

Malignant Melanoma among Older Adults

Wey Leong, MSc, MD, Department of Surgical Oncology, Princess Margaret Hospital, University Health Network, University of Toronto, ON.

Alexandra M. Easson, MSc, MD, Department of Surgical Oncology, Princess Margaret Hospital and Mount Sinai Hospital, University of Toronto, ON.

Michael Reedijk, PhD, MD, Department of Surgical Oncology, Princess Margaret Hospital, University Health Network, University of Toronto, ON.

Melanoma must be considered in the differential diagnosis of any skin lesion in older adults. With the incidence of melanoma increasing in general and even more so among older people, more older adults are being diagnosed with melanoma than in the past. Among older adults, melanomas display more aggressive histological features with worse prognosis and treatment outcomes than among younger individuals. Furthermore, older individuals have fewer surgical and medical treatment options because of age-associated comorbidities. This article reviews the epidemiology and management of melanoma with emphasis on the older adult population.

Key words: older adults, melanoma, aged, cancer, skin neoplasm

Introduction

Malignant melanoma originates from melanocytes, pigment-producing cells of neural crest origin that acquire the ability to invade and metastasize. While melanoma represents one of the rarer forms of skin cancer, it is responsible for the majority of skin-cancer-related deaths. The overall incidence of melanoma has increased significantly in the past decades and the incidence of melanoma is higher among older adults.¹ Melanoma must be considered in the differential diagnosis when managing any skin lesion. Unfortunately, melanoma appears to confer a worse prognosis among older adults² and available surgical and medical treatment options may be limited in this age group due to the associated morbidity and toxicity. This article reviews the epidemiology and management of melanoma with a focus on the older adult population.

Epidemiology of Malignant Melanoma

Although melanoma is a relatively uncommon cancer, its rate is increasing among all age groups in countries with a Caucasian majority, including Canada. The reason for this is not clear. Among men, the incidence of melanoma rose more than 50% in the last decade (1993–2002), making it the 4th highest rate of increase after prostate, thyroid, and testicular cancer. Similarly, the incidence rose about 30% among women, making it the second fastest increasing cancer in women after thyroid cancer. The number of deaths caused by melanoma also increased by more than 40% among men (the greatest increase in death rate among all male cancers) and 20% in women (ranked 5th amongst all female cancers).¹ Overall, melanoma is the 8th most common malignancy, accounting for 3% of all cancers.¹

In Canada, there were approximately 4,500 new cases of melanoma in 2005. In

the same year, melanoma accounted for 880 deaths, making it the 14th most common cause of cancer death.¹ In 2001, the lifetime risk of melanoma was 1 in 77.1 among men and 1 in 92.8 among women, leading to a lifetime cancer death rate of 1 in 303 for men and 1 in 526.3 for women. It is slightly more common among men 70 years and older; the 10-year risk of being diagnosed with melanoma rises from 3 per 1,000 below age 70 to 4 per 1,000 above age 70. The incidence of melanoma among women is less affected by age and is about 2 per 1,000 before age 70 rising to slightly above 2 per 1,000 after age 70.¹ The reason for the age-related increase in incidence is unknown but is believed to be due to the cumulative effects of sun exposure or sun damage to the skin, one of the most important risk factors for the development of melanoma.

The incidence of nonmelanoma skin cancers (NMSC), which include basal cell carcinoma and squamous cell carcinoma, has also increased, particularly among older adults.³ Nonmelanoma skin cancers are the most common human malignancies, accounting for more cases than all other cancers combined. Nonmelanoma skin cancers are generally nonfatal; thus the incidence is not accurately documented. It is estimated that 1 in 6 men and 1 in 7 women will be diagnosed with a NMSC, a two- to threefold increase in the 1990s compared to 1960s.³ Since older adults also have more NMSC, physicians must be able to reliably differentiate melanoma from the other skin conditions. Important clinical features of melanomas include growth or change of preexisting nevi, new or growing pigmented or nonpigmented skin lesions, variations in colours or contour, ulceration, bleeding, and pruritis (Figure 1).

Advanced age (>65 years) has been identified as an independent predictor for worse overall, cancer-specific, and disease-free survival in many studies worldwide.^{4–6} This trend does not stop at any specific age (Table 1). The association between advanced age and poor outcome in melanoma is likely multifactorial. When compared to younger individuals, melanomas in older individuals tend to be thicker at diagnosis,^{4–7} are

more often ulcerated,^{8,9} and more often demonstrate regression.^{8,10} These three factors have been associated with more adverse cancer biology and worse treatment outcomes.^{2,8}

Melanomas can be classified into four histological types: superficial spreading, nodular, acral lentiginous, and lentigo maligna. Nodular melanoma has the worst prognosis and occurs more frequently among older individuals.^{6,11} Various theories have been proposed to explain this, including altered skin thickness among older adults and impaired immunological responses.⁷ Reduced concern for self-appearance resulting in a delay in diagnosis may also play a role.¹²

