



Analysis of Teledermoscopy and Face-to-Face Examination of Atypical Pigmented Lesions: a Cross-Sectional, Retrospective Study

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ABSTRACT **Introduction:** Malignant melanoma (MM) is one of the most fatal skin cancers. Early detection and treatment are crucial for metastasis prevention. The growing number of MM cases has led to an increased need for skin examinations, increasing the healthcare demand in dermatology departments.

Objectives: The purpose of this cross-sectional, retrospective study was to analyze the accuracy and reliability of two different methods, teledermoscopy (TD) and face-to-face examination (FTF), with two different patient groups for MM detection in Jönköping County.

Methods: In teledermoscopic evaluation, a general practitioner takes photographs of a suspected skin lesion (clinical and dermoscopic images) and sends TD referrals to a dermatologist for digital assessment. In the FTF group, the diagnosis was made during regular clinical visits to the dermatology department by a dermatologist.

Results: The TD group comprised 55 women and 57 men, and an FTF group comprised 72 women and 66 men. Based on the histopathology report, in the TD group, 75% of suspected MM lesions were accurately classified as MM compared with 57% of suspected MM lesions correctly diagnosed in the FTF group. When compared with histopathology report, the diagnostic concordance of TD and FTF examinations were 80% and 69%, respectively.

Conclusions: We report a high diagnostic concordance between TD and the final histopathological diagnosis. Metrics analyzed for diagnostic accuracy confirmed that TD is an effective and accurate method for early diagnosis of MM. TD is suitable, non-inferior and a useful alternative to FTF examination.

Introduction

Malignant melanoma (MM) is one of the most serious and fatal skin cancers that has steadily increased worldwide over the recent decades [1]. When a skin lesion is clinically suspected to be MM, it is examined with a dermatoscope [2]. If dermoscopic examination strengthens the suspicion of melanoma, the entire lesion is excised and sent to the laboratory for histopathological examination under acute procedure (standardised care process [SCP]) [3]. The term atypical melanocytic lesion (AML) should be used when clinical evaluation fails to fully determine whether the skin lesion is melanoma or a benign pigmented lesion. In teledermoscopic (TD) evaluation, a general practitioner takes photographs of a suspected skin lesion and sends TD referral to the dermatology department. The first regions to introduce TD in Sweden were Council County Västerbotten and Gävleborg in 2014. Since then, many regions have introduced TD. Some studies compared the reliability between teledermoscopic and face-to-face (FTF) examinations, with diagnostic reliability ranging from 81% to 91% full or partial diagnostic concordance [4]. Other studies showed similar precision between TD and FTF examinations and some studies found that TD was significantly superior to FTF examination while other studies showed that the diagnostic accuracy of TD was inferior to FTF examination. [5-9]. Data on the accuracy and reliability of TD in Sweden are scarce. There are no major scientific studies on the proportion of AML surgically removed via TD referrals compared with FTF in Jönköping County, Sweden. The growing number of MM cases has led to an increased need for skin lesion examination, increasing the healthcare demand in dermatology departments [10].

Objectives

The aim of our cross-sectional, retrospective study was to assess the diagnostic reliability of TD and FTF examinations. It is important to note that the reliability measurements reported in this study are specific to the TD service being evaluated.

Methods

This cross-sectional, retrospective study was performed between 1 January and 30 June 2020 at the Department of Dermatology, Ryhov County Hospital in Jönköping,

Sweden. Clinical data, histopathological results, age, sex, heredity, and history of skin cancer were obtained from the electronic patient journal system CAMBIO Cosmic (Swedish health care information system, version 8.0). The International Statistical Classification of Diseases, 10th revision (ICD-10), code D229F was used to identify all patients with clinically suspect AML and MM in Cosmic. The assessment of pigmented lesions via FotoFinder (Systems GmbH) is not included in this study because the patients who are regularly followed by FotoFinder may carry CDKN2A mutations, which may bias the study results. Otherwise, all patients were included in this study without any restrictions.

