ORIGINAL RESEARCH

Characteristics, treatment and outcomes of 589 melanoma patients documented by 27 general practitioners on the Skin Cancer Audit Research Database

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ABSTRACT

Background and objective: General practitioners manage more melanomas than dermatologists or surgeons in Australia. Previously undescribed, the management and outcomes of melanoma patients treated by multiple Australasian general practitioners are examined.

Methods: The characteristics, management and outcomes of 589 melanoma patients, managed by 27 Australasian general practitioners and documented on the Skin Cancer Audit Research Database (SCARD), were analysed.

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INTRODUCTION
Cutaneous melanoma is the third most common major cancer in Australia and New Zealand and the leading cause of skin cancer death in both countries.1,2 General practitioners (GPs) manage more melanomas than either dermatologists or surgeons in Australia, and their proportion increased from 45% to 49% between 2003 and 2014.3 This change has occurred in the context of a rise in the rate of melanoma in situ diagnosis relative to invasive melanoma.4 The increase in management by GPs has raised questions about the quality of management in that setting, for which limited data are available.5

Relevant to management outcomes, the 5-year survival rate for primary invasive cutaneous melanoma was 92% in Australia in 2015–20175 and 90% in New Zealand in 2010–2011.6

In this retrospective, cross-sectional study of 657 melanomas managed by 27 GPs in Australia and New Zealand in 2013, we have evaluated the characteristics of the 589 patients, the diagnostic and therapeutic management, and the related outcomes. The characteristics of the 657 melanomas in this study have been previously described.7

METHODS
This study is based on a subset of the Skin Cancer Audit Research Database (SCARD) concerning patients treated during 2015.

SCARD was established in 2007 as a free, patient safety, lesion-tracking, self-audit and research tool for professionals managing skin malignancies.7 Its functions and workflow have been described.8 Over one million unique lesions from over 415 000 patients have been entered on SCARD by more than 1500 practitioners, the majority being GPs working in Australasia.7

We invited GPs who guaranteed completeness of data during 2015, to participate in the study. Twenty-seven consented, 24 from Australia and 5 from New Zealand, representing 18.6% of those on SCARD in 2015, who contributed 55.6% of the melanomas diagnosed that year.7

Data drawn directly from SCARD included coded patient and lesion identifiers, patient demographics, diagnostic data, biopsy and management data and histopathological diagnosis. Further data were added during 2020 via a questionnaire built into the GPs’ SCARD interfaces. Patients with unknown survival status were deemed lost to follow-up. Additional information was obtained by correspondence with participants when clarification was necessary.

This is a retrospective, observational study, on de-identified data, and ethics exemption #2019000909 was granted by the Ethics Committee of The University of Queensland, Australia.

Statistical analysis
The proportion of invasive specimens for patients under 40, or 40 and over, were compared using Fisher’s exact tests.9 The average Breslow thickness of tumours definitively excised by GPs was compared with those excised by other specialists using an unpaired Mann–Whitney test (chosen due to results of appropriate normality testing).10,11 In both cases, GraphPad Prism 9.5.0 software was used for analysis, \( P < 0.05 \) was considered significant, and two-sided tests were used.

Survival and tumour-free survival probabilities were estimated using the Kaplan–Meier model. Survival analysis included only patients with primary invasive melanomas with known Breslow thickness \( (n = 205, 115 \text{ males, mean age: } 60 \text{ years}) \). One patient with an invasive melanoma of unknown Breslow thickness was excluded from analysis (desmoplastic subtype, sentinel lymph node biopsy (SLNB) negative, negative for metastasis and surviving). If multiple melanomas were recorded in the same patient, only the thickest melanoma was included in the survival analysis. All survival analyses were performed using the software package ‘survival’ and R.12

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RESULTS

We analysed 589 patients with 637 melanomas treated by 27 GPs in 2013. Most patients (58.9%) were males, and melanoma incidence peaked in the seventh decade (Fig. 1, Table 1).

Most (65%) of the 637 melanomas were in situ, and of 215 primary invasive melanomas with known Breslow thickness, in 205 unique patients, 72.5% were thin (Breslow thickness ≤1 mm).

