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Agreement on classification of clinical photographs of pigmentary lesions: Exercise after a training course with young dermatologists

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Abstract
Smartphone apps may help promoting the early diagnosis of melanoma. The reliability of specialist judgment on lesions should be assessed. Hereby, we evaluated the agreement of six young dermatologists, after a specific training.
Clinical judgment was evaluated during two online sessions, one month apart, on a series of 45 pigmentary lesions. Lesions were classified as highly suspicious, suspicious, non suspicious or not assessable. Cohen's and Fleiss' kappa were used to calculate intra- and inter-rater agreement.
The overall intra-rater agreement was 0.42 (95% confidence interval - CI: 0.33-0.50), varying between 0.12-0.59 on single raters. The inter-rater agreement during the first phase was 0.29 (95% CI: 0.24-0.34). When considering the agreement for each category of judgment, kappa varied from 0.19 for not assessable to 0.48 for highly suspected lesions. Similar results were obtained in the second exercise.
The study showed a less than satisfactory agreement among young dermatologists. Our data point to the need for improving the reliability of the clinical diagnoses of melanoma especially when assessing small lesions and when dealing with thin melanomas at a population level.

Introduction

Increasing the awareness of melanoma with the promotion of self-examination by informed people, and early access to dermatological advice for suspected lesions, are possible ways to anticipate the melanoma diagnosis and to improve survival, at a population level, in a sustainable way.[1,2]
Smartphones are largely available in the general population, and may be exploited to transfer clinical images taken by the patient, directly to a physician through an app.[3,4]
In spite of the fact that dermoscopy may improve the clinical classification of pigmentary lesions,[5] the simplest way to use the app for such a purpose by the general public, is to transfer photographs of lesions as they appear macroscopically. We already did a validity study on an app called "Clicca il Neo", comparing distant assessment of such kind of photographs with the direct clinical evaluation of original lesions. A small number of well experienced dermatologists with a high level of documented agreement participated in the study.[6]
With the aim of expanding the number of collaborating dermatologists, also enrolling young dermatologists with a limited level of clinical experience, we conduced, a new agreement study on a set of photographs selected among those sent by app users during the above mentioned previous validity study. We evaluated the agreement after an online course aimed at improving the identification and classification of pigmentary lesions.

Materials and methods

This was an agreement study, conducted after an online course, enrolling a total of six young dermatologists. The online course was organized in in collaboration with the Italian League for the Fight Against Cancer (LILT) and the Scientific Publisher Zadig of Milan, in the period February-March 2021. The course was based on an atlas of pigmentary lesions and on several recognition exercises.
At the end of the course, the reproducibility and consistency of the clinical judgments was evaluated during two online sessions, one month apart. During the sessions, the same series of 45 pigmentary lesions were presented with different order, and participants were asked to classify them as highly suspicious, suspicious, non suspicious or not assessable. The lesions were randomly selected from the validated database of the "Clicca il Neo" project. These lesions were originally classified by consensus among three experienced dermatologists as highly suspicious (5 lesions, mainly thin melanomas, all confirmed histologically); suspicious, (10 lesions, either thin melanomas or atypical nevi, also documented histologically), non suspicious (25 lesions, clinically classified as a variety of melanocytic nevi or other benign pigmentary lesions), not assessable (5 lesions, where a need for a dermoscopic examination was considered as a pre-requisite).

Statistical analysis

For descriptive purposes, data were reported as means with standard deviations (SD) or absolute numbers with percentages for continuous and nominal variables respectively. Cohen's and Fleiss' kappa were used to calculate intra- and inter-rater agreement along with their 95% confidence intervals (CI). Kappa was interpreted as follows: <0 poor, 0.01-0.20 slight, 0.21-0.40 fair, 0.41-0.60 moderate, 0.61-0.80 substantial, 0.81-1.00 almost perfect agreement. The analyses were performed with SPSS software v.26 (IBM Corp, Armonk, NY).

Results

Demographics, phenotypic features and clinical characteristics of subjects and lesions considered are reported in **Table 1**. Most subjects were females (66.7%) with an average age of 39.8 ± 14.0 years (mean ± SD). The most common phenotypic type was brown hairs (68.9%) and eyes (55.6%). Lesions were mainly located on the legs (28.9%), anterior trunk (26.7%) or back (22.2%), with a diameter between 6-15 mm in 51.1% of cases and with a large portion of subjects (44.4%) reporting recent changes in the lesion.

