ABCD+E в исследуемых группах не было получено. Визуальная клиническая оценка локального статуса на первичном приеме имела субъективный характер. На сравнительном примере групп с морфологически подтвержденным диагнозом меланомы (85) и «меланом», которые оказались впоследствии немеланомами (67), правило продемонстрировало свою несостоятельность в половине случаев. Более того, у пациентов, пигмент которых изначально оценили как невоидный, а впоследствии оказалось, что это кожная меланома (17), ни в одном из случаев не было заподозрено заболевания по суммарной оценке критерия – он у них был в 2 раза достоверно более низким. Наиболее специфичными явились критерии А (асимметрия) и В (неровность краев) – 96% и 67% соответственно. Их чувствительность оценивалась как низкая (для А – экстремально низкая, 8%). Признаки С (цвет) и D (диаметр) характеризовались невысокими показателями как чувствительности, так и специфичности. Чувствительность Е (эволюция элемента) была самой высокой – 62%, но его специфичность в 33% не может рассматриваться как

достаточная. Корреляционной зависимости между толщиной меланомы и суммой критериев правила ABCD+E не получено.

Закключение. Даже максимальное количество баллов правила ABCD+E не может быть надежным свидетельством того, что врач имеет дело с меланомой, и, наоборот, низкий показатель суммы может соответствовать злокачественному новообразованию. Первичный дерматоонкологический прием требует обязательной оценки индивидуальных относительных рисков развития меланомы кожи и проведения дерматоскопического исследования пигмента.

Ключевые слова: кожная меланома, правило ABCD+E.

■ INTRODUCTION

The annual incidence of malignant melanoma in European countries ranges from 3–5 per 100,000 (northern and central parts) to 12–35 per 100,000 (Mediterranean countries), while in Australia and New Zealand this figure reaches 50 or more. The incidence of melanoma has shown a generally upward trend over the past four decades, with a relative stabilization of mortality, except for older men. [3]. Melanoma can develop at any age, with a peak incidence at age 65 [4]. The mortality/morbidity ratio in Eastern European countries is higher than in Western European countries, which indicates the need to improve prevention and early diagnosis in Eastern Europe [5].

Fig. 1–4 show the data of the Belarusian Cancer Register for the last 20 years. The absolute numbers of newly diagnosed cases of melanoma (whole population, men and women) have increased by more than 2.5 times during this period (Fig. 1). The peaks of registration of melanoma (rate per 100,000) are in the elderly age group (the higher the age, the higher the risks of developing melanoma); the highest rates are for people in the 8th and 9th decades of life (Fig. 2). Standardized indicators of the incidence

Fig. 1. Melanoma (2009–2019): the absolute numbers of newly diagnosed cases [8]

Fig. 2. Melanoma (2009–2019): age-specific incidence rates [8]

of melanoma in Belarus (Fig. 3) tend to increase both among urban and country populations, with a higher gender growth rate in men ($1.9/1.7=M/F$), with a lower detection rate ($5.7/6.8=M/F$ per 100,000 in 2015–2019). On the positive side, there is an increased incidence of melanoma detected in the early stages. For example, over the past 20 years the percentage of registration at stage I has increased by 14.6% (Fig. 4).

It is generally accepted that ultraviolet (UV) radiation is the leading carcinogen involved in the genesis of melanoma. The nature of UV and exposure time directly affect tumor development. Melanomas that develop on covered skin areas of the body (trunk and limbs usually have intermittent insolation regimes in continental climate zones) are more often associated

Fig. 3. Melanoma (2009–2019): standardized incidence rates [8]

Fig. 4. Melanoma (2009–2019): dynamics of the distribution of newly diagnosed cases by stages [8]

with sunburns received in childhood and adolescence. Melanomas on open areas of the body (head, neck) usually develop as a result of chronic UV exposure to the skin. At the same time, there are some subtypes of melanoma (acral melanoma, mucosal melanoma), the development of which is not associated with UV exposure.