Delays in diagnosis do appear to occur more often among older populations^{7,12} and are associated with a poorer prognosis.¹³ When compared to younger populations, older individuals also have a higher incidence of melanomas on the feet,^{14,15} head, and neck,⁴ areas recognized to be associated with diagnostic delay.¹⁶ Benign moles have a higher rate of transformation into melanomas in the older populations (age >60) (1 in 200,000 vs. 1 in 33,000).¹⁷ The risk of developing a second melanoma (overall 5%) also increases with time,¹⁸ making new primary lesions more common among older adults.

Management of Malignant Melanoma Screening

Melanoma has a relatively low incidence rate, and screening is therefore not generally recommended for the average fair-skinned population. While melanoma can occur in those with dark skin, it occurs at a much lower rate. However, in an American study, melanoma screening had a higher chance of detecting a melanoma for those over 50 years old (2.6 vs. 1.5 per 1,000 screening).¹⁹ Screening is recommended for those with a personal or family history of melanoma and atypical moles, and a history of excessive sun exposure, especially at young age.

Diagnosis

Any skin lesions with some or all the clinical features of melanoma should under-

Table 1: Five- and Ten-year Survival Rates by Age for Stages I and II Melanoma Patients Demonstrating Survivals Are Increasingly Worse with Age

Age group (Years)	No.	Survival Rates	
		5-Year% ± SE	10-Year% ± SE
10–19	238	87 ± 2.6	81 ± 3.5
20–29	1,400	87 ± 1.1	77 ± 1.6
30–39	2,518	86 ± 0.8	77 ± 1.2
40–49	3,006	85 ± 0.8	75 ± 1.2
50–59	2,945	82 ± 0.9	69 ± 1.3
60–69	2,805	78 ± 1.0	63 ± 1.6
70–79	1,500	71 ± 1.7	56 ± 2.7
≥80	333	60 ± 5.0	43 ± 7.0

Source: Balch, et al., 2001.²

go a diagnostic excisional, incisional, or punch biopsy (see Figure 1). It is important to remember that not all melanomas are pigmented, so biopsies should be done on any new or changing lesion, especially if it is itching or bleeding. Clinicians who feel comfortable doing a punch or excisional biopsy in the office should do so: it is not necessary to refer prior to diagnosis. A full-thickness skin biopsy allows for accurate diagnosis as well as an assessment of the tumour thickness or depth which is essential to guide further management. This can be obtained by an excisional or punch biopsy under local anesthetic in the office or a referral to a dermatologist can be made. For small lesions, an excisional biopsy with 0.5 cm margins is recommended. Punch biopsies are used for larger skin lesions and lesions in cosmetically sensitive areas such as the face. Shave biopsy is not recommended as it does not allow an accurate assessment of tumour depth and may interfere with accurate depth assessment at definitive excision.

Surgery

Wide local excision is the primary surgical treatment for melanoma. The width of surgical margins is guided by the pathologic thickness of the lesion and its anatomic location. A general consensus can be

derived from randomized trials that have examined the optimal lateral resection margin in order to reduce local recurrence. For melanoma in situ, a margin of 0.5–1.0 cm around the primary lesion or biopsy scar is appropriate. For invasive melanoma less than 1.0 mm (thin melanoma), a 1 cm margin is advised.^{20,21} For lesions between 1.0 and 2.0 mm in depth, the adequacy of a 2.0 cm margin (if the anatomic site allows) is implied by several studies.^{20,22,23} A margin of 2.0 cm for melanomas between 2.01 and 4.0 mm thickness is sup-

Figure 1: Atypical Melanoma



An atypical melanoma that arose in a pre-existing scar demonstrates features that should raise clinical suspicion. These include A: asymmetry, B: an irregular border, C: variations in colour, and D: an increasing diameter.

