Development and validation of a scoring system for SIAscopic diagnosis of pigmented skin lesions in primary care

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ABSTRACT

Background Pigmented skin lesions (PSLs) are a common presenting problem in general practice but differentiating malignant melanomas from other pigmented lesions is challenging. SIAscopy using the Moncrieff scoring system (MSS) increases diagnostic accuracy for melanoma in referred populations but has not previously been tested in primary care.

Objectives To develop and validate a scoring system for SIAscopic diagnosis of PSLs in primary care.

Methods Patients presenting with a PSL were recruited from 6 general practices in Cambridgeshire. The following data were obtained for each lesion: clinical history including 7-point checklist; digital photograph; SIAscan image, and digital dermoscopy. SIAscan images were interpreted by an expert and validated against histopathology where possible, or expert clinical review of all available data for each lesion.

Results 630 lesions from 389 patients were recruited. Most lesions were benign naevi (69.7 % n=439) or seborrhoeic keratoses (22.2 % n =140); 5 (0.79%) were melanoma. The MSS showed the following characteristics for the diagnosis of 'suspicious' (95% CI): sensitivity 54.2% (35.1-72.1%); specificity 77.4% (73.0-81.2%); PPV 12.6% (7.5-20.4%); NPV 96.5% (93.9-98.1%), and for the diagnosis of melanoma: sensitivity 66.7% (20.8-93.8%); specificity 75.9% (71.6-79.7%); PPV 1.9% (0.5-6.8%); NPV 99.7% (98.2-99.9%). A primary care scoring algorithm (PCSA) was developed to improve the ability to distinguish seborrhoeic keratoses and haemangiomas from melanoma. The PCSA had the following characteristics for the diagnosis of 'suspicious': sensitivity 50.0% (18.7-81.2%); specificity 84.2% (78.5-88.5%); PPV 8.6% (3.0-22.4%); NPV 98.3% (95.0-99.4%). Using simulation modelling to provide tighter estimates for the diagnosis of melanoma, the PCSA had a sensitivity of 94.0% and specificity of 83.5% for melanoma.

Conclusions The PCSA could have a useful role in improving primary care management of pigmented skin lesions. Further work is needed to validate the PCSA in other primary care populations, and to evaluate GP performance after training in SIAscopy use.

Word count 299

KEYWORDS

Pigmented skin lesion, melanoma, SIAscopy, primary care, diagnostic aid

INTRODUCTION

Pigmented skin lesions are a common presenting problem in general practice and, while the majority are benign naevi or non-melanocytic lesions (seborrhoeic keratoses, haemangiomas), a small minority are malignant melanomas. Melanoma is a serious skin cancer, responsible for 2% of all cancers and 1% of all cancer deaths in the UK, with about 8,000 new cases and 1,800 deaths a year (CRUK 2004). Worldwide, the incidence of melanoma is increasing faster than any other cancer with an approximate doubling of rates every 10-20 years in countries with white populations [1].

General practitioners (GPs) are relatively poor at differentiating melanomas from other pigmented lesions [2,3], probably because an individual GP will encounter melanoma infrequently [4]. There have been conflicting findings about the performance of GPs who have been trained in melanoma diagnosis either face to face [5] or via the internet [6]. However, in a primary care setting the ability to distinguish lesions that are either benign or suspicious is as important as a clinical diagnosis of melanoma in making the decision to reassure or refer urgently for dermatological review.

New approaches are therefore required to improve GPs' assessment of pigmented skin lesions. Dermoscopy has been shown to improve the diagnostic accuracy for melanoma in the specialist setting [7], and in one randomised controlled trial in general practice [8]. However, dermoscopy is a relatively time-consuming technique to learn [9] and has not been shown to improve the management of benign lesions [8]. In a recent trial of dermoscopy and digital monitoring, Australian GPs required up to 30 hours of internet-based learning to acquire adequate skills (Menzies, Emery et al; *in submission*).

An innovative approach uses SIAscopy, a non-invasive multispectral scanning technique which gains micro-architectural information about the skin within seconds. SIAscans are high-resolution images of the collagen and haemoglobin content of the papillary dermis, and melanin content of the epidermis and papillary dermis. Patterns within the SIAscans of pigmented skin lesions (such as the presence of dermal melanin and blood displacement with erythematous blush) indicate the histopathology and pathophysiology consistent with melanoma. Previous studies have demonstrated the diagnostic accuracy of SIAscopy for melanoma in referred populations using the Moncrieff scoring system [10], but this has not

previously been validated in primary care. The aim of this study was to develop and validate a scoring system for SIAscopic diagnosis of pigmented skin lesions in primary care.

METHODS

Ethical approval for this study was obtained from the Cambridge Research Ethics Committee (REC Ref 04/079) and research governance approval from Cambridge City and South Cambridgeshire Primary Care Trusts (Project number L00569). Data collection occurred between January 2005 and January 2006.

