SKIN CANCER (E TONGDEE AND O MARKOWITZ, SECTION EDITORS)

Screening and Managing Melanoma: Who Is (Should Be) Doing It?

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Abstract



Purpose of Review The detection and management of melanoma is moving toward a more interdisciplinary approach. This review provides a specialty-based framework to characterize the roles of dermatologists and non-dermatologist healthcare professionals in detecting and managing cutaneous melanoma and data on outcomes of management by specialty and training. **Recent Findings** Dermatologists manage thinner, earlier stage melanoma compared with surgical specialties and have higher survival rates than non-dermatologists. While teledermatology, primary care physicians, and advance practice practitioners offer potential solutions to the shortage of dermatologists, there is insufficient data demonstrating comparable detection and management are emerging as settings for collaborative care.

Summary Early detection and diagnosis of melanoma is vital to prognosis, so the involvement of non-dermatologist healthcare professionals is important to providing timely care to patients. Increased education for detecting melanoma can increase the incidental detection of early melanoma by non-dermatologist healthcare professionals. While there is no consensus on who should be managing melanoma, collaborative care in MDMCs may become more important as treatment options for earlier disease continue to rise.

Keywords Melanoma \cdot Melanoma screening \cdot Melanoma histopathologic diagnosis \cdot Melanoma surgical management \cdot Melanoma surveillance \cdot Multidisciplinary models

Introduction

The incidence of cutaneous melanoma (CM) continues to rise, which raises the question: who should be diagnosing and managing melanoma? The management of melanoma is a complex task, requiring multidisciplinary approaches, particularly for patients with advanced disease. The primary management of CM may be dictated by the stage of disease, patient preference, and physician or specialist availability [1, 2]. One study of outpatient melanoma

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³ Hillman Cancer Center, University of Pittsburgh Medical Center, Pittsburgh, PA, USA follow-up visits in the United States (US) from 1979 to 2010 found a significant increase in the proportion of dermatology visits and a corresponding decrease in visits to primary care physicians (PCPs) and surgeons [3]. A national study conducted in Germany revealed about 84% of invasive melanomas were surgically excised by dermatologists, followed by general surgeons (15.5%), plastic surgeons (3.6%), and finally general practitioners (1.1%) who will be referred to as primary care providers (PCPs), the term used to describe their US counterparts, in this manuscript [4•]. In general, dermatologists tend to manage thinner, earlier stage CM compared with other surgical specialties or medical oncologists [5].

The 2019 American Academy of Dermatology (AAD) guidelines support the collaboration of dermatologists with medical, surgical, and radiation oncologists in caring for advanced melanoma patients; however, they do not explicitly delineate which discipline should be the primary driver of management decisions [6•]. Moreover, with the current shortage of dermatologists, melanoma diagnosis and management increasingly involves other healthcare providers (HCPs) including PCPs and advance practice practitioners (APPs), such

as nurse practitioners (NPs) and physician assistants (PAs). Surgical treatment of melanoma is performed by general surgeons, plastic surgeons, surgical oncologists, otolaryngologists, PCPs, APPs, and dermatologists; however, there are few studies investigating outcomes by specialty or training. Even within the field of dermatology, the role of Mohs micrographic surgery (MMS) in managing melanoma in situ (MIS) is the subject of ongoing debate [7, 8•]. Here, we review the literature on who is diagnosing and treating melanoma along with data on the outcomes of management by specialty and training.

Screening and Diagnosis of Melanoma

In 2015, there were about 74,000 melanomas diagnosed in the US and nearly 352,000 melanomas diagnosed worldwide [9]. Melanoma incidence continues to rise likely due to sun exposure practices and an increase in melanoma awareness and screening [10]. Melanoma may first be discovered by the patient or as part of a routine physical or dedicated skin cancer screening. Guidelines on melanoma screening are vague, and the United States Preventive Services Task Force (USPSTF) states there is insufficient evidence to recommend for or against melanoma screening in asymptomatic populations [11]; however, it does recommend that PCPs, including pediatricians, counsel patients and parents about the importance of avoiding ultraviolet radiation [12].