UV radiation causes clear signs of DNA damage and increasing of mutations per megabase, Mb [6]. The best prevention is physical protection with clothing. One randomized study showed that prevention of UV exposure, including the regular use of sunblock creams, reduced the incidence of primary skin melanoma in the Australian population [7]. Primary prevention continues to play an important role in reducing the incidence of melanoma and non-melanoma skin cancers but is unlikely to change incidence rates in the foreseeable future, considering current trends. Further research will be required to optimize early detection and screening in order to reduce morbidity and mortality from melanoma and non-melanoma skin cancers.

■ THE AIM OF THE STUDY

Was to assess the effectiveness of using the ABCD+E rule in clinical practice for the early diagnosis of pigmented skin lesions.

■ MATERIALS AND METHODS

The study was carried out in 2018–2019 and based at the outpatient surgery department of the N.N. Aleksandrov Oncology Center of Belarus. The study is direct, diagnostic, observational, retrospective, longitudinal, and single-centered.

Table 1
Study inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
1. Patients with pigmented skin lesions who applied for a initial examination by an oncologist for the purpose of surgical treatment on the basis of outpatient surgery department	None
2. Age: 18 or older	

Table 1 shows the inclusion and exclusion criteria which the authors used when developing the study design. The primary selection of candidates was carried out by outpatient oncologists. All patients (854) with pigmented lesions were divided into two groups: 1st – 135 patients with suspicion of melanoma (Suspicio M), 2nd – 719 patients with nevi. The volume and nature of the surgical aid were determined by the staff of the oncology department (outpatient surgery department), depending on the clinical diagnosis and following the Belarusian Clinical Protocols "Algorithms for the diagnosis and treatment of malignant neoplasms" [1]. After receiving the results of the postoperative morphological examination, two new groups were formed with final diagnoses: 1st – 85 patients with a diagnosis of Melanoma (M), 2nd – 769 patients with other diagnoses, Nevi + Non-Nevi.

The study design is shown in Fig. 5.

Statistical processing of the results was carried out using the Statistica 10.0 software package. The obtained variation series were checked for compliance with the normal distribution by the Shapiro – Wilk method. A pairwise comparison of variation series was carried out using the Mann – Whitney test. Evaluation of correlations for the specified parameters in the

Fig. 5. Study design

study groups was carried out using the Spearman coefficient. P values less than 0.05 were considered statistically significant. Data are presented by values of the median and the mean $\pm$ error of the mean.

■ RESULTS

Young people (3–4–5 decades of life) were more likely to visit the oncologist for the initial appointment for pigmented lesions (70%), the average age of those who came for the appointment (854) – 42 years (Fig. 6).

There were no gender differences within group M, melanoma was equally common in both men and women (42/43 = M/F). The average age in group M (85) was 48 years, which is statistically significantly higher compared to the general group (Fig. 7). The course of the curves of the distribution frequency (%) of melanoma in different age categories of the general group (854) and group M (85) mostly imitated each other (orange and gray graphs, Fig. 7). However, when calculating the percentage (%) of the incidence of melanoma within age groups, there was a clear upward trend of the incidence of melanoma within older age categories, with peaks in the 8th decade of life (yellow graph of Fig. 7).

Lesions localized on the skin sites “head and neck” and “abdominal wall” were equally often observed in both men and women in group M (85) (Table 2). More than half of male melanoma cases were developed on the back and shoulder area (25); there are three sites in the “leaders” for women – the skin of the lower extremities (13), upper extremities (11), back, and shoulder area (11). The localization of pigmented lesions in the Suspicio M group (135) generally repeats the above-described tendency, which gives the authors the right to assert that initial admission doctors have sufficient alertness according to the “characteristic localization of cutaneous melanoma”.

Fig. 6. Distribution of patients by age (n=854)

Fig. 7. Group M (85): Distribution of patients by age

The interpretation of the skin pigmented lesions characteristics according to the criteria of the ABCD+E rule by doctors deserves special attention. There was no significant difference in the SC in the following groups: M (2.08 ± 0.29), Suspicio M – M (2.31 ± 0.32), Suspicio M (2.24 ± 0.22), Suspicio M – Non-Melanoma (2.171 ± 0.3). This means that the visual clinical assessment of the local status at the initial admission is very subjective, and in the comparative example of the M (85) and M – Non-Melanoma (67) groups, it demonstrates its inconsistency in half of the cases (Fig. 8). Furthermore, SC in the cases with pigmented lesions that initially were assessed as nevi and later turned out to be cutaneous melanoma (17) was 2 times significantly lower.

