

# Characteristic Clinical Features of Melanoma in Patients With Excised Skin Lesions

OLIWIA MAJEWSKA<sup>1</sup>, PIOTR KULIG<sup>2</sup>, PAWEŁ BRZEWSKI<sup>2,3,4</sup>, JAN KULIG<sup>3</sup> and ANNA MARKIEWICZ<sup>5,6</sup>

<sup>1</sup>Department of Pediatrics and Pediatric Endocrinology, Saint John Paul II Upper Silesian Child Health Centre, Katowice, Poland;

<sup>2</sup>Andrzej Frycz Modrzewski University, Faculty of Medicine, Krakow, Poland;

<sup>3</sup>Jagiellonian University Medical College, Krakow, Poland;

<sup>4</sup>Department of Dermatology and Venereology of the Stefan Zeromski Municipal Hospital in Krakow, Krakow, Poland;

<sup>5</sup>Department of Ophthalmology and Ocular Oncology, Faculty of Medicine, Jagiellonian University Medical College, Krakow, Poland;

<sup>6</sup>Department of Ophthalmology and Ocular Oncology, University Hospital, Krakow, Poland

## Abstract

**Background/Aim:** The aim of this study was to assess the risk of melanoma in patients with excised skin lesions (ESLs) considering their clinical features.

**Patients and Methods:** A total of 126 cases of ESLs were collected between December 2021 and April 2025. The clinical features of 109 benign skin lesions (BSLs), 10 non-nodular melanomas (NNMs), and seven nodular melanomas (NMs) were analyzed according to the ABCDE criteria, the ABCDE-EFG method, and the 7-point checklist (7-PCL) scale.

**Results:** In univariate analysis, compared to BSLs, NNMs presented more common irregular borders ( $p=0.029$ ), color variegation ( $p=0.015$ ), diameter greater than 6 mm ( $p=0.031$ ), evolution in size, shape or color within six months ( $p=0.005$ ), rapid growth within six weeks/atypical skin lesion *de novo* ( $p=0.019$ ). NMs, compared to BSLs, were more likely to show evolution in size, shape or color within six months ( $p=0.003$ ), elevation ( $p=0.003$ ), firm to touch ( $p<0.001$ ), and rapid growth within six weeks/atypical skin lesion *de novo* ( $p<0.001$ ). In the Firth's penalized logistic regression, rapid growth within six weeks/atypical skin lesion *de novo* was significantly more frequent in NNMs compared to BSLs [odds ratio (OR)=31.36, 95% confidence interval (CI)=1.42-11350.06,  $p=0.028$ ], and in both NNMs and NMs compared to BSLs (OR=27.32, 95% CI=3.64-540.48,  $p<0.001$ ). Color variegation (OR=25.06, 95% CI=2.80-681.62,  $p=0.002$ ) and evolution in size, shape or color within six months (OR=6.02, 95% CI=1.21-55.19,  $p=0.027$ ) were also found to be significant in differentiating for both NNMs and NMs compared to BSLs. However, in multivariate analysis, for NMs alone, no clinical features were significantly more frequent compared to BSLs.

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Oliwia Majewska, Witkowice Nowe 23, 31-235 Krakow, Poland. Tel: +48 660351374 or 883220224, e-mail: oliwia.m09@op.pl

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**Conclusion:** The most important clinical features increasing the risk of melanoma were rapid growth within six weeks/atypical skin lesion *de novo*, color variegation and evolution in size, shape or color within six months, but not for NMs cases alone in the Firth's penalized logistic regression.

**Keywords:** Melanoma, nodular melanoma, clinical features, dermatosurgery.

## Introduction

According to global cancer data, an estimated 331,722 new cases and 58,677 deaths due to malignant melanoma of the skin (MM) were reported in 2022 (1). In the United States, MM was diagnosed with a 104,960 new cases and 8,430 deaths in 2025 (2, 3). In Europe, MM accounts for more than 80% of malignant skin neoplasm deaths (4, 5). In Poland, the number of cases and deaths due to MM in 2021 was 4,094 (1,876 men and 2,218 women) and 1,277 (661 men and 616 women), respectively (6).