Several initiatives run by the AAD in the United States and by Euromelanoma in the European Union have provided data about the effectiveness of large dermatologist-based screening programs. In 1985, the AAD launched an initiative to provide free skin cancer educational programs and free, open screenings and found a suspected melanoma rate of 0.8% and histological confirmed rate of 0.15% in about 640,000 patients screened between 1985 and 1999 [13]. From 2009 to 2010, the Euromelanoma campaigns found an average suspected melanoma rate in their screening population to be about 2.8% (ranging 1.1–19.4% across all countries) and an average biopsy-confirmed detection rate of 0.35% (ranging 0.09-1.9% across all countries) [14]. Publications from both initiatives acknowledge that screening has never been proven effective in decreasing mortality, speculating that the screening programs attract younger, more female, higher socioeconomic populations who are at lower risk of melanoma mortality due to greater access and utilization of care. Thus, both initiatives recommended more studies to increase future detection rates in populations who would be at highest risk for melanoma mortality, particularly male patients over 50 years of age in a lower socioeconomic class [13, 14].

Between 2003 and 2004 in the German state of Schleswig-Holstein, the largest investigation into the effect of melanoma screening on mortality was performed primarily by PCPs after they received 8 h of training in skin cancer detection [15]. In 1 year, about 360,000 patients over 19 years of age were screened, and the initial analysis showed almost 50% reduction in melanoma mortality in 2008-2009 (1.0 and 0.7 in 100,000 men and women, respectively) when compared with 1998-1999 (1.9 and 1.4 in 100,000 men and women, respectively) [16]. However, further analysis following the initiation of a national program, in which PCPs performed screening every 2 years for patients 35 years or older, did not show a reduction in melanoma mortality and thus no clear benefit of screening [17•]. In another program that provided online training for PCPs in melanoma screening and detection in western Pennsylvania, screened patients were more likely to be diagnosed with melanoma (adjusted risk ratio of 2.4; p < 0.01) and had thinner lesions (median thickness 0.37 mm vs. 0.65 mm; p < 0.001) than those who were not screened; having said this, there was no statistically significant reduction in the incidence of melanoma lesions thicker than 1 mm [18•]. The melanoma detection rate of these PCP-led screening programs was 0.16% in the initial German 1-year intervention and 0.094% in the western Pennsylvania population, which are both lower than the values for the dermatologist-led programs by the AAD and Euromelanoma group discussed previously [15, 18. Regardless, these findings are encouraging and suggest that PCP-driven screening exams may improve melanoma early detection when included as part of a routine physical examination; in addition, the German experience suggests that such programs must be routinely and systematically evaluated to ensure they are performed in the most beneficial way possible [18•].

Outside of population-based screening programs, large databases (such as the Surveillance, Epidemiology, and End Results [SEER] Program and Medicare) are sources of information about who is diagnosing melanoma and, in some cases, outcomes associated with diagnosing HCP. One study found greater dermatologist density is associated with higher melanoma survival [19•], with 0.001 to 1 dermatologist per 100,000 people in the population being associated with a 35.0% reduction in melanoma mortality [20]. A study of Medicare beneficiaries in the US found that areas of high versus (vs) low PCP density had an increased incidence of thin melanomas with no difference in mortality rate nor incidence of stage III and IV melanomas, even when adjusting for dermatologist density; this suggests that PCP density may primarily increase detection of early, less aggressive disease [21]. Pennie et al. compared outcomes among patients diagnosed by a dermatologist vs a non-dermatologist using a database of Medicare patients and saw earlier stage disease; higher survival rates at 6 months, 2 years, and 5 years (98%, 87%, and 74% vs 95%, 79%, and 69%, respectively; p < 0.05); and lower cancer-related (13% vs. 21%; p < 0.01) and overall mortality (29% vs. 37%; p < 0.01) among patients diagnosed by dermatologists [22•]. Similarly, in the US, one

study found that dermatologists had a greater ability than PCPs when deciding when to biopsy and refer patients (p < 0.01) [23]. Another study found that patients who had their melanoma biopsied and diagnosed through a nondermatologist had a higher likelihood of delayed excision (more than 1.5 months) compared with those through dermatologists (31% vs. 16% probability) [24]. Adding to this analvsis, recent studies analyzing patient satisfaction with patientprovider interactions at the time of diagnosis showed that patients were more likely to report fair/poor satisfaction, lower levels of compassion, and poorer knowledge of melanoma if seen by a non-dermatologist [25]. Given dermatologists' focus on melanoma, dermatology practices are likely more streamlined to facilitate efficient melanoma triaging, timely and compassionate treatment, and malignant biopsy followup which minimize delayed excisions and increase patient satisfaction.

