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Early melanoma detection and acral lentiginous melanoma: evidence from Central-Eastern Europe

Ph.D. thesis

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TABLE OF CONTENTS

LIST OF PUBLICATIONS

This doctoral thesis is based on the following publications:

I I Csányi, N Houshmand, M Szűcs, H Ócsai, L Kemény, J Oláh, E Baltás. Acral lentiginous melanoma: a single-center retrospective review of four decades in East-Central Europe. J Eur Acad Dermatol Venereol. 2020;34(9):2004-2010. **D1, IF: 6.166**

II I Petrovszki, I Csányi, M Szűcs, H Ócsai, N Houshmand, L Kemény, J Oláh, E Baltás. Factors influencing early detection of malignant melanoma. Orvosi Hetilap. 2016;157(51):2028-2033. **Q4, IF: 0.349**

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I NK Kovács, ÁÁ Balogh, I Csányi, M Manczinger, AT Fülöp, L Asztalos, J Dombi, G Weszelovszky, R Gyulai, L Kemény, E Baltás. Image-based education enhances public accuracy in identifying concerning pigmented skin lesions. [*submitted for publication*]

II BT Papp, K Toplenszky, H Ócsai, I Csányi, L Kemény, R Gyulai, J Oláh, E Baltás. Ten Years of Euromelanoma in Hungary: Nationwide Trends and Risk Factors for Skin Cancer in Central–Eastern Europe. Cancers. 2025;17(23):3749. **Q1, IF: 4.4***

III B Nagy, N Kovács, K Ónodi, I Csányi, H Ócsai, J Oláh, L Kemény, R Gyulai, E Baltás. Skin-directed therapies in early-stage mycosis fungoides. Bőrgyógyász Venerol Szle. 2025;101(5):261-267.

IV P Rózsa, BT Papp, E Szederkény, G Vass, Cs Hánis, I Csányi, H Ócsai, E Baltás, J Oláh, L Kemény, R Gyulai, E Kis. Electrochemotherapy for multiple nonmelanoma skin tumors in immunosuppressed patients: a prospective cohort analysis. J Dermatol Ther. 2025. **Q1, IF: 3.4***

V P Rózsa, I Csányi, G Vass, E Varga, IB Németh, I Korom, H Ócsai, E Baltás, J Oláh, R Gyulai, E Kis. Electrochemotherapy, as a novel therapeutic approcach in the management of lentigo maligna, lentigo maligna melanoma and acral lentiginous melanoma. J Dermatol Treat. 2025;36(1):2495096. **Q1, IF: 3.9***

VI E Tóth-Molnár, A Vass, N Polgár, SzA Sándor, D Ágoston, P Rózsa, I Csányi, H Ócsai, E Baltás, J Oláh, E, Kis. The role of electrochemotherapy in the treatment of locally advanced or recurrent eyelid-periocular basal cell carcinoma: Long-term results. Int J Dermatol. 2025;64(1):111-118. **Q1, IF: 3.3***

VII H Ócsai, E Baltás, I Csányi, R Gyulai, J Oláh. Az onkológiában alkalmazott immun- és target terápiák leggyakoribb dermatológiai mellékhatásai. Orvos Továbbképző Szemle. 2024;31(11).

VIII B Pósfai, M Szentkereszty, F Sánta, Z Bajory, A Simon, Zs Kozéki, I Csányi, M Akgul, L Kuthi. Penile melanoma: a pathological report of two cases. Diagn Pathol. 2023; 18:117. **Q2, IF: 2.4**

IX E Kis, E Baltás, H Ócsai, I Csányi, A Ottlakán, Gy Lázár, G Vass, D Ágoston, P Rózsa, K Bottyán, Sz Dalmády, A Nagy, E Tóth-Molnár, J Oláh. Milestones of electrochemotherapy. Bőrgyógyász Venerol Szle. 2023;99(2):116-120.

X E Baltás, H Ócsai, I Csányi, A Varga, J Oláh, on behalf of the Oncology Team and its members. Advances and challenges of the past twenty years in our dermatooncological center. Bőrgyógyász Venerol Szle. 2023;99(2):109-115.

XI M Gaál, I Csányi. Challenges of the STI outpatient clinic at the Department of Dermatology and Allergology University of Szeged in the past 19 years. Bőrgyógyász Venerol Szle. 2023;99(2):155-160.

XII D Ágoston, Cs Hánis, H Ócsai, I Csányi, E Varga, I Korom, I Németh, E Kis, L Kemény, J Oláh, E Baltás. Multimodal treatment options for Merkel cell carcinoma. Bőrgyógyász Venerol Szle. 2022;98(5):240-246.

XIII A M van Huizen, S P Menting, et al. International eDelphi Study to Reach Consensus on the Methotrexate Dosing Regimen in Patients With Psoriasis. JAMA Dermatol. 2022;158(5):561-572.

XIV I Csányi, H Ócsai, I Korom, E Varga, A Varga, K Hideghéty, L Krenács, E Bagdi, T Gurbity Pálfi, K Piukovics, Z Borbényi, L Kemény, J Oláh, E Baltás. Prognostic markers of mycosis fungoides by means of two cases. Bőrgyógyász Venerol Szle. 2020;96(5):223-229.

XV Á Korom, I Csányi, E Baltás, J Oláh, Z Borbényi, T Gurbity Pálfi. Malignant melanoma in our patients with chronic lymphocytic leukemia. Haematológia-Transzfúziológia. 2019;52(4):232-236.

XVI J Oláh, A Varga, I Csányi, G Emri, N Kiss, E Varga, IB Németh, Zs Lengyel, P Holló. Clinical aspects and diagnosis of malignant epithelial skin cancers. Updates 2018. Bőrgyógyász Venerol Szle. 2018;94(5):227-236.

XVII I Csányi, H Ócsai, J Varga, I Korom, E Varga, I Németh, K Hideghéty, L Kemény, J Oláh, E Baltás. Clinical experiences with vemurafenib treatment of peripheral primitive neuroectodermal tumor in a patient suffering from malignant melanoma. Bőrgyógyász Venerol Szle. 2017;93(4):173-178.

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LIST OF ABBREVATIONS

AJCC: American Joint Committee on Cancer

ALK: anaplastic lymphoma kinase

ALM: acral lentiginous melanoma

AM: acral melanoma

BRAF: v-Raf murine sarcoma viral oncogene homolog B1

CCND1: cyclin D1

CDK4/6: cyclin-dependent kinase 4/6

CDKN2A: cyclin-dependent kinase inhibitor 2A

c-KIT: receptor tyrosine kinase (CD117)

CMM: cutaneous malignant melanoma

CTLA-4: cytotoxic T-lymphocyte-associated protein 4

DEJ: dermoepidermal junction

DM: desmoplastic melanoma

FDA: Food and Drug Administration

GAB2: GRB2-associated binding protein 2

GIST: gastrointestinal stromal tumor

HOX13: homeobox paralog group 13

HR: hazard ratio

HRAS: Harvey rat sarcoma viral oncogene homolog

ICI: immune checkpoint inhibitor

IL-2: interleukin-2

KIT: v-Kit Hardy-Zuckerman 4 feline sarcoma viral oncogene homolog

KRAS: Kirsten rat sarcoma viral oncogene homolog

LM: lentigo maligna

LMM: lentigo maligna melanoma

MAPK: mitogen-activated protein kinase

NF1: neurofibromin 1

NM: nodular melanoma

NRAS: neuroblastoma RAS viral oncogene homolog

NTRK3: neurotrophic tyrosine receptor kinase 3

PAK1: p21-activated kinase 1

PD-1: programmed cell death protein 1

PRKCA: protein kinase C alpha

RLND: regional lymph node dissection

SLN: sentinel lymph node

SLNB: sentinel lymph node biopsy

SPRED1: sprouty-related EVH1 domain-containing protein 1

SSE: skin self-examination

SSM: superficial spreading melanoma

TERT: telomerase reverse transcriptase

TIL: tumor-infiltrating lymphocyte

TNM: tumor–node–metastasis

US: United States

UV: ultraviolet

VEGF: vascular endothelial growth factor

WHO: World Health Organization

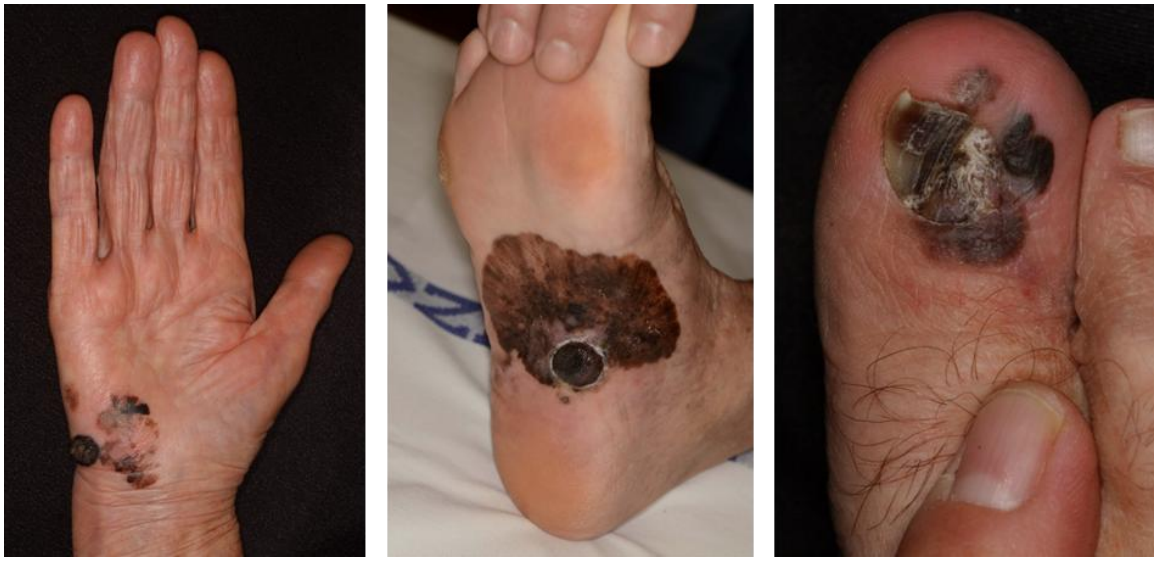
1. INTRODUCTION

1.1. Acral melanoma

1.1.1. Terminology and classification

Acral melanoma (AM) is defined in the medical literature as a distinct subtype of cutaneous melanoma that arises on the glabrous (non-hair-bearing) skin of the palms, soles, and nail apparatus (subungual region) (Figure 1).[1-5] The anatomical boundary of glabrous skin is not sharply defined, Wallace lines provide a practical clinical guide during physical examination.[1,6-11]

Figure 1. Acral melanoma on the palm (85-year-old female; right palm; pT3b), sole (81-year-old female; right sole; pT3b) and of the nail apparatus (44-year-old male; right great toe; pT1a)

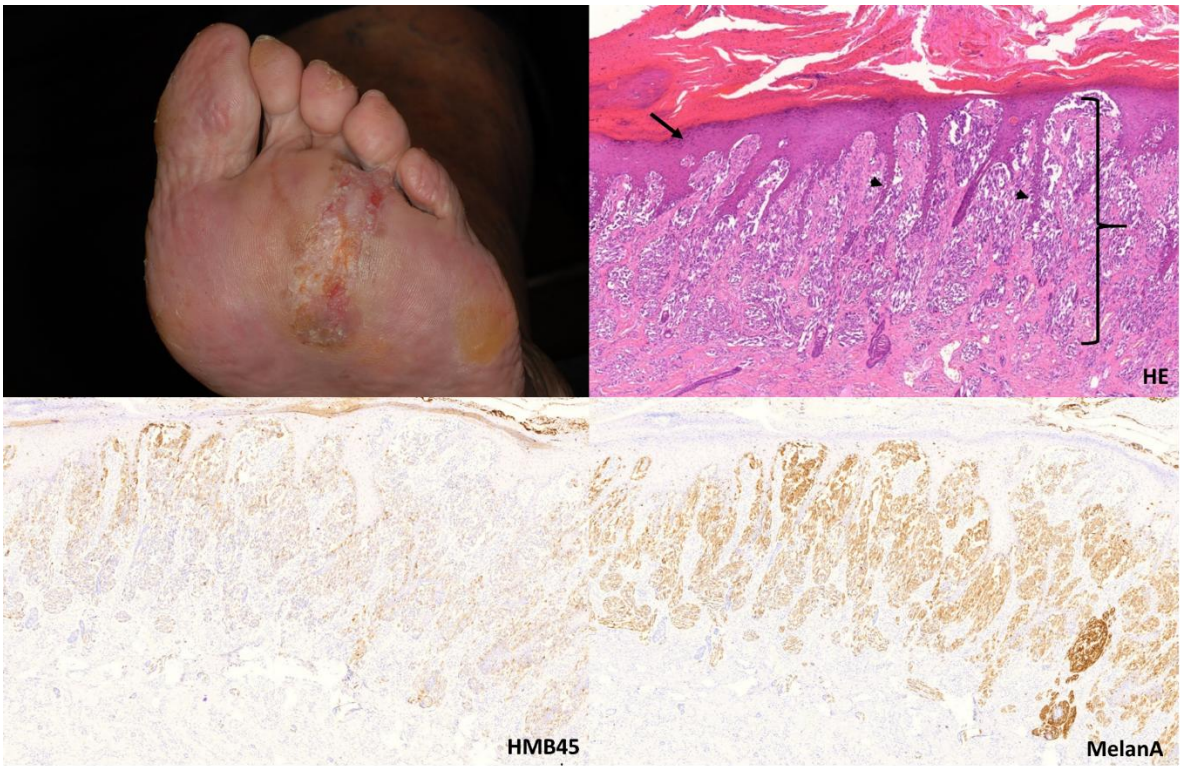


Acral melanoma includes all histologic subtypes occurring at these locations. The most common histopathologic variant is acral lentiginous melanoma (ALM), defined by Reed in 1976 as a lentiginous proliferation of atypical intraepidermal melanocytes along the dermoepidermal junction, accompanied by epidermal hyperplasia and an expanded, inflamed papillary dermis (Figure 2).[1-3,5,9,12-17] Thus "acral melanoma" denotes anatomical location, while "acral lentiginous melanoma" refers to a specific histological growth pattern, which accounts for the majority–but not all– melanomas arising at acral sites.[2,3]

Multiple histological subtypes may arise on acral skin, including superficial spreading melanoma (SSM), nodular melanoma (NM), desmoplastic melanoma (DM), and unclassified variants.[9,18-20] Reported proportions of ALM on acral skin vary considerably across studies

between 40–80%, largely due to differences in anatomical definitions and classification criteria.[9,16-18,21,22]

Figure 2. Clinical and histological images (40x, HE, HMB45, MelanA) of a clinically amelanotic acral lentiginous melanoma (pT3a) on the left sole of a 78-year-old female patient. Main histopathological features on the hematoxilin-eosin (HE) stained image: atypical melanocytes in a lentiginous pattern along the dermoepidermal junction (DEJ) (arrowhead), epidermal hyperplasia (arrow), and expanded, inflamed papillary dermis (curly bracket).



In a seminal study, Kuchelmeister *et al.*, who classified the dorsal hands and feet as acral sites, demonstrated that all histologically confirmed ALMs (60%) were confined to palmoplantar or subungual regions, whereas SSMs (30%) occurred almost exclusively on the dorsal aspects of the hands and feet, with NM distributed across both locations.[9] They confirmed that all ALMs are acral melanomas, but not all acral melanomas exhibit the acral lentiginous histological pattern.[2,3] In summary, histological subtype distribution is therefore strongly site-dependent, with palmoplantar and subungual melanomas showing a lentiginous growth pattern, in contrast to dorsal acral surfaces where SSM and NM are more common.[9,20,23]

The 2018 World Health Organization (WHO) classification introduced a multidimensional framework integrating etiological pathways, clinical features, anatomical site, and molecular characteristics.[5,23,24] Within this system, melanomas are broadly categorized as ultraviolet (UV)

radiation-associated or non-UV-associated, reflecting fundamental differences in pathogenesis rather than morphology alone.[5]

Acral melanoma is classified as a melanoma not consistently associated with solar damage, characterized by its anatomical location and a distinct molecular profile, including a low UV mutational signature and recurrent structural genomic alterations.[4,5,23] This classification separates amplification-driven melanomas, such as acral and mucosal melanoma, from UV-induced cutaneous subtypes.[5]

At the molecular level, acral melanoma is biologically distinct from from UV-driven cutaneous melanoma. It exhibits a low tumor mutational burden (approximately 2.76–4.6 mutations/Mb), lacks a dominant UV mutation signature, and is characterized by frequent copy-number alterations and complex chromosomal rearrangements[4,25-29].