Table 1 - Demographics, phenotypic features and clinical characteristics of subjects and lesions selected in the study

		N=45	%
Gender	Male	15	33.3%
	Female	30	66.7%
Age (years)	*Mean, SD*	*39.8*	*14.0*
Hair colour	Black	5	11.1%
	Brown	31	68.9%
	Red	1	2.2%
	Blond	6	13.3%
	Other	2	4.4%
Eye colour	Black	2	4.4%
	Brown	25	55.6%
	Green	6	13.3%
	Light blue	11	24.4%
	Other	1	2.2%
Lesion site	Head/face/neck	4	8.9%
	Shoulders/armpits	4	8.9%
	Arms	2	4.4%
	Anterior trunk	12	26.7%
	Back	10	22.2%
	Legs	13	28.9%
Lesion diameter	<6 mm	19	42.2%
	6-15 mm	23	51.1%
	>15 mm	1	2.2%
	Unknown	2	4.4%
Recent onset	No	34	75.6%
	Yes	6	13.3%
	Unknown	5	11.1%
Recent changes	No	15	33.3%
	Yes	20	44.4%
	Unknown	10	22.2%
Personal history of melanoma	No	33	73.3%
	Yes	6	13.3%

		N=45	%
	Unknown	6	13.3%
Family history of melanoma	No	30	66.7%
	Yes	8	17.8%
	Unknown	7	15.6%
Sunburns in lifetime	No	28	62.2%
	Yes	12	26.7%
	Unknown	5	11.1%
Ongoing immunosuppressive therapies	No	43	95.6%
	Yes	1	2.2%
	Unknown	1	2.2%

SD: standard deviation

Table 2 shows the distribution of dermatologists' assessment in the first and second phase of the study. In the first phase 37.0% of lesions were judged as not assessable, 27.8% as non suspected, 27.0% as suspected and 8.1% as highly suspected. The distribution of judgments on the same pictures in the second phase, after 1 month, was similar. More specifically, the overall intra-rater agreement, as assessed by Cohen's kappa, was 0.42 (95% CI: 0.33-0.50), varying from 0.12 to 0.59 on single raters (**Table 3**). When combing suspected and highly suspected lesions together, the overall kappa was 0.47 (95% CI: 0.39-0.56), ranging from 0.16 to 0.67.

Table 2 - Distribution of dermatologists' assessment of lesions in the first and second phase of the study

Study phase	Judgment	Assessor												**Total**	
		1		2		3		4		5		6			
		N	%	N	%	N	%	N	%	N	%	N	%	**N**	**%**
I	Not assessable	22	48.9%	20	44.4%	16	35.6%	20	44.4%	8	17.8%	14	31.1%	**100**	**37.0%**
	Non suspected	8	17.8%	13	28.9%	16	35.6%	10	22.2%	18	40.0%	10	22.2%	**75**	**27.8%**
	Suspected	11	24.4%	8	17.8%	10	22.2%	10	22.2%	14	31.1%	20	44.4%	**73**	**27.0%**
	Highly suspected	4	8.9%	4	8.9%	3	6.7%	5	11.1%	5	11.1%	1	2.2%	**22**	**8.1%**
II (4 weeks after)	Not assessable	28	62.2%	16	35.6%	18	40.0%	10	22.2%	14	31.1%	14	31.1%	**100**	**37.0%**
	Non suspected	3	6.7%	14	31.1%	13	28.9%	17	37.8%	17	37.8%	10	22.2%	**74**	**27.4%**
	Suspected	12	26.7%	10	22.2%	10	22.2%	11	24.4%	12	26.7%	17	37.8%	**72**	**26.7%**
	Highly suspected	2	4.4%	5	11.1%	4	8.9%	7	15.6%	2	4.4%	4	8.9%	**24**	**8.9%**

Table 3 - Intra-rater agreement between first and second phase of the study

Assessor	Phase I judgment	Phase II judgment (4 weeks after)								Kappa (95% CI)*
		Not assessable		Non suspected		Suspected		Highly suspected		
		N	%	N	%	N	%	N	%	
1	Not assessable	19	67.9%	0	0.0%	3	25.0%	0	0.0%	0.49 (0.28, 0.71)
	Non suspected	5	17.9%	3	100.0%	0	0.0%	0	0.0%	0.54 (0.32, 0.76)**
	Suspected	4	14.3%	0	0.0%	7	58.3%	0	0.0%	
	Highly suspected	0	0.0%	0	0.0%	2	16.7%	2	100.0%	
2	Not assessable	12	75.0%	4	28.6%	3	30.0%	1	20.0%	0.53 (0.33, 0.72)
	Non suspected	2	12.5%	10	71.4%	1	10.0%	0	0.0%	0.56 (0.36, 0.76)**
	Suspected	2	12.5%	0	0.0%	5	50.0%	1	20.0%	
	Highly suspected	0	0.0%	0	0.0%	1	10.0%	3	60.0%	
3	Not assessable	12	66.7%	2	15.4%	2	20.0%	0	0.0%	0.59 (0.40, 0.78)
	Non suspected	5	27.8%	11	84.6%	0	0.0%	0	0.0%	0.67 (0.48, 0.85)**
	Suspected	1	5.6%	0	0.0%	7	70.0%	2	50.0%	
	Highly suspected	0	0.0%	0	0.0%	1	10.0%	2	50.0%	
4	Not assessable	7	70.0%	10	58.8%	3	27.3%	0	0.0%	0.37 (0.18, 0.57)
	Non suspected	2	20.0%	7	41.2%	1	9.1%	0	0.0%	0.45 (0.25, 0.64)**
	Suspected	1	10.0%	0	0.0%	6	54.5%	3	42.9%	
	Highly suspected	0	0.0%	0	0.0%	1	9.1%	4	57.1%	
5	Not assessable	1	7.1%	5	29.4%	2	16.7%	0	0.0%	0.12 (-0.07, 0.30)
	Non suspected	5	35.7%	10	58.8%	3	25.0%	0	0.0%	0.16 (-0.04, 0.36)**
	Suspected	7	50.0%	1	5.9%	5	41.7%	1	50.0%	
	Highly suspected	1	7.1%	1	5.9%	2	16.7%	1	50.0%	
6	Not assessable	7	50.0%	3	30.0%	4	23.5%	0	0.0%	0.35 (0.14, 0.56)
	Non suspected	4	28.6%	5	50.0%	1	5.9%	0	0.0%	0.41 (0.19, 0.62)**
	Suspected	3	21.4%	2	20.0%	12	70.6%	3	75.0%	
	Highly suspected	0	0.0%	0	0.0%	0	0.0%	1	25.0%	
Total	Not assessable	**58**	**58.0%**	**24**	**32.4%**	**17**	**23.6%**	**1**	**4.2%**	**0.42 (0.33, 0.50)**
	Non suspected	**23**	**23.0%**	**46**	**62.2%**	**6**	**8.3%**	**0**	**0.0%**	**0.47 (0.39, 0.56)****
	Suspected	**18**	**18.0%**	**3**	**4.1%**	**42**	**58.3%**	**10**	**41.7%**	
	Highly suspected	**1**	**1.0%**	**1**	**1.4%**	**7**	**9.7%**	**13**	**54.2%**	