MM develops primarily *de novo* or from dysplastic nevus; however, any suspicious skin lesion seen in patients should be evaluated by a dermatologist for potential surgical removal. Clinical evaluation of skin lesions often includes the ABCDE criteria, such as asymmetry (A), irregular borders (B), color variegation (C), diameter greater than 6 mm (D), and evolution in size, shape, or color (E), which aid in the diagnosis of MM. For better detection of nodular MM, the extended ABCDE-EFG method incorporates the following: elevation (E), firm to touch (F), and rapid growth within several weeks (G) (7-10). The Glasgow 7-point checklist (7-PCL) is a clinical scale also used in the recognition of MM. It includes additional signs such as inflammation, oozing or crusting, and sensory changes like itching (11).

From the incorporation of the ABCDE criteria and the 7-PCL scale in clinical diagnosis to modern advancements of computer algorithms and genetic markers, early detection of MM has improved significantly. To more accurately evaluate skin lesions, artificial intelligence-based techniques with computer-aided diagnosis are used in combination with non-invasive diagnostic imaging methods, including reflectance confocal microscopy,

optical coherence tomography, electrical impedance spectroscopy, and especially video/dermatoscopy. However, a "good clinical eye" is still the basis for diagnosis in selecting MM among multiple skin lesions. A skin self-examination by patients and skin examination by clinicians should include all relevant clinical features for early recognition of MM, because early detection is crucial for prognosis (12-14).

In the early stages of MM - stage 0 (MM *in situ* - tumor cells in the epidermis) or stages I-II, according to the eighth edition TNM classification, surgical resection of the primary lesion without lymphadenectomy, immunotherapy, radiotherapy, or chemotherapy may be the only method of treatment. Five-year survival rates for stage I-II MM are 99.4% in U.S.A, declining to 68.0% in stage III and 29.8% in stage IV. In Poland, survival rates range from 60-90% in stages I-II, 20-70% in stage III, and only 5-10% in stage IV (2, 6, 15-18).

In this study, we evaluated multiple clinical symptoms including ABCDE-EFG criteria and the 7-PCL scale as potential prognostic factors influencing the detection of MM. We assessed whether any of the clinical features were significantly more frequent in MM than in benign skin lesions (BSLs).

## Patients and Methods

**Patient cohort.** From December 2021 to April 2025, a total of 138 cases of skin lesions in 122 patients with skin lesions were surgically excised at PZU Zdrowie Medical Center, Krakow, Poland. Skin lesions were referred for excision due to suspected malignancies, a history of irritation, crusting, recurrent bleeding, or at the patient's request for cosmetic reasons. To obtain a more

homogeneous group of patients for comparing BSLs with MM of the skin, cases of basal cell carcinoma, squamous cell carcinoma and other skin cancers were not included in this study. Before surgery, clinical evaluation including a patient interview, visual and palpable examination was performed, and ESLs were documented with photographs. However, in-person, not image-based, evaluation all cases of ESLs was performed to collect clinical features. A patient database was created that included clinical features and histopathological analysis of all ESLs. Based on histopathological verification, patients were separated into three groups as follows: Group 1 - BSLs, Group 2 - non-nodular melanomas (NNMs), and Group 3 - nodular melanomas (NMs). The clinical features of individual ESLs were analyzed according to routine guidelines, including the ABCDE-EFG criteria, recommended by the American Academy of Dermatology Association, and the weighted 7-PCL rule, recommended by the UK's National Institute for Health and Care Excellence (NICE) (4, 7-11). All ESLs were measured based on the maximum length (criterion D of the ABCDE-EFG features) in histopathological sample. Evolution in size, shape or color was understood as changes in these clinical features within a period of six months (synonym for criterion E of ABCDE-EFG features). A clinical feature defined as rapid growth within six weeks/atypical skin lesion *de novo* was considered as growing fastly within six weeks (synonym for criterion G of ABCDE-EFG features) or a new skin lesion with ABCDE-EFG features.

