MELANOMA

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Introduction

Malignant melanoma (MM) is a life-threatening skin cancer that arises from melanocytes, which are the pigment-producing cells within the skin. Although melanoma typically arises within the skin, it can often metastasize, or spread, to other parts of the body, including lymph nodes, lung, brain and liver. According to the Surveillance Epidemiology and End Results (SEER) data, it is projected that 68,720 men and women will be diagnosed with and 8, 650 patients will die of melanoma in the year 2009. Men tend to be affected slightly more than women, although data compiled from Carolina Medical Center - NorthEast in 2008 showed equal distribution of cases between men and women (63 cases each). The median age at diagnosis for MM is roughly 59 years; however, the ages at which we are seeing MM vary greatly: 0.9% under the age of 20; 7.8% between 20-34; 12% between 35-44; 18.9% between 45-54; 19.8% between 55-64; 17.7% between 65-74; 16.8% between 75-84; and 5.7% greater than 85. Moreover, it has also been demonstrated that white patients have a slightly higher risk of developing MM, yet other races/ethnicities such as African-Americans, Asians, Hispanic, and American Indians can also be affected.

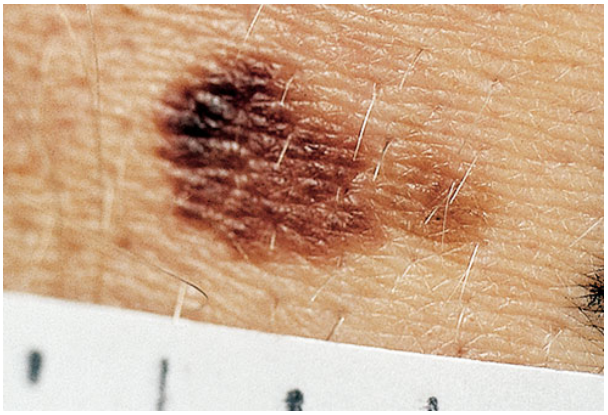
Risk Factors

Perhaps one of the greatest challenges in the prevention, diagnosis, and treatment of MM is identifying the patient populations at most risk. These risk factors can be roughly divided into two general categories: genetic/hereditary (family) and environmental. For example, those patients who carry certain genetic mutations have an increased risk, which can occur within families. Those individuals with a personal or family history of MM are also at increased danger, as are those with a large number and size of moles. Despite a lack of agreement, some authors suggest having greater than 50 moles or those that have moles larger than 5mm (about the size of a pencil eraser) are more likely to develop MM. Furthermore, patients who have skin types I and II (those that always or usually sunburn, respectively) tend also to be affected. On the other hand, exposure to UV rays from the sun is the most important cause in MM. Those patients who have a history of blistering sunburns, exposure to man-made UV sources (tanning booths), and live close the equator all have a greater predisposition to MM. Also, individuals who are immunosuppressed i.e. HIV/AIDS or those with other types of cancers undergoing chemotherapy are more likely to be affected.

Clinical Features

Although MM can rarely arise on non-skin areas such as the eye and inner ear, the majority are diagnosed within the skin. There are four main types of MM: superficial spreading, nodular, lentigo maligna, and acral lentiginous. Superficial spreading MM is the most frequently-encountered type and can be seen almost anywhere on the body in fair-skinned people, even though it tends to favor the chest and back in male patients and the lower legs

in female patients. This type of melanoma may arise within a pre-existing mole or develop abruptly. Asymmetry (lop-sidedness) within a mole, irregular borders, color variation, and changing size are all clues that a lesion on your body may be a MM. One popular misconception is that melanoma's are typically raised "bumps", whereas the superficial-spreading types are usually completely flat and may resemble a freckle.


reference: http://www.webmd.com/melanoma-skin-cancer/slideshow-precancerous-skin-lesions-and-skin-cancer

Nodular melanomas occur most commonly on the head, neck and trunk areas, and are more common in men than woman. They may appear as rapidly enlarging, brown/black or blue nodules that oftentimes bleed or ulcerate. These changes may take place over the course of weeks to months. Lentigo maligna melanoma is typically seen in older patients in their 60-70's, and occur in areas of chronic sun exposure i.e. head/neck and arms. These skin cancers may appear as an ill-defined brown or black spot, displaying irregular borders and color variation. Finally, the acral lentiginous variant, which is the least common type, is seen in individuals with darker skin types and tends to favor the palms and soles and in rare instances, affect the nails. Oftentimes, patients will miss-identify these cancers as trauma, which usually causes a delay in seeking diagnosis and treatment.

