Selection of Patients for Long-term Surveillance With Digital Dermoscopy by Assessment of Melanoma Risk Factors

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Objective: To identify patients at increased melanoma risk who benefit from long-term surveillance with digital dermoscopy.

Design: Prospective, nonrandomized, observational study.

Setting: University-based surveillance program.

Participants: Six hundred eighty-eight patients prospectively categorized into defined melanoma risk groups and followed up (mean, 44.3 months) by clinical examinations, dermoscopy, and, for atypical nevi, sequential digital dermoscopy.

Main Outcome Measure: Association between patient risk factors and detection of melanomas.

Results: Odds ratios from a multivariate logistic regression analysis indicated a highly increased melanoma risk for patients with familial atypical mole and multiple melanoma (FAMMM) syndrome, atypical mole syndrome (AMS), or previous melanoma. Each digitally documented atypical lesion (range, 1-17 lesions per patient) denoted a significant 10% increase in melanoma risk. Patients with higher melanoma risk (1) showed a higher percentage of melanomas detected by digital dermoscopy (FAMMM syndrome group, 50%; AMS group, 22%), (2) more often developed multiple melanomas within shorter intervals, and (3) showed a ratio of melanoma to benign results for lesions excised because of dynamic changes of 1:15 (AMS group) or 1:4 (FAMMM syndrome group). Melanomas detected by digital dermoscopy were significantly thinner (0.41 mm in mean Breslow thickness) compared with melanomas detected by other means (0.62 mm; P = .04).

Conclusions: We suggest an individualized surveillance plan, with digital dermoscopy performed at follow-up intervals of 3 months for patients with FAMMM syndrome and 6 to 12 months (depending on additional risk factors) for those with AMS. Patients with multiple common nevi and no additional risk factors had no benefit from sequential digital dermoscopy.

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FAMMM syndrome) indicates an exceedingly high risk for the development of melanoma. Patients with FAMMM syndrome also carry a greater risk for multiple melanomas, even at an early age.16-19

Without systematic selection of patients and lesions for sequential digital dermoscopy, the cost-effectiveness and the overwhelming workload of observing hundreds of nevi per patient were recently identified as considerable concerns.20 The aim of the present prospective study was to better allocate resources to patient groups that benefit most from long-term follow-up surveillance by sequential digital dermoscopy.

**METHODS**

**PATIENT EXAMINATION**

All clinical investigations were conducted according to the Declaration of Helsinki. Written informed patient consent was obtained for all invasive procedures. Patient characteristics, including age, sex, hair color, eye color, skin type (I-IV, Fitzpatrick classification), presence of ephelides, estimated whole-body nevus count, personal/family history of previous melanoma, histologic results of former biopsies from the patient and first-degree relatives, presence of a high nevus count in first-degree relatives (anamnestic data), and number of atypical nevi (as reflected by the number of digitally stored lesions) were prospectively entered into a database.

Moreover, patients were assigned to 3 defined risk groups depending on the presence of risk factor combinations21-23 (Table 1): multiple nevi (MN) group, 461 patients; atypical mole syndrome (AMS) group, 219 patients; and FAMMM syndrome group, 8 patients. Data from 688 patients with at least 1 follow-up examination were collected during a period of 10 years (December 1, 1998, through February 28, 2008). Of the 688 included patients, 125 (18.2%) were lost to follow-up during the analyzed 10-year period (86 of the 461 patients in the MN group [18.7%] and 39 of the 219 in the AMS group [17.8%]) as defined by more than 24 months without attending any further follow-up appointments.

At first-visit examinations (Figure 1), overview images were taken and the entire integument was examined by the unaided eye and conventional dermoscopy (EpiScope, 10× magnification, contact plate; Welch Allyn, Skaneateles Falls, New York). The 7-point checklist algorithm was used to differentiate between benign melanocytic lesions and melanoma.24 Lesions suspected of being malignant (score, ≥3 points) were excised immediately. Lesions scoring less than 3 points but presenting defined clinical or dermoscopic criteria of atypia (eg, asymmetry in shape, irregular margin, variegated color, or prominent pigment network)25 were marked on digital overview images and electronically stored (FotoFinder dermoscope, Teachscreen Software GmbH, Bad Birnbach, Germany; or Hikoscopes, Hiko, Pirmasens, Germany).