Another measure of efficacy in melanoma screening and detection includes the number needed to screen to detect one melanoma (NNS) or number needed to biopsy to detect one melanoma (NNB), with lower values indicating greater efficacy. Several studies from individual institutions and clinics have investigated the NNS and NNB by dermatologists which have been found to be 215-400 and 7.9-28, respectively [26-29]. Although some studies have compared other HCPs' and dermatologists' NNS and NNB, this is difficult to do via retrospective analysis since the latter group tends to see a population at higher risk of skin cancer. One study found the NNB to be significantly higher in APPs vs. dermatologists (32.8 vs. 17.4, respectively, p = 0.04) [30]. Similarly, a study comparing PAs and dermatologists found a higher NNB (39.4 vs. 25.4, respectively) and a higher rate of detection of melanoma in situ but not invasive melanoma or non-melanoma skin cancer, by dermatologists [31•]. While studies are lacking on PCPs' NNB in the US, PCPs in Australian skin cancer clinics had a NNB of 23 in one study when excluding biopsies of seborrheic keratoses [32]. These data suggest that dermatologists have higher accuracy in finding melanomas than other providers. Shahwan et al. highlighted the importance of a low NNB to reduce overall healthcare costs, called for more studies on interventions to improve HCP's NNB as a healthcare cost reduction strategy, and suggested that one cost-effective option may be having a dermatologist make the final biopsy decision for pigmented lesions [33•].

Notably, however, the workforce is not sufficient for all melanoma screening and diagnoses to be performed by dermatologists. As of 2015, there were about 11,500 clinical practicing dermatologists in the US, corresponding to about 36 dermatologists per 1 million people [34]. If all adults over 34 years old in the US were to be annually screened (totaling about 170 million people according to the 2016 US Census Bureau) [35], each dermatologist would need to perform about 15,000 screenings per year, or 57 per workday, 52 weeks a year. In fact, there is already a shortage of access to dermatologists in the US, and one study has reported an average of 39day wait time for an appointment to evaluate a changing mole [36]. Thus, other clinicians have a role in the diagnosis of melanoma, and the use of APPs and PCPs to provide skin cancer screenings has increased to meet the growing demand [34]. A recent study found that over 780,000 diagnostic skin biopsies by APPs were billed independently in 2015, a trend that has continued to increase over the 2012–2015 study timeframe [37]. One pilot study found that training in skin cancer identification resulted in a sensitivity of 50–100% and specificity of 99–100% for appropriate referral of suspicious lesions by NPs; this suggests that formal skin cancer education may result in higher diagnostic accuracy among non-dermatologists [38].

A newer development in the management of CMs is the emergence of teledermatology, which can extend dermatologic care to underserved regions. One study found that agreement rates for pigmented lesions between in-person clinic dermatologists and teledermatologists ranged from 52.8 to 80.1% (kappa 0.49-0.67) for the primary diagnosis and 66.7 to 79.8% (kappa 0.18–0.42) for the recommended management plan, with statistically significant improvement in agreement based on the use of contact immersion dermoscopy [39]. Moreover, with the rising shortage of specialists, especially in rural areas, teledermatology-directed surgical excision by PCPs has facilitated their management of melanoma with guidance from remote dermatologists. One national study conducted among veterans in the Veterans Affairs system found that melanoma excisions could often be safely performed in rural clinics by trained PCPs with teledermatology guidance [40]. However, complication rates of wide local excisions (WLEs) performed by PCPs were still higher at 7.7% compared with 2.5% for WLEs performed by specialists [40]. A systematic review in 2017 gave a grade 2A recommendation (weak recommendation) for teledermatology when a face-to-face was not feasible as a triage tool [41]. However, because the quality of the evidence was only B for all of its recommendations (indicating lower quality studies due to mostly small trials in the literature), authors called for more rigorous studies to verify diagnostic accuracy in patients without access to dermatologic care [41].