Table 2
Localization of pigmented lesions

Site	Suspicio M (n=135)		Suspicio M → Nevi + Non-Nevi (n=67)		M (n=85)		Nevi → M (n=17)	
	M (65) abs./%	F (70) abs./%	M (41) abs./%	F (36) abs./%	M (42) abs./%	F (43) abs./%	M (8) abs./%	F (9) abs./%
Head and neck	8/53	7/47	5/45	6/55	1/50	1/50	–	–
Back and shoulders	31/63	18/37	13/62	8/38	25/69	11/31	5/83	1/17
Rib cage ¹	4/40	6/60	3/50	3/50	2/33	4/67	–	1/100
Abdominal wall	6/50	6/50	4/57	3/43	3/50	3/50	1/100	–
Upper extremities	11/48	12/52	3/50	3/50	8/42	11/58	2/50	2/50
Lower extremities ²	5/19	21/81	13/87	13/87	3/19	13/81	–	5/100

Notes: ¹ anterolateral surface; ² pelvis and legs.

Assessment of criteria of the clinical rule ABCD+E individually showed the following results (Table 3). For group M (85), criterion A (asymmetry) was negative in 92% of the cases, with the probability of its detection 0.082 ± 0.0596 (0 – no sign, 1 – there is a sign). Criterion B (border irregularity) and C (heterogeneity of color) were also negative in more than half of the cases – in 60% and 59%, and the probability of their verification did not exceed 0.4 in both cases (Table 4). Criteria such as diameter (more than 5–7 mm) D and evolution (growth) of element E were positive at 56% and 62%, respectively. The majority of lesions were less than 5–7 mm in diameter, as the indicator of detecting a sign was 0.57 ± 0.11 . The only criterion that demonstrated its "viability" in more than half of the cases was E (0.62 ± 0.105). However, the E criterion is not objective during the initial examination, since it is based on the patient's feelings that cannot be checked.

Fig. 8. ABCD+E Rule: Effectiveness Evaluation

Table 3
Efficiency of the criteria of the rule ABCD+E in groups

M (n=85)				
Criterion	Criterion		Criterion	
	n	%	n	%
A	78	92	7	8
B	51	60	34	40
C	50	59	35	41
D	37	44	48	56
E	32	38	53	62
Nevus-M (n=17)				
Criterion	Criterion–		Criterion+	
	n	%	n	%
A	16	94	1	6
B	13	76	4	24
C	16	94	1	6
D	10	59	7	41
E	10	59	7	41
Suspicio M (n=135)				
Criterion	Criterion–		Criterion+	
	n	%	n	%
A	125	93	10	7
B	82	61	53	39
C	64	47	71	53
D	57	42	78	58
E	44	33	91	74
Suspicio M – Non-M (n=67)				
Criterion	Criterion–		Criterion+	
	n	%	n	%
A	64	95	3	5
B	45	67	22	33
C	30	44	37	56
D	30	44	37	56
E	22	33	45	67

There is no statistically significant difference in A, B, C, D, and E in patients with suspected melanoma (135), with confirmed melanoma (85), and melanoma, which was described as a nevus at the stage of clinical examination (17) (Table 4). In the Nevi group (67), the C feature (heterogeneity of color of the element) did not work – 0.0625 ± 0.12 ; if we take into account that even in group M it did not rise above 0.41 ± 0.1 , then it can be stated that its diagnostic value is generally low in any of the studied groups.

The most specific criteria in the clinical assessment of melanoma were criteria A (asymmetry) and B (border irregularity) – 96% and 67%, respectively (Table 5). However, their sensitivity can be assessed as low (for A – extremely low, 8%). Criteria C (color) and D (diameter) had low indicators of both sensitivity and specificity. Sensitivity of criteria E (evolving) was the highest – 62%, but its specificity of 33% cannot be considered sufficient.