Patients aged less than 40 years had fewer melanomas, but in that cohort most melanomas were invasive, a higher proportion compared with those aged 40 years or older (P < 0.0001) (Fig. 1). Most patients (95.5%) had a single melanoma in 2015, 5.6% had two, and the balance (n = 5) had between 3 and 7 melanomas. Only 8.7% of patients had a history of a first-degree relative with melanoma, but 22.8% had previous melanoma and the majority (52.6%) had previous keratinocyte carcinoma (Table 1).

Most (55.9%) melanomas were diagnosed following an elliptical excision biopsy, the balance by shave to mid-dermis (32.2%), punch (8.5%) and saucerisation (deep to subcutis) (1.3%) (Table 2). Biopsy margins were uninvolved in 88.8% of elliptical excision biopsy specimens compared with 44.9%, 27.8% and 37.5% for shave, punch and saucerisation biopsies respectively (Table 2). The rates of unintended positive margins were 4.5% for ellipses, 58.3%, for shaves and 40% for punch biopsies.

Shave biopsy was preferred, by a narrow margin, for lesions 10.1–20 mm in diameter, but elliptical excision biopsy was preferred for all melanomas smaller or larger with known diameter (Table 3). For lesions with known diameter, 63.8% of punch biopsies were performed on small lesions ≤6 mm in diameter.

Most superficial spreading melanomas (60.5%) were subjected to elliptical excision biopsy, but lentiginous melanoma was subjected to excision and shave biopsy with similar frequency (45.4% and 43.8% respectively) (Table 3).

The diagnostic procedure was intended as definitive treatment for 9.4% (n = 60) of the 637 melanomas, but further surgery was required for 29 of these to achieve appropriate margins.

For patients with primary invasive melanomas (n = 205), either thin (≤1 mm) or thick, SLNB was discussed with 22 and 46, and proceeded with for 2 and 30 of them, respectively. Of the 32 SLNB performed, 5 were positive, all for thick melanomas, and all had completion lymphadenectomy. Of the five patients with positive SLNB, one had subsequent lymph node metastasis but was lost to follow-up, and four were surviving in 2020, without documented disease progression. Of 27 patients with negative SLNB, four were lost to follow-up, two died from non-melanoma causes, one had subsequent lymph node and distant metastasis followed by melanoma-specific death, and one had just distant metastasis followed by melanoma-specific death with 19 surviving disease-free.

Figure 1 Numbers of in situ and invasive melanomas by age. Exact counts are shown on corresponding bar segments. A single primary invasive melanoma with unknown thickness was excluded from this analysis. Statistical analysis to compare proportion of invasive and in situ melanomas for those aged under 40, or 40 and over, were performed using a Fisher’s exact test.
Definitive re-excision was performed by the treating GP for 74.9% of the melanomas, with 10.8% and 6.8% being treated by plastic and general surgeons respectively (Fig. 2, Table S1). GPs excised 84.5% of \textit{in situ} melanomas. The average Breslow thickness of invasive melanomas definitively excised by GPs was 0.67 mm (range 0.07–8 mm), and of those referred to and excised by other specialists, 1.99 mm (range 0.15–10 mm) \((P < 0.0001)\). Plastic surgeons definitively excised similar numbers of \textit{in situ} and invasive melanomas, 47.8% from females, most on the face, including the nose and ear, while those treated by general surgeons were mainly invasive, only 54.9% being from females, most not on the face, with none on nose or ear.

Current Australasian guidelines in 2015\cite{15} (5 mm peripheral clinical margins for melanoma \textit{in situ}, and 10 mm, or 10-20 mm, for Breslow thickness $\leq$1 mm or $>1$ mm respectively, with deep margins through full subcutis for all melanomas) were adhered to for 95.1% of excisions for peripheral margins (Table S1). Recommended deep margins were complied with for 55.6% of excisions, 41.4% alternatively having the deep margin within subcutis. For 4.2% of melanomas \((n = 26)\), no definitive re-excision was performed, and as a result, there were seven melanomas with deep clearance recorded as being within dermis (Table S1).

