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Clinical and Digital Follow-up of Cutaneous Melanoma

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Abstract

Background: Follow-up of melanoma patients allows early detection of both recurrences and new invasive melanomas. Early recognition of cutaneous melanoma is the most efficient strategy to improve prognosis of this potentially fatal disease. Currently there is no universally accepted surveillance protocol for melanoma patients. Self-examination along with history taking and physical examination must be performed regularly for every patient. Imaging can be considered for patients with advanced stages. Clinical follow-up is supported by digital follow-up consisting of total-body photography and digital dermoscopy.

Introduction

Cutaneous melanoma is the most dangerous skin neoplasm while being the least common. However, incidence of cutaneous melanoma continues to increase worldwide, and the disease accounts for 90% of skin cancer mortality [**1,2,3**]. After the diagnosis, staging and management, an appropriate surveillance of these patients is necessary for two main purposes: the early detection of disease recurrence and early diagnosis of a new primary melanoma [**4**]. In this article, we will discuss the clinical and digital follow-up of patients with cutaneous melanoma.

Clinical follow-up

All patients with a diagnosis of cutaneous melanoma should be instructed about self-examinations of the skin and lymph nodes. This is of utmost importance as the majority of the recurrences are recognized by patients themselves [**5**]. Skin examinations are done by naked eye, using a hand mirror and a wall mirror [**6**]. Though not reliable tools yet, smartphone applications may also help patients with self-examinations in the future [**7**]. Patients should be informed about the measures of sun protection and also the increased risk for melanoma of themselves and their family [**8**].

Critical period for the close follow-up of cutaneous melanoma patients is defined as the first 5 years after diagnosis. This is due to the fact that 90% of all melanoma metastases are detected in this period and there is 0.5% risk of development of a secondary melanoma per year. However, because of the risk of late metastases, lifelong follow-up care should be advised [**1,8,9**].

Currently, there is no universally accepted melanoma follow-up guideline and the recommendations about melanoma follow-up included in various guidelines are based on low-level evidence and expert opinions [**10**].

In clinical practice, National Comprehensive Cancer Network (NCCN) guidelines are one of the most commonly recognized guidelines.

According to NCCN guidelines, stage 0 patients should be evaluated annually by history taking and physical examination. History taking and physical examination should be done every 6-12 months for the first 5 years when following-up stage IA and IIA patients. If the physical examination yields equivocal results, assessment by regional lymph node ultrasound can be performed. For stage IIB-IV melanoma, history taking and physical examination should be performed every 3-6 months for the first 2 years and every 3-12 months for the following 3 years. Annual clinical examinations are recommended after 5 years. Consideration of imaging modalities including chest x-ray, chest/abdominal/pelvic computed tomography (CT) with intravenous contrast or whole body positron emission tomography (PET) with or without brain MRI is recommended every 3-12 months. Imaging is not recommended beyond 3-5 years if the patient is asymptomatic [**11**]. Follow-up strategies of NCCN guideline are summarized in (**Table 1**).

Recommendations for imaging modalities differ widely among various melanoma guidelines. For instance, the American Academy of Dermatology does not advise routine imaging to follow-up asymptomatic patients, with the exception of high-risk patients. On the other hand, the guidelines for the Management of Melanoma in Australia and New Zealand recommend only ultrasound imaging for advanced cases. European Society for Medical Oncology suggests performing CT with or without PET scans in high risk patients [**12**]. Despite these controversies, advanced stage patients are expected to benefit from imaging tests. Recently, in a retrospective study, Kurtz et al. reported that routine whole body imaging detected 50% of recurrences for stage IIC and IIIA-C melanoma [**13**].

Digital follow-up

Digital follow-up of patients with a history of melanoma is a screening for these individuals who are at increased risk of developing new primary melanomas. Digital follow-up is an important adjunct to clinical examination and comprises total body photography and dermoscopy, the so-called “two-step method” discussed below [**14, 15**].

Dermoscopy is superior to naked eye examination for the early detection of melanoma. Thus, routine management of pigmented lesions by means of dermoscopy is strongly recommended [**16**]. Nevertheless, it may be impossible to differentiate incipient melanomas from melanocytic nevi clinically and dermoscopically. In a study evaluating the baseline and follow-up images of 499 melanocytic skin lesions, it was shown that 61% of melanomas were lacking any of the 8 positive features described by Menzies et al. at baseline imaging. However changes between current and previous images identified during follow-up helps detect melanoma while the lesions are still inconspicuous. By the use of sequential dermoscopic imaging melanomas lacking specific features to warrant excision may be recognized and removed at an early stage. Short term monitoring at an interval of 3 months is used for single melanocytic lesions that do not show specific dermoscopic features of melanoma but that are still considered as suspicious melanocytic lesions. In this technique, except for an overall increase or decrease in pigmentation due to sun exposure and for the change in the number of the milia-like cysts, identification of any change

Table 1. Clinical Follow-op of Melanoma Patients as Recommended by NCCN Guidelines

Stage	Physical examination	Routine imaging
Stage 0	Annually	Not recommended
Stage IA-IIA	1st 5 years: every 6-12 months	Not recommended
	After 5 years: annually	
Stage IIB-IV	1st 2 years: every 3-6 months 2-5 years: every 3-12 months After 5 years: annually	Consider every 3-12 months After 3-5 years: not recommended

warrants excision of the lesion. Medium and long-term monitoring at intervals of 6 and 12 months respectively aims at surveillance of multiple inconspicuous lesions in patients with multiple nevi and patients with high risk phenotypes. Asymmetrical enlargement, foca l changes in pigmentation and structure, regression features, or change in color are considered as significant changes during follo w-up and require an excisional biopsy [**17, 18**].

The "two-step method" is the combined use of total-body photography and digital dermoscopy. This technique allows detection of the changes in pre-existing lesions and the identification and evaluation of new lesions. This method aids in diagnosis of featureless and de novo melanomas that might be unrecognized performing dermoscopy alone. Digital follow-up of patients at high risk for melanoma using the "two-step method" allows the early detection of melanomas with a low rate of excisions [**15**].

In a prospective study evaluating the impact of total body photography and sequential dermosocopy imaging on detecting melanoma in 311 individuals at extreme high risk, 62.3% of melanomas were shown to have histologic evidence of an associated nevus while the remaining 37.7% were identified as de novo melanomas. These results clearly emphasize the importance of the detection of both changing and novel lesions during the surveillance [**19**].

Meta-analysis of 14 studies indicates that more than half of the melanomas diagnosed during sequential dermoscopy were in situ and the remaining melanomas were invasive melanomas not thicker than 1 mm. The analysis also reported that the longer the follow-up period, the higher were the chances of detecting melanoma. It can be conferred that digital follow-up should be maintained over time in high-risk patients [**20**].

Conclusion

In conclusion, follow-up of patients with a history of melanoma should be undertaken for the early detection of recurrences and new primary melanomas. Although there is no consensus about the surveillance protocol, patients with higher stages need more close examination along with whole-body imaging studies. Digital follow-up is another important tool allowing the early detection of melanomas.

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