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Diagnosing melanoma: how do we assess how good we are?

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Summary

Background. Evaluating and improving diagnostic accuracy in identification of melanomas is important for both conservation of healthcare resources and reduction in patient morbidity. Useful indicators in assessing this accuracy include the number needed to treat (NNT) and the benign:malignant (B:M) ratio. Both of these methods lack sensitivity, as they do not account for the ability to detect early or *in situ* melanomas.

Aim. To assess the NNT and B:M ratio for a busy hospital serving a population of 650 000 over a 5-year period, and to assess a new ratio of diagnostic accuracy by calculating the ratio of invasive (malignant) melanomas to melanoma *in situ* (MM:MMIS) as a marker of sensitivity.

Methods. This was a retrospective analysis of data on all melanocytic lesions excised during two separate years (2006 and 2011) with a 5-year interval between them. The lesions were divided into benign naevi (BN), dysplastic naevi (DN), MMIS and MM.

Results. In 2006, 650 melanocytic lesions were excised (462 BN/DN, 45 MMIS, 143 MM). The NNT was 3.46, the B:M ratio was 2.46 and the MM:MMIS ratio was 3.18. In 2011, 730 melanocytic lesions were excised (464 BN/DN, 99 MMIS, 167 MM). The NNT was 2.74, the B:M ratio was 1.74 and the MM:MMIS ratio was 1.69.

Conclusions. The NNT and B:M ratios from our study compare favourably with those in the published literature. The fall in the MM:MMIS and B:M ratios over this 5-year study appears to be an indicator of the ability to detect early disease and is probably secondary to the changes to our skin cancer service. This study may encourage physicians to aim not only for low B:M ratios but also low MM:MMIS ratios.

Introduction

In the current climate of austerity measures, there is growing pressure on healthcare systems to reduce the economic burden of unnecessary referrals and procedures.[1] Dermatologists, as well as all clinicians involved in skin-cancer diagnosis, have a responsibility to maintain high standards of melanoma diagnosis. In primary care, the diagnostic challenge is well recognized, and is focused on referring a case mix of suspicious lesions with as few benign nonmelanocytic lesions as possible,[2,3] whereas in secondary care, the challenge is to reduce the number of benign moles removed while ensuring that no malignancies are missed.

Measuring diagnostic accuracy in melanoma recognition is difficult to quantify without the histological assessment of all moles evaluated during a clinical examination. In order to assess the true sensitivity of diagnosis, the proportion of false negatives (i.e. the melanomas left behind on patients) is required. Numerous studies in the literature[4–12] have bypassed this requirement by estimating diagnostic accuracy using surrogate measures such as the benign:malignant (B:M) ratio

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[the number of benign naevi removed compared with the total number of melanomas; also known as the naevi to melanoma ratio (NMR)] and the number needed to treat (NNT; the number of melanocytic lesions excised for each melanoma). However, these measures have limitations when used in isolation. The B:M ratio gives an indication of the proportion of unnecessary procedures, but the ratio of malignant melanoma (MM) to melanoma *in situ* (MMIS) (the MM:MMIS ratio) is a marker of the proportion of early disease, with a lower ratio indicating a higher pickup of *in situ* disease relative to invasive (malignant) melanoma (MM). Measuring both these parameters gives not only a marker of ability to distinguish melanoma from benign lesions but also an indication of the sensitivity to detect early melanoma.

The aim of this study was to examine the NNT, B:M ratio and MM:MMIS ratio over a 5-year period in a busy teaching hospital in Oxford, serving a population of approximately 650 000 patients, and to assess the effects on diagnostic accuracy of changes made to the skin-cancer service.

Methods

We carried out a retrospective analysis of data from the histopathological database of all melanocytic lesions excised in the Oxford Dermatology Department from January 2006 to December 2006 and then from January to December 2011. Only excision biopsies were included, and all reports of benign naevi (BN), dysplastic naevi (DN), MMIS and MM were collected. All shave, incisional and punch biopsies were excluded. Table 1 shows how each of the ratios were calculated.