While BRAF mutations occur in only 9–34% of cases and NRAS mutations in 12–28%, KIT alterations are more prevalent (5–36%), with activating mutations or amplifications detected in approximately 10–23% of tumors.[25-27,30-34]

Beyond canonical driver mutations, acral melanoma demonstrates considerable molecular heterogeneity, including MAPK-pathway-activating fusions (e.g., BRAF, NTRK3, ALK, PRKCA), NF1 and SPRED1 inactivation, among others.[25,27,33,35-37] Whole-genome sequencing studies further highlight aneuploidy, whole-genom duplication, and structural rearrangements, underscoring the complex genomic architecture of this subtype.[25,36,37]

1.1.2. Epidemiology

The global incidence of malignant melanoma has risen steadily over recent decades in light-skinned populations. In Europe, age-standardized rates increased from approximately 11–12 per 100,000 person-years in 2012 to 15–16 in 100,000 by 2018.[6,8,38-42] Although incidence continues to rise in most European countries, plateauing trends in younger age groups have been reported in high-risk regions such as Australia, Scandinavia, the United Kingdom, and the United States, likely reflecting the impact of prevention and early initiatives.[38-41]

In Hungary, melanoma incidence increased between 2011 and 2015, followed by a decline after 2015, with overall rates comparable to those observed in neighboring Central-European countries.[41] Within this broader epidemiological context, AM remains rare in Caucasian populations, accounting for less than 10% of cases, but disproportionately represented in East Asian (30–46%) and African (50–70%) populations.[16,28,43-46] In both the United States (US)

and Hungary, SSM is the predominant histotype of melanoma, whereas ALM represents one of the least frequently diagnosed forms of melanoma.[16,44-47]

1.1.3. Pathogenesis

Accumulating evidence indicates that melanoma subtypes differ not only clinically but also in their pathobiology, genetic drivers, and biological behavior. Wheater AM constitutes an intrinsically more aggressive melanoma subtype remains debated.[16,48-52]

Acral skin possesses unique anatomical and microenvironmental characteristics, including a thick stratum corneum, absence of hair follicles and sebaceous glands, specialized neuro-epidermal contacts and microvasculature, and a dense network of eccrine glands, which may serve as an alternative source of melanocytes. Mechanical stress and repeated trauma at weight-bearing and high-pressure sites, such as the soles and palms, have been proposed as contributory factors in tumor initiation and progression.[4,17,35,53,54]

Unlike melanomas arising on sun-exposed skin, AM pathogenesis appears to be largely independent of UV radiation, as reflected by its anatomical distribution and lacks a UV mutation signature. Instead, non-UV carcinogenic mechanisms, or site-specific microenvironmental factors, are thought to play a central role.[4,16,17,25,35,48,53-55]

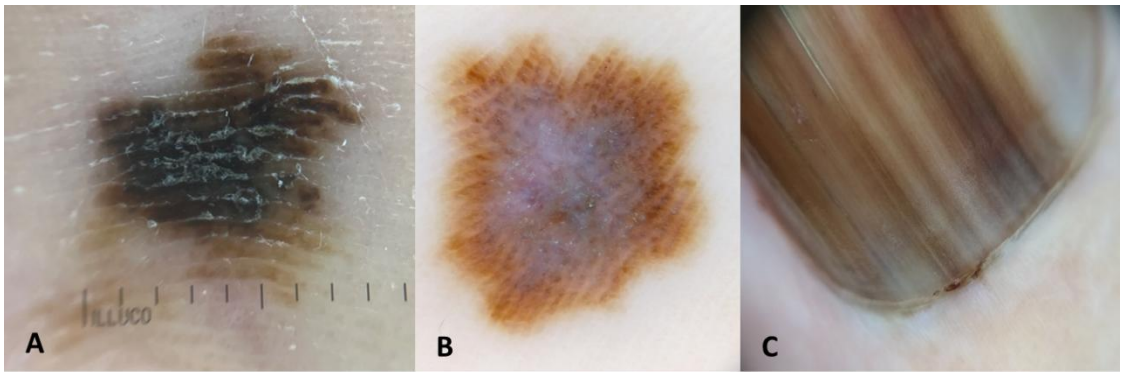
At the cellular level, melanocytes at acral skin differ biologically from melanocytes at non-acral sites, showing distinct patterns of melanin synthesis, cell–matrix interactions, and growth-signal responsiveness.[4,17,53-55] Resent work has demonstrated that anatomical position itself determines oncogenic susceptibility, with acral melanocytes expressing a positional identity gene program dominated by posterior HOX13 genes that synergizes with specific oncogenic alterations.[56] These intrinsic features likely contribute to the pathogenesis of AM.

1.1.4. Diagnosis and differential diagnosis

The clinical presentation of AM is highly variable and, together with its frequently concealed localization on the feet and nail apparatus, contributes substantially to delayed detection. Lesions may present as irregularly pigmented macules or patches, ulcers, or verrucous, bleeding tumors. In subungual melanoma, early brown discoloration of the nail plate may progress to nail dystrophy or complete nail destruction, while Hutchinson’s sign refers to periungual pigmentation of the proximal nail fold. Diagnostic recognition is further complicated by the relatively high proportion of amelanotic lesions compared with other CMM subtypes (Appendix 1).[6-8]

The ABCDEF rule proposed by Levit *et al.* summarizes key clinical warning signs of nail unit melanoma, including A (age in the 5th–7th decades and high-risk ethnic groups), B (a brown–black nail band ≥3 mm with irregular borders), C (change in the band or lack of response to treatment), D (involvement of characteristic digits), E (extension of pigment to the periungual skin, Hutchinson's sign), and F (a personal or family history of dysplastic nevi or melanoma).[57] Dermoscopy plays a critical role in the early recognition of AM (Figure 3). Characteristic dermoscopic features on volar skin include pigmentation accentuated along the ridges of parallel skin markings (parallel-ridge pattern) and irregular diffuse brown, gray, or black pigmentation.[58-60] The parallel-ridge pattern has a sensitivity of approximately 86% and specificity of 99% for early acral melanoma, making it one of the most reliable dermoscopic criteria in this setting.[61] In advanced cases, multicomponent pattern is seen, with dermoscopic features specific to melanoma on non-acral skin (irregular dots/globules, atypical vascular pattern, atypical pigment network, regression structures etc.).[25,27,33,35-37] The BRAAFF checklist is a 6-point dermoscopic algorithm used to diagnose acral melanoma on the palms and soles by evaluating four malignant (positive) and two benign (negative) features, with a total score of ≥1 suggesting melanoma (sensitivity: 93.1%, specificity: 86.7%). It includes irregular blotch (+1), parallel ridge pattern (+3), asymmetry of stuctures (+1) and colors (+), parallel furrow pattern (-1) and fibrillar pattern (-1).[62] In nail unit melanoma, irregular longitudinal lines with heterogeneity in color, spacing, width, and loss of parallelism are considered the most suggestive early dermoscopic findings.[63] According to the International Dermoscopy Society consensus study, suspicion for nail unit melanoma is highest when pigmentation involves more than two-thirds of the nail plate or shows gray or black coloration, with additional warning signs including color and band-width heterogeneity, Hutchinson or micro-Hutchinson signs, and granular pigmentation (Figure 3).[64]

Figure 3. Characteristic dermoscopic patterns of palmoplantar (parallel ridge pattern: A, B) and nail apparatus melanoma (longitudinal pigmented lines with irregular color and width: C)



During digital dermoscopic follow-up of acral melanocytic lesions, the emergence of new colors, granular pigmentation, or progressive darkening should prompt histopathological evaluation. Digital dermatoscopy facilitates serial monitoring and teledermoscopic consultation, while reflectance confocal microscopy provides non-invasive, in vivo, cellular-level assessment of equivocal acral lesions, improving diagnostic confidence and reducing unnecessary excisions.[65] However, it must be noted, that confocal imaging of acral melanocytic lesions faces significant imitations (limited imaging depth, hyperkeratosis and acanthosis, mechanical constrains, etc.).

Given the clinical heterogeneity of AM, the differential diagnosis is broad and includes benign melanocytic lesions (naevus pigmentosus, dysplastic naevus, Spitz nevus, Reed nevus, blue nevus), viral lesions (verruca vulgaris), epithelial tumors (pigmented basal cell carcinoma, squamous cell carcinoma, appendageal tumors), vascular lesions (angiokeratoma, hemangioma, pyogenic granuloma, Kaposi sarcoma, glomus tumor), and dermatofibroma. In subungual localization, distinction from benign longitudinal melanonychia (subungual lentigo and naevus, melanocyte activation) is particularly critical (Appendix 2).[6,7]

1.1.5. Treatment

Surgical management remains the cornerstone of treatment for acral melanoma, as excision is required both for definitive histopathological diagnosis and local disease control.

Whenever oncological safe, digit-sparing, function-preserving surgical approaches are preferred, while amputation is reserved for cases with extensive local invasion or unresectable disease. Nevertheless, anatomical constraints at acral sites often render complete excision technically challenging.[38,44,66,67]

Sentinel lymph node biopsy (SLNB) is routinely recommended for staging in clinically and radiologically node-negative patients, though AM has been associated with a relatively high rate of sentinel lymph node positivity compared with other cutaneous melanoma subtypes.[16,38,44,67,68]

Systemic therapy for advanced or metastatic AM largely follows treatment principles established for cutaneous melanoma in general; however, therapeutic responses differ substantially. Immune checkpoint inhibitors (ICI) targeting programmed cell death protein 1 (PD-1) or cytotoxic T-lymphocyte-associated protein 4 (CTLA-4) have markedly improved melanoma outcomes overall, yet multiple studies report lower response rates and shorter

survival in AM in both metastatic and adjuvant setting, likely reflecting its low tumor mutational burden and distinct immune microenvironment.[11,15,50,69-72]

Targeted therapy options are more limited in AM, as activating BRAF mutations are relatively uncommon. Instead, KIT mutations and amplifications represent the most relevant actionable alterations, and KIT inhibitors such as imatinib have demonstrated modest, but clinically meaningful activity in selected patients.[48,69,73-75] Responses, however, are often heterogeneous and short-lived, underscoring the need for improved molecular stratification.

Despite recent advances, patients with BRAF wild-type AM remain an underserved population. Greater emphasis is therefore needed on developing targeted strategies addressing alternative oncogenic pathways frequently altered in AM, including KIT, CDK4/6, TERT, and other cell-cycle–and telomerase-related mechanisms.[4,11,15,17,69,76-78]

Combination treatment strategies are under active investigations. The combination of the PD-1 inhibitor toripalimab with the vascular endothelial growth factor (VEGF) inhibitor axitinib has shown encouraging antitumor activity in mucosal melanoma and is frequently discussed in the context of other non-cutaneous subtypes, including AM.[69] Another emerging immunotherapeutic approach is nemvaleukin alfa, an engineered interleukin-2 (IL-2) variant designed to preferentially activate antitumor immune effector cells while minimising systemic toxicity. Although it has received Foof and Drug Administration (FDA) fast-track designation in mucosal melanoma, its potential role in AM remains under investigation.[69] Adoptive tumor-infiltrating lymphocyte (TIL) therapy has demonstrated durable responses in advanced melanoma, including non-cutaneous subtypes such as acral melanoma, although evidence remains limited and largely derived from mixed-subtype cohorts, while bispecific antibodies—designed to simultaneously engage immune checkpoints and tumor-associated antigens—represent a promising but still largely unexplored strategy in AM.[79-81]

Given the poor prognosis and frequent advanced presentation of AM, optimal management requires a multidisciplinary approach, integrating dermatology, surgical, radiation and medical oncology, pathology, and radiology. Prospective studies specifically addressing neoadjuvant and adjuvant systemic therapies in AM are still lacking, as current evidence is largely extrapolated from cohorts dominated by non-acral melanoma subtypes.[82,83]

1.1.6. Survival and prognostic factors

Survival outcomes differ substantially between AM and other cutaneous melanoma subtypes, with AM generally associated with a poorer prognosis. Whether this disadvantage primarily

reflects greater Breslow thickness and more advanced stage at diagnosis, or indicates intrinsically more aggressive tumor biology, remains unresolved.[16,35,44,66,84] The importance of early detection is underscored by survival statistics, with reported 5-year survival rates of 98.3 % for localized disease, 62.4 % for locoregional metastases, and approximately 16 % in the presence of distant metastases.[85]

Marked geographical variation in survival has been also reported, with 5-year survival rates of 53–60 % in Asian cohorts compared with 70–80 % in European and US populations.[35,41,43,86-89] By contrast, the overall 5-year survival for all cutaneous melanomas in New Zealand is approximately 91 %, reflecting earlier detection and broad access to healthcare.[89] Despite overall improvements in melanoma outcomes over recent decades, AM continues to show persistently poorer survival than non-acral subtypes, highlighting ongoing diagnostic challenges and possibly distinct biological differences.[16,35,43,86-89]

Across studies, AM is consistently associated with an unfavorable prognosis compared with other histological subtypes and anatomical sites.[44,66,90,91] Age, ulceration, Breslow thickness, and stage at diagnosis emerge as the most robust prognostic factors, mirroring those identified in other melanoma subtypes.[17,44,92-95] Consequently, inferior outcomes in AM have traditionally attributed to diagnostic delay rather than to universally accepted intrinsic biological aggressiveness.[10,94]

Nevertheless, evidence regarding intrinsic tumor biology remains conflicting. Phan *et al.* reported worse survival in patients with amelanotic or hypomelanotic AM, potentially indicating more aggressive biological behavior, although these findings have not been consistently replicated.[16] Mandalà *et al.*, in a large international cohort, identified the acral lentiginous histotype as an independent adverse prognostic factor in stage I–II melanoma after adjustment for conventional variables.[96] In contrast, Susok and Gambichler observed comparable survival between stage- and site-matched Caucasian patients with ALM and SSM, supporting diagnostic delays as the predominant driver of poor outcomes.[97]

Beyond established clinicopathological parameters, additional histological features—including regression, high mitotic rate, and vascular invasion—may further influence prognosis. The unique anatomical, vascular, and neurological characteristics of acral sites may also contribute, although data specific to AM remain limited and inconsistent. Distinct molecular and genetic characteristics of AM may additionally affect prognosis and therapeutic response.

Despite extensive investigations, the clinical course of AM remains difficult to predict. Early detection is likely the single most important modifiable determinant of outcome and depends not only on careful clinical examination but also on patient awareness and healthcare-provider

education.[98,99] Although population-based screening remains controversial, targeted strategies for high-risk groups may help reduce diagnostic delay and improve outcomes.

In summary, the unfavourable prognosis associated with acral melanoma is multifactorial, reflecting delayed diagnosis, advanced stage at presentation, distinct molecular characteristics–including low tumor mutational burden–and reduced responsivenes to immune checkpoint inhibitors and targeted therapies.[2-4,28]

1.2. Factors influencing early detection of malignant melanoma

The prognosis of patients with malignant melanoma is strongly determined by the stage at which the disease is diagnosed.[67] When melanoma is detected at an *in situ* or early invasive stage, treatment is typically limited to surgical excision performed under local anesthesia. In contrast, advanced-stage disease often requires surgery under general anesthesia and systemic therapies, and is associated with substantially higher morbidity and mortality.