![Figure 1](https://archderm.jamanetwork.com/article-fig1.png)

**Figure 1. Decision tree for first visit and follow-up examinations.**

![Table 1](https://archderm.jamanetwork.com/table-1.png)

**Table 1. Definition of Risk Groups**

<table>
<thead>
<tr>
<th>Risk Group Stratification (n=688)</th>
<th>MN (n=461)</th>
<th>AMS (n=219)</th>
<th>FAMMM Syndrome (n=8)</th>
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</thead>
<tbody>
<tr>
<td><strong>Follow-up data</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Digitally monitored lesions</td>
<td>6349</td>
<td>4553</td>
<td>235</td>
</tr>
<tr>
<td>Total No.</td>
<td>8</td>
<td>19</td>
<td>31</td>
</tr>
<tr>
<td>Median No./patient</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Appointments</td>
<td>1645</td>
<td>1540</td>
<td>77</td>
</tr>
<tr>
<td>Total No.</td>
<td>4</td>
<td>7</td>
<td>10</td>
</tr>
<tr>
<td>Median No./patient</td>
<td>12</td>
<td>11</td>
<td>8</td>
</tr>
<tr>
<td>Median follow-up interval, mo</td>
<td></td>
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<td></td>
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<tr>
<td><strong>Abbreviations:</strong></td>
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<tr>
<td>AMS, atypical mole syndrome; FAMMM, familial atypical mole and multiple melanoma; MN, multiple nevus.</td>
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<tr>
<td><strong>Definition</strong></td>
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<tr>
<td>≥50 Common and/or ≤3 atypical nevi</td>
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<tr>
<td>≥50 Common and &gt;3 atypical nevi</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Family history of ≥2 melanomas in 1st- or 2nd-degree relatives and presence of AMS criteria</td>
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</tbody>
</table>

aCommon nevi (≥3 criteria): well-defined border, regular margin, uniform color, and macular or papular surface; atypical nevi: asymmetry in shape, ill-defined border, irregular margin, variegated color, and macular and papular components.
At follow-up examinations (Figure 1), patients were asked about new or changing nevi and overview images were compared with the corresponding body surface. The whole integument was examined by the unaided eye and conventional dermoscopy. Nevi that had been digitally documented during a previous visit (n = 11 137) were again digitally stored and then compared side by side with the corresponding baseline image on a split screen. Newly developed lesions were treated as described for first-visit examinations. The median follow-up interval during the study was 11 months (range, 1-71 months), with significant differences between the risk groups (MN group, 12 months; AMS group, 11 months; FAMMM syndrome group, 8 months; MN vs AMS group, P < .001; MN vs FAMMM syndrome group, P < .001; and AMS vs FAMMM syndrome group, P = .007; 2-sided t test).

All examination procedures were performed by dermatology residents (n = 13) formally trained in dermoscopy and supervised by an experienced attending dermatologist (H.A.H. or S.E.). The presence or absence of given criteria in a lesion and all diagnoses were agreed on by at least 2 dermoscopy-experienced clinicians (H.A.H., T.B., K.M.K., and S.E.).

EXCISIONAL BIOPSIES
Criteria leading to the excision of a lesion were either a 7-point checklist score of 3 points or more or a combination of a score of less than 3 points plus complementary information making the diagnosis of melanoma probable. Complementary information at first-visit examinations included the lesion history (eg, increase in size, itching, scaling, change in color, and intermittent bleeding) and the “ugly duckling” sign. In addition to this information, follow-up examinations included the analysis of morphologic changes of lesions that were digitally stored. Beyond a threshold of 17 stored lesions (range, 18-68), each additional lesion was reflected the number of highly atypical nevi because those were digitally stored and a comparison of digital overview images with the body surface to detect new lesions. In agreement with previous studies, we did not excise lesions that developed a darker or lighter overall pigmentation or lesions with a decrease in the number of initially present black dots.