Source: Courtesy Dr. Alexandra Easson

Malignant Melanoma

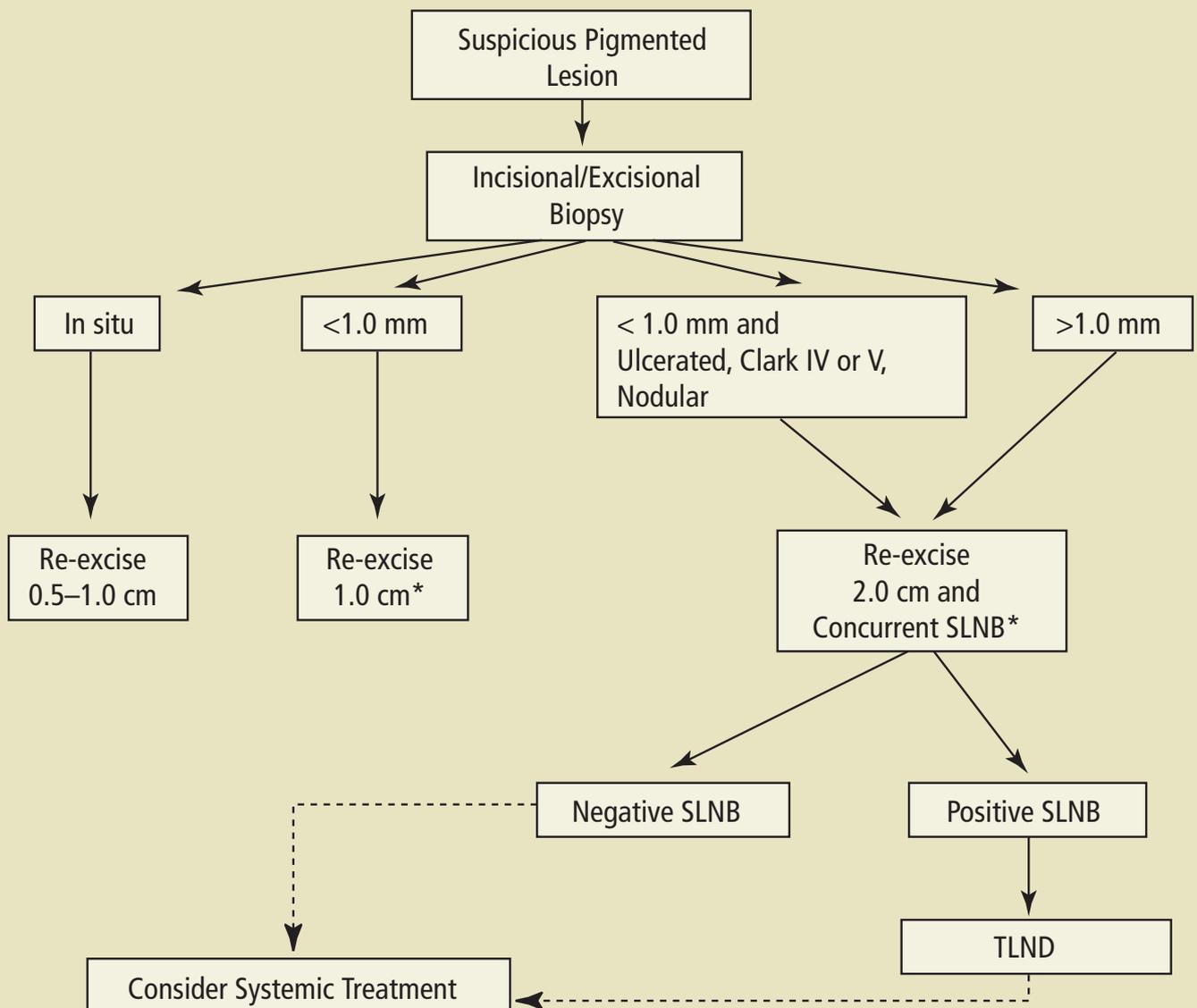
ported by two trials.^{24,25} Similarly, for melanoma >4.0 mm depth, a margin of 2.0 cm has been shown to be adequate²⁶ as larger margins do not reduce recurrence or survival and result in higher wound complications (Figure 2).

Provided there are no medical contraindications, surgical treatment of the primary site of melanoma among older

adults should be carried out without any compromise of the recommended surgical margins. Depending on the location and size of the primary, a skin graft or rotational flap closure might be necessary to close the anticipated skin defect. A clear understanding of the surgical anatomy is necessary when considering extensive reconstructive procedure and a

consultation with a plastic surgeon may be required. Wide local excision of thin, small melanomas can often be done under local anesthesia (LA), but more extensive excision with complicated closure will likely require the procedure to be performed under general anesthesia (GA). This may require a preoperative referral to a cardiologist or anesthesiolo-

Figure 2: An Algorithm for the Primary Management of a Malignant Melanoma



Abbreviations

FNAB: Fine needle aspiration

TLND: therapeutic lymph node dissection (removal of all lymph nodes in the lymph node basin (axilla or groin))

SLNB: sentinel lymph node biopsy (1st draining lymph node and draining the area of skin where melanoma was, usually located in closest lymph node basin (groin or axilla))

*If clinical assessment of local lymph nodes suggests involvement, this should be confirmed with FNAB on excisional biopsy followed by therapeutic lymphadenectomy in node-positive cases.

gist for older patients with substantial comorbidities.