*Surgical and treatment approach.* Biopsies were performed using spindle-shaped surgical excisions under local infiltration anesthesia with 1-2% lignocainum hydrochloricum WZF solutions. The surgical specimen contained epidermis, dermis, and some adipose tissue, with surgical margins ranging from 1 to 10 mm. The wound was primarily sutured with single or continuous non-absorbable sutures Ethilon, Daflon, Amfilin M 3/0 or 4/0, which were removed during a routine follow-up visit after 12-14 days. All ESLs were primary skin lesions. In 16 of 17 patients diagnosed with MM, initially curative

resection was performed, with no cancer cells detected microscopically at the lesion site or surgical margins. However, patients with detected MM usually underwent secondary extended surgical excision, with surgical margins of 1-20 mm using the same surgical principles. In some cases of MM, sentinel lymph node biopsy was used in the surgical approach and/or immunotherapy, radiotherapy, or chemotherapy as the additional treatment.

*Statistical analysis.* Clinical characteristics, including asymmetry, irregular borders, color variegation, diameter greater than 6 mm, evolution in size, shape, or color within six months, elevation, firm to touch, rapid growth within six weeks/atypical skin lesion *de novo*, inflammation, oozing or crusting, sensory changes (*e.g.*, itching), white spot in lesion, and other symptoms in each case of ESLs, including melanomas, in the patient database were coded in binary form. The R computing environment, version 4.0.3 (2020-10-10) (Vienna, Austria) was used for the calculations. The R project website: <https://www.r-project.org/>. CRAN package repository: <https://cran.r-project.org/>. Fisher's exact test and penalized Firth's logistic regression were used to determine the association between clinical features of ESLs and the risk of melanoma. A *p*-value of  $\leq 0.05$  was considered statistically significant. All statistical analyses were performed using R software (version 4.0.3; R Foundation for Statistical Computing, Vienna, Austria; <https://www.r-project.org/>).

## Results

*Database characteristics.* The database contained 138 cases of ESLs from 122 patients. After excluding ten cases of basal cell carcinoma and two cases of squamous cell carcinoma, a total of 126 ESLs were included in the final analysis. The 126 ESLs included: 109 BSLs, 10 NNMs, and seven NMs. The highest median age was in Group 3 (NMs) – 54 years (range=40-67 years). BSLs (Group 1), and melanomas (Groups 2, and 3) were more commonly found in female patients: 57.8%, 60%, 57.1%, respectively.

In 109 BSLs (Group 1), the most common were: compound nevus, 46 (42.2%); marginal nevus, 17 (15.6%); intradermal nevus, 14 (12.8%); seborrheic keratosis, 8 (7.3%); and dermatofibroma, seven (6.4%). In 17 melanomas cases, there were eight cases of superficial spreading melanoma, seven cases of NM, one case of lentigo malignant melanoma, and one case of acral lentiginous melanoma. The highest median diameter was in NNMs (Group 2) – 7 mm (range=5-8 mm) compared to BSLs – 5 mm (range=1-12 mm), and NMs – 5 mm (range=2-8 mm). BSLs were most commonly located on the back (20.2%), abdomen (14.7%), and arm (11%). In 10 cases of NNM, the locations were as follows: the abdomen, two cases; foot, two cases (including one acral lentiginous melanoma); back, one case; shin one case; scalp, one case, neck, one case; thigh, one case; face one case (one case of lentigo maligna melanoma). Locations of NMs were back, three cases; shin, two cases; thigh, one case; face, one case. All cases of NMs, nine cases of 10 NNMs and 103 cases of 109 BSLs underwent complete primary excision (Table I).

*Clinical recognition of malignant melanoma of the skin - univariate analysis.* In BSLs, the most common clinical features were asymmetry (71.6%), irregular borders (65.1%), and color variegation (62.4%). The incidence of asymmetry, irregular borders, color variegation, diameter greater than 6 mm, evolution in size, shape, or color within six months in NNMs cases was 100%, 100%, 100%, 60%, 90%, respectively. The most common clinical features in NMs were elevation, 100%; firm to touch, 100%; evolution in size, shape, or color within six months, 100%; asymmetry, 85.7%; color variegation, 85.7%; and rapid growth within six weeks/atypical skin lesion *de novo*, 71.4%. In Fisher's exact test, in comparison with the BSLs, NNMs had more common irregular borders ( $p=0.029$ ), color variegation ( $p=0.015$ ), diameter greater than 6 mm ( $p=0.031$ ), evolution in size, shape or color within six months ( $p=0.005$ ), rapid growth within six weeks/atypical skin lesion *de novo* ( $p=0.019$ ). In univariate analysis, NMs also demonstrated statistically significant