Table 4
Average values for individual criteria of the rule ABCD+E*

Criterion	Suspicio M (n=135)	M (n=85)	Nevus-M (n=17)	Nevi (n=67)
A	0.067±0.043	0.082±0.0596	0.045±0.05	0.0625±0.12
B	0.388±0.084	0.4±0.1	0.33±0.12	0.235±0.22
C	0.53±0.086	0.41±0.11	0.56±0.12	0.0625±0.12
D	0.58±0.085	0.57±0.11	0.56±0.12	0.412±0.25
E	0.74±0.082	0.62±0.105	0.67±0.12	0.412±0.26

Note: * average value of the sample (where 0 – no feature, 1 – feature) + statistical error.

Table 5
ABCD+E rule: sensitivity/specificity (n=854)

A	8%	96%
B	40%	67%
C	41%	44%
D	57%	44%
E	62%	33%

It was difficult for the authors to assess the effectiveness of dermoscopy in the diagnostics of pigmented lesions due to the insufficient number of performed/fixed visualizations. The total number of such examinations is 21 (Table 6). In accordance with the developed 7-point scoring system (Argenziano) of pigmented lesions, doctors indicated the presence of melanoma with an atypical pigment network, a blue-white veil, irregular globules, and uneven pigmentation more often than others [9]. Atypical vascular pattern, regression structures, and irregular streaks were not described in any of the cases.

Table 7 presents the discrepancy between clinical and morphological diagnoses. Non-pigment neoplasms were diagnosed in 20.4% (147) of patients who were initially diagnosed with nevi: seborrheic keratosis, keratopapilloma, dermatofibroma, basal cell carcinoma, etc. Cutaneous melanoma was diagnosed in 17 patients (2.4%).

Table 6
Dermoscopic examination results (n=21) in patients with pigmented lesions according to a 7-point system (Argenziano)

Criteria	M (12)		Non-M (9)	
	Abs.	%	Abs.	%
Atypical pigment network	4	67	2	22
Blue-whitish veil	4	67	4	44
Atypical vascular pattern	–	–	–	–
Irregular streaks	–	–	–	–
Regression structures	–	–	1	11
Irregular blotches	2	33	4	44
Irregular dots/globules	3	50	2	22

In the group of patients with a clinical diagnosis of melanoma, every second patient did not receive its morphological confirmation. "Dysplastic nevus" was identified in 16% of the cases, basal cell skin cancer was found in another 4%.

The percentage of the discrepancy between clinical and final diagnoses in the clinically formed patient groups "Nevi" and "M" was 23% and 50%, respectively. The second indicator should influence the revision of approaches in the early diagnosis of cutaneous melanoma. The amount of unreasonably performed radical excisions using anesthetic aids is too high.

The verified morphological types of the identified melanomas (Table 8) were distributed in descending order as follows: superficial spreading (28%), nodular melanoma (26%), lentigo maligna (22%), melanoma in situ (19%), spindle-cell low pigment melanoma (1%).

Thin melanomas (in situ and Breslow 1 – up to 0.75 mm thick) were diagnosed in more than half of the cases (Table 9). The higher the detection

Table 7
Clinical and final diagnoses: discrepancies

Morphological diagnosis	Treated as "Nevus"		Treated as "Melanoma"	
	Abs.	%	Abs.	O,7
Actinic keratosis			1	3.7
Basal cell carcinoma	8	1.1	5	5.2
Intradermal nevus	212	29.5	7	3.7
Hemangioma	10	1.4	5	1.5
Histiocytoma	–	–	2	3.0
Blue nevus	17	2.4	4	1.5
Dermatofibroma	10	1.4	2	15.6
Dysplastic nevus	70	9.7	21	–
Keratopapilloma	24	3.3	–	1.5
Lentigo	–	–	2	–
Melanos	4	0.6	–	50.4
Melanoma	17	2.4	68	–
Reed's nevus	3	0.4	–	1.5
Papilloma	–	–	2	–
Papillomatous nevus	41	5.7	–	–
Polypus	1	0.1	–	5.2
Seborrheic keratosis	88	12.2	7	2.2
Compound nevus	84	11.7	3	–
Mixed nevus	119	16.6	–	0.7
Tricholemmoma	1	0.1	1	1.5
Fibrosis of the skin	–	–	2	–
Epidermal cyst	2	0.3	–	2.2
Junctional nevus	8	1.1	3	0.7
Total	719	100	135	100
Discrepancy with clinical diagnosis	23%		50%	