Melanoma staging was upgraded following definitive re-excision for 10 invasive melanomas, five due to positive SLNB. Of the remaining 5, the preceding biopsy was ellipse \((n = 2)\), shave biopsy \((n = 2)\) and punch biopsy \((n = 1)\). Both radial and deep margins were positive for one ellipse and one shave, and the deep margin was positive for the other ellipse and shave, with no margin positivity reported for the punch.

Although in 2015, there was no Australasian qualification in dermatopathology, as distinct from anatomical pathology, 347 (54.7%) of the 637 melanomas in the current study were histopathologically assessed by pathologists who reportedly identified themselves as dermatopathologists.

Outcomes for the 205 unique patients with at least one primary invasive melanoma in 2015 are presented in Figure 3.

In four cases, a subsequent lesion arose continuously with a scar from a melanoma excised in 2015. Three were confirmed as melanoma, while the other, arising in 2015, was histopathologically diagnosed as (dysplastic) naevus. The three recurrent melanomas were all on the face, two of the preceding melanomas being lentiginous and the other superficial spreading.

Fourteen patients diagnosed with at least one primary invasive melanoma in 2015 had subsequent metastasis (Table S2). Most (64.3%, \(n = 9)\) of these were male, with mean age 74.6 years (range 46–92). Two had multiple invasive melanomas in 2015, one with three (as well as four \textit{in situ}) and the other with two. Three of these 14 melanomas were located on each of the back and leg, two on each of the face, neck and thigh, one on the scalp and one on the arm. Seven were nodular, five superficial spreading and two lentiginous. Mean Breslow thickness was 5.9 mm (range 0.5–10.0). For seven of the nine patients with melanoma-specific death, that death was linked to a single
primary invasive melanoma. Five of these were nodular and two superficial spreading, one with a Breslow thickness of only 0.5 mm.

The median follow-up time of the 205 patients with primary invasive melanomas (115 males, mean age: 60 years) was 7.0 years (interquartile range: 6.5–7.3). The 5-year survival rate for all patients with invasive melanoma was 95.2% (95% CI: 91.2–98.5%).

DISCUSSION

Studies on melanoma demographics, diagnosis and management by GPs are limited, and the available evidence from Australasia suggests that while gender and age distribution of patients are similar to tertiary care-based studies, the proportion of in situ and thin-invasive melanomas is higher. The proportion of males was similar at 58.9% vs 57.1% as was the mean age at diagnosis, of 60 years (range 18–96) vs 57 years (range 19–95). In both of these primary care studies, most melanomas were in situ (65% vs 74.2% in the current and Brisbane study respectively) contrasting with only 23.8% being in situ in a tertiary care-based study on 5141 melanomas in Victoria and only 59.9% in a New Zealand, population-based study of 974 patients. Considering primary invasive melanomas, 71.5% in the current study were thin (<1 mm thick) compared with 84% in the Brisbane primary care study (<0.8 mm thick) contrasting with only 47.4% in the tertiary care-based study in Victoria (<1 mm thick).

Australasian guidelines applicable in 2015 and in Australia currently recommend elliptical excision biopsy for suspected melanoma, with 2-mm peripheral margins undermined in the subcutis, and in the current study, this was adhered to for 55.9% of lesions. Shave biopsy has been proposed as an expedient and reasonable alternative in certain circumstances, and this was the method used for 52.2% of cases in the current study. The fact that unintended positive margin involvement was eightfold more likely for shave versus excisional biopsy (Table 2) is a reminder of potential hazards to consider when deviating from guidelines.

For excisional-biopsy specimens, the objective was complete sampling for 95%, compared with 75% for shave biopsy (Table 2). This was not related to large size as ellipses were favoured for all lesions with documented diameters and were strongly favoured for lesions ≥20 mm diameter (Table 3). Punch biopsy is known to be the method most associated with errors in diagnosis of melanoma. Excluding cases with unknown diameter, 65.8% of punch biopsies were performed on lesions ≤6 mm. While for all punch biopsies, there were high rates of both radial and deep margin positivity, there were no cases of documented deep margin positivity where the radial margins were reported clear (Table 5). A similar pattern has
Figure 2  Practitioners providing the definitive treatment (secondary wide excision) of in situ and invasive melanomas. Exact counts are shown above the corresponding bar. A single primary invasive melanoma with unknown thickness was excluded from this analysis. Abbreviations: GP, general practitioner; WLE, wide local excision.