differences compared to BSLs, with more frequent presence of evolution in size, shape, or color within six months ( $p=0.003$ ), elevation ( $p=0.003$ ), firm to touch ( $p<0.001$ ), rapid growth within six weeks/atypical skin lesion *de novo* ( $p<0.001$ ). Differences in the prevalence of clinical features between melanoma subgroups (Group 2 vs. Group 3) and between melanoma groups combined (Groups 2 and 3) versus BSLs (Group 1) are presented in Table II. In the comparison of melanoma groups (Group 2 vs. Group 3), statistically more frequent were irregular borders in NNMs ( $p=0.015$ ), elevation ( $p<0.001$ ), and firm to touch ( $p<0.001$ ) in NMs (Table II).

*Clinical recognition of malignant melanoma of the skin - multivariate analysis.* The Firth's penalized logistic regression showed that only rapid growth within six weeks/atypical skin lesion *de novo* was statistically more common in NNMs than in BSLs (OR=31.36, 95% CI=1.42-11350.06,  $p=0.028$ ) (Table III).

In multivariate analysis, NMs cases did not show statistically significant differences in the analyzed clinical features compared to BSL (Table IV).

Multivariate analysis of clinical feature occurrence in all melanomas (both NNMs and NMs) compared with BSLs is presented in Table V. The Firth's penalized logistic regression revealed that color variegation (OR=25.06, 95% CI=2.80-681.62,  $p=0.002$ ), evolution in size, shape or color within six months (OR=6.02, 95% CI=1.21-55.19,  $p=0.027$ ), and rapid growth within six weeks/atypical skin lesion *de novo* (OR=27.32, 95% CI=3.64-540.48,  $p<0.001$ ) were independent prognostic factors of melanoma (Table V).

## Discussion

*ABCDE criteria.* First described by Robert Friedman in 1985, the ABCD criteria were expanded in 1998 to include the feature (E), evolution in size, shape, or color, forming the well-known ABCDE rule used in the clinical recognition of MM (7-10, 19). However, the ABCDE criteria are also observed in BSLs, and some of them are absent in

Table I. Patient groups with excised skin lesions – characteristics.

Parameters	Excised skin lesions (n=126)		
	Group 1 – Benign skin lesions (n=109)	Group 2 – Non-nodular melanomas (n=10)	Group 3 – Nodular melanomas (n=7)
Age (years), median (range)	41 (19-76)	44 (32-60)	54 (40-67)
Sex, n (%)			
Male	46 (42.2)	4 (40)	3 (42.9)
Female	63 (57.8)	6 (60)	4 (57.1)
Histopatological recognition, n (%)			
Compound nevus	46 (42.2)		
Intradermal nevus	14 (12.8)		
Marginal nevus	17 (15.6)		
Dermatofibroma	7 (6.4)		
Seborrheic keratosis	8 (7.3)		
Fibrous histiocytoma	2 (1.8)		
Capillary hemangioma	2 (1.8)		
Cavernous hemangioma	1 (0.9)		
Arteriovenous hemangioma	1 (0.9)		
Keratoacanthoma	1 (0.9)		
Blue nevus	2 (1.8)		
Skin tag	2 (1.8)		
Angiogramuloma	3 (2.7)		
Lichen planus	1 (0.9)		
Granuloma annulare	1 (0.9)		
Fibrolipoma	1 (0.9)		
Superficial spreading melanoma		8 (80)	
Lentigo maligna melanoma		1 (10)	
Acral lentiginous melanoma		1 (10)	
Nodular melanoma			7 (100)
Diameter (mm), median (range)	5 (1-12)	7 (5-8)	5 (2-8)
Location, n (%)			
Hand	1 (0.9)		
Finger	2 (1.8)		
Forearm	7 (6.4)		
Arm	12 (11)		
Foot	6 (5.5)	2 (20)	
Toe	2 (1.8)		
Shin	3 (2.7)	1 (10)	2 (28.6)
Thigh	6 (5.5)	1 (10)	1 (14.3)
Buttock	1 (0.9)		
Groin	3 (2.7)		
Back	22 (20.2)	1 (10)	3 (42.8)
Abdomen	16 (14.7)	2 (20)	
Chest	5 (4.6)		
Breast	2 (1.8)		
Axilla	3 (2.7)		
Neck	3 (2.7)	1 (10)	
Scalp	6 (5.5)	1 (10)	
Ear	1 (0.9)		
Face	8 (7.3)	1 (10)	1 (14.3)
Primary radical surgical excision, n (%)			
Yes	103 (94.5)	9 (90)	7 (100)
No	6 (5.5)	1 (10)	