Early melanoma detection is a multistep process involving the patient, the physician, and the healthcare system. In line with previous studies, early detection is commonly defined by a Breslow tumor thickness of ≤1 mm, while late detection refers to melanomas thicker than 1 mm (>1 mm).[100,101] In nodular melanoma, which is characterized by rapid vertical growth, a higher threshold of 2 mm has been proposed to distinguish early from late detection.[100]

1.2.1. Patient-, physician-, and healthcare system–related factors

Patient-related determinants of early melanoma detection have been extensively investigated and reflect a complex interplay between knowledge, attitudes, and behaviors. Regular skin self-examination (SSE), awareness of melanoma warning signs, and positive attitudes toward skin cancer surveillance are consistently associated with thinner melanomas at diagnosis.[100-102] Female sex, younger age, higher educational level, higher socioeconomic status, and marital status have also been linked to earlier detection.[101-104] Conversely, low melanoma awareness, delayed help-seeking behavior, and misinterpretation of early symptoms—such as attributing lesion changes to benign conditions—are associated with diagnostic delay. Notably, self-detection of features such as elevation, bleeding, or pain often reflects more advanced disease.[103,105]

Physician-related factors play a critical role in diagnostic timing. Melanomas detected by dermatologists are generally thinner and diagnosed at earlier stages than those detected by

primary care physicians or by patients themselves.[103,104] Barriers to timely diagnosis include limited dermatologic training, time constraints during consultations, competing comorbidities, and misdiagnosis.[100,103,106,107] Inappropriate treatment without histopathological confirmation and delays in referral to specialist care further contribute to prolonged diagnostic intervals.[100,103]

Healthcare system–related factors substantially influence melanoma outcomes. Limited access to dermatologic services—particularly in rural or socioeconomically disadvantaged areas—is associated with later-stage diagnosis.[100,103] Insurance status is a major determinant of access to care in some countries, with uninsured patients more likely to present with advanced disease.[100,103] Geographic disparities have been consistently reported, with rural populations experiencing longer diagnostic delays and higher rates of late-stage melanoma compared with urban populations.[108-110] Additionally, insufficient public awareness campaigns, lack of structured screening programs, and language barriers may further impede timely diagnosis, particularly among racial and ethnic minority populations.[100,106]

1.2.2. The Melbehav questionnaire

To systematically assess patient-, physician-, and healthcare system–related determinants of melanoma detection, Susan Swetter and colleagues developed a comprehensive questionnaire composed of 75 items.[100] Using this instrument, they demonstrated that early melanoma detection was associated with regular skin self-examination and dermatologic screening.[100]

Talaganis and colleagues subsequently applied the same questionnaire in a Greek cohort.[101] In that study, factors associated with earlier detection included female sex, non-nodular melanoma subtypes (SSM, LMM, and ALM), and primary tumor's localization on the upper extremities or head and neck. Early detection was more common among patients who were married in the year preceding diagnosis or who regularly performed SSE, whereas physician-performed physical examination did not emerge as an independent determinant of early detection.[101]

Evidence from additional studies suggests that regular SSE may reduce melanoma-specific mortality by up to 63%. Robinson *et al.* investigated determinants of SSE performance and effectiveness, reporting that approximately 70% of patients regularly performed self-examinations. SSE performance was influenced by patient attitudes, prior dermatologic examinations, a history of skin cancer within the preceding three years, and the belief that SSE could be performed effectively.[111]

1.2.3. Determinants of early melanoma detection in Central–Eastern Europe

Data from Central–Eastern Europe regarding determinants of early melanoma detection remain limited but are gradually emerging. A large retrospective single-center study from Hungary including 6,267 melanoma patients demonstrated a decline in annual median Breslow thickness over time, suggesting improvements in early detection. Female sex and younger age were associated with thinner tumors and better survival, highlighting the impact of secondary prevention measures.[112]

In Romania, a single-center cohort study reported that higher educational level and participation in awareness campaigns were significantly associated with shorter diagnostic delay for skin cancers, including melanoma.[113] Another Romanian study found that low rates of SSE and physician-performed skin examinations contributed to late-stage diagnosis, underscoring the importance of population-level educational interventions.[114] A further cross-sectional study from Northwestern Romania identified younger age, high nevus count, and predominantly indoor activity as factors associated with earlier melanoma diagnosis and emphasized the need for targeted public health strategies.[115]

Collectively, these studies indicate that education, awareness campaigns, age, sex, and health-related behaviors are key determinants of early melanoma detection in Central–Eastern European single-center cohorts.[100,101,112,113]

1.2.4. Physician-led skin cancer screening campaigns in Central–Eastern Europe

The impact of physician-led skin examinations and population-based screening programs in Central–Eastern Europe has been evaluated primarily through the Euromelanoma campaign and national initiatives. Our working group–together with other dermatooncological centers–investigated in Hungary a decade of Euromelanoma screening, and identified atypical nevi, a personal history of skin cancer, and heavy sunbed use as strong predictors of suspicious skin lesions. Detection rates were higher among participants attending screening because of a changing lesion, whereas routine checks and family history were less predictive, supporting a risk-stratified screening approach.[116]

Across 20 European countries, including Hungary, Croatia, the Czech Republic, and Romania, the Euromelanoma campaign demonstrated that full-body skin examination combined with dermoscopy improved the detection of clinically suspicious melanoma, with positive predictive values reaching up to 13%. However, the screened population was relatively young, and

detection rates varied substantially between countries, suggesting that targeting high-risk populations and optimizing screening strategies may improve effectiveness.[117]

Romanian single-center studies similarly reported that low rates of both self-examination and physician-performed skin examination contributed to late melanoma diagnosis, while higher educational level and participation in awareness campaigns were associated with shorter diagnostic delay.[100,113]

Overall, these findings indicate that targeted, physician-led screening and educational campaigns may improve early detection rates, whereas routine or untargeted approaches appear less effective. Population-wide mass screening programs remain controversial due to uncertain benefit and high costs.[100,113,114,116,117]

2. AIMS

2.1. Acral lentiginous melanoma: a single-center retrospective review

Acral melanoma is a rare but clinically significant melanoma subtype; however, data from Central-Eastern Europe remain limited.[9,10,92,94,118]

The aims of our work were to address key knowledge gaps in acral melanoma using the long-term experience of a single dermato-oncology center, with particular focus on epidemiology, clinicopathological characteristics, survival outcomes, prognostic factors, and diagnostic delay. In addition, we thought to compare our findings with published international data. Through this center-based analysis, we aimed to provide the first detailed characterization of acral melanoma from Central-Eastern Europe.

The specific aims were as follows:

- To describe the demographic, clinical, and histopathological characteristics of acral melanoma diagnosed at our center over a 40-year period.
- To analyse survival outcomes and identify prognostic factors associated with acral melanoma, including patient- and disease-related characteristics.
- To evaluate temporal trends in epidemiology, diagnostic characteristics, and outcomes across four decades, reflecting changes in awareness and therapeutic approaches.
- To contextualize our results by comparing them with previously published international data, thereby contributing novel epidemiological and outcome data from Central–Eastern Europe.

2.2. Factors influencing early detection of malignant melanoma

The primary aim of our work was to identify patient-, physician-, and healthcare system-related factors associated with the early detection of malignant melanoma in a Hungarian single-center cohort, using a standardized questionnaire-based approach.

The specific aims were as follows:

- To characterize patient and tumor characteristics associated with melanoma thickness.
- To investigate melanoma patients' awareness, knowledge, attitudes, and preventive behaviors—including skin self-examination practices—and their association with melanoma thickness.
- To evaluate medical access, health care use, and physician skin examinations in relation to early melanoma detection.
- To analyse the circumstances of melanoma recognition (patient-, layperson-, or physician-detected) and their relationship to Breslow thickness at diagnosis.
- To compare the findings of this cohort with previously published international studies from the United States and Greece using the same questionnaire.

3. MATERIALS AND METHODS

We conducted a single-center, retrospective cohort study over a 40-year period (1976-2016) including patients diagnosed with acral melanoma at the Department of Dermatology and Allergology, Albert Szent-Györgyi Health Center, University of Szeged.

Because anatomical definitions and classification criteria for acral melanoma vary across the literature, and because the acral lentiginous subtype represents the predominant histotype in acral locations, we defined our study population using combined anatomical and histopathological criteria. Eligible cases included melanomas exhibiting acral lentiginous histological subtype and arising on the glabrous skin of the extremities (palms, heels, soles, fingers) or within the nail apparatus. Based on these criteria, the term acral lentiginous melanoma was used throughout the study as the most precise and consistent designation.

In addition, determinants of early melanoma detection were investigated in a separate prospective, questionnaire-based study conducted over a one-year period, including all melanoma cases diagnosed between January and October 2015.

Both studies were conducted in accordance with the Declaration of Helsinki and were approved by the National Council of Health Sciences, Scientific and Research Ethics Committee, as well as the Regional and Institutional Review Board of Human Investigations at the University of Szeged (registration number: 40/2015 (3521), protocol number: MEL-RETRO-001; registration number: 36/2015 (3518) , protocol number: MEL-PREVENT-001).

3.1. Acral lentiginous melanoma: a single-center retrospective review

3.1.1. Patients and data collection

More than 25,000 histopathological reports were reviewed. Inclusion criteria comprised patients with a histologically confirmed diagnosis of invasive acral lentiginous melanoma arising on glabrous (non-hair-bearing) skin of the extremities, including the palms, soles, heels, fingers, or subungual regions. Exclusion criteria included melanoma *in situ*, non-ALM histological subtypes occurring at acral sites, and cases with incomplete or missing key clinicopathological data.

Clinical and pathological data were extracted from handwritten medical records for the period of 1976–1996 and from the institutional electronic database (Medsolution) for 1997–2016.

Collected variables included patient demographics, primary tumor characteristics (anatomical site, macroscopic appearance, Breslow thickness, Clark level, ulceration), sentinel lymph node (SLN) status, disease stage according to the AJCC 8th edition TNM classification, and treatment modalities.[67]

Patient-related diagnostic delay was defined as the time interval between the patient's initial recognition of the lesion and the first consultation with a physician. Temporal trends in incidence, Breslow tumor thickness, and survival were also assessed. Our findings were compared with international data. These comparisons were qualitative and descriptive in nature, based on reported proportions and associations, and no direct statistical testing between populations was undertaken.

3.1.2. Statistical analysis

Overall and disease-specific survival probabilities were estimated using the Kaplan–Meier method, with group comparisons performed using the log-rank test, applying Bonferroni correction for multiple comparisons where appropriate.

Differences in mean Breslow thickness between SLN-positive and SLN-negative patients were evaluated using Student's t-test. Temporal trends in patient age and Breslow thickness were analysed using analysis of variance (ANOVA) and Poisson regression, as appropriate.

The impact of clinicopathological variables on survival was assessed using univariate and multivariate Cox proportional hazards regression models. Covariates included: sex, Clark level (II/III vs. IV/V), ulceration, dermal mitotic rate ≥1/mm², tumor site (hand vs. foot), SLN status, nodal involvement, presence of distant metastases. Age and Breslow thickness were treated as continuous variables. Variables showing a p-value < 0.05 in univariate analyses were entered into the multivariate model, and a p-value < 0.001 was regarded as statistically significant. All analyses were performed using R statistical software (version 3.2.1).

3.2. Factors influencing early detection of malignant melanoma

3.2.1. Patients and the Melbehav questionnaire

All adult patients (≥18 years) diagnosed with malignant melanoma between January and October 2015 were eligible for inclusion. Patients were stratified by Breslow thickness into three groups: melanoma *in situ*, invasive melanoma with Breslow thickness ≤1 mm, and invasive melanoma with Breslow thickness >1 mm. Early detection of a primary melanoma was defined with a Breslow thickness of ≤1 mm and no clinical or radiological evidence of locoregional and/or distant metastases at the time of diagnosis. Patients were excluded if key clinicopathological or questionnaire data were incomplete or missing.

Patient-, physician-, and healthcare system-related determinants of early detection were assessed using the Melbehav questionnaire, developed by Susan M. Swetter *et al.* and previously validated in cohorts from the United States and Greece.[100,101] The instrument comprises 74 items covering 10 thematic domains. The questionnaire was translated into Hungarian and pilot-tested for clarity and feasibility prior to administration (Appendix 3). To contextualize our results, key findings were descriptively compared with published data from US and Greek melanoma cohorts.

3.2.2. Statistical analysis

Association between potential predictors and early detection was analysed using chi-square tests, Fisher's exact test, and Spearman's rank correlation, as appropriate. Statistical analyses were performed using R statistical software (version 3.2.1), with p-value < 0.05 considered statistically significant. Comparisons with cohorts from the US and Greece were conducted in

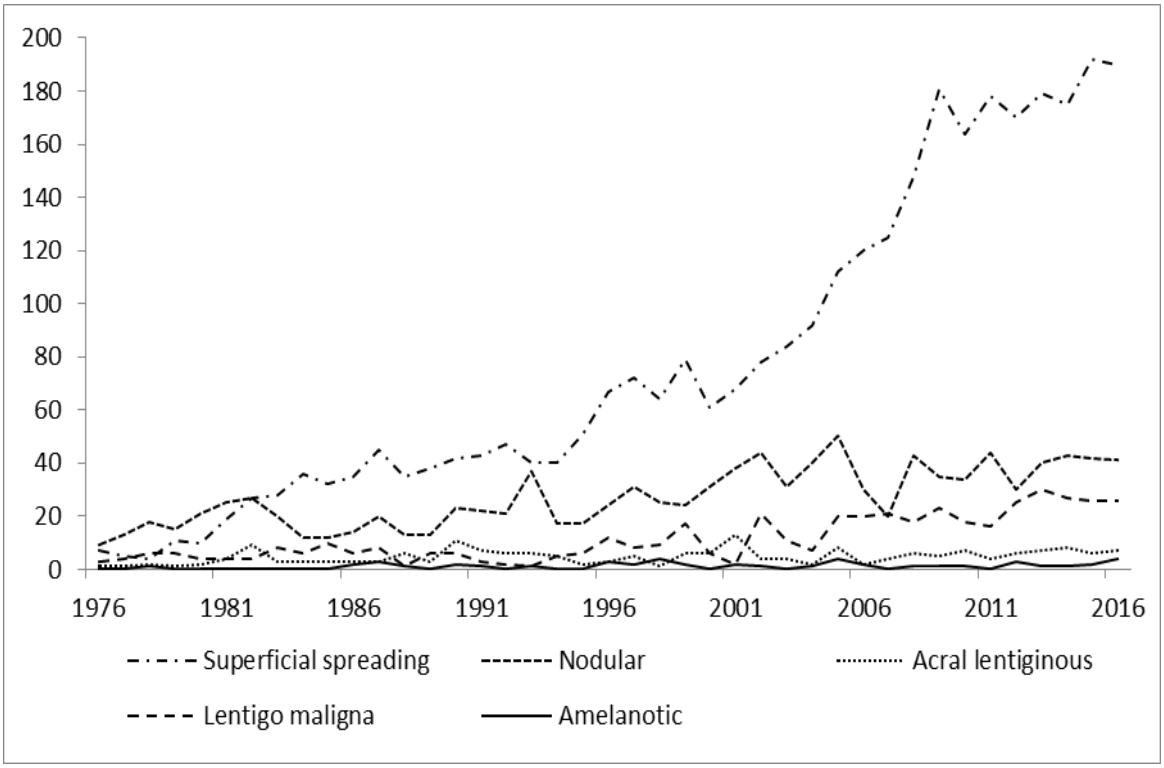
a qualitative and descriptive manner, relying on reported proportions and associations, and did not include direct statistical testing between populations.

4. RESULTS

4.1. Acral lentiginous melanoma: a single-center retrospective review

Between January 1976 and December 2016, a total of 4,593 patients were diagnosed with CMM at our center (Figure 4). Among these, 176 patients (3.83%) had histologically confirmed ALM arising on the glabrous skin of the extremities (palms, heels, soles, fingers), or in the subungual region.

Figure 4. Distribution of cutaneous melanoma subtypes among 4,593 patients diagnosed at our center over a 40-year period (1976-2016)



4.1.1. Patient demographics and primary tumor characteristics

All patients were of Caucasian ethnicity. The mean age at diagnosis was 66.17 years (range: 29–92 years, SD ±12.97), with 73.29% of cases diagnosed after the age of 60. Mean age at diagnosis was 64.50 years (±11.51) for males and 67.54 years (±13.93) for females. The male-

to-female ratio was 1:1.26, and 55.68% of tumors occurring in woman over 60 years of age (Table 1).

Table 1. Acral lentiginous melanoma: patient demographics and location of the primary tumors

Characteristics	Values
Sex (n)	
Male, n (%)	78 (44.32)
Female, n (%)	98 (55.68)
Male:female ratio	1:1.26
Age at diagnosis (year)	
Range	29–92
Median	67.43
Mean (±SD)	66.17 (±12.97)
Mean age male (±SD)	64.50 (±11.51)
Mean age female (±SD)	67.54 (±13.93)
Location of the primary tumor	
Upper extremity, n (%)	20 (11.37)
Palms	9 (5.12)
Nails	9 (5.12)
Other	2 (1.13)
Lower extremity, n (%)	156 (88.63)
Soles	86 (48.86)
Heels	41 (23.30)
Nails	16 (9.09)
Other	13 (7.38)
n: number of the patients, SD: standard deviation	

Most ALMs were located on the lower extremities (88.63%). Tumors most commonly arose on the soles (48.86%) and heels (23.30%). Subungual melanoma accounted for 14.21% of cases and was more frequently observed on the lower extremities. Upper extremity ALMs comprised 11.37% of all cases.