Setting

Six general practices were recruited from Cambridge city and the surrounding suburban and rural area covering a registered population of 52,913. The researcher (JH, a trainee plastic surgeon) set up a regular designated clinic in each practice for twelve months, where any patient with concerns about a pigmented skin lesion who had been seen by their GP within the preceding two weeks could attend, regardless of the GP's diagnosis.

Data collection

For each pigmented skin lesion the following data were collected:

1. SIAscan image;
2. Clinical history including completion of the 7-point checklist[11];
3. Clinical photograph (Canon Powershot G5; images compressed into JPEG format; resolution 640 x 480 pixels comparable to established quality for telemedicine diagnosis [12;13]
4. Digital dermoscopy (Heine Dermaphot system; images compressed into JPEG format; resolution 1440 x 960 pixels comparable to established quality for teledermoscopy diagnosis [14;15]

SIAscan scoring

SIAscan images were scored independently by two experts in SIAscopic diagnosis (JH, SC) blinded to the clinical history and dermoscopy images. Clinical and SIAscopic features that were assessed included those previously associated with melanoma [10]: size of lesion, age of patient, dermal melanin, collagen holes and blood displacement with blush. Additional

features that were also scored were: blood vessels, white dots on the collagen view, blood lacunes and a cerebriform melanin pattern (see Figure 1)

[Figure 1 about here]

Diagnostic reference standards

Given that it would have been ethically unacceptable to obtain histological diagnosis on every recruited lesion, we applied the following hierarchical approach to reference standard diagnosis:

1. Histopathology (n = 41);
2. Expert clinical review (PH) of the lesion including 7-point checklist and dermoscopy (n = 44);
3. Expert review of 7-point checklist, clinical photograph and digital dermoscopy image (n = 545) (MM, PH).

The expert reviewers were blinded to the SIAscan images. For the reference standard diagnosis we categorised lesions in two complementary ways relevant to primary care decision-making: melanoma or other pigmented lesion; and 'suspicious' or benign. The definition of suspicious was a lesion that, if seen in general practice, would warrant referral, excision or short-term monitoring.

Analysis

A 66% sub-sample of lesions was used to validate the Moncrieff scoring system (the Development Lesion dataset). A Primary Care Scoring Algorithm (PCSA) was developed to account for the different prevalence of certain pigmented skin lesions seen in primary care. This was validated against the remaining 33% sub-sample of lesions (the Validation Lesion dataset).

Given the inevitably low prevalence of melanomas in the dataset, we could not estimate sensitivity and specificity for the PCSA to diagnose melanoma very precisely. We therefore conducted a simulation modelling exercise adding random samples of 38 additional melanomas to the dataset. These melanomas came from a larger image bank of lesions recruited from previous studies conducted by the authors (PH, MM) and from data shared by colleagues at Frenchay Hospital, Bristol. The PCSA was run on 10,000 different random datasets (total lesions in each dataset: 246 including 40 melanomas) to provide more precise estimates of sensitivity and specificity for the diagnosis of melanoma. This modelling exercise

however, could not improve the precision of our estimates of the positive and negative predictive values for our primary care algorithm because of the large effect of melanoma prevalence on these calculations.

Sensitivity, specificity, positive and negative predictive values and their associated 95% confidence intervals were calculated using standard approaches including the Wilson method to account for small sample sizes in some of the cells [16]. Receiver operating characteristic (ROC) curves were created to explore different cut-off scores for the PCSA.

RESULTS

Interpretable SIAscans were obtained on 630 lesions from 389 patients who presented to their GP with concerns about the lesion. The mean age of patients in the study was 44.9 years; 68.6% were female. Table 1 shows the types of lesion represented in the dataset. There were 5 melanomas (mean Breslow thickness = 0.56mm). No pigmented basal cell carcinomas were recruited. All patients with non-pigmented lesions who were invited into the study by their GP were excluded by JH.

[Table 1 about here]

Table 2 presents the performance of the Moncrieff scoring system for the diagnosis of 'suspicious' and for melanoma for the Development Lesion dataset (n=422). In this subset there were 24 suspicious lesions and 3 melanomas, including 1 atypical melanoma with significant regression. The Moncrieff scoring system did not perform that well for the diagnosis of 'suspicious'. This was predominantly due to misclassification of seborrhoeic keratoses and haemangiomas. In particular, of the 101 seborrhoeic keratoses in the sample, 55 were misclassified as suspicious due to apparent 'dermal melanin' on the SIAscopic image. Specific SIAscopic features of seborrhoeic keratoses were identified as: white dots on the collagen view, analogous to milia-like cysts seen on dermoscopy [17], and a cerebriform appearance on the total melanin view. Haemangiomas were identified by the presence of blood lacunes on the SIAscan 'blood' view.