Table II. *Clinical features of excised skin lesions - univariate analysis.*

Clinical features	Excised skin lesions			Group1 vs. Group 2	Group1 vs. Group 3	Group2 vs. Group 3	Group1 vs. Groups 2+3
	Group 1 – Benign skin lesions, n (%)	Group 2 – Non- nodular melanomas, n (%)	Group 3 – Nodular melanomas, n (%)				
							<i>p</i> -Value*
Asymmetry	78 (71.6)	10 (100)	6 (85.7)	0.062	0.672	0.412	0.069
Irregular borders	71 (65.1)	10 (100)	3 (42.9)	0.029	0.252	0.015	0.420
Color variegation	68 (62.4)	10 (100)	6 (85.7)	0.015	0.419	0.412	0.011
Diameter greater than 6 mm	28 (25.7)	6 (60)	2 (28.6)	0.031	1.000	0.335	0.086
Evolution in size, shape or color within 6 months	45 (41.3)	9 (90)	7 (100)	0.005	0.003	1.000	<0.001
Elevation	46 (42.2)	1 (10)	7 (100)	0.086	0.003	<0.001	0.794
Firm to touch	28 (25.7)	1 (10)	7 (100)	0.448	<0.001	<0.001	0.086
Rapid growth within 6 weeks/ Atypical skin lesion <i>de novo</i>	5 (4.6)	3 (30)	5 (71.4)	0.019	<0.001	0.153	<0.001
Inflammation	19 (17.4)	2 (20)	2 (28.6)	1.000	0.609	1.000	0.513
Oozing or crusting	24 (22)	2 (20)	2 (28.6)	1.000	0.653	1.000	0.1000
Sensory changes ( <i>e.g.</i> , itching)	30 (27.5)	3 (30)	3 (42.9)	1.000	0.404	0.644	0.567
White spot in lesion	6 (5.5)	1 (10)	0 (0)	0.468	1.000	1.000	1.000
Other symptoms	17 (15.6)	0 (0)	2 (28.5)	0.354	0.322	0.154	1.000

\*Fisher's exact test.

Table III. *The Firth's penalized logistic regression for non-nodular melanomas.*

Clinical features	OR	95% CI	<i>p</i> -Value
Asymmetry	1.56	0.15-157.06	0.736
Irregular borders	1.88	0.21-169.04	0.609
Color variegation	10.99	0.76-1,762.81	0.085
Diameter greater than 6 mm	2.81	0.55-17.01	0.212
Evolution in size, shape or color within 6 months	4.07	0.67-42.61	0.134
Elevation	1.12	0.09-8.78	0.916
Firm to touch	0.15	0.00-5.46	0.279
Rapid growth within 6 weeks/atypical skin lesion <i>de novo</i>	31.36	1.42-11,350.06	0.028
Inflammation	0.21	0.01-2.15	0.194
Oozing or crusting	1.89	0.19-18.52	0.559
Sensory changes ( <i>e.g.</i> , itching)	2.49	0.36-19.23	0.325
White spot in lesion	3.79	0.20-66.01	0.343
Other symptoms	0.22	0.00-2.50	0.270

OR: Odds ratio; CI: confidence interval.

MM cases. Numerous reports have questioned the stand-alone diagnostic utility of the ABCDE rule, stating that it cannot reliably distinguish MM from BSLs and therefore should not be used as the sole method for diagnosing (4, 20-24). In a review of the global literature, we identified only a few reports demonstrating quite well results in

detecting MM using the ABCDE criteria as a diagnostic method (9, 19, 25-28). First, we present a pioneering study from the United States, where the ABCDE criteria were developed and where the rule is widely practiced. In the study by Thomas *et al.*, there were 680 BSLs (typical nevi or dysplastic nevi) and 460 MM cases. The sensitivity

Table IV. The Firth's penalized logistic regression for nodular melanomas.