Figure 3  Details of outcomes for 205 patients with at least one primary invasive melanoma in 2013. Details of each segment are presented in adjacent text. One patient with a primary invasive melanoma of unknown Breslow thickness was excluded from analysis (sentinel lymph node biopsy negative, negative for metastases and surviving). Abbreviations: SLNB, sentinel lymph node biopsy; LNMet, lymph node metastasis; DMet, distant metastasis; IntransitMet, in-transit cutaneous metastasis.

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been previously documented suggesting that punch biopsy is being favoured where the punch comfortably encompasses the lesion, although it must be accepted that even in this situation undetected positive margins will be frequent. The fact that one punch biopsy with reported clear margins was followed by upstaging of the diagnosis following wide excision, is a reminder of the limitations of margin-assessment for punch biopsy specimens.

Superficial spreading melanomas typically have well-defined margins, and 60% in the current study were diagnosed following elliptical excision biopsy in contrast to lentiginous melanomas, frequently with indistinct margins, which were just as likely to be diagnosed following a shave or elliptical excision biopsy (Table 5).

In the current study, 74.9% of lesions were definitively managed by the treating GP, 17.6% by a surgeon and 0.5% by a dermatologist (Table S1), compared with 49%, 54% and 16% reported nationally in Australia in 2015-2014 respectively. Referral for definitive treatment of a melanoma by a GP is likely to be in response to a surgical challenge, probably explaining the low rate of referral to dermatologists in this context. The distribution of definitive management between plastic and general surgeons with respect to patient gender, anatomical site and invasive status was consistent with the traditional focus of each of these specialties.

For the vast majority (95.1%) of definitive re-excisions, the peripheral margin clearance complied with guidelines (Table S1). The lower compliance with guidelines for deep margin within the subcutis, is arguably reasonable, given the context of current Australian guidelines, which include an option of measuring the deep margin as for the peripheral margin where the subcutis is thick. Adverse outcomes were not increased with deep margins in the subcutis. Of index primary invasive melanomas with the deep margin within the subcutis, 4.5% had adverse outcomes (n = 2/46) compared with 7.5% with deeper margins (n = 12/159).

Guidelines recommend a discussion with the patient concerning SLNB with thick melanomas (>1 mm) and some high-risk thin melanomas although this is not without controversy. In the current study, SLNB was discussed with 80.7% of patients with thick melanomas, and performed in 52.6%, compared with rates ranging from 55% to 55% in tertiary care-based studies. The SLNB positivity rate in the current study of 15.6% compared with 20.8% in the Multi-centre Selective Lymphadenectomy Trial. Of patients with positive SLNB, 80% remained disease-free compared with a published rate of 24%, and of those with negative SLNB with follow-up data, 8.7% progressed to metastasis compared with a published rate of 11%

The most useful indicator of adequacy of wide local excision is the rate of local recurrence. In the current study, there were three documented local recurrences of melanoma, four if the ‘recurrence’ diagnosed as (dysplastic) naevus is included. This would give a local recurrence rate of 0.6%, compared with 1.36% of cases in a study of 11,290 thin (T1) melanomas. The characteristics of the 14 melanomas progressing to metastatic disease, including the nine that progressed to melanoma-specific death, are consistent with tertiary care-based studies (Table S2). Half of these 14 melanomas were located on previously defined high-risk sites on the scalp, neck, back and arm. Nodular melanoma is disproportionately associated with adverse outcomes, and although it only comprised 12.6% of the invasive melanomas in the current study, it was responsible for 50% of the 14 cases progressing to metastatic disease. The average Breslow thickness of the 14 melanomas progressing to metastasis, 5.9 mm, is consistent with the known association of this measurement with adverse outcomes. However, the fact that two of the melanomas were thin, one with a Breslow thickness of 0.5 mm resulting in melanoma-specific death, is a reminder that until technology can prospectively identify instances of melanoma overdiagnosis (diagnosis of melanomas that will not progress to adverse outcomes), all melanomas must be managed as potentially life-threatening.