In the present study, patients were divided into two groups according to their assessment mode: FTF and TD. The clinical images in the TD group were obtained by different general practitioners using a standardized, uniform system for our county (using digital camera Canon Ixus 185 for pictures from a distance and a dermoscopic photo using Heine delta 20 SLR photoadapter attached to Canon camera) in polarized mode without using flash. The pictures for the TD assessment were uploaded by a general practitioner to the Cosmic electronic journal system and then analyzed by one of totally thirteen different dermatologists (mostly senior). All low-quality images were excluded from the beginning and sent back to the referral doctor to retake and resend higher-quality pictures for new examination.

The diagnosis was made based on a patient history and clinical and dermoscopic image (TD) evaluation. In the FTF group, the diagnosis was made during regular clinical visits to the dermatology department by one of same dermatologists as in TD group.

Pigmented lesions in the TD and FTF groups were subdivided into two groups: clinically suspected MM and AML. Histopathological results were obtained for all patients. Each subdivision was further divided depending on the histopathological diagnosis of benign nevus, mild, moderate, severe dysplastic naevi and MM (malignant melanoma including melanoma in situ). The results for clinically suspected MM in these two groups were compared for reliability. The histopathological results for MM and severe dysplastic naevus were both classified as MM and are summarized in a MM group and this due to the fact that at our department, we adhere to the national guidelines for the surgical removal of dysplastic nevi and melanoma in situ. For cases of severe

dysplastic nevus and melanoma in situ, primary excision with a 5mm margin is recommended. Re-excision is required only if the histopathological free margin is less than 2mm. However, for cases of low-grade dysplastic nevus, primary excision with a histopathological-free margin, even if it is less than 2mm, does not necessitate re-excision. Distinguishing between severe dysplastic nevi and melanoma in situ can be challenging. Moderately-to-severely and severely dysplastic nevi are more frequently associated with melanoma compared to mildly or moderately dysplastic nevi.

Results for mild and moderate dysplastic naevi and benign lesions were included in a benign lesion group (Figure 1).

Statistical Analysis

Quantitative and demographic data were presented using descriptive statistics. Chi-square and Fisher exact tests were used to compare the number of benign and malignant cases in the FTF and TD groups. Statistical significance was set at $P < 0.05$. Diagnostic accuracy describes the ability of a diagnostic test to distinguish between disease and health. To measure and compare the diagnostic accuracy of the TD and FTF examinations, the metrics sensitivity, specificity, and positive and negative predictive values (PPV and NPV, respectively) were calculated and presented as percentages. A receiver operating characteristic (ROC) curve was constructed, and the area under the curve (AUC) was calculated [11-13]. Furthermore, diagnostic effectiveness, expressed as the proportion of correctly classified subjects among all subjects was analyzed.

Results

Study Population

The TD group comprised 55 women and 57 men, and the FTF group comprised 72 women and 66 men. The number of patients and sex distribution in both groups were nearly similar. In the FTF group, the median age of patients at the time of diagnosis was higher than in the TD group. The rate of family history of non-melanoma skin cancer (NMSC) was higher in the FTF group than in the TD group, and the rate of family history of MM was approximately five times higher in the FTF group than in the TD group. Even the rate of personal history of skin cancer, including NMSC and MM, was higher in the FTF group (Table 1).

No Significant Differences in MM Detection between the TD and FTF Groups

Of the 101 cases in the TD group, 61 cases were included in the suspected AML group and 40 cases in the suspected MM group. Of the 134 cases in the FTF group, 96 cases were included in the suspected AML group, and 38 cases in the suspected MM group. Based on histopathology reports, 75% cases in the suspected MM group of the TD group were classified accurately as MM compared with 57% in the suspected MM group of the FTF group. No statistically significant difference was observed in the frequency of correctly diagnosed MM between the TD and FTF groups (Chi-square test, $P = 0.109$; Fisher test, $P = 0.15$), suggesting that TD and FTF examinations are equivalent in detecting MM. The total