Clinical features	OR	95%CI	p-Value
Asymmetry	1.69	0.03-210.87	0.777
Irregular borders	0.28	0.00-4.44	0.402
Color variegation	2.75	0.10-312.04	0.513
Diameter greater than 6 mm	0.87	0.08-7.16	0.892
Evolution in size, shape or color within 6 months	10.16	0.53-665,483.14	0.131
Elevation	0.85	0.01-77.48	0.925
Firm to touch	15.33	0.50-6,724.17	0.133
Rapid growth within 6 weeks/atypical skin lesion <i>de novo</i>	5.66	0.56-998.66	0.146
Inflammation	0.65	0.00-14.12	0.768
Oozing or crusting	0.37	0.00-6.40	0.479
Sensory changes ( <i>e.g.</i> , itching)	0.63	0.01-14.31	0.725
White spot in lesion	4.19	0.00-1,068.24	0.591
Other symptoms	8.29	0.28-6,521.24	0.216

OR: Odds ratio; CI: confidence interval.

Table V. The Firth's penalized logistic regression for both non-nodular and nodular melanomas.

Clinical features	OR	95% CI	p-Value
Asymmetry	1.56	0.21-25.15	0.690
Irregular borders	1.64	0.29-12.46	0.582
Color variegation	25.06	2.80-681.62	0.002
Diameter greater than 6 mm	1.90	0.46-8.18	0.373
Evolution in size, shape or color within 6 months	6.02	1.21-55.19	0.027
Elevation	1.49	0.19-10.44	0.688
Firm to touch	0.80	0.11-8.38	0.835
Rapid growth within 6 weeks/atypical skin lesion <i>de novo</i>	27.32	3.64-540.48	<0.001
Inflammation	0.19	0.01-1.26	0.090
Oozing or crusting	1.28	0.24-6.52	0.765
Sensory changes ( <i>e.g.</i> , itching)	2.52	0.55-14.31	0.237
White spot in lesion	4.62	0.33-50.09	0.226
Other symptoms	0.52	0.06-2.88	0.472

OR: Odds ratio; CI: confidence interval.

of the individual criteria for the recognition of MM was 57%, 57%, 65%, 90%, and 84% for ABCDE, respectively. The specificity of every criterion of the ABCDE rule for differentiation of MM was 72% for criterion A, 71% for criterion B, 59% for criterion C, 63% for criterion D, and 90% for criterion E. The incidence of the ABCDE criteria was significantly different between typical nevi (1.24±1.26) and MM (3.53±1.53) ( $p<0.001$ ). However, there also were a two conclusions questioning the effectiveness of the ABCDE rule. The first, no significant difference was found between melanomas and atypical nevi. The second, the sensitivity for diagnosis of MM was

89.3% if two criteria of ABCDE rule occurred, compared to 65.5% if three criteria of ABCDE rule occurred (19).

Abbasi *et al.* reported that the diameter criterion (D) in the ABCDE rule has an important meaning in MM detection, with a significant increase in the proportion of MM among ESLs greater than 6 mm. From 1,657 excised ESLs in their study, 853 (51.5%) were 6 mm in diameter or less, and 804 (48.5%) were greater than 6 mm in diameter. In 138 MM diagnoses among 1,657 cases, 84 were *in situ* MM and 54 invasive MM. The *in situ* MMs were diagnosed in 22 of 853 cases (2.6%) that were 6 mm or less in diameter and in 62 of 804 cases (7.7%) that were

greater than 6 mm in diameter. The invasive MM were diagnosed in 13 of 853 cases (1.5%) that were 6 mm or less in diameter and in 41 of 804 cases (5.1%) that were greater than 6 mm in diameter. Based on these findings, the authors suggested that preserving the original greater than 6 mm D criterion according to the ABCDE rule is a relevant prognostic factor in clinical detection of MM (27). Abbasi *et al.* also emphasized the importance of criterion E of the ABCDE rule. They concluded that while not every lesion that evolves in size, shape, or color is MM, any skin lesion showing change over time warrants close monitoring or possible surgical excision (9, 27). However, in the study by Jitian Mihulecea *et al.*, where 47 skin lesions were excised between 2017 and 2019 including seven typical nevi (14.9%), 33 dysplastic nevi (70.2%), and seven MMs (14.9%), evolution in size, shape, or color (criterion E) appeared in all patients with dysplastic nevus. Notably, all the ABCDE criteria were present in all seven cases of MM (28).