The mean Breslow tumor thickness was 3.861 mm (range 0.000–14.516; DS ±2.66 mm), with a median thickness of 3.344 mm. Overall, 75.00% of tumors were thicker than 2 mm, and 37.50% exceeded 4 mm. Clark level IV or V invasion was observed in 56.25% of cases. Histological ulceration was present in 71.59% (n=126) of tumors, while macroscopic ulceration was documented in 35.79%. Clinical bleeding was reported in 14.20% of cases (Table 2).

Information on patient-related diagnostic delay was available in 138 cases. The interval between patient recognition of the lesion and first physician consultation ranged from 1 month to 10 years, with a mean delay of 18 months. More than half of patients (51.45%) waited longer than one year before seeking medical help, and 11.59% delayed consultation for more than three years.

Table 2. Acral lentiginous melanoma: histological characteristics of the primary tumor

Characteristics	Values
Breslow tumor thickness (mm)	
Range	0.000–14.516
Median	3.344
Mean (±SD)	3.861 (±2.66)
Breslow tumor thickness, n (%)	
≤1 mm	18 (10.23)
1.01–2.00 mm	26 (14.77)
2.01–4.00 mm	66 (37.50)
>4 mm	66 (37.50)
Clark level, n (%)	
I	2 (1.14)
II	16 (9.09)
III	59 (33.52)
IV	68 (38.64)
V	31 (17.61)
Microscopic ulceration, n (%)	
Present	126 (71.59)
Not present	47 (26.70)
No data	3 (1.71)
n: number of the patients, SD: standard deviation	

4.1.2. Survival analysis and prognostic factors

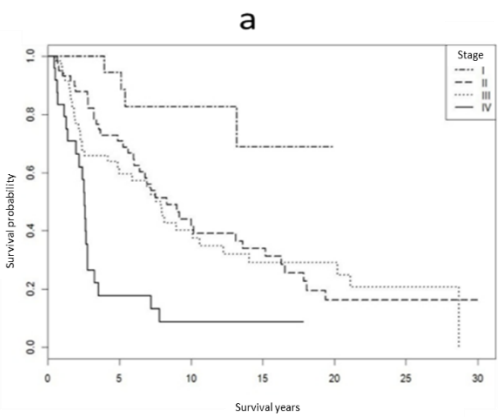
Sentinel lymph node biopsy (SLNB) has been routinely performed at our center since 1999. In total, 58 patients (32.95%) underwent SLNB, of whom 60.30% were SLN-positive. SLN-negative patients were predominantly female (male-to-female ratio 1:4) and had significantly lower mean Breslow thickness compared with SLN-positive patients (2.02 ± 0.36 mm vs. 4.66 ± 0.45 mm; $p < 0.001$). No significant differences were observed between SLN-positive and SLN-negative patients regarding age, tumor location, or patient-related diagnostic delay.

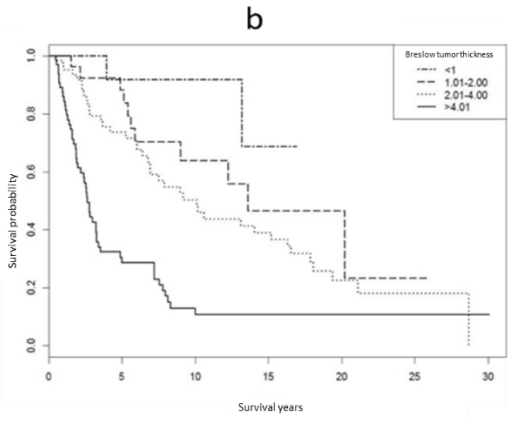
The 5- and 10-year overall survival rates of patients with ALM were 60.51% (95% CI, 53.27–68.75) and 41.59% (95% CI, 34.10–50.72), respectively. Disease-specific survival differed significantly by TNM stage ($p < 0.001$), with patients diagnosed at stage I showing significantly better outcomes than those with stages II–IV (Figure 5). No significant survival difference was observed between stages II and III; however, both groups had significantly better survival than stage IV patients ($p < 0.001$).

Stratification by Breslow thickness demonstrated a pronounced survival gradient. Five-year disease-specific survival was 92.31% (95% CI, 78.90–100.00) for T1 tumors and 28.56% (95% CI, 19.03–42.87) for T4 tumors ($p<0.001$) (Figure 5). Similarly, SLN-negative patients had

significantly higher 5-year disease-specific survival compared with SLN-positive patients (84.21% vs. 54.61%; p<0.001) (Figure 5).

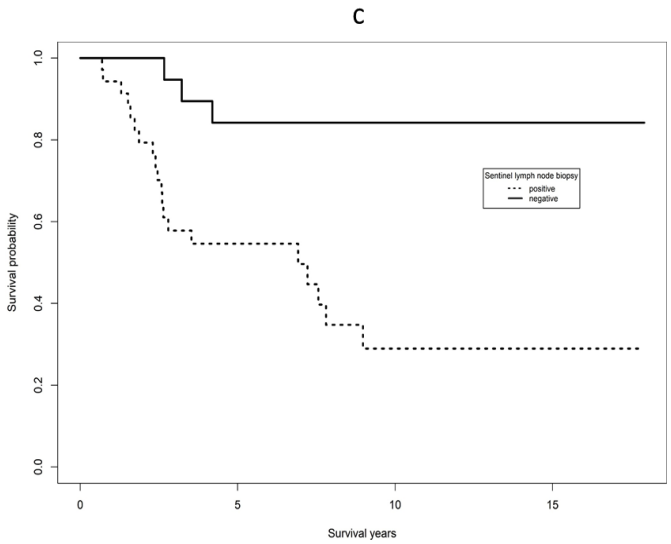
Figure 5. Kaplan–Meier disease-specific survival curves for patients with ALM, stratified by (a) TNM stage, (b) Breslow primary tumor thickness categories, and (c) sentinel lymph node status
CI: confidence interval; Br. t. (mm): Breslow tumor thickness in mm; SLNB: sentinel lymph node biopsy.





Stage	5-year survival, % (95% CI)	10-year survival, % (95% CI)
I	94.44 (84.43 – 100.00)	82.64 (66.55 – 100.00)
II	70.80 (59.67 – 84.00)	44.08 (31.93 – 60.86)
III	59.56 (47.73 – 100.00)	40.30 (28.35 – 57.29)
IV	17.71 (7.30 – 42.98)	8.85 (2.36 – 33.20)

Br. t. (mm)	5-year survival, % (95% CI)	10-year survival, % (95% CI)
<1	92.31 (78.90 – 100.00)	92.31 (78.90 – 100.00)
1.01 – 2.00	88.11 (76.32 – 100.00)	63.83 (46.13 – 88.32)
2.01 – 4.00	73.67 (63.03 – 86.11)	50.34 (38.21 – 66.31)
>4.01	28.56 (19.03 – 42.87)	12.85 (6.36 – 25.99)



SLNB	5-year survival, % (95% CI)
Positive	54.61 (39.95 – 74.65)
Negative	84.21 (69.31 – 100.00)

SLNB	10-year survival, % (95% CI)
Positive	28.96 (15.09 – 55.59)
Negative	84.21 (69.31 – 100.00)

In univariate Cox regression analysis, age, sex, Breslow thickness, Clark level, ulceration, SLN positivity, nodal involvement, and presence of distant metastases were all significantly associated with disease-specific survival ($p < 0.05$). Tumor site and dermal mitotic rate were not significantly associated with survival. In multivariate analysis, increasing age (HR 1.058,

95% CI 1.035–1.083), Breslow thickness (HR 1.187, 95% CI 1.099–1.282), and presence of distant metastases (HR 3.002, 95% CI 1.850–4.871) remained independent predictors of worse disease-specific survival (Table 3).

Table 3. Univariate and multivariate Cox proportional hazard regression analyses of clinicopathological variables associated with disease-specific survival in patients with ALM

	Univariate		**Multivariate**	
	HR (95% CI)	p-value	HR (95% CI)	p-value
Age	1.046 (1.027–1.065)	<**0.001**	1.058 (1.035–1.083)	<**0.001**
Female sex	0.652 (0.443–0.960)	0.030	0.506 (0.326–0.784)	0.002
Breslow thickness (mm)	1.253 (1.173–1.339)	<**0.001**	1.187 (1.099–1.282)	<**0.001**
Clark level IV/V **(**vs II/III)	2.842 (1.871–4.316)	<**0.001**	1.768 (1.071–2.918)	0.026
Presence of ulceration	3.625 (1.934–6.795)	<**0.001**	2.591 (1.302–5.154)	0.006
Presence of dermal mitoses ≥1/mm^2	1.149 (0.601–2.195)	0.674		
Anatomical site: foot (vs hand)	1.471 (0.714–3.032)	0.296		
SLNB* positivity	6.087 (1.799–20.600)	0.004		
Positive nodal status	1.714 (1.154–2.156)	0.008	2.585 (1.088–6.139)	0.031
Presence of distant metastasis	2.834 (1.840–4.364)	<**0.001**	3.002 (1.850–4.871)	<**0.001**

**Analysis of 58 patients.*

4.1.3. Treatment patterns

All 176 ALM patients underwent wide local excision of the primary tumor with varying safety margins during the 40-year study period (Table 4). Regional lymph node dissection (RLND) was performed electively until 1998 in 24 patients (28.5%). From 1999 onward, after the introduction of SLNB at our department, 58 ALM patients underwent it, followed by complete RLND in 26 cases (28.2%). In patients with clinically detectable lymph node metastases, RLND was performed in 20 patients (23.8%) until 1998, and in 7 patients (7.6%) thereafter.

Regarding adjuvant systemic therapy, dacarbazine was predominantly used until 1998 (19.0%), whereas interferon-alpha (22.8%) became the preferred systemic drug from 1999. For unresectable and/or metastatic disease, chemotherapy was the systemic treatment of choice until 2015 (11.9% before 1998; 20.6% from 1999).

In 2015, novel therapeutic options—including targeted and immuno-oncological treatments—have become available and were administered to 14 patients in total (imatinib: n=2; dabrafenib + trametinib: n=1; ipilimumab: n=4; nivolumab: n=4; pembrolizumab: n=3).

Radiotherapy was used in 16.5% of patients in either adjuvant or metastatic settings (cutaneous: n=7; lymph node: n=2; brain: n=11). From 2007, electrochemotherapy was used in 2.2% of patients for loco-regional cutaneous melanoma metastases.

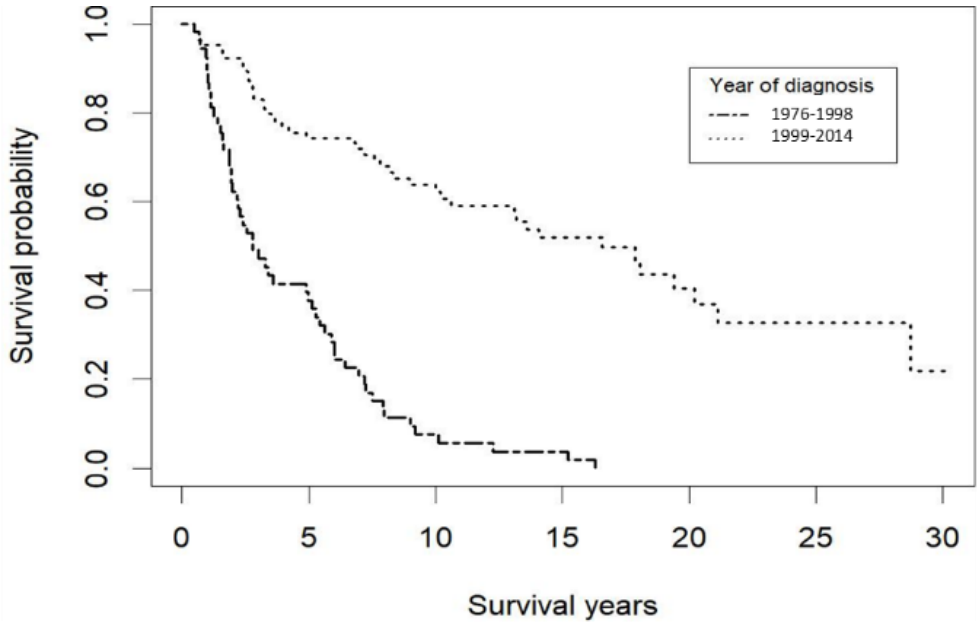
Based on treatment availability, three periods were defined (1976–1998, 1999–2014, 2015–2016). Comparison between the first two periods showed no significant differences in age, sex

distribution, or Breslow thickness. Clinically detectable nodal metastases were more frequent in the earlier period (20 vs. 5 patients). Kaplan–Meier analysis demonstrated significant differences in overall survival between patients treated in 1976-1998 and those treated in 1999-2014 ($p < 0.001$) (Figure 6).

Table 4. Treatment modalities for acral lentiginous melanoma across three time periods

Time periods		**1976–1998**	**1999–2014**	**2015–2016**
Number of ALM patients (n)		84	78	14
Mean age (years)		65.68	67.53	62.42
Male:female ratio		1:0.95	1:1.68	1:1.30
Mean Breslow thickness (mm)		4.056	3.583	4.528
Median Breslow thickness (mm)		3.450	2.812	3.496
Surgery (excision: 100%, SLNB: 32.9%, RLND: 43.8%)				
Primary tumor wide local excision (n)		84	78	14
Sentinel lymph node biopsy (n)		-	53	5
Regional lymph node dissection (RLND)	Elective (n)	24	-	-
	Clinically occult (SLN positivity) (n)	-	24	2
	Clinically detectable LN metastasis (n)	20	5	2
Adjuvant Systemic Treatment (22.7%)				
Dacarbazine (n)		16	3	-
Interferon-alpha (n)		-	20	1
Systemic Treatment of Irresecable/Disseminated Melanoma (25%)				
Dacarbazine (n)		6	10	1
Other chemotherapy (*cisplatin, BOLD regimen, fotemustine*) (n)		4	8	-
Targeted treatment (*imatinib*, *dabrafenib + trametinib*) (n)		-	-	3
Immunotherapy (i*pilimumab*, *nivolumab*, *pembrolizumab*) (n)		-	-	11
Radiotherapy (16.5%)				
Adjuvant (lymph node region) (n)		2	3	4
Metastases (lymph node, cutan, brain) (n)		6	13	1
Electrochemotherapy (2.2%)				
Locoregional cutan/subcutan metastasis (n)		–	3	1

Figure 6. Kaplan–Meier overall survival curves of patients with ALM treated during two time periods according to the availability of the sentinel lymph node biopsy technique (1976–1998 and 1999–2014)

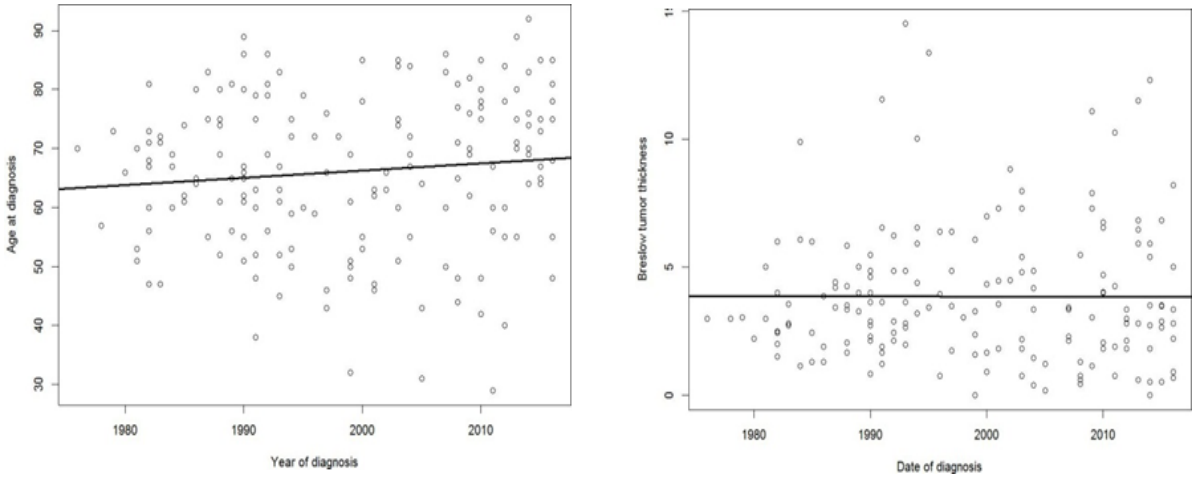


Year of diagnosis	5-year survival, % (95% CI)	10-year survival, % (95% CI)
1976-1998	37.74 (26.70-53.33)	7.55 (2.94-19.36)
1999-2014	74.33 (66.10-83.59)	63.72 (54.36-74.70)

4.1.4. Temporal trends over four decades

Across the four decades analyzed, no significant changes were observed in mean Breslow thickness (p = 0.964) or mean patient age at diagnosis (p = 0.157) (Figure 7).