Table 8
Group M (n=85): morphological variants

Morphological variants	N/%
In situ	16/19%
Lentigo maligna	19/22%
Nodular melanoma	22/26%
Superficial spreading	24/28%
Spindle-cell low pigment	1/1%
Not indicated	3/4%

Table 9
Group M (n = 85): tumor thickness (mm, Breslow)

Thickness M, mm	n	Breslow	n
in situ	23	1 (dermal component thickness is less than 0.75 mm)	25
до 1	30	2 (0.75–1.5 mm)	17
1.1–1.5	10	3 (1.51–3.0 mm)	14
1.5–3	18	4 (3.0–4.0 mm)	3
3.1–4	2	5 (more than 4 mm)	3
More than 4	2	in situ	23

rate of thin melanomas, the better the survival rates in the near future. The correct and effective organization of early diagnosis of pigmented neoplasms and screening of risk groups for melanoma, in our opinion, will lead to the predicted increase in the incidence of melanoma, mainly due to thin variants and a decrease in mortality rates.

No correlation was found between the thickness of the melanoma and the sum of the ABCD+E rule criteria (Table 10). Even the maximum score of the ABCD+E rule cannot be reliable evidence that the doctor is dealing with melanoma, and vice versa, a low score does not guarantee the absence of a malignant neoplasm.

There are several classifications of malignant melanoma, which allow a differentiated approach to the diagnosis and treatment of the disease. Unfortunately, none of them is recognized as universal, therefore, over time, the systems are revised, updated and/or supplemented. The most significant

Table 10
M (n=85): Breslow and ABCD+E rule

Breslow	Σ ABCD+E						
	0	1	2	3	4	5	
1	4	5	4	6	2	2	r=0.003. There is no correlation between the thickness of melanoma and the sum of the ABCD+E rule criteria
2	0	6	4	3	2	1	
3	2	4	3	3	1	0	
4	0	0	1	2	0	0	
5	1	0	1	1	0	0	

Table 11
Classification of melanoma, category T (primary tumor) according to the AJCC version (8th and 7th revisions), adapted from [12]

T	8 th revision AJCC (2018)		7 th revision AJCC (2010)	
	Thickness	Ulceration	Thickness	Ulceration
TX	Not applicable	Not applicable	Not applicable	Not applicable
T0	Not applicable	Not applicable	Not applicable	Not applicable
Tis	Not applicable	Not applicable	Not applicable	Not applicable
T1	≤1.0 mm	Unknown or not specified	≤1.0 mm	Unknown or not specified
T1a	<0.8 mm	Without ulceration	≤1.0 mm	Without ulceration and <1 mitosis/mm ²
T1b	<0.8 mm	With ulceration	≤1.0 mm	With ulceration and ≥1 mitosis/mm ²
	0.8–1.0 mm	With/without ulceration	≤1.0 mm	
T2	>1.0–2.0 mm	Unknown or not specified	1.01–2.0 mm	Unknown or not specified
T2a	>1.0–2.0 mm	Without ulceration	1.01–2.0 mm	Without ulceration
T2b	>1.0–2.0 mm	With ulceration	1.01–2.0 mm	With ulceration
T3	>2.0–4.0 mm	Unknown or not specified	2.01–4.0 mm	Unknown or not specified
T3a	>2.0–4.0 mm	Without ulceration	2.01–4.0 mm	Without ulceration
T3b	>2.0–4.0 mm	With ulceration	2.01–4.0 mm	With ulceration
T4	>4.0 mm	Unknown or not specified	>4.0 mm	Unknown or not specified
T4a	>4.0 mm	Without ulceration	>4.0 mm	Without ulceration
T4b	>4.0 mm	With ulceration	>4.0 mm	With ulceration