Histologic Diagnosis of Melanoma

Once biopsied, the correct diagnosis needs to be made histologically, and discrepancies in the diagnosis of melanocytic lesions by dermatopathologists vs general pathologists have been documented. Overall, interobserver variability between general pathologists and expert dermatopathology consultation can be up to 68.8–84.8% [42]. Expert consultation can result in changes in management, which can include recommending wider surgical margins in 7.9-12% and sentinel lymph node biopsies in 8.6-16% of cases [42-44]. Other discrepancies include reclassifying lesions from MIS to invasive CM in 20.5% and invasive CM to MIS in 7.3% of cases [42]. In one study examining the discordance rate between outside dermatopathologists or surgical pathologists vs specialized dermatopathologists at the University of California San Francisco, there was a discordance rate of 14.3% in the diagnosis of melanomas and nevi; although this may seem like a low percentage, if one considers that 1,500,000 to 4,500,000 biopsies were performed in the US in 2008, this would roughly translate to a discordance of 215,000 to 644,000 cases annually [45]. Ideally, the histologic diagnosis of melanoma should be made by a board-certified dermatopathologist or a pathologist with extensive experience in the evaluation of pigmented skin lesions.

Surgical Management of Melanoma

Little data is available comparing melanoma surgical treatment outcomes by specialty. One small study performed at a single center in the US compared adherence to the National Comprehensive Cancer Network (NCCN) guidelines for surgical margins and utilization of sentinel lymph node biopsy by the specialty of the treating physician. The authors reported that treatment by a surgical oncologist was associated with higher rates of margin compliance (95% vs 38% of cases) and compliance with the lymph node management guideline in place at the time (92% vs 67% of cases) compared with all other specialties, including dermatologists, general surgeons, otolaryngologists, and plastic surgeons [46]. One study in Scotland between 1979 and 1997 found the management of CM by dermatologists compared with that of general surgeons, plastic surgeons, and PCPs was associated with improved overall survival, disease-free survival, and recurrence-free survival. General surgeons were also found to use wider surgical margins than other specialists. The authors suggested that this data show dermatologists should be central to the management in melanoma. However, the melanomas managed by dermatologists were also lower risk (thinner, less likely to be ulcerated, and more likely to occur in women and younger patients), which likely accounted for most of these differences in outcomes. [47] Another study of practitioners in Scotland found that patients receiving initial excision for their CMs by PCPs do not have worse survival or increased morbidity over an 8-year study period compared with those with CMs excised by specialists [48•].

In contrast, other studies have found that PCP management did not meet the standard of care of management compared with specialists. For example, one retrospective study in the United Kingdom (UK) found that excision by surgical consultants was more likely to be complete compared with excision by PCPs (83.8% vs. 48%, p < 0.05) and to be compliant with known guidelines (70.5% vs 29.8%, p < 0.05). As a result, this study recommended that the UK melanoma guidelines aggressively enforce urgent referral of melanomas to specialists [49]. In a New Zealand study of pathology reports from all skin excisions over a 3-month period, dermatologists excised a greater percentage of malignant lesions when compared with PCPs, PCPs interested in skin surgery, and surgeons (93% vs. 63%, 71%, and 72%, respectively), and had more complete excision of the lesions with lower percentages of positive margins (0% vs. 23%, 21.5%, and 20%, respectively) [50].