STATISTICAL EVALUATION
The statistical analysis was performed with SAS software version 9.1.3 (SAS Institute Inc, Cary, North Carolina). The data were prospectively entered and stored in a database (Access; Microsoft Corp, Redmond, Washington). Plausibility, accuracy, and completeness were verified. All recorded melanoma risk factors were entered as independent variables into a backward stepwise logistic regression analysis to determine which of them remained significantly associated with the diagnosis of melanoma while simultaneously adjusting for all other criteria included in the regression model. The results were expressed as odds ratios (ORs) with 95% confidence intervals (CIs).

RESULTS

GENERAL DATA
Data from 688 patients (mean age, 42 years; 295 female, 393 male) were collected during a period of 10 years. The mean follow-up time was 44.3 months (median, 46 months; range, 2-123 months). Patients were prospectively stratified into 3 risk groups: 461 (67.0%) were assigned to the MN group, 219 (31.8%) to the AMS group, and 8 (1.2%) to the FAMMM syndrome group (Table 1). A large proportion of patients had a personal history (201 [29.2%]) and/or family history (90 [13.1%]) of melanoma and/or a high number (>50) of nevi (388 [56.4%]).

Of 1219 excised lesions, 127 melanomas (10.4%) were confirmed by histopathologic examination. Of these, 50 (39.4%) were in situ melanomas. The mean Breslow tumor thickness of 77 invasive melanomas was 0.57 mm (median, 0.45 mm).

RELEVANT MELANOMA RISK FACTORS FROM UNIVARIATE ANALYSIS
All documented risk factors were included into univariate statistical analysis to detect those with a significant effect on the risk for developing melanoma during the study. Five of 10 risk factors (assignment of risk group, personal and family history, number of nevi, skin type, and number of digitally documented lesions) were significantly associated with an increased relative risk of melanoma (Table 2). The highest risk was found for patients in the FAMMM syndrome group (OR, 135.30; 95% CI, 24.26-754.00; P < .001; Table 2). Interestingly, we found a substantial increase in melanoma risk for each digitally stored lesion (range of 1 to 17 stored lesions: OR, 1.18; 95% CI, 1.09-1.28; P < .001). The number of digitally documented lesions reflected the number of highly atypical nevi because those were digitally stored. Beyond a threshold of 17 stored lesions (range, 18-68), each additional lesion was associated with a lesser, but still significant, further increase in melanoma risk (Table 2).

As expected, patients with a better ability to tan carried a significantly decreased risk of melanoma (skin type, Cochran-Armitage test for trend, P = .01; Table 2).

INDEPENDENT MELANOMA RISK FACTORS FROM MULTIVARIATE REGRESSION ANALYSIS
All risk factors were also entered into a backward stepwise logistic regression analysis as independent variables to determine which of them remained significantly associated with melanoma while simultaneously adjusting for all other criteria included in the regression model (Table 3). Three of 10 risk criteria remained significantly associated with the risk to develop melanoma during the study (assignment of risk group, personal history of melanoma, and number of digitally documented lesions). The number of nevi and skin type did not reach statistical significance as independent risk factors. In agreement with the univariate analysis, the highest relative risk was found for patients of the FAMMM syndrome group (OR, 37.11; 95% CI, 6.03-228.39; P < .001). Patients assigned to the AMS group (OR, 8.06; 95% CI, 3.86-16.80; P < .001) carried the second highest relative risk, followed by patients with previous melanoma (OR, 6.23; 95% CI, 3.34-11.63; P < .001). A higher number of digitally documented lesions in the range from 1 to 17 also remained an independent risk factor in the multivariate analysis (Table 3).
The follow-up time of 461 patients in the MN group totaled 1252 years, and 11 melanomas were detected (1 melanoma per 114 years of follow-up). For the patients in the 3 risk groups, we calculated the total number of melanomas per 114 years of follow-up, respectively.

