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Localized melanoma in older patients, the impact of increasing age and comorbid medical conditions

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Abstract

Background: Elderly patients experience a different spectrum of disease and poorer outcomes than younger patients. This study investigated the impact of age and medical comorbidities on the management and outcome of patients ≥65 years.
Methods: A retrospective review of all patients ≥65 years (481 patients with 525 primary melanomas) presenting with AJCC clinical stage I–II melanoma to an Australian cancer centre between 2000 and 2008.
Result: The median age was 74 years (65–94) with a male predominance (313 males, 65.0%) and median tumour thickness of 1.90 mm (IQR = 0.40–2.90, T1 = 33%, T2 = 20%, T3 = 24%, T4 = 23%). Inadequate surgical margins of excision (<10 mm) were common in older patients independent of site, thickness and ulceration (OR = 1.04, 95%CI = 1.00–1.07, p = 0.038). Inadequate excision margins were strongly associated with time to local recurrence, independent of age, thickness, ulceration and mitotic rate (HR = 3.00, 95% CI = 1.49–6.03, p = 0.0021), but not time to progression (p = 0.10) or disease specific survival (DSS, p = 0.27). Overall survival (OS) was strongly related to increasing age (HR = 1.04, 95%CI = 1.01–1.07, p = 0.015) and comorbid medical conditions (HR = 1.26, 95%CI = 1.12–1.42, p < 0.001), as assessed by the Charlson comorbidity index (CCI). DSS was significantly related to CCI (HR = 1.20, 95%CI = 1.01–1.42, p = 0.041) and not age (p = 0.46), when adjusting for thickness, ulceration and mitotic rate on multivariate analysis.
Conclusion: Older patients present with poor prognosis melanomas yet are less likely to receive adequate surgical excision margins resulting in higher rates of local recurrence. In melanoma patients ≥65 years, the increasing number of medical comorbidities explains much of the age related variations in OS and DSS and should be considered when planning treatment.

Keywords: Melanoma; Aged; Comorbidity; Mortality; Disease progression

Introduction

The management of melanoma in older patients poses an emerging challenge to health care systems for two major reasons. First, the global population is in the midst of an unprecedented demographic transformation characterized by a rapid and disproportionate expansion in the number of older persons. The World Health Organisation predicts between 2000 and 2050, the proportion of the world's population over 60 years of age will have doubled from 11% to 22%, while the number of people aged over 80 years of age will have quadrupled.[1] Second, the disease burden of melanoma is borne disproportionately by older persons. In the USA, the largest proportion of new melanoma cases is in people >60 years[2] and while melanoma mortality is decreasing for those <65 years, it continues to increase for persons >65 years, particularly older men.[3]

Older patients with melanoma appear to present with more advanced primary tumours and have a poorer prognosis than younger patients.[4–8] Elderly patients are also increasingly more likely to have other age-related comorbid medical conditions, which may impact on the delivery of care. The impact of increasing age and comorbidities

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amongst older patients with respect to their presentation, management and outcome is not well understood. The aim of this study was to investigate the impact of age and increasing medical comorbidities on the management and outcome of patients ≥65 years.

Method

Patients

The study was a retrospective review of all patients aged 65 years and over presenting to the Peter MacCallum Cancer Centre (PMCC), a tertiary referral cancer hospital in the state of Victoria, Australia. Subjects were accessed via the 'Health Information Services' registration database. Data was sourced from PMCC records and where necessary follow up data from the Victorian Cancer Registry or contact with the patients general practitioner.

All patients aged 65 years or over who presented to PMCC from the 1st of January 2000 to the 31st of December 2008 with AJCC[9] clinical stage I or II melanoma were eligible for the study. In total 481 patients presenting with 525 primary melanomas were identified and all were included in the study. Patients with more than one primary melanoma over the specified interval (n = 32) had only their most advanced melanoma considered when reporting survival and demographic data.

The age threshold of 65 years to define 'older' was adopted in view of the use of this cut off in previous reports[4,6,10] and as it commonly marks the end of full time employment in Western industrialized societies.[11]

Patients were managed according to a unit protocol based on the Australian Cancer Society Guidelines for the Management of Cutaneous Melanoma.[12] Generally, SNB was not recommended for patients over 85 years of age but left up to the treating clinician, predominantly due to concerns that patients may not derive a benefit from SNB as well as a desire to avoid hospitalization and a general anaesthetic in frail patients. Patients over 85 years were excluded from any analysis involving SNB. Excision margins were calculated from histopathology specimens by summing the margin from the initial diagnostic biopsy and from the wide excision and multiplying by a factor of 1.25 to account for shrinkage during histology processing.[13] For this study, a complete excision margin of 10.00 mm or greater for any invasive melanoma was considered acceptable.

The Charlson comorbidity index (CCI), a validated system of stratifying patients' risk of mortality was used to assess the magnitude of patients comorbid medical conditions.[14,15] CCI scores are calculated by summing comorbidity scores based on the International Classification of Diseases (ICD) diagnosis codes. Each comorbidity has an associated weight, based on its adjusted risk of mortality and the sum of all medical comorbidities results in a single patient comorbidity score. A high CCI score reflects multiple and/or significant medical comorbidities and indicates a high predicted 10-year mortality. A non-age adjusted version of the CCI exists and was used in this study due to the inclusion of age as a variable in multivariate analysis. Cutaneous melanoma was not included in the calculated CCI score for patients in this study.

The number of medications (including vitamin supplements) were obtained from pharmacy records. The histologic subtypes of spindle, acral lentiginous and desmoplastic morphologies were classified as 'other' for the purposes of this study as they accounted for only 8.2% of melanomas. Absolute mitotic rate refers to the number of mitotic figures visualised per mm^2.

Statistical analysis

Data was analysed using 'R' statistical software, version 3.0.3. A two sided p-value < 0.05 was considered statistically significant. Quantitative variables were described as mean (standard deviation) or median (range or IQR) according to their distribution. Odds and hazard ratios were specified per 1-year increase in age or 1-unit increase in CCI unless otherwise specified.

Comparative analysis of patient demographics, tumour characteristics and management were performed using simple and multivariate linear and logistic regression treating age as a continuous quantitative variable. Although age was modelled as a continuous variable, patients fell into three clinically relevant age groups; mature patients aged between 65 and 74 years, elderly patients aged between 75 and 84 years and very elderly patients aged 85 years and over. These groups have been used to summarise the data in the tables and graphs.

Cox proportional hazard modelling was used to examine disease specific survival (DSS), overall survival (OS), time to progression and time to local recurrence. Time to progression was defined as the period between histological confirmation of disease and time to disease progression. Disease progression was defined as the development of either regional (nodal or in-transit metastasis) or distant disease, patients who died without evidence of disease were censored at their date of death. Time to local recurrence was defined as the time from histological confirmation of disease to the development of a local recurrence. Local recurrence was defined as tumour regrowth within 2 cm of the surgical scar following definite excision, patients without an initial local recurrence were censored at the date of regional or distant recurrence or date of last follow up. Recurrences were documented as per clinical notes (letters, clinical notes) and pathology reports. Unless otherwise specified, multivariate analysis included the variables age, CCI, Breslow thickness, ulceration and mitotic rate.

Approval to conduct this study was obtained from the Peter MacCallum Cancer Centre Ethics Committee on 12/03/2014, project number 14/40R.