Diagnostic sentinel lymph node biopsy (SLNB) has become an accepted part of the surgical treatment of primary melanoma in patients without clinical, radiological, or histological evidence of local-regional or distant metastases.²⁷ Sentinel lymph node biopsy is relatively contraindicated when done subsequent to a previous rotational flap closure due to higher false negative rates^{28,29}; therefore, it is preferred to do both procedures at the same time. Patients with primary tumours demonstrating depth >1.0 mm or tumours of any depth and Clark IV and V level invasion, ulceration, or nodular subtype are offered SLNB²⁷ (see Figure 2). The objective of SLNB is to perform accurate minimally invasive lymphatic staging. Patients with positive sentinel lymph nodes are offered a therapeutic lymph node dissection (TLND), removal of residual nodes in the lymph node basin (usually axilla or groin), followed by adjuvant interferon therapy.

For older patients, the decision to perform SLNB must be individualized. Older individuals should be made aware of the possibility that this procedure may not be as accurate as in the general population.^{8,30–32} Preoperative lymphoscintigraphy to identify the sentinel node may be helpful in planning surgery and the type of anesthesia needed. Sentinel nodes in the groin or axilla may be amenable to excision under LA or GA; sentinel nodes in the neck, popliteal fossa, or multiple nodal basins may necessitate GA. The stress of a procedure under LA may not be appropriate for individuals with angina; however, existing comorbidities may make LA a better choice for some patients. Follow-up TLND (in the case of positive nodes) must be performed under GA and so there is no sense to performing SLNB in patients whose comorbidities preclude GA. Patients who present with clinically palpable positive lymph nodes at presentation are offered a TLND under GA for local control.

Systemic Therapy

The mainstay of adjuvant medical treatment for high-risk malignant melanoma

Key Points

The incidence of melanoma is increasing, especially among the older adult population.

Melanoma among older adults has a worse prognosis than among younger patients.

Melanoma should be considered in the differential of any new or changing lesion, particularly if it itchy or bleeding. A melanoma is usually, but not always, pigmented.

Full-thickness biopsy will diagnose the lesion and allow the assessment of the depth of the lesion, which is essential to guide further management.

Wide local excision and sentinel lymph node biopsy (SLNB) is the current accepted management strategy for individuals with an early melanoma. Among older adults, the benefit of SLNB is particularly not clear; thus, it should be offered on an individual basis.

is interferon alpha-2b. Three studies have demonstrated improved relapse-free survival, two showing improved overall survival, among patients administered high-dose interferon for stage III (lymph node-positive) melanoma.^{33–35} High-dose interferon alpha-2b has many side-effects including headache, fatigue, nausea, weight loss, myelosuppression, and depression.³⁴ Interferon may be considered for patients with high-risk disease (lesions >4.0 mm or local lymph node involvement cleared surgically) in whom the potential benefits outweigh the possible toxic side effects. Patients being considered for systemic treatment should be without serious comorbidities and should have a premonitory life expectancy greater than 10 years.³⁶ These recommendations appropriately exclude many older adults from interferon alpha-2b treatment.

The above discussion regarding systemic treatment requires a brief review of the role for SLNB among older adults. There is currently no convincing evidence that SLNB followed by TLND in patients with positive sentinel nodes improves disease-free survival that is attributable to the procedure alone.^{25,37} Rather, SLNB allows selection of patients who may benefit from systemic treatment. It follows that many older adults, who are not eligible for systemic treatment with interferon, should not be offered SLNB. Close follow-up with TLND performed when there is clinical/pathological evidence of local nodal lymphatic metastases is an appropriate alternative.

Metastatic Melanoma

Metastatic melanoma is generally noncurative in most patients and confers a grave prognosis. These patients have a 5-year survival of less than 5% and a mean survival of 6–19 months.³⁸ Chemotherapy and immunochemotherapy (interferon alpha-2b or interleukin-2) remain the mainstay of treatment but no therapy that has been shown to impact on survival in metastatic disease.^{39,40} In any case, because of their toxicity, these regimens are not an option for most older individuals.

For the palliative management of symptomatic metastases (Figure 3) local radiation to soft tissue metastases can be very effective, with reduction of symptoms in most.⁴¹ A topical cream applied to skin metastases, imiquimod 5% (Aldara), has

Figure 3: Locally Advanced Melanoma on a Shin Presenting with Multiple Satellite Lesions



Source: Courtesy Dr. Alexandra Easson.

also been effective for older adults who cannot tolerate other therapies.⁴²

Conclusion

The rapid rise in the incidence of melanoma, particularly among older adults, means that any changing or new skin lesion deserves special attention in this age group. Melanomas among older adults often display more aggressive biology and a worse prognosis. Therefore, public awareness and a heightened index of suspicion by primary care physicians are necessary to avoid a delay in diagnosis and to allow intervention during the curable phase of this disease. Unfortunately, comorbidity frequently precludes the use of aggressive definitive surgical and/or medical management of more advanced melanoma among older adults.



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