In 2006, suspected skin cancers were seen in both general clinics and skin-cancer clinics; the general clinic physicians were not trained in dermoscopy. Not all melanocytic lesions had a consultant review pre-excision. In 2011, all tumours or suspected tumours were seen in a dedicated consultant-led skin cancer clinic. All patients underwent a full body screen unless they declined. All clinicians working in this clinic were trained in dermoscopy, and dermoscopes were available in all clinic rooms and theatres. All melanocytic lesions also had a consultant review before excision, and were also dual reported by two members of the same accredited experienced panel of expert dermatopathologists for the duration of the study period.

Statistical analysis

The χ^2 test was used for comparisons, with significance defined as $P < 0.05$.

Results

The total number of melanocytic lesions excised in 2006 was 650, of which there were 462 benign (BN + DN), 45 MMIS and 143 MM. The calculated NNT was 3.46, the B:M ratio was 2.46, and the MM:MMIS ratio was 3.18 (Table 2). Five years later, in 2011, there were 730 melanocytic lesions excised, of which 464 were benign (BN + DN), 99 were MMIS and 167 were MM. The calculated NNT was 2.74, the B:M ratio was 1.74 and the MM:MMIS ratio was 1.69 (Figs 2 and 3; Table 2). Using the χ^2 test, the increase in the proportion of MMIS seen in 2011 was found to be significant ($P < 0.001$).

The different histological variants of the benign naevi are summarized in Fig. 1.

Discussion

Dermatologists need to demonstrate quality and standards as part of their clinical governance. There are relatively few easily measured parameters to measure diagnostic accuracy in identifying melanomas. Incidence of melanoma detection cannot be used alone as a marker of diagnostic accuracy, as it relies heavily on population characteristics. However, this can be overcome by looking at the surgical activity as a marker for diagnostic accuracy, as the background variation in population characteristics will be negated.

A number of studies in the literature[4–13] have suggested other measures of accuracy for melanoma

Table 1 Calculations of ratios.

Ratio	Definition	Calculation
Benign:malignant (B:M) ratio	Ratio of benign naevi to malignant melanomas	(BN + DN)/ (MMIS + MM)
Number needed to treat (NNT)	Number of naevi needed to be removed to discover a melanoma	(BN + DN + MMIS + MM)/(MM + MMIS)
Malignant melanoma to malignant melanoma *in situ* (MM:MMIS) ratio	Ratio of invasive (malignant) melanoma to melanoma *in situ*	(MM/MMIS)

BN, benign naevi; DN, dysplastic naevi.

Table 2 Histopathological results for lesions excised during 2006 and 2011 with calculated ratios.

	2006	2011
Benign	462	464
No dysplasia	300	176
Mild to moderate dysplasia	100	248
Severe dysplasia	62	40
MMIS	45	99
MM	143	167
B:M ratio	2.46	1.74
NNT	3.46	2.74
MM:MMIS	3.18	1.69

B:M, benign:malignant; MM, malignant melanoma; MMIS, malignant melanoma *in situ*; NNT, number needed to treat.

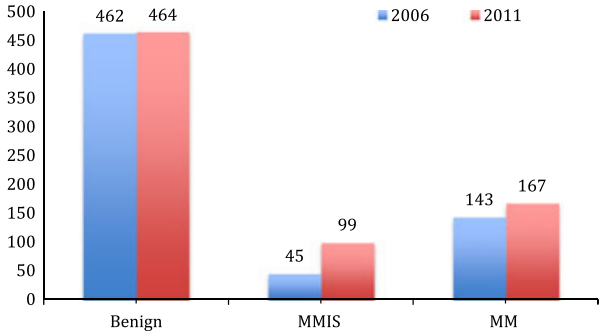

Figure 1 Histological distribution of melanocytic lesions excised in Oxford in 2006 and 2011.