Management of Melanoma Within the Field of Dermatology

Even among dermatologists, there is some disagreement as to who should treat melanoma and how it should be done. One area of controversy in managing melanoma within the field of dermatology is the role of Mohs micrographic surgery (MMS) vs wide local excision (WLE). Several arguments against using MMS in treating CMs or MIS include the inferiority of frozen sections in comparison with paraffin-embedded tissue for melanocytic lesions, inability to permanently document margin of clearance, and the potential for skip lesions (areas of tumor-free skin) within melanoma [7]. In spite of these concerns, there was a documented 60% increase in SEER melanomas treated with MMS from 2003 to 2008. It is important to note though that these only totaled to be about 3.5% of all treated melanomas [51]. Many studies have documented no significant differences in outcomes between MMS vs WLE for MIS with one recent retrospective study showing no significant differences in recurrence rate (1.8% vs 5.7%, respectively; p = 0.07), 5-year overall survival (92% vs 94%, respectively; p = 0.28), or melanoma-specific mortality (0.7% vs 3.4%, respectively; 95% CI 0.17-3.80) [8•]. The Mohs Appropriate Use Task Force determined in 2012 that the use of MMS to treat melanoma is appropriate in anatomically constrained sites when used for the purposes of tissue sparing for lentigo maligna and MIS, except for lesions on the trunk or extremities (for which is was rated "uncertain" appropriateness); notably, invasive melanomas were excluded in these criteria [52].

Another procedure commonly used to treat melanoma of the head and neck area is staged excision, which is also referred to as "slow Mohs" or the square procedure. This technique allows 100% margin assessment but uses paraffin-fixed and hematoxylin- and eosin-stained tissue processed in vertical sections rather than the frozen tissue and immunohistochemistry used to evaluate melanoma by traditional Mohs surgery. This reduces the variability from the use of frozen tissue, but it does not permit excision and repair to be completed on the same day as is typically done with Mohs surgery. A study of 806 lesions treated using this technique in a single center with a median follow-up of 9.3 years demonstrated local recurrence rates of 1.4% at 5 years, 1.8% at 7.5 years, and 2.2% at 10 years [53•].

Another area in which management by dermatologists has some variation is in the decision to involve other specialists. In a study of patients initially biopsied by dermatologists from 1985 to 1997, WLE was performed by general surgeons in 64%, plastic surgeons in 23%, and dermatologist in 13% of cases with an increasing percentage of dermatologist-performed WLE throughout the course of the study [47]. In 2015, another study surveying practice patterns in the US found dermatologists referred excisions to surgical specialties for MIS, CM less than 1 mm, and CM greater than 1 mm in 11%, 22%, and 67% of cases, respectively [54•]. Dermatologists who completed their training less than 10 years ago were more likely to personally treat MIS (95% vs 87%; p < 0.01) and CM less than 1 mm (86% vs 74%; p < 0.01) than their counterparts who completed residency more than 10 years ago [54•]. However, dermatologists across all settings are more likely to refer cases to surgeons and other specialties for excision and management with increasing Breslow thickness, especially for sentinel lymph node biopsies and adjuvant therapies [55]. Notably, one French retrospective study evaluated differences in follow-up practices for stage I CMs between dermatologists practicing in outpatient, private practice settings vs inpatient, public hospital settings, and found that patients managed primarily in the former were more likely to be lost to follow-up and at higher risk of developing metastases [56].

Surveillance of the Melanoma Patient

While the value of screening the asymptomatic population for melanoma may be debatable, it is generally agreed that surveillance after a melanoma diagnosis is important. The probability of developing a second primary melanoma at 5 and 10 years is 5.58% and 8.04%, respectively, and the median time to first development of a second primary melanoma is 8.39 years, which highlights the importance of a long-term follow-up [57]. A retrospective study on the detection of melanoma relapse found that the largest proportion of recurrences were detected by dermatologists (43%), followed by patients (33%), radiologists (18%), and PCPs (6%) [58]. In fact, second primary melanomas have been found to be thinner among patients with routine follow-up with a dermatologist vs those without follow-up (0.36 mm vs. 1.22 mm mean thickness, p =0.019), suggesting that dermatologic management after initial diagnosis is vital for surveillance of the patient with melanoma [59]. The AAD guidelines recommend co-management with medical oncology for patients at higher risk of recurrence (stages IIB–IV), who may benefit from radiologic surveillance to detect occult metastases.