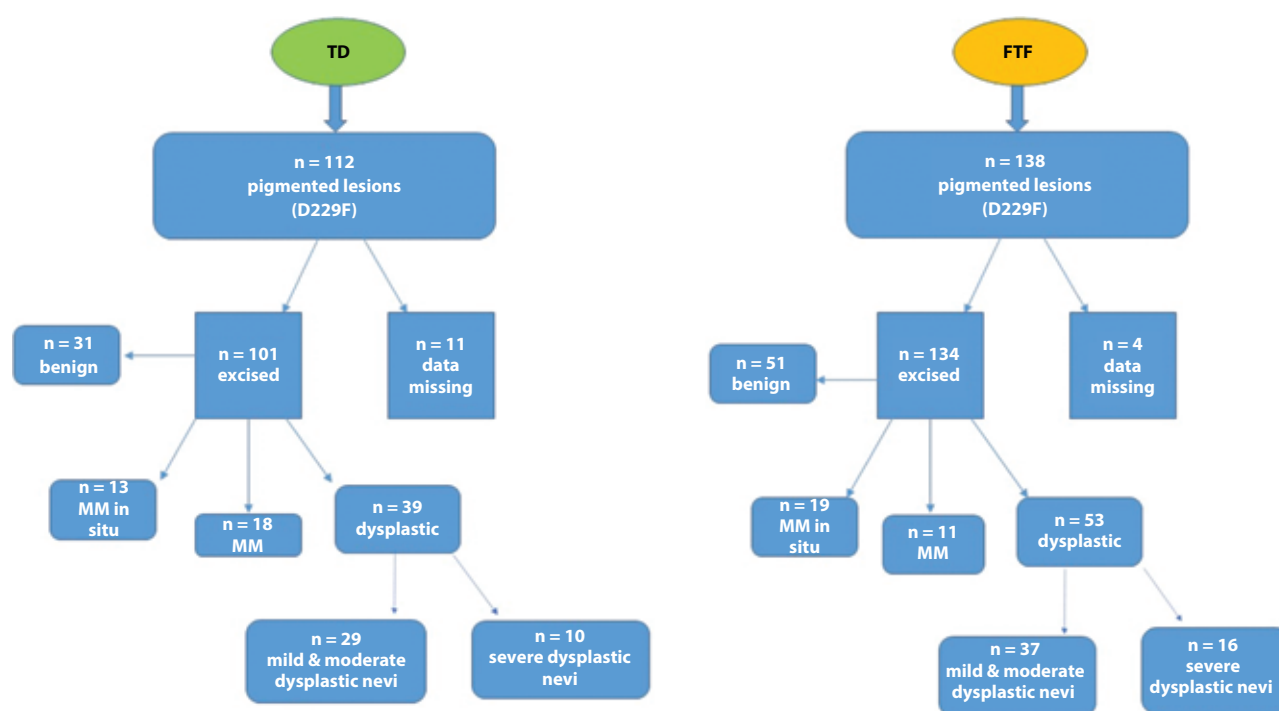


Figure 1. Flow Chart.

TD = teledermoscopy; FTF = face-to-face; MM = malignant melanoma.

Table 1. Demographic data for all patients with pigmented lesions included in this study.

		TD	FTF
Sex	male, N (%)	57 (50.9)	66 (47.8)
	female, N (%)	55 (49.1)	72 (52.2)
Age	median (min–max)	55 (18–91)	68 (43–92)
Age depending on histopathological diagnosis	benign	45 (18-86)	56(10-92)
	mild and moderate dysplastic	50 (19-86)	53 (27-88)
	severe dysplastic	63 (45-68)	48 (29-81)
	MM	64 (36–91)	75 (58-82)
Family history of skin cancer	NMSC, N (%)	3 (2.9)	6 (4.4)
	MM, N (%)	1 (1.0)	26 (19.1)
Personal history of skin cancer	NMSC, N (%)	2 (1.8)	24 (21.4)
	MM, N (%)	13 (11.6)	31 (27.7)

AUC = area under curve; FTF = face-to-face; NPV = negative predictive value; PPV = positive predictive value; ROC = receiver operating characteristic analysis; TD = teledermoscopy.

number of patients with suspected MM was similar in the TD and FTF groups (Figure 2).