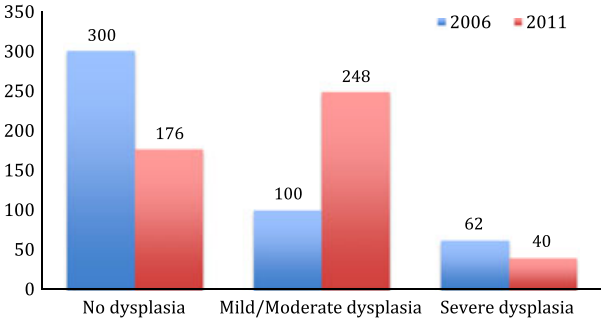

Figure 2 Histology of the benign melanocytic lesions excised in Oxford in 2006 and 2011.

diagnosis, such as the number of benign naevi removed compared with the total number of melanomas (the B:M ratio), or the number of melanocytic lesions excised for each melanoma (NNT). Some studies have also included all pigmented lesions (including seb-orrhoeic keratoses) in their NNT.[9,11] However, these ratios have limitations when used in isolation. In order to reflect diagnostic sensitivity, the additional ability to detect early disease, not just thick obvious melanomas, needs to be taken into account.

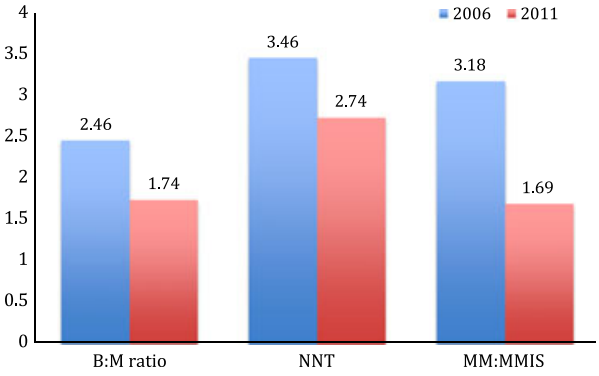

Figure 3 Benign:malignant (B:M) ratio, number needed to treat (NNT), and malignant melanoma to malignant melanoma *in situ* (MM:MMIS) ratio calculated for melanocytic lesions excised in Oxford in 2006 and 2011.

We believe this can be achieved by assessing the proportion of *in situ* disease compared with invasive disease. There are no published data on the validity of using the MM:MMIS ratio in the literature, but our data shows an improvement in B:M and MM:MMIS ratios over the 5-year period of the study, indicating not only the ability to distinguish melanoma from benign lesions but also the sensitivity to detect early melanoma.

The NNT and the B:M ratio in this study compare very favourably with those in the published literature. Internationally, reports of NNT or of numbers needed to excise have varied from 4 to 40, with lower NNTs generally being documented in specialist dermatology clinics.[4,5,12] Recently, Sidhu *et al.*[6] published the first data for NNT for melanoma diagnosis in the British National Health Service in a region with a population of 600 000, a similar size to ours. They had an overall NNT of 6.3 over 5 years of excisions. In this context, our NNT of 2.74 in 2011 is highly encouraging, and adds to this small body of evidence from dermatology departments in the UK.

Over the 5-year period studied, our data show an approximately two-fold increase in the proportion of MMIS detected, with a corresponding reduction in the MM:MMIS ratio from 3.2 to 1.69. This implies higher sensitivity, with the ability to detect melanoma at an earlier stage coinciding with a decrease in our B:M ratio. Critics may suggest that the increase in our proportion of MMIS is an artefact of over-reporting, resulting from a potential diagnostic drift, with a tendency for reporting severely dysplastic naevi as melanoma.[14] However, evidence to support a real phenomenon is the fact that all melanocytic lesions were dual reported by the same accredited experienced panel of expert

dermatopathologists for the duration of this study period, making individual diagnostic drift less likely. Our data also show a reduction in the number of benign naevi excised within this timeframe, with an increase in reports of moderate dysplasia and a reduction in severe dysplasia. If there had been a diagnostic drift, we would expect an increase in severely dysplastic naevi (which would previously have been classified as moderate dysplasia), which was not the case in our findings. Ultimately, to confirm or refute this theory, a study to re-report a cohort of tumours from past patients compared with current patients would be required. Unfortunately, owing to working pressures within the histopathological service within our NHS hospital, this has not been possible. Interestingly, our data from this time period has shown a trend towards providing our dermatopathologists with an increasingly more complex case mix for interpretation. Although the number of excisions of melanocytic lesions has not increased during this time period, we have shown that the number of excisions of benign naevi without dysplasia has reduced, while there has been a proportional increase in the number of excised lesions that are abutting the diagnostic threshold between benign and malign. This trend should warrant further evaluation on its effects, particularly when planning future provision of histopathology services.