Notes: TX – the thickness of the primary tumor cannot be determined (for example, when diagnosed as a result of curettage); T0 – absence of signs of a primary tumor (for example, unknown primary or completely regressed melanoma); Tis – melanoma in situ.

changes were made to the classification of melanoma staging in 2010. Recommended by the AJCC (American Joint Committee on Cancer), they began to include an accurate diagnosis and prognosis of the development of the disease [10]. In 2018 this classification was also revised (Table 11) [11].

For the analysis of the international melanoma database used in the 8th revision AJCC classification, patients with primary melanoma without signs of a regional or distant metastatic process were divided into 8 subcategories according to the T criterion (T1a–T4b). Patients with T1 melanoma were included in the data analysis if clinical or pathological findings were corresponding to T1N0. Patients with T2–T4 melanoma were included only if they had undergone lymphatic mapping and sentinel lymph node (SLN) biopsy and had no tumor-bearing SLN or satellites or in-transit metastases at the time of diagnosis or after completion of initial treatment (pN0 melanoma).

Primary tumor thickness (Breslow) and ulceration are major predictors of survival and T grade stratification in cutaneous melanoma [13–15]. The 8th revision of AJCC recommends measuring the thickness of the tumor with an accuracy of 0.1 mm, and not with an accuracy of 0.01 mm (as in previous versions). At the same time, category T, as before, is defined by the threshold values for melanoma thickness of 1.0, 2.0 and 4.0 mm. Thus, tumors ranging

in size from 0.95 to 1.04 mm should be rounded to 1.0 mm (i.e., T1b); previously (AJCC 7th revision) melanomas of 1.01–1.04 were defined as T2 (a – without ulceration; b – with ulceration) [10, 11]. The clinical outlook (if any) of this small subset of patients in a lower stage, according to the 8th revision of the classification, has not yet been formally studied [16].

In previous versions of the classification, the clinically significant threshold in patients with T1 melanoma was defined by 0.7–0.8 mm [14–16]. In the eighth edition of the AJCC, a multivariate analysis was used to analyze a cohort of patients with T1 melanoma to predict melanoma-specific survival (MSS); i.e., tumor thickness, ulceration, number of mitoses, as a dichotomous variable (<1 mitosis/mm² versus ≥1 mitosis/mm²) showed that the dichotomy of tumor thickness as <0.8 mm and 0.8–1.0 mm and ulceration were better predictors of MSS than the mitotic rate (as a dichotomous variable) [11, 17]. The definitions of T1a and T1b have been revised so that T1a melanoma includes those <0.8 mm without ulceration, while T1b melanoma includes those 0.8–1 mm with or without ulceration and those <0.8 mm with ulceration.

Even though the number of mitoses (mitosis per 1 mm²) remains the main prognostic factor for melanomas of all thickness categories, this feature is no longer used as a criterion for category T in the eighth version of the classification. However, it is strongly recommended to document this feature for all patients [11].

Table 12 provides information on category T of final diagnoses in group M.

The issue of unification of the primary dermato-oncological approach should be revised. The ABCD+E rule should be considered as an initial descriptive stage. The following categories should also be added to the examination checklist: genotype, personal and family history of skin lesions, the number of nevi and their nature (dysplastic nevi), phenotypic signs (hair color, freckles, eye color, tanning regime). The relative risks for each of the above criteria are described by Psaty E.L. et al. in 2010 (table 13) [1].

Dermoscopy should be considered as the final and obligatory link in the non-invasive pigment assessment. Several studies show that the widespread introduction of imaging techniques into dermato-oncological practice not only improves the quality of melanoma diagnostics but also makes it possible to reduce the number of unnecessary surgical interventions by 30% [18–20].

Table 12
Group M (85): distribution of final diagnoses by category T

pT	n	ulceration
pTis	21	–
pT1a	34	–
pT1b	2	0
pT2a	17	–
pT2b	3	3
pT3a	2	–
pT3b	3	3
pT4a	1	–
pT4b	2	2

Note: pTis – melanoma in situ.