[Table 2 about here]

The Primary Care Scoring Algorithm (PCSA)

We set out to develop a new diagnostic algorithm to improve the ability to distinguish seborrhoeic keratoses and haemangiomas from melanoma, lesions which are more prevalent in primary care than in referred populations. An additional feature, the presence of blood vessels, was entered into the Moncrieff model to examine its role in improving the diagnostic performance for melanoma. ROC curves were plotted, using data from the Development Lesion dataset, to examine the different point scores for the presence of blood vessels (Figure 2a). The performance of the Moncrieff score for 'suspicious' was improved if lesions classified as seborrheoic keratoses or haemangiomas, based on SIAscopic features, were excluded from the dataset (Figure 2.b). For the diagnosis of melanoma, performance was improved by scoring 2 points for the presence of blood vessels and by excluding lesions classified as seborrheoic keratoses or haemangiomas, based on SIAscopic features (Figure 2c). On this basis a new Primary Care Scoring Algorithm (PCSA) was developed that aims to identify lesions with features of seborrheoic keratoses or haemangiomas first and then apply a scoring system based on the presence of other features associated with melanoma (see Figure 3).

[Figures 2a, 2b, 2c and 3 about here]

The new PCSA was tested against the 208 lesions in the Validation Lesion dataset, which included 6 suspicious lesions and two melanomas. The performance of the PCSA is presented in Table 3. *S*imulation modeling with a higher prevalence of melanomas in the dataset confirmed high sensitivity and specificity for the diagnosis of melanoma with the PCSA (Figure 4). The mean sensitivity and specificity of the PCSA for the diagnosis of melanoma was 94.0% and 83.5% respectively.

[Table 3 and Figure 4 about here]

DISCUSSION

This is the first study to test the use of SIAscopy in a primary care population. The Moncrieff scoring system was found to be less accurate than in the secondary care setting [10] due to the different prevalence of lesions among the primary care population. In order to account for the higher prevalence of non-melanocytic lesions, such as seborrhoeic keratoses and haemangiomas, we developed a new Primary Care Scoring Algorithm which improved the diagnostic accuracy of SIAscopy for melanoma in the primary care setting. The PCSA was

also slightly more specific than the Moncrieff scoring system for 'suspicious' but no more sensitive. It was reassuring that the PCSA's relatively poor sensitivity for 'suspicious' does not appear to be reflected in its sensitivity for melanoma. This may reflect the difficulty that the secondary care experts had in defining 'suspicious', which is a less familiar concept than it would be for GPs. Ultimately, although a primary care algorithm should be good at identifying 'suspicious' pigmented lesions, its ability to accurately identify melanomas is probably more important.

There are several limitations of this study which reflect the challenges of conducting this type of research in primary care. First, the practices were recruited via individual practitioners' interest, and often expertise, in dermatology. Second, the patients often had to return to the practice for their appointment with the researcher. The sample therefore may not be totally representative of patients who usually present to their GP about a PSL, or of the whole practice population, as it may under-represent certain groups such as the elderly or housebound. Third, as the incidence of melanoma in a primary care population is very low, we used simulation modelling with a higher prevalence of melanoma in the dataset to provide tighter estimates of sensitivity and specificity of the PCSA for the diagnosis of melanoma. Increasing the prevalence of melanomas in the dataset in the modelling exercise is a valid approach to inform sensitivity and specificity but it cannot provide more precise estimates of the positive and negative predictive values for melanoma in a primary care population. We accept that, even though we recruited 630 lesions from 389 people, because of the low prevalence of suspicious lesions in primary care, further validation of the PCSA is now needed. Two studies in progress, the Molemate Trial in the UK and a validation study in Western Australia will provide important additional data to test the accuracy of the PCSA in primary care.

In this study we used experts in SIAscopy to interpret the SIAscans. This therefore reflects the best performance of SIAscopy in primary care and not how it would perform in the hands of GPs. We believe that the features of SIAscopy may be easier to learn than those of dermoscopy which can take a long period of training in which to become proficient. A recent study we have conducted suggests that SIAscopy features can be learnt by GPs using a CD-rom based tutorial in approximately two hours [18]. This tool may therefore have utility for a much wider group of primary care practitioners than dermoscopy.

CONCLUSIONS

The PCSA for SIAscopy could have an important role in improving the management of pigmented skin lesions in primary care. Further work is required to validate the PCSA in other primary care populations, and to examine the impact of training GPs in SIAscopy on their clinical management of pigmented skin lesions.

Conflict of interest disclosure

SC is employed by, and PH has provided consultancy services for, Astron Clinica Ltd which produces devices that use SIAscopic technology.

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