The ratios can be plotted graphically (Fig. 4), and a tendency towards the origin on the *x*-axis corresponds to an increasing proportion of MMIS relative to MM being diagnosed, whereas the *y*-axis corresponds to fewer benign naevi being excised for each MM.

The fall in NNT, B:M ratio and MM:MMIS ratio over the past 5 years has coincided with a number of changes within our department. Firstly, all tumours or suspected tumours are seen in a dedicated consultant-led skin-cancer clinic; secondly, all clinicians working in this clinic have been trained in dermoscopy, and dermatoscopes are available in all clinic rooms and theatres; thirdly, all melanocytic lesions have a consultant review before excision. We, like other authors, believe that dermoscopy has played an essential part in the reduction in these ratios.[15–19] Similar findings were seen by Carli *et al.*,[15] who showed an improved B:M ratio when dermoscopy was introduced into their clinical practice.

Our study is limited by the lack of comparative data in the literature of the MM:MMIS ratio. To validate this ratio as a potential marker of clinical accuracy, we compared our data with two large published studies from recognized cancer centres, for which the components required for measurement were available for analysis. Soares *et al.* published a histopathological retrospective review of 1547 pigmented lesions excised at the Mayo

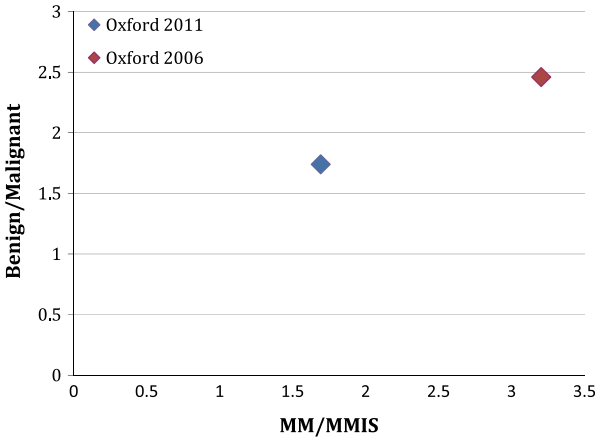

Figure 4 Change in the malignant melanoma to malignant melanoma *in situ* (MM:MMIS) and benign:malignant (B:M) ratios over a 5-year period.

Clinic (Scottsdale, AZ, USA) over a 12-month period in 2005,[20] and found that 1398 naevi were excised, with 147 of these being melanomas (of which 74 were MM and 73 were MMIS). This provides a B:M ratio of 9.5 and an MM:MMIS ratio of 1.0. More recently, Kovalyshyn *et al.* published a retrospective histopathological review of melanoma data from the Memorial Sloan-Kettering Cancer Center (MSKCC; New York, NY, USA) over a 10-year period between 1998 and 2008. They reported 394 melanomas (171 MM and 323 MMIS) excised, and a B:M ratio of 5.4 : 1 for the period, suggesting total naevi excision of approximately 2127 (5.4 × 394) over this 10-year period,[21] giving an MM:MMIS ratio of 0.53. Although crude comparisons can be made, care should be taken when interpreting results, as clearly there are different population characteristics between these groups. The USA and Australia have a higher prevalence of MMIS compared with the UK, reflecting the higher ongoing background UV intensity in those countries. Until more data is available on the MM:MMIS ratio, it may be more appropriate if it is used as an indicator of diagnostic accuracy to initially compare centres looking after patients with the same background population characteristics. MM:MMIS may become a useful tool for those involved in commissioning skin cancer services in the future, as it not only reflects diagnostic accuracy but also resource utilization.