Figure 7. Distribution of (a) mean age at diagnosis and (b) mean Breslow primary tumor thickness of ALM cases across four consecutive decades (1976-2016)



The absolute number of ALM cases diagnosed per decade remained relatively constant. In contrast, when considering all CMM cases diagnosed at our center, the relative proportion of ALM decreased significantly over time ($p < 0.001$), coinciding with a marked increase in the incidence of SSM (Figure 4).

4.1.5. Comparisons with other published international cohorts

Comparisons with European ALM cohorts involving predominantly Caucasian populations (Table 5) revealed broadly similar patient demographics and tumor characteristics, including older age at diagnosis, female predominance, and preferential involvement of the lower extremities. Mean Breslow thickness exceeded 2 mm in all comparative studies; however, the thickness observed in our cohort (nearly 4 mm) was among the highest reported, second only to data form the United Kingdom.[10,92,94,118]

Table 5. Comparison of our data with other studies involving Caucasians.[10,92,94,118]

	France (2006)	**Spain (2009)**	**United Kingdom (2014)**	**Germany (2017)**	**Hungary (2019)**
Duration period	1996–2004	1987–2007	1996–2006	1983–2015	1976–2016
N	126	89	87	2243	176
Non-Caucasian Patients (n)	Asian (1)	Asian (2)	–	–	–
Mean age (years)	63.0	61.6	67.0	63.1	66.2
Male:female ratio	1:1.86	1:1.69	1:1.71	1:1.48	1:1.26
Mean Breslow tumor thickness (mm)	2.51	2.8	7.9	3.08	3.86
Location	87.3%, lower extremities 37%, nails	79.8%, lower extremities 24.7%, nails	84%, lower extremities no data	82.1%, feet 35.6%, nails	88.6%, lower extremities 14.2%, nails

4.2. Factors influencing early detection of malignant melanoma

A total of 153 patients were enrolled in the study and completed the questionnaire in 2015; of these, 139 patients were eligible for statistical analysis.

4.2.1. Patient demographics and primary tumor characteristics

The mean age of the study population was 59 years (range: 22–93 years). No statistically significant differences in the mean age were observed across tumor thickness categories (*in*

situ: 57.3 years; ≤1 mm: 57.8 years; >1 mm: 62.5 years). Overall, 12% of patients were younger than 40 years, 40% were between 40-60 years, and 48% were older than 60 years. Among patients diagnosed with melanomas thicker than 1 mm, 63% were over 60 years of age.

Gender distribution was nearly equal (70 males, 69 females). Regarding educational attainment, 19% of respondents had primary education, 31% vocational training, 27% secondary education, and 23% higher education (Table 6).

Table 6. Demographic characteristics of patients (n=139)

Demographic characteristic	Value
Mean age at diagnosis, years	59 (22-93)
Age groups, n (%)	
<40 years	16 (12%)
40-60 years	56 (40%)
>60 years	67 (48%)
Gender, n (%)	
Male	70 (50%)
Female	69 (50%)
Educational level, n (%)	
Primary school	26 (19%)
Vocational school	43 (31%)
Secondary school	38 (27%)
Higher level	32 (23%)
Caucasian Ethnicity, n (%)	139 (100%)

The mean Breslow thickness of the primary excised melanomas was 1.645 mm (range: 0.152-17.024 mm). Nineteen percent of patients were diagnosed with melanoma *in situ*, 44% with melanoma ≤1 mm, and 37% with melanoma >1 mm.

Histopathological evaluation revealed that the superficial spreading melanoma was the predominant subtype (69%), followed by nodular melanoma (16%), lentigo maligna melanoma (6%), acral lentiginous melanoma (4%), and lentigo maligna (1%). Among thin melanomas (≤1 mm), SSM predominated, whereas in melanomas >1 mm, SSM and NM occurred at comparable frequencies.

Histological ulceration was present in 20 tumors (14%), of which 15 cases (75%) occurred in melanomas thicker than 1 mm. The most common tumor location was the trunk (53%), followed by the lower extremities (20%), head and neck (15%), and upper extremities (12%).

Among melanomas >1 mm, the trunk (45%) and the lower extremities (31%) were most frequent sites (Table 7).

Table 7. Clinicopathological characteristics of primary melanomas

Clinicopathological characteristic	Value
Mean Breslow thickness, mm (range)	1,65 (0,15-17,02)
Breslow thickness category, n (%)	
melanoma *in situ*	26 (19%)
≤1 mm	62 (44%)
>1 mm	51 (37%)
Anatomical location, n (%)	
trunk	73 (53%)
lower extremities	28 (20%)
head and neck	21 (15%)
upper extremities	17 (12%)
Histological subtype, n (%)	
superficial spreading melanoma	96 (69%)
nodular melanoma	23 (16%)
lentigo maligna melanoma	9 (6%)
acral lentiginous melanoma	5 (4%)
lentigo melanoma	1 (1%)
other	5 (4%)
Microscopic ulceration present, n (%)	20 (14%)

4.2.2. Melanoma patients' preventive behaviors, including skin self-examination

General health awareness was assessed through participation in cancer screening programs and routine health monitoring. Among female patients, 71% reported previous participation in mammography and 77% in cervical cancer screening, while 30% of male respondents had undergone prostate cancer screening. Colonoscopy participation was 20% in both sexes.

In the year preceding melanoma diagnosis, 94% of patients were aware of their blood pressure values and 70% knew their cholesterol levels. In contrast, adherence to photoprotective behaviors was limited: 27% regularly used sunscreen, 23% wore wide-brimmed hats, and 28% reported using protective clothing (Table 8).

Skin self-examination practices were also evaluated. Thirty-five percent of respondents (n=, 49) did not perform any skin self-examination. Among those who did, nearly half examined more than six of the thirteen predefined body regions. No significant differences were observed among tumor thickness groups in the frequency or thoroughness of self-examination ($p > 0.05$).

Only six patients (4%) reported consulting melanoma-specific visual reference materials prior to self-examination.

Approximately half of the respondents reported assistance from partners, family members, or friends in monitoring nevi (46%) or performing skin examinations (52%). Although 61% of patients were married and 77% lived with someone, neither marital status nor cohabitation was significantly associated with earlier melanoma detection ($p > 0.05$).

Table 8. General health awareness and preventive behavior of patients

Variable	n/N	%
Participation in cancer screening programs		
Mammography (female patients only)	49/69	71.0
Cervival cancer screening (female patients only)	53/69	77.0
Prostate cancer screening (male patients only)	21/70	30.0
Colon cancer screening (both sexes)	28/139	20.1
General health awareness		
Aware of blood pressure value in the year preceding diagnosis	131/139	94.2
Aware of cholesterol level in the year preceding diagnosis	98/139	70.5
Photoprotective behaviors		
Regular sunscreen use	37/139	26.6
Regularly use of a wide-brimmed hat	32/139	23.0
Regularly use of protective clothing	39/139	28.1

4.2.3. Knowledge and attitudes of melanoma patients toward skin cancer

In the year preceding diagnosis, 71% of patients considered themselves attentive to their health; however, only 15% actively sought information on early detection of skin cancer. Patients who regarded the monitoring of suspicious skin lesions as unimportant were diagnosed with significantly thicker melanomas, whereas 80% of *in situ* and ≤1 mm melanoma occurred among patients who considered early detection as important ($p = 0.027$).

Prior to diagnosis, 74% of respondents did not perceive themselves to be at risk for melanoma, and only 13% believed their risk was higher than that of others. Furthermore, 38% were unaware that melanoma is a malignant skin tumor before diagnosis. Even after diagnosis, 29% did not consider melanoma a serious disease, and 44% did not anticipate substantial health consequences.

4.2.4. Health care utilization and physician skin examination

In the year preceding melanoma diagnosis, 72% of patients reported at least one physician visit for any reason (Table 9). A skin examination was performed in only 28% of these encounters, of which 72% were full-body examinations and 28% were partial examinations. Slightly more than half (54%) occured as part of routine care, while 46% were initiated by the patient or a relative/friend.

Only 13% of patients had ever discussed melanoma with a healthcare professional, 9% had been informed of their personal melanoma risk, 8% had received specific instructions regarding skin self-monitoring, and 6.5% were aware of having atypical nevi.

Table 9. Healthcare utilization and physician-patient communication related to skin cancer in the year preceding the melanoma diagnosis

Variable	n/N	%
Healthcare utilization		
At least one physician visit in the year preceding diagnosis	100/139	71.9
Physician skin examination during medical visit		
Any skin examination performed	39/139	28.1
full-body skin examination	28/39	71.8
partial (lesion-focused) examination	11/39	28.2
Initiation of skin examination		
Performed as part of routine clinical care	21/39	53.8
Initiated by patient or relative/friend	18/39	46.2
Physician–patient communication		
Discussion of melanoma with a physician	18/139	12.9
Informed of increased personal melanoma risk	12/139	8.6
Received specific guidance on skin self-monitoring	11/139	7.9

4.2.5. Circumstances of initial melanoma detection

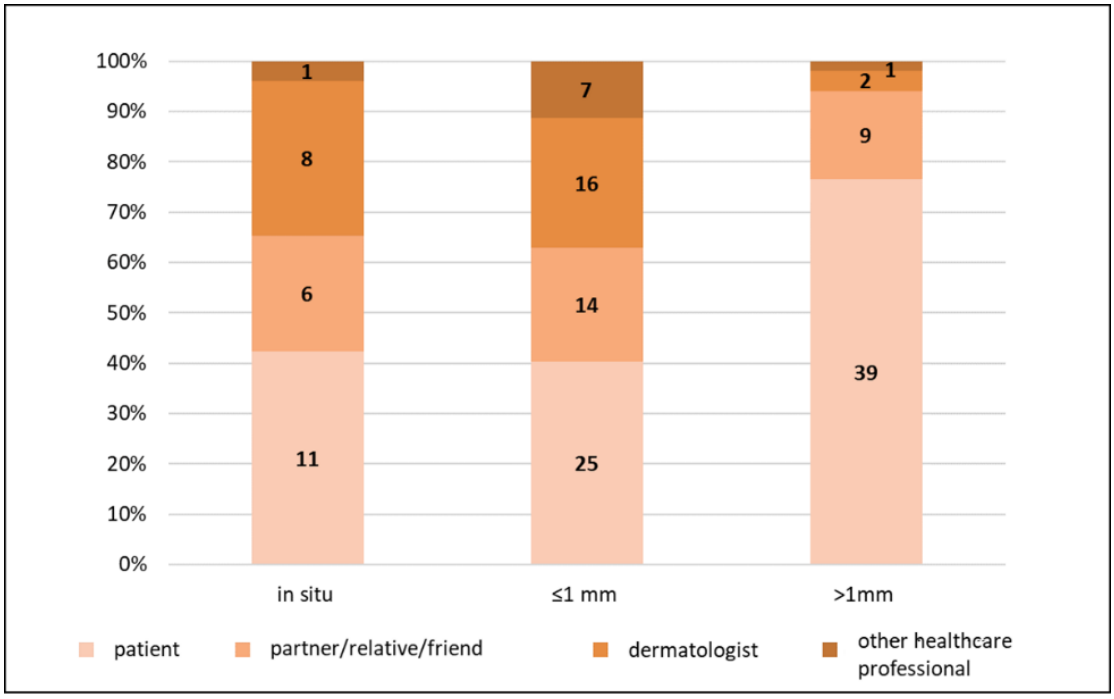
In 54% of cases, the lesion later diagnosed as melanoma was first noticed by the patient; 25% were first identified by physicians (18% by dermatologists and 7% by other physicians); and 21% by partners, family members, or friends (Figure 8). Across all tumor thickness categories, patients were the most frequent initial detectors of melanoma.

Among melanomas thicker than 1 mm, 94% were initially detected by patients or laypersons, whereas approximately 65% of *in situ* or ≤1 mm melanoma were identified by these groups. Mean Breslow thickness varied according to the initial detector: dermatologist (0.384 mm), another physician (1.003 mm), relative (1.913 mm), and patient (2.048 mm).

Patients most reported noticing changes in lesion size (50%), color (40%), elevation (33%), or overall appearance (37%). Seven percent reported that the lesion had always been present, 32%

noticed it more than one year prior to diagnosis, 45% within one year, and 17% only at the time of diagnosis. Among patients who delayed seeking medical attention, the most frequently cited reason was lack of concern about the lesion (48%), followed by time constraints and competing health issues. Once medical consultation occurred, 88% of patients received specialized assessment and/or surgical excision within approximately 10 days.

Figure 8. Person first noticing the skin lesion later diagnosed as melanoma (%, n)



5. DISCUSSION

5.1. Acral lentiginous melanoma: a single-center retrospective review

ALM is a rare subtype of CMM in Caucasian populations, accounting for less than 10% of cases, yet it is consistently associated with advanced stage at diagnosis and inferior survival outcomes.[10,90] Over the past four decades, ALM represented 3.83% of all cutaneous melanoma patients treated at our center. In line with previous reports, ALM predominantly affected elderly individuals, with most cases diagnosed in patients aged 70 or older.[10,44,66,90] The mean age at diagnosis in our cohort exceeded 65 years, aligning with findings from previous research.[94]

The literature on sex predominance in ALM is conflicting.[92] While some studies, such as that by Phan *et al.*, reported a female predominance with female sex as an independent prognostic

factor, others found no significant sex-based differences.[10,66,90,92] In our study, the male-to-female ratio was 1:1.26, supporting the absence of a strong sex predilection.

ALM in our study was commonly diagnosed at an advanced tumor thickness, as reflected by the mean Breslow thickness of nearly 4 mm, with 75% of tumors exceeding 2 mm and more than half invading Clark level IV or V. This thickness in substantially higher than that reported in most Caucasian ALM series.[10,16,92,94] These prevalent adverse histopathological features–including also microscopic ulceration–were indicating biologically aggressive disease at presentation. Anatomically, ALM lesions occurred in nearly 90% of cases on the lower extremities, most commonly on the soles and heels. Subungual melanoma comprised 14.2% of cases and was more frequently observed on the lower extremities, consistent with previous reports.[92] While tumor location and patient age were comparable to other studies, the Breslow thickness at presentation was greater in our cohort.[46,92,119]

SLN biopsy has been routinely performed at our institution since 1999. In our study, SLN-positivity was significantly more common ($p < 0.001$) than that reported by Pavri *et al.*, and was strongly associated with greater Breslow thickness, underscoring the close relationship between primary tumor burden and early regional metastatic spread.[120]

Patients with ALM have consistently poor survival and an unfavorable prognosis. In the landmark study by Bradford *et al.*, the 5- and 10-year melanoma-specific survival rates for patients with cutaneous malignant melanoma were 91.3% and 87.5%, respectively, whereas patients with ALM experienced significantly worse outcomes, with corresponding survival rates of 80.3% and 67.5%.[44] Notably, survival outcomes in our cohort were inferior to those reported in most Caucasian ALM series (5-year OS: 70%–80%; 10-year OS: 56%–67%), with 5- and 10-year overall survival rates of 61% and 42% respectively, confirming the particularly unfavorable prognosis in our population.[44,66,92]

Disease-specific survival was strongly stage-dependent, demonstrating a clear and progressive decline in survival with advancing TNM stage. The most pronounced survival differences were observed between stages I and III, as well as between stages I and IV, underscoring the major prognostic impact of regional lymph node involvement and distant metastases. Primary tumor thickness exerted a similarly strong influence on outcome: the most substantial survival difference was observed between tumors ≤2 mm (T1–T2) and those >4 mm (T4). Across all analyses, tumors exceeding 4 mm in Breslow thickness were consistently associated with markedly reduced survival, highlighting advanced tumor thickness as a major determinant of poor prognosis. In summary, survival in acral lentiginous melanoma was poor and strongly dependent on disease stage, primary tumor thickness, and sentinel lymph node status. Early-

stage disease and thin tumors were associated with favorable outcomes, whereas advanced stage, increased Breslow thickness, and nodal involvement predicted significantly worse survival. Age (HR 1.058), Breslow thickness (HR 1.187), and presence of distant metastases (HR 3.002) were the strongest independent predictors of worse disease-specific survival.