The number of lesions classified as AML was almost 40% higher in the FTF group than in the TD group. The proportion of clinically misdiagnosed AML, in which histopathology showed MM or severe dysplastic naevi, was higher in the FTF group (25%) than in the TD group (18%). However, no statistically significant difference was observed in the frequency of misdiagnosed MM between the groups (Chi-square test, $P = 1.19$; Fisher test, $P = 0.235$), suggesting that TD and FTF examinations are comparable for detecting MM. In addition, the diagnosis of MM and benign naevus was twice as high in the FTF group as in the TD group; nevertheless, the number of cases of mild, moderate, and severe dysplastic naevi was nearly similar (Figure 2).

TD and FTF are Comparative in Detecting MM

To investigate the reliability of TD and FTF examinations in differentiating malignant from benign lesions, the sensitivity, specificity, predictive value, and diagnostic effectiveness were calculated. Compared with the histopathological diagnosis, the diagnostic effectiveness of TD was 80% with a sensitivity of 75%, specificity 83.9%, PPV 75% and NPV 83.6%, and for the FTF examination, it was 69% with a sensitivity of 47.8%, specificity 81.2%, PPV 57.9%, and NPV 74.7% (Table 2).

In this study, TD evaluation of pigmented lesions showed slightly higher scores for sensitivity and accuracy but nearly similar specificity compared to FTF diagnosis.

The AUC for TD was 0.79, indicating good accuracy, whereas the FTF evaluation of pigmented lesions showed sufficient accuracy (AUC=0.64).

Conclusions

Our study results are consistent with those of other studies [14-17]. We report a high (80%) diagnostic accuracy between TD and the final histopathologic diagnosis, similar to some previous studies.

Compared to other TD studies that have shown comparable diagnostic accuracy between TD and FTF examinations [4,5,18], the diagnostic accuracy of FTF in our study was slightly lower (69%) than TD (80%), which may be due to the different study designs. In our study, the TD and FTF groups included different patients. Most patients in the FTF group were older and high-risk patients with a higher rate of personal and family history of skin cancer, making the group-comparison difficult. It is possible that the higher incidence of missed melanomas in FTF group occurs in patients with extensive sun damage or atypical nevus syndrome could be related to the comprehensive full-body exams conducted during these checks, as opposed to TD referrals that typically focus on one to three specific lesions. Some studies have reported false-negative diagnoses in the management of high-risk patients [19].

In contrast to our study, other studies have shown the inferiority of TD in terms of accuracy compared to FTF examination [20]. Börve et al reported 66.7% accuracy for FTF examination which is similar to our study. However, the same study has shown a diagnostic accuracy of 50.7% and 60.9% for TD by teledermoscopists 1 and 2, respectively, which is lower than that of our study. Notably, the number of cases (69) in this study was smaller, and the study period (16 weeks) was shorter than in our study [20]. Moreover, both examinations were performed by the same dermatologist, which was not the case in our retrospective study. Although