The percentage of melanomas among all excisions from patients in the MN group (11 melanomas, 369 excisions) was very low in contrast to those in the AMS group (100 melanomas, 778 excisions) and FAMMM syndrome group (16 melanomas, 72 excisions) (Figure 2B).

The cost-effectiveness of digital dermoscopy may be estimated from the number of appointments that were necessary to detect 1 melanoma. In the MN group, 150 appointments resulted in the detection of 1 melanoma (1645 appointments, 11 melanomas). In the AMS group, 1 melanoma was detected in every 5 appointments (1540 appointments, 11 melanomas), and in the FAMMM syndrome group, 1 melanoma was diagnosed in every 5 appointments (77 appointments, 16 melanomas).

The mean age of patients at the time of the first melanoma diagnosis during the study was also analyzed in relation to the 3 risk groups. There were nonsignificant differences in the mean age of patients with melanoma between the FAMMM syndrome and AMS groups (42.7 vs 38.5 years; P=.33) and between the FAMMM syndrome and MN groups (47.4 vs 38.5 years; P=.31, 2-sided t test).

**Table 3. Multivariate Analysis of Melanoma Risk Factors**

<table>
<thead>
<tr>
<th>Patient Subgroup Characteristics</th>
<th>OR (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk group</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AMS group (n=219) vs MN group</td>
<td>3.71 (9.03-22.89)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>FAMMM syndrome group (n=8) vs MN group</td>
<td>8.06 (3.86-16.80)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>AMS group vs MN group</td>
<td>8.06 (3.86-16.80)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Personal history of previous melanoma</td>
<td>6.23 (3.34-11.63)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>No. of digitally documented lesions</td>
<td>1.11 (1.02-1.21)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

**Table 2. Frequencies of Patients With Melanoma in Defined Risk Groups as Detected During the Study**

<table>
<thead>
<tr>
<th>Patient Subgroup Characteristics</th>
<th>No. of Patients With ≥1 Melanoma (n=79)</th>
<th>OR (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk group</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AMS group (n=219) vs MN group</td>
<td>63 (18.21 (9.12-36.37)</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>FAMMM syndrome group (n=8) vs MN group</td>
<td>6 (135.30 (24.26-754.00)</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>Personal and family history vs no history</td>
<td>63 (13.44 (7.52-24.02)</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>Personal history of melanoma (n=201)</td>
<td>60 (3.54 (2.07-6.08)</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>Personal history of dysplastic nevi (n=347)</td>
<td>5 (3.96 (1.32-11.94)</td>
<td>.01</td>
<td></td>
</tr>
<tr>
<td>&gt;1 Melanoma in 1st-degree relatives (n=15)</td>
<td>17 (2.11 (1.17-3.82)</td>
<td>.01</td>
<td></td>
</tr>
<tr>
<td>Family history of dysplastic nevi (n=87)</td>
<td>1 (0.43 (0.19-0.97)</td>
<td>.04</td>
<td></td>
</tr>
<tr>
<td>No. of nevi (estimated)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>50-100 (n=259) vs &lt;50</td>
<td>38 (2.54 (1.43-4.53)</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>&gt;100 (n=129) vs &lt;50</td>
<td>22 (3.04 (1.58-5.84)</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>Skin type (I-IV)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type III (n=183) vs type I</td>
<td>13 (0.43 (0.19-0.97)</td>
<td>.04</td>
<td></td>
</tr>
<tr>
<td>No. of digitally documented lesions</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-17 (n=410)</td>
<td>24 (1.18 (1.09-1.28)</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>&gt;17 (n=278)</td>
<td>55 (1.03 (1.01-1.06)</td>
<td>&lt;.001</td>
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</tr>
</tbody>
</table>

**DISTRIBUTION OF MELANOMAS BY RISK GROUP**

Although patients in the AMS (n=219) and FAMMM syndrome (n=8) groups accounted for only 33.0% of the study population (227 of 688 patients), they developed 91.3% of the melanomas (116 of 127 melanomas). For better comparability of melanoma events in different risk groups, we calculated the total number of melanomas per total years of follow-up for each risk group (Figure 2A).