Diagnostic delay is a well-recognized hallmark of ALM and is widely considered one of the major contributors to its poor prognosis. Previous studies have reported average diagnostic delays exceeding seven months, attributable to factors such as advanced patient age, cognitive decline, hidden anatomical location, atypical or amelanotic presentation, limited public awareness, and misdiagnosis or delayed referral by healthcare professionals.[92,118] Rex *et al.* and Teramoto *et al.* have suggested that the unfavorable outcomes of ALM are driven primarily by diagnostic delay rather than intrinsic biological aggressiveness.[10,94] In our cohort, more than half of patients delayed seeking medical attention for over one year, and nearly 12% for more than three years. While Phan *et al.* reported delays ranging from 2 months to 30 years; the interval in our study ranged from 1 month to 10 years, emphasizing the persistent and clinically relevant nature of this problem.[92] These prolonged delays may contribute to the excessive Breslow thickness and advanced stage observed in our patients at diagnosis.

Our long-term study enabled us to evaluate temporal trends in epidemiology, diagnostic characteristics, and outcomes across four decades, reflecting changes in awareness, diagnostic practices, and therapeutic approaches.

The absolute number of ALM cases remained stable over the four decades studied, while the relative proportion of ALM among all cutaneous malignant melanomas declined significantly, in parallel with a marked increase in superficial spreading and lentigo maligna melanoma.

No significant improvements in diagnostic characteristics were observed over time, as mean Breslow thickness and age at diagnosis remained unchanged, indicating persistently late-stage presentation of ALM despite increasing melanoma awareness.

Beyond tumor- and patient-related factors, treatment advances have undoubtedly influenced melanoma survival over the four decades. Surgical management evolved significantly, with a transition from elective regional lymph node dissection to sentinel lymph node biopsy, improving nodal staging accuracy and surgical practice. Overall survival improved significantly after 1999, coinciding with changes in surgical management; however, patients treated in the earliest period more frequently presented with clinically advanced disease (nodal metastases). Therapeutic strategies evolved substantially during this period, particularly with the introduction of modern systemic therapies. Kaplan–Meier analyses suggested an overall improvement in survival over time; however, due to the heterogeneity and continuous evolution

of treatment modalities, and the low sample size undergoing novel systemic therapies; reliable conclusions regarding their impact on survival cannot be drawn from our retrospective analysis. In summary, over four decades, the epidemiology of acral lentiginous melanoma remained largely unchanged in terms of absolute case numbers, with no improvement in tumor thickness at diagnosis or patient age at presentation. While advances in surgical staging were associated with improved survival, substantial diagnostic delay persisted, and the limited use of systemic therapies prevented meaningful assessment of their effect on outcomes.

Our findings were largely comparable to those reported in other Caucasian cohorts, including patient demographics (older age, slight female predominance) and anatomical distribution (preferential involvement of the lower extremity) of ALM. Mean Breslow thickness exceeded 2 mm across all comparative European studies, confirming that ALM is generally diagnosed at an advanced stage in Caucasian populations. Tumors in our cohort exhibited among the greatest Breslow thicknesses reported, second only to data from the United Kingdom, indicating particularly advanced disease at diagnosis. This finding provides a plausible explanation for the poor survival outcomes observed in our region.[10,16,66,90,92,94,118]

In conclusion, this first single-center, long-term analysis of ALM from Central-Eastern Europe demonstrates that, despite improvements in melanoma awareness and diagnostic practices, ALM continues to be diagnosed at an advanced stage with excessive tumor thickness in our region.[121] While patient demographics and tumor distribution are comparable to those reported elsewhere, the pronounced diagnostic delay observed in our cohort represents the most important modifiable determinant of prognosis. These findings underscore the urgent need for targeted educational and preventive strategies aimed specifically at improving early detection of ALM, particularly among elderly patients and healthcare professionals.

5.2. Factors influencing early detection of malignant melanoma

From a clinicopathological perspective, increasing melanoma thickness was associated with older age, the presence of ulceration, and more aggressive histological subtypes. Superficial spreading melanoma predominated among thin lesions, whereas nodular melanoma occurred with comparable frequency in tumors thicker than 1 mm. Thicker melanomas were more commonly located on the trunk and lower extremities. Sociodemographic factors, including sex and educational level, were not significantly associated with melanoma thickness in our cohort.

General health awareness among melanoma patients appeared high, as reflected by participation in routine screening programs and cardiovascular health monitoring. However, melanoma-specific preventive behaviors were limited, particularly with respect to photoprotection and skin self-examination. Skin self-examination was infrequent and often incomplete, and neither its frequency nor thoroughness was associated with thinner melanoma at diagnosis, suggesting limited effectiveness of unstructured self-examination practices. Knowledge and attitudes toward melanoma were also insufficient: most patients underestimated their personal risk and lacked basic awareness of melanoma as a malignant disease prior to diagnosis, with a substantial proportion maintaining this misconceptions even after diagnosis. Notably, perceived importance of early detection was significantly associated with melanoma thickness, as patients who regarded monitoring suspicious lesions as unimportant were diagnosed with significantly thicker tumors. Social support, measured by marital status or cohabitation, did not translate into earlier diagnosis, indicating that informal assistance alone is insufficient to reduce diagnostic delay.

Despite frequent healthcare utilization–most patients reported at least one physician visit in the year preceding melanoma diagnosis–opportunities for early detection were often missed. Physician-performed skin examinations occurred in fewer than one-third of medical consultations, despite regular contact with the healthcare system. When conducted, skin examinations were frequently opportunistic rather than systematic, and nearly half were initiated by patients or relatives rather than by physicians. Melanoma-specific counseling by healthcare professionals was rare, with only a small minority of patients receiving information on melanoma risk, skin self-monitoring, or atypical nevi. Overall, our findings point out, that limited physician engagement in skin cancer prevention and early detection likely contributes to delayed melanoma diagnosis, despite sufficient healthcare utilization.

Patients were the most frequent first detectors of melanoma across all tumor thickness categories, underscoring the central role of self-recognition in the melanoma diagnostic pathway. Importantly, melanomas first identified by physicians–especially dermatologists–were diagnosed at significantly thinner stages, indicating more effective early detection through professional skin examination. In contrast, melanomas thicker than 1 mm were predominantly detected by patients or laypersons, whereas physician detection was more common among *in situ* and thin melanomas. This finding demonstrating a clear association between the initial detector and Breslow thickness at diagnosis.

Delays in seeking medical attention were primairly attributable to low perceived concern about the lesion, rather than delayed access to specialist care, as diagnostic work-up and/or surgical

excision occurred rapidly after first consultation. Collectively, these findings indicate that while patient self-detection represents the most common route to melanoma recognition, it is less effective for early-stage detection than physician-led identification. This underscores the need for improved public awareness and more systematic skin self-examinations in routine clinical practice.

A substantial body of literature has examined patient-, physician-, and healthcare system-related factors influencing early melanoma detection.[104,122-130] To date, only two studies–conducted in the United States and Greece–have applied the standardized Melbehav questionnaire developed by Susan M. Swetter *et al.* to investigate these determinants.[100,101] These studies provide an important comparative framework for interpreting our findings.

In the US cohort, most respondents were male (61%), the median Breslow thickness was 1.25 mm, and more than half of melanomas (57%) exceeded 1 mm at diagnosis. Thin melanomas (≤1 mm) were more frequently associated with SSM and LMM subtypes, absence of ulceration, extremity or trunk localization, younger age (≤60 years), female sex, higher educational attainment, and participation in routine medical care. Early detection was also more common among individuals who performed skin self-examination using melanoma-specific photographic references or who had been informed about atypical nevi. Among men older than 60 years, thinner melanomas were more likely to be detected when a full-body skin examination was incorporated into routine medical visits.[100]

In the Greek study, thinner melanomas were more commonly located on the head, neck, and upper extremities, and educational level was not significantly associated with Breslow thickness.[101] Instead, self-examination practices and marital status emerged as the strongest determinants of early detection, with married individuals being more than three times as likely to be diagnosed with melanoma ≤1 mm compared with unmarried participants.[101]

By applying the same standardized questionnaire, our study provides the first Central-Eastern European dataset directly comparable with US and Greek cohorts.[100,101] Unlike those studies–where self-examination practices, marital status, or educational level were associated with thinner melanomas–none of these factors independently predicted early detection in our population.[100,101] These findings indicate that the determinants of early melanoma detection are population- and healthcare system–dependent, and that strategies effective in other countries cannot be directly extrapolated to Central-Eastern Europe without careful contextual adaptation.

6. LIMITATIONS

The present PhD thesis integrates two studies that together provide novel and clinically relevant insights into acral lentiginous melanoma and factors influencing early detection of melanoma in a Central–Eastern European setting. The strengths and limitations of each study should be considered when interpreting the findings.

6.1. Acral lentiginous melanoma: a single-center retrospective review

A major strength of this study is that it represents the first comprehensive regional evaluation of acral lentiginous melanoma in Central–Eastern Europe. The analysis spans four decades, allowing detailed assessment of clinicopathological characteristics, survival outcomes, prognostic factors, and temporal trends across substantial changes in melanoma diagnosis and management. The application of clearly defined anatomical and histopathological inclusion criteria ensured a homogeneous ALM cohort, while standardized survival analyses enabled the identification of independent prognostic determinants.

The main limitations of this analysis stem from its retrospective, single-center design, which may limit generalizability and is inherently subject to incomplete documentation and potential selection bias, particularly in earlier decades. Patient-reported diagnostic delay may also be affected by recall bias. Although staging was harmonized according to the AJCC 8th edition where possible, residual heterogeneity in diagnostic criteria, staging systems, and therapeutic approaches over the 40-year study period may have influenced survival analyses. In addition, the limited availability of molecular data and the late introduction of modern systemic therapies restricted evaluation of biological factors and contemporary treatment effects. Comparisons with international cohorts were descriptive in nature, as differences in study design, population characteristics, and reporting standards precluded formal statistical analyses.

6.2. Factors influencing early detection of malignant melanoma

A key strength of the second study is the use of the validated Melbehav questionnaire, which enabled a systematic assessment of patient-, physician-, and healthcare system–related determinants of early melanoma detection and allowed direct comparison with cohorts from the United States and Greece. The integration of questionnaire data with clinicopathological variables provided a comprehensive overview of the melanoma diagnostic pathway. Together, these methodological strengths enhance the internal validity, comparability, and clinical relevance of the findings and support their applicability to region-specific prevention and early detection strategies.

Several limitations should also be acknowledged. The questionnaire-based design relied on self-reported data, which are subject to recall bias and social desirability bias, particularly with respect to preventive behaviors and healthcare utilization. Although the Melbehav questionnaire is a validated instrument and was translated and pilot-tested for use in this study, cultural and healthcare system differences may have influenced the interpretation of certain items. The relatively modest sample size may have limited statistical power to detect weaker associations. Furthermore, comparisons with US and Greek cohorts were qualitative and descriptive rather than statistical, limiting direct cross-population inference. Despite these limitations, the consistency of findings across both studies supports the robustness of the main conclusions.

7. CONCLUSIONS

7.1. Acral lentiginous melanoma: a single-center retrospective review

Our study provides novel regional data on epidemiology, clinicopathological features, survival, and diagnostic delay of acral lentiginous melanoma. The findings underscore the persistent clinical challenges associated with this melanoma subtype, particularly delayed diagnosis, advanced disease stage at presentation, and its consistently unvavorable prognosis.

Key conclusions:

- This study represents the first comprehensive, long-term, single-center cohort analysis of acral lentiginous melanoma from Central–Eastern Europe, addressing a major gap in regional melanoma epidemiology and outcome data.
- Acral lentiginous melanoma is a rare melanoma subtype that predominantly affects elderly patients and is characterized by unfavourable histopathological features and advanced stage at diagnosis.
- Survival in acral lentiginous melanoma is poor, with age, Breslow thickness and stage at diagnosis representing the main independent prognostic factors.
- Across four decades, no substantial changes were observed in epidemiology, tumor thickness, or patient age at diagnosis.
- Demographic and anatomical characteristics of ALM were largely comparable to other Caucasian cohorts; however, Breslow thickness was among the highest reported.

7.2. Factors influencing early detection of malignant melanoma

This single-center study identified patient-, physician-, and healthcare system–related determinants of early melanoma detection in a Central-Eastern European cohort. Early detection was driven primarily by patients' attitudes toward skin monitoring and the perceived importance of early diagnosis, rather than by demographic, educational, or social characteristics. Although skin self-examinations was commonly reported, it was ineffective in the abscence of melanoma-specific knowledge and guidance.

Key conclusions:

- This study provides the first Central-Eastern European data on early melanoma detection using a previously developed, standardized questionnaire.

- Greater Breslow thickness (>1 mm) was associated with unfavorable clinicopathological profile, including older age at diagnosis, ulceration, and nodular subtypes, while no clear association was observed with gender or eductional level.
- Early melanoma detection depend primarly on patients' attitudes toward skin monitoring and the percieved importance of early diagnosis, while skin self-examination alone–without melanoma-specific knowledge–was insufficient to ensure early detection.
- Despite frequent healthcare utilization, low rates of physician-performed skin examination and melanoma-specific counseling represented substantial missed opportunities for early detection.
- Melanomas detected by healthcare professionals were diagnosed at significantly thinner stages than those identified by patients or laypersons.
- Determinants of early detection differed from those reported in the US and Greek cohorts, underscoring the need for region-specific, healthcare system-adapted early detection strategies.

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DECLARATION

The studies were conducted in accordance with the Declaration of Helsinki, approved and permitted by the National Council of Health Sciences, Scientific and Research Ethics Committee (MEL-RETRO-001, 23/FEB/2015) and the Regional and Institutional Review Board of Human Investigations in University of Szeged (MEL-RETRO-001, 23/FEB/2015).