Table 13
Melanoma: Estimated Risk Factors, adapted from [1]

Categories	Signs	Risk (as relative risk with 95% confidence interval, unless otherwise noted)
Genotype	Xeroderma pigmentosum	About one in five people develop melanoma
	CDKN2A Suspicious: In families with multiple melanomas or pancreatic cancer CDK4 (very rare) BRCA2 – families with breast and ovarian cancer MC1R Suspicious: Caucasians with red hair, freckles OCA2 Suspicious: Patients with family history of albinism	35–70 times 67% lifetime risk Significantly increased 2.58 (1.28–5.17) 2–3.5 Low risk, regardless of phenotype
	Melanoma	1–8% of melanoma patients will be re-diagnosed with melanoma
	Non-melanoma skin cancers (including actinic lesions)	4.28 (2.8–6.55)
Family history	Relatives	1.74 (1.41–2.14)
	Parent	2.4 (2.1–2.72) 3.2 (2.6–3.9) for men of North America 4.4 (3.5–5.2) for women of North America
	Siblings	2.98 (2.54–3.47) 3.2 (2.6–3.9) for men of North America 4.4 (3.5–5.2) for women of North America
	Two first-line relatives Parent with multiple primary melanomas	8.92 (4.25–15.31) 61.78 (5.82–227.19)
Atypical nevi	0	1.0
	1	1.45 (1.31–1.6)
	2	2.1 (1.71–2.54)
	3	3.03 (2.23–4.06)
	4	4.39 (2.91–6.47)
	5	6.36 (3.8–10.33)
Nevi	0–15	1.0
	16–40	1.47 (1.36–1.59)
	41–60	2.24 (1.9–2.64)
	61–80	3.26 (2.55–4.15)
	81–100	4.74 (3.44–6.53)
	101–120	6.89 (4.63–10.25)
Phenotypic traits		
Hair color	Red vs dark	3.64 (2.56–5.37)
	Blonde vs dark	1.96 (1.41–2.74)
	Light blond vs dark	1.62 (1.11–2.34)

Table 13 end

Freckles	Large vs small amount	2.1 (1.8–2.45)
Eye color	Light (green, light brown, blue) vs brown	~1.5
Tanning (mode)	Intermittent	2.35 (1.78–3.09)
	Chronic	0.98 (0.85–1.12)
	History of sunburns	2.02 (1.73–2.34)
	Solarium	Ever vs never. 1.15 (1.0–1.31)

Why does dermoscopy help to better diagnose cutaneous melanoma? First, the method is capable of detecting pathognomonic micro visual signs that become apparent much earlier than clinical changes. Second, a physician skilled in the dermoscopic assessment of pigmented lesions is more concerned with checking for trite-looking lesions, considering it a «level 1» screening tool. Thirdly, the doctors get the opportunity of detailed observation of the lesion using high-precision digital dermoscopy [21]. The unification of the initial clinical examination should be followed by the unification of the dermoscopic assessment of the pigment. An adequate and convenient scale/system of the algorithm for detecting pigmented lesions should be based on several comparative studies to assess their sensitivity and effectiveness. Carrying out morpho-dermoscopic correlations will facilitate the search for new visual non-invasive characteristics/signs of pigmented lesions.

■ CONCLUSION

The ABCD+E rule nowadays does not have sufficient sensitivity and specificity and can be considered only as a descriptive characteristic of the local status of pigmented lesions. The initial dermato-oncological examination should be carried out taking into account the assessment of the individual relative risks for developing skin melanoma. The checklist must contain information about genotype, personal and family history of skin neoplasms, the number, and quality of recorded nevi (dysplastic nevi), phenotypic traits (hair color, freckles, eye color, tanning regime). Dermoscopy should be considered as a mandatory option for non-invasive pigmented lesions assessment, capable of providing early verification of melanoma at the preclinical stage.

The unification of the algorithm for non-invasive diagnostics will contribute to the development of an authentic screening program for melanoma and non-melanoma skin cancers in Belarus.

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