With respect to patients with multiple primary invasive melanomas, a study from Queensland, Australia, on 52,861 patients with melanomas, found that the hazard ratio of death within 10 years was two times higher for those with two melanomas, and nearly three times higher for those with three, compared with a person with a single melanoma. In the current study, 5% of patients with multiple primary invasive melanomas in 2013 progressed to metastatic disease (2 out of 6 patients), compared with only 6% of those with a single primary invasive melanoma (12 out of 199 patients). A larger sample size is necessary to test the significance of this trend.

Notwithstanding the limitations of comparing survival metrics in the current study with age-adjusted population-based metrics, melanoma-specific 5-year survival in the current study of 95.2%, is similar to national figures for Australia (92%) and New Zealand (90%).

LIMITATIONS

Completeness and accuracy of data were not independently verified, and the absolute number of melanoma patients was small, as a proportion of the total managed by GPs in Australasia in 2015. This study is based on a subset of a database, and the participants are not necessarily typical of Australasian GPs. With respect to their level of qualification, the majority have a Master’s degree or PhD in the field of skin cancer, and as an indication of their experience, they each excised an average of 23.6 melanomas in 2013, compared with national figures for GPs, surgeons and dermatologists of 0.7, 7.5 and 13.8, respectively.

CONCLUSIONS

In this study on melanoma management and outcomes for a subset of GPs in Australasia, patient gender and age demographics were similar to those of tertiary care-based studies, but the majority of melanomas were in situ or thin-invasive. While melanoma in situ predominated overall, invasive melanoma was more prevalent under the...
age of 40 years. Diagnostic and therapeutic management was closely aligned with current guidelines, with elliptical excision biopsy followed by wide excision being performed for the majority. The much higher rate of margin involvement with shave and punch biopsies, along with the fact that most punches were performed on small lesions which could easily have been excised, argues strongly in favour of a recommendation for elliptical excision biopsy. Most in situ and thin melanomas were definitively re-excised by GPs, with thick melanomas preferentially referred to surgeons. Melanomas with adverse outcomes, as in tertiary care-based studies, tended to be thick, half of nodular subtype, but with all major subtypes, as well as thin melanomas, being represented. Five-year survival with respect to invasive melanoma was at least as favourable as national population-based metrics. Further studies are warranted.

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ETHICAL APPROVAL

The Human Ethics Research Office of The University of Queensland, Australia, provided ethics exemption for this study.

AUTHOR CONTRIBUTIONS

Author Wilson administers SCARD and provided the raw data for analysis. Author C Rosendahl performed data cleaning. Authors Hay, Keir, Jimenez Balcells, Coetzee-Botha, Wilson, Clark, Kittler and C Rosendahl made substantial contributions to conception and design, acquisition of data, analysis and interpretation of data, were involved in drafting and critically revising and finally approving the manuscript and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of the work have been appropriately investigated and resolved. Harald Kittler calculated the survival distribution. Most strongly in favour of a recommendation for elliptical excisions which could easily have been excised, argue the fact that most punches were performed on small lesions.

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Supporting Information

Additional Supporting Information may be found online in Supporting Information:

Table S1 Definitive management providers, clinical guidelines adherence, deep margin location, sentinel lymph node biopsy metrics and impact of definitive excision on tumour staging. A single primary invasive melanoma with unknown thickness was excluded from this analysis. Abbreviation: GP, general practitioner; SLNB, sentinel lymph node biopsy.

Table S2 Characteristics of patients and their index melanomas (thickest melanoma as per Breslow thickness) for those with at least one primary invasive melanoma in 2013 who progressed to in-transit cutaneous, nodal or distant metastasis (n = 14) (single primary invasive melanoma with unknown thickness excluded). Abbreviations: NM, nodular melanoma; SSM, superficial spreading melanoma; LM, lentiginous melanoma; SLNB, sentinel lymph node biopsy.