
Risk factors and outcomes of cutaneous melanoma in women less than 50 years of age

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Background: Melanoma is the fifth most common cancer in the United States, with recent reports indicating increasing incidence among young women.

Objective: This study sought to investigate histopathology, staging, risk factors, and outcomes of cutaneous melanoma in women younger than 50 years.

Methods: All female patients aged up to 49 years with biopsy-proven diagnosis of melanoma between 1988 and 2012 were included. Patients with a follow-up of less than 2 years were excluded.

Results: A total of 462 patients were identified, with mean age of 34.7 years. Invasive melanoma was less common in women 19 years of age or younger ($P < .0008$). Positive sentinel node status ($P < .008$), recurrence rates, metastatic disease ($P < .001$), and death rates ($P < .008$) were higher for women ages 40 to 49 years. The 41 patients with a pregnancy-associated melanoma had a significantly worse prognosis in comparison with a control group of nonpregnant patients, with a 9-fold increase in recurrence ($P < .001$), 7-fold increase in metastasis ($P = .03$) and 5-fold increase in mortality ($P = .06$).

Limitations: This was a retrospective study.

Conclusion: The increasing incidence of melanoma for women younger than 50 years suggests that regular skin checks and self-examinations are warranted. In addition, in women given the diagnosis of melanoma during or within 1 year after childbirth, regular follow-up and monitoring for recurrence are recommended. (*J Am Acad Dermatol* 2016;74:731-8.)

Key words: melanoma; pregnancy; pregnancy-associated melanoma; outcomes; sentinel node; survival; young.

The incidence of malignant melanoma (MM) has been increasing at a rapid pace in the last few decades.¹ Surveillance, Epidemiology, and End Results showed an increase in female MM incidence rates by year from 7.44 cases per 100,000 in 1975 to 18.35 cases per 100,000 in 2011.^{2,3} Recent epidemiologic studies showed that the incidence of melanoma is rapidly increasing in women between 20 and 40 years of age.⁴

Although pregnancy-associated melanoma (PAMM) is considered a rare occurrence, the number

Abbreviations used:

AJCC: American Joint Committee on Cancer
MM: malignant melanoma
PAMM: pregnancy-associated malignant melanoma

of cases may be expected to rise given the corresponding increase of melanoma among women of childbearing age. In fact, a recent population-based

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Funding sources: None.

Conflicts of interest: None declared.

Accepted for publication November 12, 2015.

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Published online January 20, 2016.

0190-9622/\$36.00

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<http://dx.doi.org/10.1016/j.jaad.2015.11.014>

study conducted in Sweden identified melanoma as the most common malignancy diagnosed during pregnancy, followed by breast and cervical cancer.⁵ Whether pregnancy itself has an adverse effect on the prognosis of MM is still unclear and remains a matter of debate.

In this single-center retrospective case-control study, a large clinical database was used to collect detailed data of cutaneous melanomas developing in women aged 49 years or younger. The odds of melanoma mortality, recurrence, and metastasis in women with MM diagnosed during or within 1 year after pregnancy were analyzed.

METHODS

This study was approved by the Cleveland Clinic Institutional Board Review. Patient population was obtained from the institutional diagnosis database. Data for all female patients up to 49 years of age who had a biopsy-proven diagnosis of cutaneous MM from 1998 to 2012 were reviewed.

Patients with less than 2 years of follow-up after diagnosis were excluded from the study. Detailed data were extracted from patients' electronic medical records and included patient demographics, tumor characteristics, sentinel lymph node biopsy, and histopathologic data. Multiple manual searches for terms "child," "children," "pregnancy," "pregnant," "delivery," "delivered," "birth," "gravida," "gestation," "miscarriage," and "abortion" were used in the electronic medical record system to identify all patients with melanoma that developed during pregnancy or within 1 year of childbirth. Cutaneous melanoma stage was assigned based on the 7th edition of the American Joint Committee on Cancer (AJCC) staging system.⁶

Melanoma outcomes included all-cause MM-specific mortality, recurrence, metastasis rate, and need for immunotherapy, chemotherapy, and radiotherapy. Length of follow-up was defined as the last office visit recorded in the electronic medical record. PAMM was arbitrarily defined as MM diagnosed during pregnancy or within 1 year after delivery.

PAMM data were compared with a control group defined as the remaining study population with no evidence of pregnancy or childbirth within

1 year of diagnosis. Patients with miscarriages and pregnancy terminations were included. Patients were categorized in 4 age groups (0-19, 20-29, 30-39, and 40-49 years) for categorical data analyses.

Statistical analysis

Statistical analysis was performed using software (Stata 11.0, StataCorp LP, College Station, TX). Mann-Whitney or Student *t* tests were used for continuous variables as deemed appropriate. The χ^2 or Fisher exact tests were used for categorical variables; Fisher was the test of choice for variables with frequency limited to 5 or fewer occurrences per subgroup. Post hoc analysis was performed for variables with multiple nominal categories and χ^2 with *P* less than .05 considered significant. To avoid high type 1 error, Bonferroni correction was applied when indicated.

Multivariate analysis was performed using logistic regression to determine if history of pregnancy, stage, location, and age group were independently associated with melanoma death, metastasis, and recurrence.

RESULTS

After applying exclusion criteria, the study cohort comprised 462 patients (Table 1). The mean age at the time of melanoma diagnosis was 34.7 years. The mean length of follow-up was 91 months. The majority of the patients in the study were aged 30 to 39 years (42.5%). The mean Breslow level was 1.14 mm. Breslow level was available for 92% of the patients. The most common anatomic location was the trunk (38%), followed by lower extremities (33%) and upper extremities (20%). All patients included in the study had information on AJCC stage.⁶

Study population

The most common pathologic stages across all age groups were stage 0 and I. Stage I was the most frequent in women presenting at 20 to 49 years of age, with approximately half of the cases (*P* < .001 vs. other subgroups). In addition, a higher proportion of patients in the youngest age group (≤ 19 years) had a stage 0 melanoma (*P* < .0008).

CAPSULE SUMMARY

- Incidence of malignant melanoma among women younger than 50 years is increasing, with highly variable reported outcomes among pregnant women.
- This study found higher rates of recurrence, metastasis, and mortality in women with pregnancy-associated melanoma.
- Women younger than 50 years, particularly those who are pregnant and at higher risk of developing melanoma, should be vigilant in monitoring changing skin lesions and maintain diligent dermatologic follow-up.

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