Conclusion

We have introduced a new ratio into our department to monitor our performance in diagnosing melanoma. The MM:MMIS ratio is a useful tool used in combination with the B:M ratio or NNT, which enables clinicians involved

in melanoma diagnosis to quantify and monitor their diagnostic accuracy in a simple and reproducible manner using readily available histopathological data. The changes made to our skin-cancer service are likely to be behind the improvement in our service delivery. There have been concerns raised in the literature that a low NNT or B:M ratio may result in more melanomas being missed, while a high NNT or B:M ratio may result in unnecessary excisions. Use of the MM:MMIS ratio utilizes a marker of sensitivity; that is, the proportion of the *in situ* disease. We believe that all departments involved in melanoma diagnosis should aim to have the lowest possible B:M ratio/NNT and MM:MMIS ratio when auditing their clinical performance.

What's already known about this topic?

- Several studies have used markers such as the number of moles removed to detect a melanoma (NNT) or the ratio of benign to malignant moles (B:M ratio) as surrogate markers of diagnostic accuracy in diagnosing melanoma.
- However, these existing markers have limitations.

What does this study add?

- This study introduces a novel ratio (malignant melanoma:malignant melanoma *in situ*; MM:MMIS) that we believe is a superior method when used in combination with the B:M ratio as an indicator of diagnostic accuracy in detecting melanoma.
- This study adds to the paucity of data on diagnostic accuracy in detecting melanoma in the UK literature.
- This study shows that the efficiency of the service has been improved by patients being seen in a dedicated skin-cancer clinic by clinicians trained in dermoscopy, and by all lesions having a consultant review prior to excision.

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CPD questions

Learning objective

To raise awareness of approaches to assessing accuracy in diagnosing melanoma using different performance indicators.

Question 1

Which one of the following is not used as a surrogate marker for estimating diagnostic accuracy in melanoma diagnosis?
(a) Benign:malignant (B:M) ratio.
(b) Number needed to treat (NNT).
(c) Malignant melanoma:malignant melanoma *in situ* (MM:MMIS) ratio.
(d) The melanoma hit rate (MHR).
(e) Naevi:melanoma ratio (NMR).

Question 2

The benign:malignant (B:M) ratio is calculated by which of the following formulae?
(a) Total number of benign naevi and dysplastic naevi divided by total number of melanomas (including *in situ* melanomas).
(b) Total number of benign naevi divided by total number of dysplastic and malignant melanomas.
(c) Total number of benign naevi (including dysplastic naevi) and *in situ* melanomas divided by total number of malignant melanomas.
(d) Total number of benign skin lesions divided by total number of malignant melanomas.
(e) Total number of malignant melanomas divided by total number of benign naevi.

Question 3

In the literature to date in the British National Health Service there is only one paper looking at the number needed to treat (NNT) for melanoma diagnosis. What was their NNT over a 5-year period?
(a) 2.1
(b) 6.3
(c) 10.5
(d) 20.7
(e) 45.2

Question 4

Which of the following is not correct? The malignant melanoma:malignant melanoma *in situ* (MM:MMIS) ratio…
(a) …acts as a marker of the sensitivity of melanoma diagnosis.
(b) …is a useful audit tool for assessing departmental performance.
(c) …is a marker of the ability to differentiate benign lesions from melanomas.
(d) …is a potential marker of the ability to pick up early melanomas.
(e) …may be a useful tool for commissioning skin cancer services in the future.

Question 5

Which factor do the authors believe has not contributed to the improvement in the efficiency of their skin-cancer service?
(a) A dedicated skin-cancer screening clinic.
(b) All physicians using and trained in dermoscopy.
(c) Smaller clinics.
(d) Consultant-led clinics.
(e) Dermatoscopes being available in all clinic rooms and theatres.

Instructions for answering questions

This learning activity is freely available online at http://www.wileyhealthlearning.com/ced.

Users are encouraged to

- Read the article in print or online, paying particular attention to the learning points and any author conflict of interest disclosures
- Reflect on the article
- Register or login online at www.wileyhealthlearning.com/ced and answer the CPD questions
- Complete the required evaluation component of the activity

Once the test is passed, you will receive a certificate and the learning activity can be added to your RCP CPD diary as a self-certified entry.