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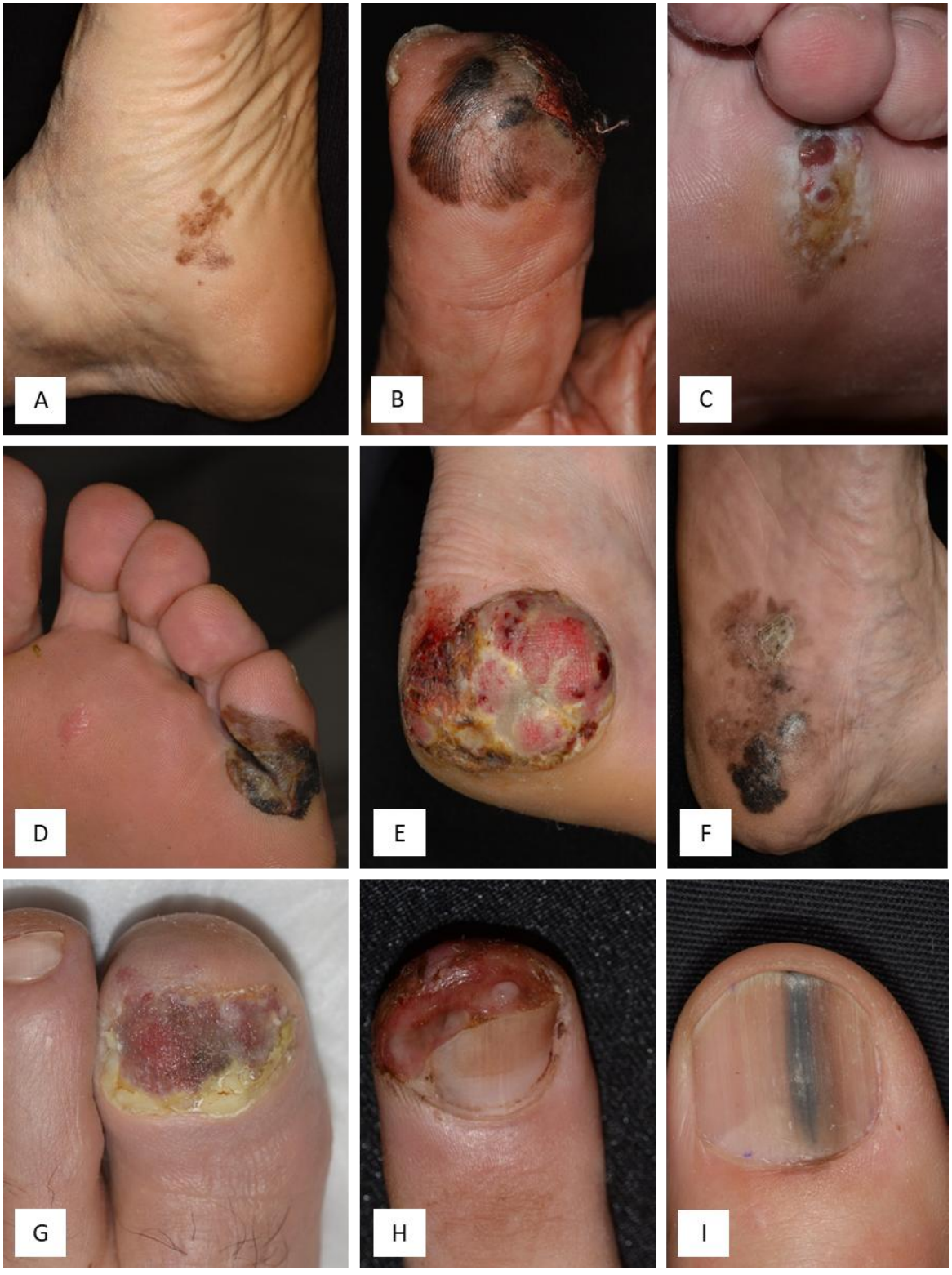
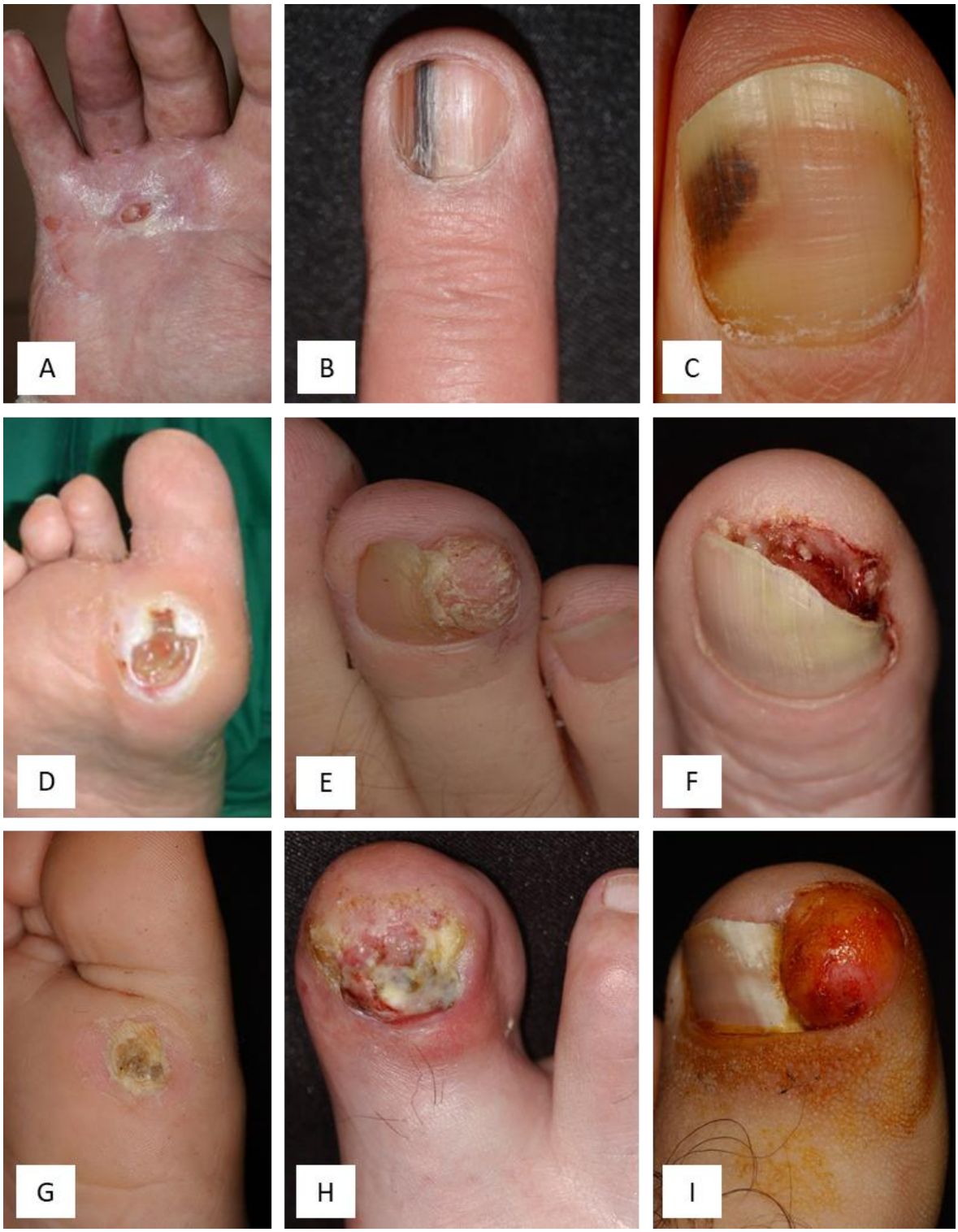
Appendix 1. Heterogenous clinical presentation of acral melanoma. (A): 74-year-old female, left sole, pT1a; (B): 82-year-old female, left thumb, pT4b; (C): 65-year-old male, left sole, pT4b; (D): 40-year-old male, left sole, pT3b; (E): 60-year-old male, right heel, pT4b; (F): 75-year-old male, right sole, pT3b; (G): 54-year-old male, left great toe, pT4b; (H): 46-year-old male, right index finger, pT4b; (I): 71-year-old male, right thumb, pT1a.



Appendix 2. Differential diagnosis for palmoplantar and nail unit melanoma. (A): squamous cell carcinoma, (B): subungual junctional lentigo with melanocyte activation, (C): subungual haemorrhage, (D): diabetic foot ulcer, (E): epitheloid sarcoma, (F): squamous cell carcinoma, (G): viral wart, (H): Langerhans cell histiocytosis, (I): periungual exostosis.



Appendix 3. An accurately translated Hungarian version of the English questionnaire created by Susan M. Swetter, which we used in our prospective questionnaire study.[100]

A melanoma sikeres korai felismerésének viselkedésbeli meghatározói

KÉRDŐÍVES FELMÉRÉS

Köszönjük, hogy beleegyezett a vizsgálatba. Felmérésünk célja, hogy a melanomában szenvedő betegeink tapasztalatairól és véleményéről minél többet megtudjunk.
A továbbiakban kérdéseket fogunk Önnek feltenni.

I. HÁTTÉR INFORMÁCIÓ

1. Mikor született? _____év_____hónap

2. Milyen nemű? ( ) férfi ( ) nő

3. Milyen végzettséggel rendelkezik? (Kérjük egyetlen választ adjon meg.)

( ) alapfokú (általános iskola)
( ) szakmunkás
( ) középfokú (érettségi)
( ) felsőfokú (főiskola, egyetem)
( ) egyéb

4. Milyen eredetű?
( ) európai
( ) ázsiai
( ) ausztrália
( ) afrikai
( ) egyéb, kérem adja meg: _____

A következő részben a melanomáról és a bőrtípusáról fogjuk kérdezni.

II. MELANOMA RIZIKÓTÉNYEZŐI

1. Ez az első melanomája? ( ) igen ( ) nem ( ) nem tudom
2a. Volt-e a melanomán kívül egyéb bőrrákja (pl.: bazalióma, laphám carcinoma)?
( ) igen ( ) nem ( ) nem tudom
2b. Amennyiben volt, figyelmeztette-e kezelőorvosa, hogy ellenőrizze a bőrrák miatt a bőrét?
( ) igen ( ) nem ( ) nem tudom
3. Első fokú rokonainál (anya, apa, testvér, gyermek) előfordult-e melanoma?
( ) igen ( ) nem ( ) nem tudom
4. Milyen színű a bőre (napozás nélkül)? (Kérjük egyetlen választ adjon meg.)
( ) nagyon világos ( ) világos ( ) közepes ( ) sötét ( ) nagyon sötét ( ) nem tudom
5. Hogyan reagál bőre, ha nyáron a déli órákban napon tartózkodik fényvédelem nélkül?
( ) mindig leég ( ) általában leég ( ) néha ég le ( ) ritkán ég le ( ) soha nem ég le
6. Hogyan reagál bőre, ha több alkalommal a napon tartózkodik fényvédelem nélkül?
( ) nagyon lebarnulok ( ) mérsékelten barnulok le ( ) enyhén vagy alkalmanként barnulok
( ) egyáltalán nem barnulok le vagy csak szeplős leszek ( ) nem tudom

Felmérésünk során minél többet szeretnénk megtudni melanomás betegeinkről a diagnózis felállítását <u>megelőző</u> időszakra koncentrálva. A kérdések megválaszolásakor a diagnózis felállítását <u>megelőző egy évre</u> gondoljon vissza. Ezáltal tanulmányozni tudjuk, hogy milyen egészségügyi szokásai voltak <u>mielőtt</u> a melanomát diagnosztizálták Önnél. Kérjük válaszoljon a kérdésekre legjobb tudása szerint.

III. DEMOGRÁFIA, EGÉSZSÉGÜGYI ÉS PREVENCIÓS SZOKÁSOK

Kérjük gondoljon vissza egészségügyi szokásaira a melanoma diagnosztizálását megelőző 12 HÓNAP-ban.

1. Milyen volt a családi állapota?
( ) házas
( ) özvegy
( ) egyedülálló-soha nem volt házas
( ) elvált vagy különélő

2. Együtt élt partnerével vagy házastársával? ( ) igen ( ) nem

3. Volt egészségügyi biztosítása? ( ) igen ( ) nem
Amennyiben igen, kérem jelölje meg az összes Önre vonatkozó típust?
( ) állami egészségbiztosítás
( ) magán, éspedig: _____
( ) egyéb: _____

4. Kérjük jelölje meg a legutolsó évet, amikor az alábbi vizsgálatok történtek Önnél. Amennyiben a felsorolt vizsgálat még nem történt meg Önnél, jelölje meg a "soha" lehetőséget.

<u>kizárólag nők számára kitöltendő:</u>

vastagbél tükrözés/colonoscopia	utolsó dátum: ____ soha ____
emlőrák szűrés (mammográfia)	utolsó dátum: ____ soha ____
méhnyakrák szűrése (Pap festés/kenet)	utolsó dátum: ____ soha ____

<u>kizárólag férfiak számára kitöltendő:</u>

vastagbél tükrözés/colonoscopia	utolsó dátum: ____ soha ____
prosztatarák szűrés (PSA vizsgálat vérből)	utolsó dátum: ____ soha ____

5. Az elmúlt évben tudott-e a következőkről**:**

vérnyomás értéke?	( ) igen	( ) nem
koleszterinszintje?	( ) igen	( ) nem

6. Amikor egy napfényes napon a szabadban tartózkodott, használt-e <u>rendszeresen</u>:

fényvédő készítményt/naptejet?	( ) igen	( ) nem
széles karimájú kalapot, mely teljesen árnyékolja az arcát?	( ) igen	( ) nem
hosszú ujjú inget/pólót, hogy teljesen védje bőrét a naptól?	( ) igen	( ) nem

7. Melyik testrészeit ellenőrizte rutinszerűen? (Minden lehetséges választ jelöljön meg.)

	igen	nem		igen	nem		igen	nem
arc	___	___	fejbőr	___	___	nyak	___	___
váll	___	___	hát felső része	___	___	hát alsó része	___	___

alsó vgtg elülső fsz ___ ___ alsó vgtg hátsó fsz ___ ___ mellkas ___ ___
has ___ ___ talp ___ ___
felső vgtg elülső fsz ___ ___ felső vgtg hátsó fsz ___ ___

8. Amikor a bőrét ellenőrizte, használt-e melanomáról készült fotót (kiadvány, poszter, betegtájékoztató füzet)? ( ) igen ( ) nem

9. Milyen gyakran:

a. ellenőrizte az összes anyajegyét, beleértve a háton lévőket is?
   1 vagy 2 havonta ( )
   6 havonta ( )
   évente ( )
   soha ( )

b. nézte meg közelebbről családtagja vagy barátja az Ön hátán lévő anyajegyeket?
   1 vagy 2 havonta ( )
   6 havonta ( )
   évente ( )
   soha ( )

IV. HÁZASTÁRS/PARTNER/ROKON/BARÁT SZEREPE AZ ÖN EGÉSZSÉGÜGYI SZOKÁSAIBAN

Gondoljon vissza, hogy vajon házastársa, partnere, közeli barátja vagy más családtagja foglalkozott-e az Ön bármilyen egészségügyi problémájával a diagnózis előtti évben.

1. A házastársam/partnerem/barátom/családtagom többet törődött az egészségügyi problémámmal, mint én.
( ) nagyon egyetértek ( ) egyetértek ( ) egyet is értek meg nem is
( ) nem értek egyet ( ) egyáltalán nem értek egyet

2. A házastársam/partnerem/barátom/családtagom sokat segített abban, hogy biztosan elmenjek az orvoshoz.
( ) nagyon egyetértek ( ) egyetértek ( ) egyet is értek meg nem is
( ) nem értek egyet ( ) egyáltalán nem értek egyet

3. A házastársam/partnerem/barátom/családtagom segített ellenőrizni a bőrömet, beleértve azokat a területeket, amiket én nem látok.
( ) nagyon egyetértek ( ) egyetértek ( ) egyet is értek meg nem is
( ) nem értek egyet ( ) egyáltalán nem értek egyet

4. Segített Önnek házastársa/partnere/barátja/családtagja a következőkben? (Kérjük minden lehetséges választ jelöljön meg.)
- többet megtudni az egészségügyi problémájáról ( ) igen ( ) nem
- beszélni az orvossal az Ön egészségügyi problémájáról ( ) igen ( ) nem
- vizsgálati időpontot egyeztetni az Ön számára ( ) igen ( ) nem
- az egészségügyi problémájával kapcsolatosan dönteni ( ) igen ( ) nem

V. HOZZÁÁLLÁS A MELANOMÁHOZ

A következő részben arról fogjuk kérdezni, hogy hogyan vélekedett a melanomáról a diagnózisát felállítását megelőző egy évben.

1. Odafigyeltem az egészségemre.
( ) nagyon egyetértek ( ) egyetértek ( ) egyet is értek meg nem is
( ) nem értek egyet ( ) egyáltalán nem értek egyet

2. Rendszeresen érdeklődtem a bőrrákok felismerésének lehetőségeiről.
( ) nagyon egyetértek ( ) egyetértek ( ) egyet is értek meg nem is
( ) nem értek egyet ( ) egyáltalán nem értek egyet

3. Fontos volt számomra, hogy figyeljem a bőrömön a melanomára utaló jeleket.
( ) nagyon egyetértek ( ) egyetértek ( ) egyet is értek meg nem is
( ) nem értek egyet ( ) egyáltalán nem értek egyet

4. Fontos volt számomra, hogy egészségügyi szakember vizsgálja meg a bőrömet.
( ) nagyon egyetértek ( ) egyetértek ( ) egyet is értek meg nem is
( ) nem értek egyet ( ) egyáltalán nem értek egyet

5. Megfelelt számomra, hogy családtagom figyelje anyajegyeimet a hátamon, illetve azokon a bőrterületeken, ahol én nem látom őket.
( ) nagyon egyetértek ( ) egyetértek ( ) egyet is értek meg nem is
( ) nem értek egyet ( ) egyáltalán nem értek egyet

6. Kellemetlennek éreztem, hogy levetkőzzek egészségügyi szakember (pl. orvos, nővér, asszisztens) előtt bőrvizsgálat során.
( ) nagyon egyetértek ( ) egyetértek ( ) egyet is értek meg nem is
( ) nem értek egyet ( ) egyáltalán nem értek egyet

VI. A KOCKÁZAT MEGÍTÉLÉSE ÉS VISELKEDÉS
A következő kérdések során arról kérdezzük, hogy hogyan ítélte meg saját kockázatát melanoma szempontjából mielőtt diagnosztizálták.