Diagnosis/Workup

Once you and your health care provider has identified a suspicious lesion, they will likely proceed with a biopsy, an easy surgical procedure in which they take a portion or all of the mole and send it for examination by a pathologist, a physician who analyzes skin samples. The pathologist will then confirm the diagnosis of melanoma, and generate a report that looks at several important variables: Breslow's depth (how deep the cancer goes down into the skin), ulceration, regression, mitotic figures, tumor infiltrating lymphocytes, regression, satellite metastases, and angioneurotropic invasion. In particular, the Breslow's depth, ulceration and more recently, mitotic figures are crucial pieces of information that will help your health care provider "stage" your melanoma, which provides both prognostic data and well as survival probabilities. For instance, according to the American Joint Committee on Cancer (AJCC) staging for melanoma (Table 1), a melanoma measuring less than 1 mm in depth and showing no ulceration is considered Stage 1A, whose 5 and 10 year survival rates are 95 and 88 %, respectively (Table 2). These "thin melanoma's" typically don't require blood or xray tests to check for lymph node spread. However, if an individual has a

melanoma whose depth is 2 mm and shows signs of ulceration, it is considered Stage IIB and has an increased risk for spread to local lymph nodes. Your health care provider will most likely order blood tests (complete blood counts, liver function tests, and lactate dehydrogenase levels), as well as radiographic studies such as chest X-rays, CT scans and even PET-scans. Your physician will also discuss the possibility of a sentinel lymph node biopsy (SLNB), a minimally invasive procedure that uses radiographic dye to identify the nodes that drain the location from which your melanoma has arisen. Although this procedure has not been shown to alter survival rates, it does play a critical role in determining your prognosis and directing appropriate treatment options. Survival rates are followed annually on the National Cancer Database (NCDB) (Table 3).

Treatment Options

The principle treatment for all melanomas is surgical excision. The amount of tissue that your surgeon will take depends on several factors, including the depth of the melanoma, as well as the location. For instance, melanoma in-situ (those melanomas confined to the epidermis, or top portion of the skin), require only roughly 1/5 of an inch to be removed around the visible mole. However, lesions whose depth is greater than 1mm require 1-2 cm margins. Oftentimes, a melanoma will occur in anatomic areas where obtaining the adequate margins is difficult, and may necessitate adjuvant treatment. Adjuvant treatment (those that alter your immune system) is used in situations where individuals have thick melanoma's, positive lymph node involvement or spread to internal organs. Several cancer drugs such as dacarbazine, temazolamide, as well as interferon-α have been used to treat patients with advanced disease. Melanoma vaccines have also been tested recently, but so far have shown no clear value.

Follow-up/Prevention

Those individuals diagnosed with melanoma have an approximately 1-8% chance of developing an additional melanoma sometime in their life. These high risk patients require regular follow-ups every 3-6 months with their health care provider, with a complete physical exam as well as a thorough review of systems. Recurrences, although most common within the first 2 years of diagnosis, can occur decades later, necessitating close monitoring. It is necessary for these patients, as well as everyone, to adhere to consistent sun protections guidelines: wearing sunglasses with UV protection, wearing SPF 30+ sunscreens (re-applying every 90 minutes), and avoiding direct sun exposure at times when the ultraviolet rays are at their peak (approximately 10 am-3 pm). Patients should also be counseled on the proper way to perform monthly self skin examinations, paying particular attention to the ABCD's of melanoma: A. symmetry, B.order irregularities, C. olor variation and D.iameter changes. While it is important to recognize changes in existing moles, remember that the majority of melanoma's occur 'from scratch'. For those patients with multiple moles or a history of melanoma, digital photography is an excellent tool to help both you and your physician track and follow your skin.

Table 1.

TNM	**DEFINITIONS**
	Primary Tumor (T)
TX	Primary tumor cannot be assessed (e.g., shave biopsy or regressed melanoma
T0	No evidence of primary tumor
Tis	Melanoma *in situ*
T1	Melanoma ≤ 1.0 mm with or without ulceration
T1a	Melanoma ≤ 1.0 mm in thickness and level II or III, no ulceration
T1b	Melanoma ≤ 1.0 mm in thickness and level IV or V or with ulceration
T2	Melanoma 1.01-2.0 mm in thickness with or without ulceration
T2a	Melanoma 1.01-2.0 mm in thickness, no ulceration
T2b	Melanoma 1.01-2.0 mm in thickness, with ulceration
T3	Melanoma 2.01-4 mm in thickness with or without ulceration
T3a	Melanoma 2.01-4 mm in thickness, no ulceration
T3b	Melanoma 2.01-4 mm in thickness with ulceration
T4	Melanoma greater than 4.0 mm in thickness with or without ulceration
T4a	Melanoma > 4.0 mm in thickness, no ulceration
T4b	Melanoma >4.0 mm in thickness, with ulceration

Table 2.