The follow-up time of 461 patients in the MN group totaled 1252 years, and 11 melanomas were detected (1 melanoma per 114 years of follow-up). For the patients in the AMS and FAMMM syndrome groups, we calculated ratios of 1 melanoma per 12 years of follow-up (100 melanomas, 1212 years of follow-up) and 1 melanoma per 3 years of follow-up (16 melanomas, 50 years of follow-up), respectively.

**ATYPICAL PIGMENTED LESIONS WITH DYNAMIC CHANGES**

We calculated the ratio of melanoma to benign lesions in those excised exclusively because of dynamic changes for patients in the 3 risk groups (Figure 2C). In the MN group, the melanoma to benign ratio for atypical lesions with dynamic changes was 1:79 (2 melanomas and 138
benign lesions). A more reasonable rate of 1:15 (22 melanomas and 324 benign lesions) was calculated for the AMS group, and, for the FAMMM syndrome group, a rate of 1:4 (8 melanomas and 31 benign lesions) was found.

**INTERVALS BETWEEN CONSECUTIVE MELANOMAS**

We assessed the mean time interval between 2 consecutive melanomas in patients who developed multiple melanomas during the study. Whenever more than 1 melanoma was detected within a given follow-up interval, we divided the interval by the number of melanomas. This statistical approach resulted in a rough estimate of a follow-up interval suitable for detecting melanomas at curable stages. There were 28 patients who developed multiple melanomas (range, 2-7 melanomas) during the study. In the MN group, only 1 of 10 patients with melanoma developed 2 melanomas, so no conclusion could be drawn (Figure 3). Of 63 patients in the AMS group who were diagnosed as having melanoma during the study, 23 (37%) developed multiple melanomas, and 37 time intervals between consecutive melanomas were included in the analysis (mean [SEM], 20.3 [3.6] months; Figure 3B). Of 6 patients with FAMMM syndrome who developed melanoma, 4 had multiple melanomas, and 10 time intervals were included (mean [SEM], 4.2 [2.3] months). The difference between the mean intervals in the AMS and FAMMM syndrome groups was statistically significant ($P = .03$, $t$ test).

**IMPACT OF DIGITAL DERMOSCOPY ON MELANOMA DETECTION**

The surgical excision of atypical pigmented lesions with dynamic changes was shown to increase the sensitivity of melanoma detection. We calculated the impact of digital dermoscopy follow-up on the sensitivity of melanoma detection within the 3 risk groups. The sensitivity of each examination technique (7-point checklist for dermoscopy, complementary information, or digital dermoscopy follow-up) was expressed as the percentage of melanomas within each risk group detected by that technique (Figure 4). Approximately 10% of melanomas were detected by complementary information across all risk groups.
3 risk groups. The relevance of conventional dermoscopy (7-point checklist) for melanoma detection decreased from 73% in the MN group to 38% in the FAMMM syndrome group patients. Despite a much higher number of digitally monitored lesions in the MN group (6349 lesions) than in the AMS group (4553 lesions) and FAMMM syndrome group (235 lesions), the percentage of melanomas detected by digital dermoscopy follow-up was lowest in the MN group (18%) and highest in the FAMMM syndrome group (50%).

Melanomas diagnosed because of dynamic changes documented by sequential digital dermoscopy were significantly thinner than those detected by other means (0.41 mm vs 0.62 mm; P = .04, t test; data not shown). It is therefore reasonable to assume that digital dermoscopy depletes some melanomas from possible later detection by conventional dermoscopy. However, whether all melanomas detected by digital dermoscopy would develop enough dermoscopic features for later detection by conventional dermoscopy cannot be addressed by the present data.