1. Soha nem gondoltam arra, hogy veszélyeztetett vagyok melanoma szempontjából.
( ) nagyon egyetértek ( ) egyetértek ( ) egyet is értek meg nem is
( ) nem értek egyet ( ) egyáltalán nem értek egyet

2. Azt gondoltam, hogy a melanoma nem túl súlyos betegség.
( ) nagyon egyetértek ( ) egyetértek ( ) egyet is értek meg nem is
( ) nem értek egyet ( ) egyáltalán nem értek egyet

3. Figyelembe véve az Ön nemét és életkorát mit gondolt, hogy milyen esélye van a melanomára másokhoz képest?
( ) sokkal kevesebb ( ) kicsit kevesebb ( ) ugyanolyan ( ) kicsit több ( ) sokkal több

4. Melanoma diagnózisa esetén milyen súlyos egészségügyi következményekre számított?
( ) egyáltalán nem súlyos ( ) kicsit súlyos ( ) mérsékelten súlyos ( ) súlyos ( ) nagyon/extrém súlyos

5. Mennyire bízott magában, hogy:
a. meg tudja vizsgálni a hátán lévő anyajegyeit?
( ) egyáltalán nem ( ) kicsit ( ) közepesen ( ) nagymértékben ( ) teljes mértékben

b. össze tudja hasonlítani a hátán lévő anyajegyeit és felismeri, ha egy anyajegy eltér a többitől?
( ) egyáltalán nem ( ) kicsit ( ) közepesen ( ) nagymértékben ( ) teljes mértékben
c. anyajegyekről készült fényképek segítségével saját anyajegyeit meg tudja ítélni?
( ) egyáltalán nem ( ) kicsit ( ) közepesen ( ) nagymértékben ( ) teljes mértékben
d. fel tudna ismerni egy melanomát saját magán?
( ) egyáltalán nem ( ) kicsit ( ) közepesen ( ) nagymértékben ( ) teljes mértékben
6. Mennyire bízott abban, hogy az orvosa fel tudná fedezni az Ön melanomáját?
( ) egyáltalán nem ( ) kicsit ( ) közepesen ( ) nagymértékben ( ) teljes mértékben
7. Mennyire aggasztotta a melanoma?
( ) egyáltalán nem ( ) kicsit ( ) közepesen ( ) nagymértékben ( ) teljes mértékben

Kérjük válaszolja meg a következő kérdéseket, amennyiben <u>Ön vagy hozzátartozója</u> fedezte fel az anyajegyet, amiből melanoma lett. Amennyiben az orvosa fedezte fel, kérem hagyja ki a kérdéseket <u>8-tól 13-ig</u>. A következőkben lehetséges okokat fogunk felsorolni arra vonatkozólag, hogy Ön miért nem kereste fel orvosát a szokatlan anyajegy felfedezésekor.

8. Túl nehéz volt (közlekedésileg) eljutni az orvoshoz.
( ) nagyon egyetértek ( ) egyetértek ( ) egyet is értek meg nem is
( ) nem értek egyet ( ) egyáltalán nem értek egyet

9. Nem volt időm, hogy elmenjek az orvoshoz.
( ) nagyon egyetértek ( ) egyetértek ( ) egyet is értek meg nem is
( ) nem értek egyet ( ) egyáltalán nem értek egyet

10. Nem tudtam elszabadulni a munkahelyemről/szabadságot kivenni, hogy elmenjek az orvoshoz.
( ) nagyon egyetértek ( ) egyetértek ( ) egyet is értek meg nem is
( ) nem értek egyet ( ) egyáltalán nem értek egyet

11. Más egészségügyi problémáim voltak.
( ) nagyon egyetértek ( ) egyetértek ( ) egyet is értek meg nem is
( ) nem értek egyet ( ) egyáltalán nem értek egyet

12. Nem igazán aggódtam egy anyajegy miatt.
( ) nagyon egyetértek ( ) egyetértek ( ) egyet is értek meg nem is
( ) nem értek egyet ( ) egyáltalán nem értek egyet

13. Nem tudtam gyermekem felügyeletét megoldani.
( ) nagyon egyetértek ( ) egyetértek ( ) egyet is értek meg nem is
( ) nem értek egyet ( ) egyáltalán nem értek egyet

A következőkben lehetséges okokat fog találni, amiért <u>nem</u> fordult bőrgyógyászhoz anyajegy vizsgálat céljából. Gondoljon vissza a diagnózis előtti évre és válaszoljon az alábbi kérdésekre:

14. Túl drága egy bőrgyógyászati vizsgálat.
( ) nagyon egyetértek ( ) egyetértek ( ) egyet is értek meg nem is
( ) nem értek egyet ( ) egyáltalán nem értek egyet

15. Nem tudtam hogyan szerezzek betegbiztosítást, amiből fedezhetem a bőrgyógyászati vizsgálatot.
( ) nagyon egyetértek ( ) egyetértek ( ) egyet is értek meg nem is ( ) nem értek egyet ( ) egyáltalán nem értek egye
16. Nem tudtam hogyan intézzek magamnak bőrgyógyászati vizsgálatot bőrrák szűrése céljából.
( ) nagyon egyetértek ( ) egyetértek ( ) egyet is értek meg nem is ( ) nem értek egyet ( ) egyáltalán nem értek egyet

VII. MELANOMÁVAL KAPCSOLATOS ISMERETEK.

Szeretnénk megtudni, hogy mennyit tudott a melanomáról a diagnózis felállítása előtt.

1. Ismerte-e az ABCD szabályt a melanomával kapcsolatban? Ezek figyelmeztető jelek bőrelváltozásokkal kapcsolatban: aszimmetria, szabálytalan szél, színváltozás, és/vagy az átmérő növekedése. ( ) igen ( ) nem

2. Tudta-e mi a különbség egy melanoma és egy közönséges bőrelváltozás között? ( ) igen ( ) nem

3. Tudta-e hogy melyik anyajegyekre kell figyelnie amikor átnézi bőrét? ( ) igen ( ) nem

4. Milyen információszerzési lehetőségeket/forrásokat használt bőrrákkal kapcsolatban?

	gyakran	**néha**	**ritkán**	**soha**
internet	( )	( )	( )	( )
TV hírek	( )	( )	( )	( )
rádió	( )	( )	( )	( )
betegtájékoztató/szórólap	( )	( )	( )	( )
napilap	( )	( )	( )	( )
heti magazin	( )	( )	( )	( )
orvosom rendelője	( )	( )	( )	( )

VIII. EGÉSZSÉGÜGYI KOMMUNIKÁCIÓ A MELANOMÁRÓL

1. A melanoma diagnosztizálása előtti évben volt-e olyan intézmény, ahová betegségével vagy egészségügyi problémáival rendszerint fordult?
   ( ) igen, orvosi rendelő, klinika, egészségügyi centrum
   ( ) igen, sürgősségi ellátó központ
   ( ) igen, egyéb hely; éspedig:_____
   ( ) nem, nem volt olyan hely ahová fordulhattam volna.

2. A melanoma diagnosztizálását megelőző évben volt-e olyan egészségügyi szakember, akihez rendszeresen járt rutin ellenőrzésre, vizsgálatra? ( ) igen ( ) nem

3. A melanoma diagnosztizálását megelőző évben fordult-e egészségügyi szakemberhez (orvos, nővér)?
   ( ) egyszer sem
   ( ) egyszer
   ( ) 2-3 alkalommal
   ( ) > 3 alkalommal

4. Ezeken a viziteken megvizsgálta-e Önt bőrrák irányában az egészségügyi szakember (beleértve a bőrét, mellkasát) legalább egyszer?
( ) igen ( ) nem ( ) nem tudom (ha nem tudja, hagyja ki a kérdéseket: 4-5)
Amennyiben igen, miért vizsgálta meg az orvos a bőrét? (Kérjük minden lehetséges választ jelöljön meg.)

( ) része volt az orvosi rutinvizsgálatnak
( ) az orvosi vizsgálat bőrrák szűrés céljából történt
( ) Ön aggódott a bőrrák miatt
( ) Ön kért bőrvizsgálatot
( ) partnere/barátja vagy más úgy gondolta, hogy Önnek szűrésre kell mennie

5. Megvizsgálta-e az orvos a teljes bőrfelületét vagy csak bizonyos bőrelváltozásait?
( ) teljes bőr ( ) bizonyos bőrelváltozás ( ) nem tudom

6. Tapasztalt-e valaha változást anyajegyeiben? ( ) igen ( ) nem

7. Amennyiben igen, beszámolt-e anyajegye változásáról orvosának vagy más egészségügyi szakembernek? ( ) igen ( ) nem

8. Beszélgetett-e valaha orvosával vagy más egészségügyi szakemberrel a bőrrákról?
( ) igen ( ) nem

9. Említette-e valaha orvosa, hogy Ön veszélyeztetett bőrrák szempontjából?
( ) igen ( ) nem

10. Említette-e orvosa, hogy Önnek van atípusos vagy dysplasticus anyajegye?
( ) igen ( ) nem

11. Említette-e valaha orvosa, hogy figyelje egy vagy több bizonyos anyajegyét?
( ) igen ( ) nem

12. Kapott-e valaha tanácsot vagy betegtájékoztató anyagot arról, hogy hogyan figyelje bőrét melanoma szempontjából? ( ) igen ( ) nem

IX. MELANOMA FELFEDEZÉSE

Most arról kérdezzük, hogy hogyan fedezték fel melanomáját. A melanoma felfedezése azt az időpontot jelenti, amikor először megtudta, hogy bőrelváltozása egy melanoma.

1. Ki volt az **első**, aki észrevette a bőrelválto,zását amiről kiderült, hogy melanoma? (csak egy válasz lehetséges)

( ) saját maga
( ) élettársa/partnere/házastársa
( ) családtag (szülő, testvér, gyermek)
( ) barát
( ) orvosa (háziorvos, nőgyógyász, egyéb kezelőorvosa stb.)
( ) bőrgyógyász, dermatoonkológus
( ) nővér
( ) orvosi asszisztens
( ) egyéb, kérem részletezze: _____

2. Mikor kezdett aggódni a bőrelváltozása miatt, melyről később kiderült, hogy melanoma?

( ) 1-3 hónappal a diagnózis előtt
( ) 4-11 hónappal a diagnózis előtt
( ) 1-2 évvel a diagnózis előtt
( ) több mint 3 évvel a diagnózis előtt
( ) kizárólag a diagnózis felállításakor

3. Mikor vette észre először a bőrelváltozását, melyről később kiderült, hogy melanoma?

( ) mindvégig tudtam róla (születésem óta volt ott)
( ) 1-3 hónappal a diagnózis előtt
( ) 4-11 hónappal a diagnózis előtt
( ) több mint 1 évvel a diagnózis előtt
( ) kizárólag a diagnózis felállításakor

4. Észlelt-e változást a bőrelváltozásban, mely később melanomának bizonyult? (Kérjük minden lehetséges választ jelöljön meg.)

( ) egyik oldala máshogy nézett ki mint a másik
( ) változott a széle (cakkos vagy szabálytalan lett)
( ) változott az alakja
( ) változott a színe
( ) változott az átmérője/mérete
( ) más lett, mint a többi anyajegyem
( ) más lett, mint korábban volt
( ) változott a vastagsága/kiemelkedése a bőrből
( ) feszülni/fájni kezdett
( ) viszketni kezdett
( ) vérezni kezdett
( ) egyéb, éspedig:_____
( ) nem változott

5. Kérjük karikázza be a 4-es kérdésnél, amely változás a leginkább aggasztotta Önt.

6. Könnyen meg tudta vizsgálni a bőrelváltozását, mely később melanomának bizonyult?
( ) igen ( ) nem ( ) nem tudom

7. Milyen volt a bőrelváltozás színe?
( ) pigmentált (barna, fekete) ( ) rózsaszín ( ) bőrszínű ( ) nem tudom

8. Mennyi idő elteltével fordult orvoshoz vizsgálat céljából, miután Ön vagy házastársa/partenere/barátja/rokona észrevette a bőrelváltozását, mely melanomának bizonyult?

( ) kevesebb, mint egy hét
( ) 1 héttől 1 hónapig
( ) 1 - 3 hónap
( ) 3 - 6 hónap
( ) 6 -12 hónap
( ) > 1 év
( ) nem vonatkozik rám a kérdés, mert az orvos vette észre először

9. Az Önt először megvizsgáló egészségügyi szakember továbbküldte-e Önt bőrgyógyászhoz vagy sebészhez gyanús bőrelváltozásának vizsgálata vagy sebészi eltávolítása céljából?
( ) igen ( ) nem

10. Amennyiben igen, mennyi idő telt el, míg kapott időpontot a bőrgyógyásznál vagy sebésznél? _____ nap vagy_____ hét

11. Amennyiben az egészségügyi szakember, aki az Ön bőrelváltozását először megvizsgálta nem küldte tovább, vett-e mintát szövettanra vagy eltávolította-e az anyajegyet?
( ) igen ( ) nem

12. A bőrelváltozásának első orvosi vizsgálatát követően mennyi idővel történt szövettani mintavétel (biopszia vagy sebészi kimetszés)?
( ) az első vizsgálat során megtörtént a szövettani mintavétel
( ) < 1 hónappal az első vizsgálatot követően
( ) 1-3 hónappal az első vizsgálatot követően
( ) 3-6 hónappal az első vizsgálatot követően
( ) > 6 hónappal az első vizsgálatot követően

X. JAVASLATOK

A következőkben néhány kérdést szeretnénk feltenni azzal kapcsolatban, hogy mit tegyünk a melanoma minél korábbi felismerése érdekében. Kérjük adjon meg 3 választ, mely Ön szerint a leghatékonyabb lenne, hogy a melanomára felhívjuk a lakosság figyelmét.

( ) társadalmi szervezetek: Lions Club
( ) egészségügyi oktató programok irodákban, munkahelyeken
( ) ingyenes egészségügyi vásárok és programok ingyenes bőrrák szűrési lehetőséggel
( ) internetes oldal vagy hírlevél a Magyar Nyugdíjasok Egyesületétől/nyugdíjas kluboktól
( ) internetes oldal vagy hírlevél a Magyar Onkológusok Társaságától
( ) gyakran olvasott egészségügyi témájú internetes oldal
( ) nyomtatott betegtájékoztatók elhelyezése olyan helyeken, ahová az emberek rutinszerűen járnak (benzinkút, szépségszalon, bevásárló központ, edzőtermek, sportesemények)
( ) nyomtatott betegtájékoztatók és plakátok orvosi rendelőkben
( ) különböző patika láncokkal való együttműködés a témával kapcsolatos információk terjesztésére
( ) rádió műsor
( ) TV műsor
( ) egyéb javaslat:_____

A melanoma diagnosztizálása előtti évben a „melanoma” kifejezés hallatán mi jutott eszébe?
( ) anyajegy szinonimája
( ) bőrbetegség
( ) bőrdaganat
( ) egyéb: _____

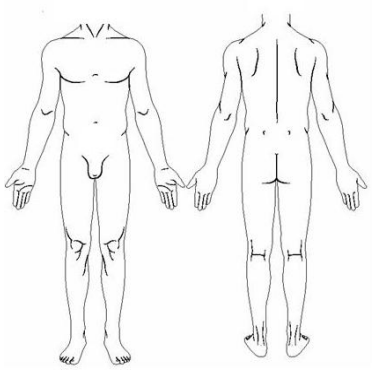
Kérjük amennyiben további ötlete/tanácsa van számunkra, hogy hogyan tudnánk a melanoma tudatosságot javítani a lakosság körében, illetve elősegíteni a betegség korai felismerését, ossza meg velünk!

_____
_____
_____
_____

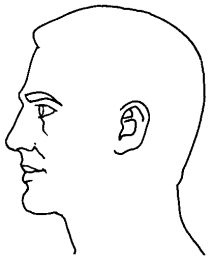
Köszönjük szépen!
Nagyon lekötelezett bennünket, hogy segítségünkre volt a kérdések megválaszolásában.

Klinikus által kitöltendő:

1. Melanoma anatómiai lokalizációja (jelöle meg X-el):



1. fejbőr ___	11. lábszár elülső f. ___
2. arc ___	12. lábfej/lábujjak ___
3. nyak elülső r. ___	13. nyak hátsó r. ___
4. mellkas ___	14. váll hátsó f/hát felső r. ___
5. has ___	15. hát also r. ___
6. suprapub./lágyék ___	16. gluteus ___
7. kar elülső f. ___	17. kar hátsó f. ___
8. kéz/ujjak ___	18. comb hátsó f. ___
9. tenyér	19. lábszár hátsó f. ___
10. comb elülső ___	20. talp ___



2. Tumor vastagsága _____ mm (amennyiben reziduális tumor, legnagyobb vastagság)

3. Szövettani ulceráció (amennyiben reziduális lézió, végleges ulcerációs státusz):
nincs. van nincs adat (karikázza be)

4. Szövettani típus (karikázza be): SSM NMM LMM ALM desmoplastikus egyéb: ___

5. Naevusok száma (ellenőrizze): 0-20_____ 20-50 _____ 50-100_____ >100_____

6. Naevusok fenotípusa: klinikailag atípusos neavus: van ( ) nincs ( )
Amennyiben igen, azok becsült száma (ellenőrizze): 1-5_____ 6-20_____ >20_____

7. Jelen **klinikai** AJCC Stádium (sentinel ill. radiológiai vizsgálatok előtt) – karikázza be:

Stádium	Breslow (mm)	Ulceráció
IA	≤1	Nem
IB	≤1	Igen
	1.01-2	Nem
IIA	1.01-2	Igen
	2.01-4	Nem
IIB	2.01-4	Igen
	> 4	Nem
IIC	>4	Igen
III	Regionális nycs(k) /In-tranzit /Szatellita(k)	
IV	bármely távoli áttét	