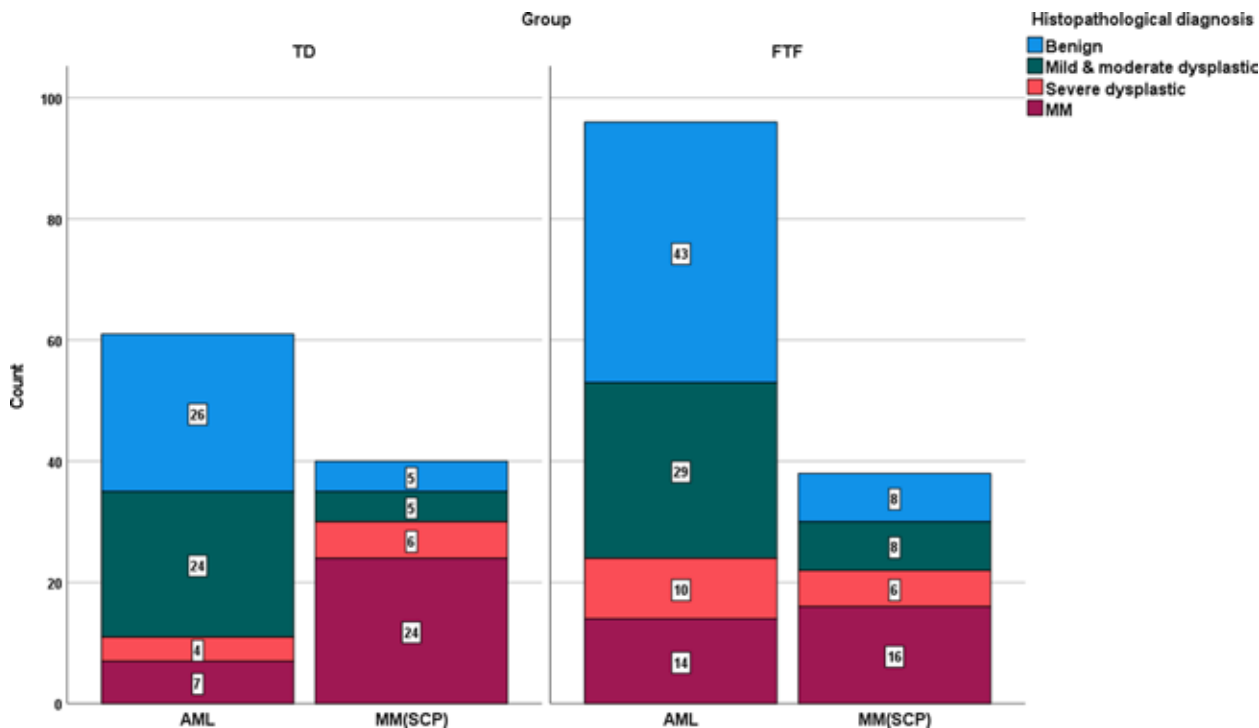


Figure 2. Number of benign or malignant lesions assessed by TD and FTF examinations for melanoma and atypical melanocytic lesion diagnosis.

TD = teledermoscopy; FTF = face-to-face; MM = malignant melanoma; SCP = standardized care process; AML = atypical melanocytic lesion.

Table 2. Diagnostic accuracy and reliability of TD and FTF examinations for all patients with suspicious MM (malignant melanoma under standardized care process).

	TD	FTF
Sensitivity (%)	75	47.8
Specificity (%)	83.9	81.6
PPV (%)	75	57.9
NPV (%)	83.6	74.7
AUC (n)	0.793	0.647
Diagnostic effectiveness	0.802	0.699

FTF = face-to-face; MM = malignant melanoma; NMSC = non-melanoma skin cancer; TD = teledermoscopy.

TD was analyzed by different dermatologists in our study, TD accuracy was slightly higher. The higher accuracy for TD reported in our study can be due to the smaller study size compared to Börve et al. Additionally, that study had a selection bias because only lesions requiring biopsy or excision were included. The teledermoscopists were aware of this fact, which may have influenced their management decisions. In addition, the teledermoscopists rated 14 different cases out of 69 as having poor image quality. In our study, we reduced the risk of selection bias by enrolling high-risk patients and

excluding low-quality images, resulting in a higher sensitivity of TD than would have been found in a general population. TD relies heavily dependent on high-quality images [21,22]. The cases included in our study consisted of only good quality images, as all low-quality images were excluded from the beginning and sent back to the referral doctor to retake and resend higher-quality pictures for new examination.