**COMMENT**

Financial and personnel resources for early melanoma detection are not infinite. The data from our study suggest that patient subgroups with a highly increased risk of melanoma benefit most from the laborious task of sequential digital dermoscopy.

In a recent series of meta-analyses, relevant risk factors for developing melanoma were reviewed.\(^1\)\(^-\)\(^3\) We have taken into account most of the known melanoma risk factors (age, sex, hair color, eye color, skin type, presence of ephelides, nevus count, personal/family melanoma history, results of former biopsies [in patients and first-degree relatives], presence of a high nevus count in first-degree relatives [anamnestic data], and number of atypical nevi). We did not record the history of sunlight exposure because several methodologic problems may bias the association between sunlight exposure and melanoma risk.\(^2\)\(^7\) The presence of certain risk factors was used to prospectively categorize patients into 3 risk groups. All risk factors were entered into both univariate and multivariate statistical analyses to assess the association with melanoma. The multivariate analysis, which is able to independently assess each risk factor while simultaneously adjusting for all other criteria included in the regression model, identified the attributed risk group, a personal history of melanoma, and the number of atypical pigmented lesions (as reflected by the number of digitally documented lesions) as significant risk factors. Although the number of common nevi was a strong and significant risk factor in the univariate analysis, the significance was lost in the multivariate regression model. This suggested that the number of common nevi is not an independent, but a closely correlated, risk factor. In our study sample, nevus counts were correlated with the assigned risk group (risk group stratification included information about nevus count). Moreover, a recent meta-analysis reported a correlation between the numbers of common and atypical nevi.\(^2\)\(^8\)\(^-\)\(^9\) Interestingly, beyond a threshold of 17 stored atypical lesions, additional lesions were not associated with a significant further increase in melanoma risk (multivariate analysis). This confirms earlier studies reporting a threshold level without a further increase in melanoma risk above a certain number of atypical nevi.\(^2\)\(^6\)\(^-\)\(^9\) For clinical application, we suggest recording all of the aforementioned risk factors and then grouping patients into the described risk groups. This stratification could be extended by assignment to subgroups according to the presence or absence of a personal and/or family history of melanoma.

The results of 2 earlier long-term monitoring studies suggested that patients with increased numbers of common nevi and no further risk factors for melanoma might not benefit from sequential digital dermoscopy.\(^2\)\(^6\)\(^-\)\(^9\) In both studies the authors predominantly monitored lesions without signs of dermoscopic atypia in low-risk patients, and no melanomas were detected. A number of other studies targeted flat atypical melanocytic lesions in high-risk patients (eg, AMS, FAMMM syndrome, and a history of previous melanoma).\(^6\)\(^-\)\(^8\)\(^,\)\(^1\)\(^1\)\(^-\)\(^1\)\(^3\)\(^,\)\(^3\)\(^2\) Higher risk of the patients included in these studies correlated with a better melanoma to benign ratio for lesions excised exclusively because of dynamic changes over time. The patient population in the study by Bauer et al\(^1\)\(^3\) showed a very high risk of melanoma (196 patients, 86% with AMS, 35% with a history of melanoma, and a mean follow-up of 24 months) and a melanoma to benign ratio of 1:16 for atypical lesions with dynamic changes. A previously published study by our group\(^5\) included a lower percentage of patients with AMS, and the melanoma to benign ratio was 1:18 (530 patients, 33% with AMS, 1% with FAMMM syndrome, 37% with a history of melanoma, and a mean follow-up of 32 months). The study by Robinson and Nickoloff\(^1\)\(^2\) monitored many common junctional nevi, and all lesions with dynamic changes were excised. This might explain the low melanoma to benign ratio of 1:47 despite a population with a very high risk of melanoma (100 patients, 100% with AMS, 81% with a history of melanoma, and a median follow-up of 36 months). Fuller et al\(^1\)\(^2\) monitored atypical lesions in
patients with a rather low risk profile for a shorter period (297 patients, no information about AMS frequency, 25% with a history of melanoma, and a median follow-up of 22 months) and reported a very low melanoma to benign ratio of 1:95.