CI: confidence interval
* Cohen's kappa

** Kappa calculated combining suspected and highly suspected lesions together

On the other side, the inter-rater agreement, as assessed by Fleiss' kappa, during the first phase was 0.29 (95% CI: 0.24-0.34) considering all the possible categories and 0.33 (95% CI: 0.28-0.39) combing suspected and highly suspected lesions together (**Table 4**). When considering the agreement for each category of judgment, kappa varied from 0.19 for not assessable to 0.48 for highly suspected lesions. Similar results were obtained in the second phase with kappa of 0.24 (95% CI: 0.19-0.29) and 0.30 (95% CI: 0.24-0.35) for all categories and for suspected and highly suspected lesions combined respectively.

Table 4 - Inter-rater agreement in the first and second phase of the study

Judgment	Phase I	Phase II (4 weeks after)
	Kappa (95% CI)*	Kappa (95% CI)*
Not assessable	0.19 (0.11-0.26)	0.19 (0.12-0.27)
Non suspected	0.34 (0.26-0.41)	0.23 (0.15-0.30)
Suspected	0.29 (0.21-0.37)	0.25 (0.17-0.32)
Highly suspected	0.48 (0.41-0.56)	0.40 (0.32-0.47)
Total	**0.29 (0.24-0.34)**	**0.24 (0.19-0.29)**
	0.33 (0.28-0.39)**	**0.30 (0.24-0.35)****

CI: confidence interval
* Fleiss' kappa calculated on total and on specific categories
** Kappa calculated combining suspected and highly suspected lesions together

Discussion

This study shows a less than satisfactory agreement among dermatologists, with a limited clinical experience, when judging about pigmentary lesions even after a training course has been performed. In addition, the study indicates that the consistency of the judgment, i.e., intra-rater agreement, varies among dermatologists with some dermatologists being more consistent than others. There are few studies assessing the agreement of dermatologists not supported by dermoscopy when judging about pigmentary lesions.[7,8] Even if dermoscopy is recognized as a pre-requisite for a clinical diagnosis, the search for suspicious lesions is usually directed by a preliminary inspection of the skin.[9]

Notably, the kappa values obtained in our study are similar to those obtained in the few similar studies published also enrolling experienced dermatologists. For example, the rates of inter- and intra-observer agreement amongst dermatologists were moderate in a concordance study where evaluation was limited to facial lesions.[8] Even when assessing dermoscopic features the level of agreement among different observers is rather low,[10,11] and adding dermoscopy to the clinical evaluation translate into a limited increase in a correct diagnosis (according to the study of Carli et al. the improvement was not higher than 15%).[12] In a meta-analysis, dermoscopy translated into an improved diagnosis of melanoma only in the hands of experienced clinicians and especially when the diagnosis was made by a group of examiners in consensus.[5]

Conclusions

All in all, these data are of practical relevance, and point to the need for improving the reliability of the clinical diagnoses of melanoma especially when assessing small lesions and when dealing with thin melanomas at a population level and not in the context of pigment lesions clinics.

To improve diagnostic reliability, assessment by an interconnected group of experts, so-called collective intelligence, has been proposed.[13] More feasible, is assessment in duplicate by two different observers with discordance being solved by consensus or third-party adjudication.
Finally, given the promising diagnostic performance of machine learning algorithms, such as deep convolutional neural networks,[14] automatic computer-based procedures are worth being assessed for melanoma early diagnosis in a "real world" setting.

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