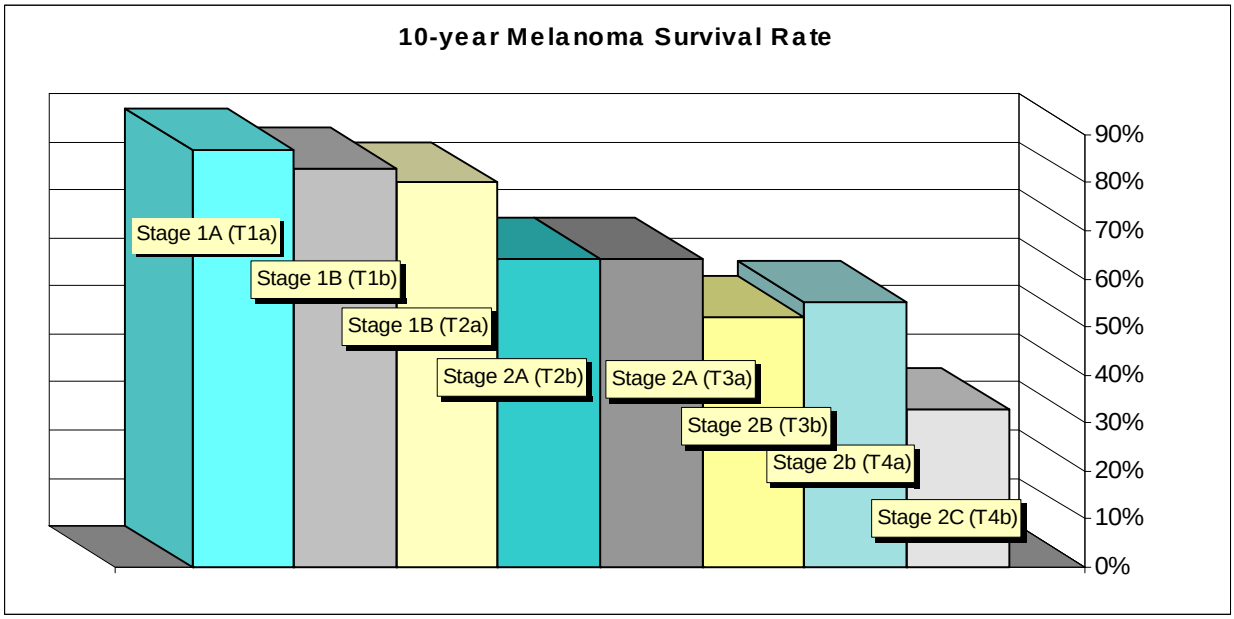
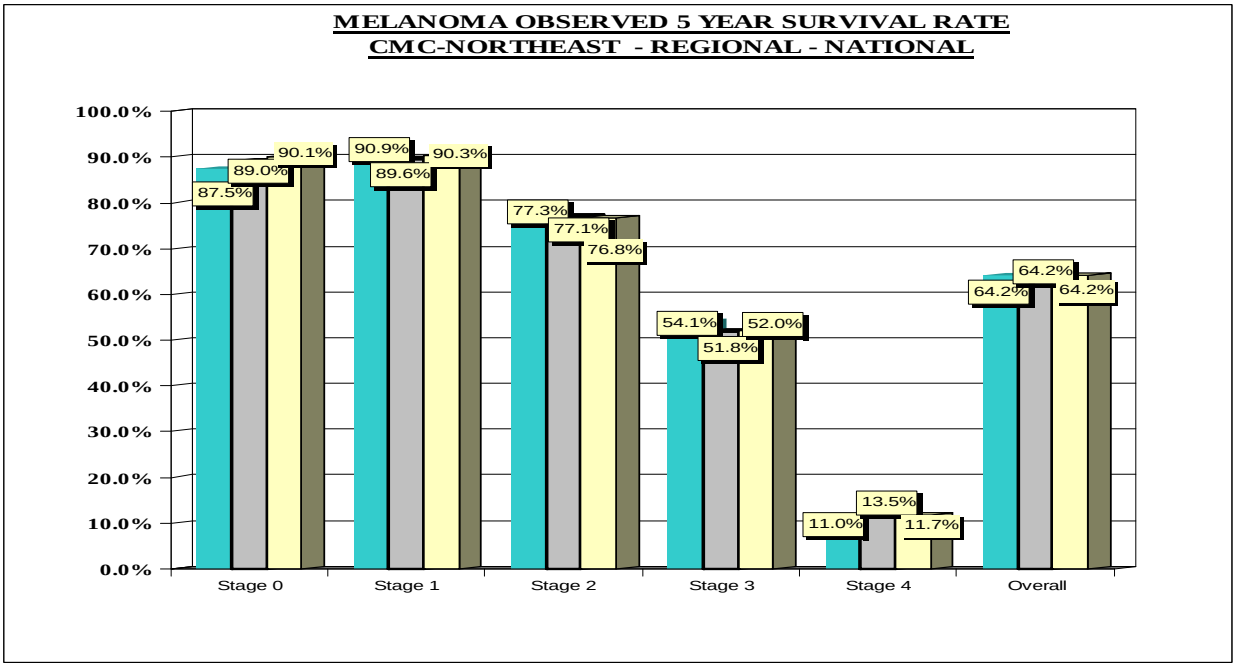


Table 3.



*CMC-NorthEast survival rates closely match state averages in our region (DE, FL, GA, MD, NC, SC, VA, & DC) and national averages.

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