Multidisciplinary Models for Melanoma Management

Given the multidimensional aspects of managing melanoma at various stages, it is not surprising that there is an effort to characterize shared care between disciplines. In a qualitative study in Australia at two specialist referral melanoma clinics, interviews of surgical oncologists, dermatologists, and PCPs, who are specially trained in melanoma, found the most interdisciplinary overlap in the management of early-stage melanoma [60]. Authors described four models of shared care for early-stage melanomas (stage I/II) with alternating combinations of specialists, PCPs, surgical oncologists, or dermatologists leading each model and recommended comparative evaluation of each model to determine costs and benefits [60]. Some interdisciplinary approaches to melanoma management have taken the form of multidisciplinary melanoma clinic (MDMC) models that are recommended for all invasive CMs by the UK guidelines and are composed of dermatologists, various surgical specialists, NP equivalents, dermatopathologists, radiologists, medical oncologists, and palliative care specialists [61]. International guidelines also reflect the movement toward a more collaborative approach between specialties [62]. MDMC models for managing invasive CMs in the US include a model created by the University of Michigan where dermatologists acted as the primary managers of non-metastatic invasive CMs; weekly tumor board conferences (TBC) involved nondermatologist melanoma specialists, such as medical and surgical oncologists, otorhinolaryngologists, plastic and general surgeons, and radiation oncologists [63]. Surgical oncologists primarily managed more advanced melanomas, minimum stage III disease, while medical oncologists primarily managed non-operable stage IV melanomas. In the MDMC model, the roles of various disciplines were clearly delineated facilitating an organized approach to healthcare for patients, encouraging interdisciplinary communication, and improving cost efficiency [63]. Care delivered in this MDMC resulted in an overall reduction in cost without affecting clinical outcomes due to reduced usage of healthcare resources, suggesting that care can be most efficiently delivered in this setting [64].

Outside of MDMC models, the movement toward shared care of melanoma patients can be observed from an increased prevalence of skin cancer–specific, multiple disciplinary TBCs. One cross-sectional survey administered to 59 National Cancer Institute-Designated Comprehensive and Clinical Care Centers supported consistency in meeting structure which was usually led by dermatologists, surgical oncologists, or medical oncologists and attended by representatives of at least ten specialties [65]. Notably, all respondents indicated that TBCs enhanced interdisciplinary communication for a shared care approach in managing CM.

Conclusion

Early detection and diagnosis of melanoma is likely one of the most important interventions to reduce melanoma mortality. Unlike most cancers, melanoma can be diagnosed at the most curable in situ stage with a simple naked-eye examination. Therefore, improving melanoma education in the medical school curriculum and including it in the training of PAs, NPs, and nurses will increase the incidental detection of early melanoma that would otherwise go unnoticed. While dermatologists have a higher diagnostic accuracy for melanoma, most patients will not be seen by a dermatologist in a given year. Therefore, there is an important role for multiple specialists in increasing early detection and counseling patients on preventative measures such as sun protection.

While dermatologists are generally well-equipped to handle MIS and stage IA disease, a multidisciplinary approach, including medical and surgical oncology, is appropriated for stage IB and higher disease. As therapeutic options for melanoma evolve, so likely will the roles that different specialists play in treatment. There is a clear role for trained surgical oncologists to perform sentinel lymph node biopsy and excision of thicker melanoma. With the proposed use of early adjuvant immunotherapy in stage II disease, and the availability of the subcutaneous anti-PD-1 antibody treatment cemiplimab for advanced cutaneous squamous cell carcinoma [66•], dermatologists could conceivably expand their role to include administration of immunotherapy in the future [67]. Furthermore, the collaboration between dermatologists and medical oncologists in the care of patients with stage II melanoma will likely expand. It will be difficult to reach full consensus as to who should be diagnosing and managing melanoma, but patients, particularly those with more advanced disease, often require and benefit from having a team of specialists manage their care. As the treatment landscape changes over time, collaborative care is likely to make treatment in an MDMC even more important for a larger number of patients as we have increased options for treatment of earlier stage disease.

Author Contributions All listed authors are qualified for authorship, had access to the data, and have participated in the preparation of the manuscript.

Compliance with Ethical Standards

Conflict of Interest Dr. Ferris is a consultant for DermTech, International, and is an investigator for Castle Biosciences. All other authors declare that they have no conflicts of interest. No funding was received for this study.

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