The data from the present study support the assumption that monitoring atypical nevi in high-risk patients will yield an acceptable melanoma to benign ratio. When the MN, AMS, and FAMMM syndrome subgroups were analyzed separately, the ratio gradually increased from 1:79 (MN group) to 1:15 (AMS group) to 1:4 (FAMMM syndrome group). The melanoma to benign ratio itself correlated well with the number of visits needed to detect 1 melanoma, which represents a good measure of the financial and personnel resources expended. For MN group patients, the ratio of 1 detected melanoma in 150 visits does not appear to represent reasonable cost-effectiveness.

From our data and earlier studies it might be concluded that the higher the individual melanoma risk, the more frequently dynamic changes in atypical nevi represent melanoma. When used in the appropriate population, digital dermoscopy contributed to the overall sensitivity and detected melanomas at a significantly thinner Breslow thickness. Because 31% to 69% of common nevi may eventually develop dynamic changes as well, their long-term follow-up in low-risk patients should be discouraged.35,36

Of note, a recent study distinguished between substantial (eg, asymmetric enlargement, architectural and color changes) and nonsubstantial long-term modifications of melanocytic lesions.3 However, limitations arise from the fact that lesions with defined nonsubstantial changes (eg, appearance or disappearance of an inflammatory reaction and disappearance of parts of the pigment network with replacement by a diffuse light-brown pigmentation) were not excised, and no data from further follow-up of lesions that developed such changes were given in the article. Until more data are made available, we recommend a cautious use of the term nonsubstantial long-term changes. Given the high-risk patient population in our study, we decided to excise all atypical melanocytic lesions with dynamic changes, except for those with a darker or lighter overall pigmentation or lesions with a decrease in the number of initially present black dots. We emphasize the need for studies that focus on the development of objective algorithms for the interpretation of dynamic changes.

Most previous long-term follow-up studies either used a standard annual follow-up interval8 or based the follow-up interval on a more subjective interpretation of the patients' individual risk of melanoma.35 In the present study, we calculated the mean time interval between the diagnosis of 2 individual melanomas within patient risk groups. The results may be used as a basis for recommendations of follow-up intervals and are in agreement with a more systematic approach used in a recent clinical trial.33 We are aware that patients with multiple melanomas represent a selected group of patients who often carry genetic changes associated with melanoma.33 At the same time, our calculated intervals showed a considerable range of variation within patients from the same subgroup, so that the recommendations should be viewed as conservative estimates. According to the calculated intervals between 2 consecutive melanomas, we suggest that patients with FAMMM syndrome be followed up at 3-month intervals. Patients with AMS should be followed up every 6 to 12 months, depending on the presence of additional risk factors (eg, history of melanoma). For better patient adherence to the reexamination schedule, a first reexamination at 3 months after the baseline visit should be considered because an earlier study reported a decrease in the adherence of patients scheduled for longer follow-up intervals.36 Because only 1 patient in the MN group developed 2 melanomas, no optimal follow-up interval could be calculated. However, in this study, patients with MN did not seem to benefit from long-term digital dermoscopy. We suggest monitoring these patients at regular intervals with the naked eye and conventional dermoscopy only. We affirm that a short-term follow-up in selected cases with a higher-grade atypia by dermoscopic criteria or a suspicious lesion history should be considered.

In conclusion, targeting the right lesions (atypical and with no suspicion of melanoma) for sequential digital dermoscopy in the appropriate patient groups (AMS, FAMMM syndrome, and MN group patients with a history of melanoma) at the correct follow-up interval should result in a reasonable melanoma to benign ratio of excised lesions and offer acceptable cost-effectiveness. Objective algorithms for the assessment of dynamic changes in pigmented lesions are required.

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