*ABCDE-EFG method.* NMs are biologically distinct and rare (approximately 10-30% of cases), and yet are the more aggressive type that grows and spreads faster than other MM types. They are associated with higher mortality, and potential delays in diagnosis owing to atypical clinical presentation of NMs that do not fit the general criteria for the early identification of MM, including the ABCDE criteria. The ABCDE-EFG method enriches the ABCDE criteria with a broader clinical evaluation of skin lesions to recognize NMs. Therefore, clinical features, such as elevation (E), firm to touch (F), and rapid growth within several weeks (G), were added to the ABCDE criteria because are more characteristic to this type of MM (10, 29-31).

The aim of the study by Coroiu *et al.* was to identify early clinical symptoms of NMs. In 66 patients diagnosed with MM, there were 34 NMs, including 16 cases with diameters of 2 mm or less. They found some unique signs for NMs with diameters of 2 mm or less: growth of a small white dot, visible blood spots underneath the skin, blue darkening-fast skin lesions, round skin lesions, which quickly become asymmetric, skin lesions developing

elevation fast, skin lesions becoming puffy and crusty over time, and an overall physical sensation that the skin lesion is different from other skin lesions. Furthermore, changes in skin lesion shape, darkening of color, and rapid vertical growth reportedly occurred mostly over a two-week period in NMs with a diameter of 2 mm or less. According to Coroiu *et al.*, clinical symptoms for the early identification of MM, such as the ABCDE criteria including the ABCDE-EFG method with additional features as elevation (E), firm to touch (F), and rapid growth over several weeks (G) or clinical features of the 7-point checklist (7-PCL) scale, capture some of the identified features of NMs with a diameter of 2 mm or less. However, clinical features such as a white coloration and very small diameter are not present in any of the ABCDE-EFG criteria or the 7-PCL scale (10).

*The 7-PCL scale.* Congdon *et al.* assessed an alternative scale of clinical detection of MM, (the 7-PCL) scale, which is used mainly in the United Kingdom. The newest weighted 7-PCL includes the following features (which are scored): asymmetry or irregular borders (2 points), color variegation (2 points), diameter of 7 mm or more (1 point), change in size (2 points), inflammation (1 point), oozing or crusting (1 point), and sensory changes including itching (1point). The first four features of the 7-PCL scale correspond with the ABCDE criteria, but the last three features are unique in the clinical recognition of MM. According to the 7-PCL scale, all skin lesions scoring  $\geq 3$  suggest a possibility of MM and should be considered for surgical excision. In their report, Congdon *et al.* performed a systematic review of the incidence of the features of the 7-PCL in 1184 cases of MM. This systemic review found change in size as the most commonly reported feature, with the range 33% to 77.9%. Color variegation and asymmetry or irregular borders were the second and third most frequent features, with the range 20% to 86.1% and 0% to 80%, respectively. A diameter  $\geq 7$  mm was the fourth most commonly occurring feature, with the range 33.3% to 76%. Itching, oozing or crusting, and inflammation, features of the 7PCL scale, were less

common and observed with the range 10% to 25%, 0% to 35%, and 0 to 25%, respectively (11).

Walter *et al.* evaluated 36 histologically confirmed cases of MM using the 7-PCL scale. The highest sensitivity for MM detection was observed for color variegation (86.1%), diameter  $\geq 7$  mm (75.0%), change in size (72.2%), and irregular borders (69.4%). The highest specificity was reported for inflammation (91.0%), oozing or crusting (90.2%), itch or altered sensation (72.3%), and irregular borders (66.6%). A weighted 7-PCL score of  $\geq 3$  was strongly associated with MM detection ( $p < 0.001$ ). At this threshold, the weighted 7-PCL achieved a sensitivity of 91.7% and a specificity of 33.1% for MM. One limitation of the 7-PCL analysis was that, although the single feature of asymmetry/irregular borders was less sensitive than a weighted 7-PCL score of  $\geq 3$  (69.4% vs. 91.7%), it was more specific (66.6% vs. 33.1%) for MM detection (32).