Interestingly, another study reported similar results, with TD showing lower accuracy and reliability than FTF examination in general practice. However, image quality was rated as good in only one-third of cases, and the diagnostic and accuracy rates were higher, particularly in cases with good quality photographs [21].

A systematic review of 21 studies [23] showed that teledermoscopist-histology accuracy was 51–85%, and in cases of FTF examination, the accuracy was higher (67%–85%). Most studies in this review had remarkable methodological limitations in terms of diagnostic accuracy. Another study found significant differences in diagnostic accuracy between TD and FTF examinations when different dermatologists evaluated lesions; this difference could be due to different definitions of the terms. [24] As in our study, it is very difficult to say whether the limited agreement in diagnoses is related to the use of the technology itself or differences in dermoscopy skills that may exist in practice. Tan et al reported higher diagnostic accuracy when the same

dermatologist performed both methods ($\kappa = 0.95$; range, 0.91–0.99) [24].

A recent large prospective study conducted in Denmark showed no significant difference in sensitivity between FTF and TD; however, the specificity for TD was lower than for FTF examination. [25] The data are inconsistent with our study, which showed no significant difference in specificity (83% versus 81%) between the two methods and a lower sensitivity for FTF examination than TD (47.8% versus 75%). This could be due to the retrospective nature of our study with different patients with higher risk factors in FTF group which influences the comparison of sensitivity of the two groups.

We believe that the higher diagnostic accuracy and sensitivity of TD in our study compared with lower diagnostic accuracy and sensitivity of FTF examination is due to several different factors. The evaluation of clinical and dermoscopic images by TD in a quiet environment and with a wide screen resolution that focuses more on a specific lesion can improve the diagnosis of benign and malignant skin tumors. The patients included in the FTF group had a higher median age and more family and personal history of skin cancer compared with patients in the TD group, complicating the diagnosis in the FTF group with several risk factors. Namely, there is a huge difference in the personal history of skin cancer between the TD and FTF groups (11.6% versus 27.7%, respectively). This difference has two important consequences. In one hand, it probably shows that the patients in TD group, as a part of their nursing care, might have easier way to a dermatologist, which shows the need for TD in an average population. In the other hand, MM survivor patients have higher chance to acquire another primary MM later. This could result in specialists will more likely decide surgical excision, perhaps resulting in higher numbers of excisions with lower accuracy and sensitivity of FTF compared to TD. This bias might be the reason for the difference in accuracy in FTF compared to TD.

The main strength of our study is an analysis of TD and FTF evaluation for assessing MM and AML in a representative population with different age groups, sex, and valid histopathological results as reference. The two groups were equal in size and sex. Moreover, the same lesions were not examined by the same clinician which might have prevented a bias, resulting from recalling the lesions from TD consultation and the associated diagnosis for the second time during FTF examination. These results are in line with the results of the systematic review of 21 studies [23].

The present study has some limitations. The study was conducted between January and June 2020, at the beginning of the Covid-19 pandemic, when some patients were recommended to follow the Ministry of Health restrictions; therefore, they might not have sought medical care. For further

research, we suggest that the same patient group be included in both TD and FTF assessments as the comparison of the two methods will be accurate with a valid gold-standard method available. Another limitation of this study was the small sample size. We suggest that TD is an effective and accurate method for early diagnosis of MM, it is suitable and non-inferior to FTF examination in detecting MM. TD reduces healthcare costs and is a useful alternative to FTF examination. TD has been shown to exhibit high reliability, resulting in a decrease in the number of unnecessary referrals and waiting time, not only for patients residing in remote rural areas but also for those facing challenges in accessing specialist care. Education in the field of dermoscopy and TD implementation in the everyday life of dermatologists may improve fast and accurate melanoma diagnosis in a larger number of patients, which may lead to earlier melanoma diagnosis and reduce morbidity and treatment costs. Larger studies are needed to confirm the results of the present study. Continued studies with a reduced risk of bias in assessing diagnostic accuracy and education in this field with advanced photography techniques will probably improve the quality of TD assessment care.

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