Dermatology Practical & Conceptual

Over-diagnosis, Overtreatment or Oversurveillance of Melanoma: Is There a Way Out?

Iris Zalaudek[1]

1 Department of Dermatology and Venereology, University of Trieste, Trieste, Italy

Citation: Zalaudek I. Overdiagnosis, Overtreatment or Oversurveillance of Melanoma: Is There a Way Out? *Dermatol Pract Concept.* 2023;13(4):e2023250. DOI: https://doi.org/10.5826/dpc.1304a250

Accepted: August 7, 2023; **Published:** October 2023

Funding: None.

Competing Interests: None.

Corresponding Author: Iris Zalaudek, Department of Dermatology and Venereology, University of Trieste, Trieste, Italy. E-mail: iris.zalaudek@gmail.com

Timely detection and prompt treatment have been declared as the key for reducing melanoma mortality. Dermoscopy and digital monitoring improves early melanoma diagnosis compared to the naked eye, which explains its wide use in almost all dermatological practices worldwide. However, epidemiologic studies reporting a significant increase in the incidence thin melanomas without a significant impact on mortality led to the discussion on melanoma over-diagnosis [1].

In this issue, Betz-Stablein et al. and Navarette Dechent et al. discuss several valid arguments related to melanoma over-diagnosis and conclude that intensified use of integrated clinical approach combined with even more innovative technologies such as 3D Total Body Photography, sequential dermoscopy images and whole slide pathology images supported by AI will have the power to resolve the dilemma of over-diagnosis. I doubt their conclusion because the current design and application of all innovative technologies focus on early melanoma detection and do not address the true problem in dermato-oncology today: how to identify biologically "dangerous" melanomas and how to differentiate them for biologically "indolent" ones. After decades of intense research and technical progresses enabling us to diagnose melanoma at all stages (from earliest to latest stage), we failed entirely to step forward in our ability to predict outcome. The single most important and reliable prognostic factor for melanoma progression remains level of invasion and thickness, which has been introduced more than 50 years ago by Alexander Breslow [2].

However obtaining reliable morphological information and to link it with biological outcome becomes increasingly complicated because of the introduction of effective treatments in adjuvant settings and the multidisciplinary approach in melanoma management today. Those specialties, who are primarily involved in diagnosis (pathologists and dermatologists) are not necessarily those, who care about treatment and follow up. Consequently, there is the natural risk of inter-disciplinary loss of information between "holders" of image collections and long-term outcomes. Clinical trials on melanoma represent powerful documentation tools on treatment efficacy and progression, but they rarely include the validation of pathological and/or clinical-dermoscopic documentation of the primary tumor. In my view, the most significant problem of melanoma over-diagnosis is not related to the diagnostic dilemma nor to treatment of equivocal lesions, but to the consequences that arise from it: namely a worldwide over-surveillance. Most clinicians and pathologists

agree on the problem of over-diagnosis but consider a simple re-excision of an equivocal melanocytic neoplasm diagnosed eventually as "early melanoma" an acceptable compromise in the management path. While this might be true for an individual patient, the problem gains a much more significance when it comes to follow up after melanoma diagnosis. Individuals diagnosed with melanoma are believed to be at higher risk for developing a subsequent melanoma, although most never do [3,4]. Only roughly 10%-20% of melanoma patients will be diagnosed with subsequent melanoma, whereby the risk of subsequent melanoma is highest within the first 3 years after initial melanoma diagnosis [5]. Notwithstanding this evidence, most guidelines and dermatologists advocate lifelong surveillance with at least annual visits for all melanoma, irrespective of tumor thickness, effective risk of recurrence/progression or presence of additional risk factors [6,7]. Addressing the problem of melanoma over-diagnosis in this light, which refers to early melanomas that will never cause symptoms or death during a person expected lifetime, the uncritical overtake of this practice results in long term over-surveillance of a significantly increasing cohort of virtually "cured" healthy individuals. Needless to underline that annual visits are unlikely to allow the timely detection of biologically aggressive melanomas/cancers or recurrent disease between two visits. In this light it is legitimate to question about the value of such recommendation and the need to seek for alternative strategies. Research on melanoma diagnosis before, during and after Covid-19 pandemic may provide us with some interesting aspects on this theme. Waiting times for dermatological services have almost doubled worldwide after the lock down and will take years to recover [8]. Several lines of evidence report on thicker tumors diagnosed during the lock down period, especially among elderly, which points towards delayed diagnosis [9]. Whether these thicker tumors are caused by suspended screening activities or result of limited patients-self referral to hospitals due to fear has not been clarified in detail. However, an increasing number of studies support the hypothesis of postponed self-referral as main cause for the increased thickness observed during lockdown, also because surgical interventions of suspicious tumors have been always guaranteed [10]. Self-referral due to symptomatic lesions has not achieved high attention during the last decades, although lines of evidence suggest more than half of melanoma are patients-self detected and referred [11,12]. At this end, I like to cite the recent wording of the USPSTF Statement on Skin Cancer Screening: "At this point it is critical to understand the differences between "screening" and "diagnostic" examinations: The term screening refers to a test (the visual skin examination) on an asymptomatic individual to determine if that individual has melanoma requiring further evaluation or intervention. In contrast, if a patient presents to a dermatologist for a concerning symptomatic mole, this is not considered a screening examination but a diagnostic examination. Thus, the relevant central clinical question in the discussion on over-diagnosis is whether individuals at average to low risk without symptomatic lesions of concern should be offered regular visual skin examination for melanoma prevention"[13]. In conclusion, over-diagnosis and over-surveillance are hot topics in dermatology and pathology, especially in the post-Covid era. Clinical trials on melanoma, if starting to include clinical – pathologic images in their design, may provide powerful tools to gain more insights into the value of morphology as potential predictive marker for patterns of progression and response to treatment. However, solid data may not be expected earlier than after 5-10 years from now.

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