*Comparison ABCDE criteria with the 7-PCL scale.* McGovern *et al.* compared the diagnostic performance of the ABCD criteria and the 7-PCL scale in detecting MM. Logistic regression analysis showed the 7-PCL scale (205 skin lesions) identified the two significant variables as follows: asymmetry or irregular borders [odds ratio (OR)=10.9,  $p=0.001$ ], and diameter greater than 1 cm (OR=6.7,  $p=0.005$ ) for MM recognition. However, the ABCD rule (192 skin lesions) identified three significant variables as follows: irregular borders (OR=9.3,  $p=0.001$ ), color variegation (OR=3.7,  $p=0.05$ ), and a diameter greater than 6 mm (OR=5.5,  $p=0.008$ ) for differentiating MM (25).

A meta-analysis by Dinnes *et al.*, including 49 studies across 51 cohorts, evaluated clinical algorithms for MM detection. The recognition of 1,076 cases of MM among 19,330 skin lesions without a clinical algorithm ( $n=21$  datasets) represented the highest diagnostic odds ratio (DOR) of 46.2 (95% CI=21.9-97.5), with a pooled sensitivity of 78% (95% CI=68%-85%) and a pooled specificity of 93% (95% CI= 88% to 96%). The ABCDE criteria applied in the diagnosis of 654 cases of MM among 5,501 skin lesions ( $n=6$  datasets) had the DOR of 36.6 (95% CI=7.94-168), with the pooled sensitivity

slightly higher 83% (95% CI=75%-88%), but a slightly lower pooled specificity of 88% (95% CI=64%-97%). At the standard threshold of 3 or above for the weighted 7-PCL algorithm to detect 18 cases of MM among 773 skin lesions ( $n=1$  dataset) the highest sensitivity of 94% (95% CI=73%-100%), with a specificity of 80% (95% CI=77%-83%) was observed. Conclusions from the meta-analysis suggest that MM could be missed if only a clinical algorithm (*i.e.*, the ABCDE criteria or the 7-PCL scale). However clinical evaluation is a fundamental component of recognizing skin lesions and a further prospective evaluation of the potential added value of using established clinical algorithms according to the prior diagnostic difficulties may be warranted (24).

*Study limitations.* First, it was a single-center study. Second, we had 126 ESLs, so the number of cases is relatively small. Third, we only had 17 cases of MM of the skin limiting robust statistical analysis. Fourth, ESLs were qualified for surgical excision due to suspected malignancy. However, the patient database also contained skin lesions removed for other indications, *i.e.*, history of irritation, crusting and recurrent bleeding or at the patient's request for cosmetic reasons. Therefore, to obtain a more homogeneous group of patients to analyze clinical features of melanoma, ESLs could be limited to only melanomas suspicious skin lesions. Fifth, in detecting MMs, we did not compare clinical features with dermatoscopic results, which broadens and improves the diagnosis in daily, routine practice.

## Conclusion

Contrary to most reports, clinical evaluation, based on features included in the ABCDE criteria, the ABCDE-EFG method, and the 7-PCL scale, was found to be useful for detecting cutaneous MM, but not in NMs cases alone. In the Firth's penalized logistic regression, rapid growth within six weeks/atypical skin lesion *de novo*, was only clinical feature statistically significant for NNMs cases. In multivariate analysis, compared to BSLs cases, rapid

growth within six weeks/atypical skin lesion de novo, color variegation and evolution in size, shape or color within six months were independent prognostic factors for both NNMs and NMs cases. However, in the Firth's penalized logistic regression were not presented significant clinical features in differentiating NMs cases from BSLs cases.

### Conflicts of Interest

The Authors declare that they have no conflicts of interest in relation to this study.

### Authors' Contributions

Oliwia Majewska: concept of the study, statistical analysis, database results analysis, reviewed articles for the discussion, writing the manuscript. Piotr Kulig: concept of the study, collection and analysis of patients database, statistical analysis, database results analysis, reviewed articles for the discussion. Paweł Brzewski: concept of the study, statistical analysis, database results analysis, critical review. Jan Kulig: concept of the study, critical review. Anna Markiewicz: database results analysis, reviewed articles for the discussion, critical review.

### Artificial Intelligence (AI) Disclosure

No artificial intelligence (AI) tools, including large language models or machine learning software, were used in the preparation, analysis, or presentation of this manuscript.

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