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CONCISE COMMUNICATION

CASH algorithm versus 3-point checklist and its modified version in evaluation of melanocytic pigmented skin lesions: The 4-point checklist

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ABSTRACT

Dermoscopy, in expert hands, increases accuracy, sensitivity and specificity in diagnosis of pigmented skin lesions of a single operator, compared with clinical examination. Simplified algorithmic methods have been developed to help less expert dermoscopists in diagnosis of melanocytic lesions. This study included 125 melanocytic skin lesions divided into melanocytic nevi, dysplastic nevi and thin melanomas (<1 mm). We compared the 3-point checklist and CASH algorithm to analyze different pigmented skin lesions. Based on preliminary results, we proposed a new modified algorithm, called the 4-point checklist, whose accuracy is similar to the CASH algorithm and whose simplicity is similar to the 3-point checklist.

Key words: 3-point checklist, CASH, dermoscopy, melanocytic nevus, melanoma.

INTRODUCTION

Dermoscopy is a non-invasive *in vivo* technique which allows investigation of colors and microstructures of the epidermis, the dermoepidermal junction and the papillary dermis.[1] Those structures are specifically correlated to histological features. Identification of specific diagnostic patterns related to the distribution of colors and dermoscopic structures allows earlier diagnosis of cutaneous melanoma as well as several other skin lesions, assisting in diagnosis of pigmented skin lesions.[1]

Qualitative and semiquantitative dermoscopic methods and algorithms have been developed in clinical practice.[1] Pattern analysis, a qualitative method, has been demonstrated to be the most sensitive and specific. Several semiquantitative algorithms have been set up to "standardize" dermatoscopic examinations, especially for non-expert dermoscopists, but complex analyses are often required to gain a score.

Simpler algorithms, such as the 3-point checklist and more recently the CASH algorithm, have been developed.[2] The 3-point checklist is the simplest algorithm, in spite of its low accuracy. The CASH algorithm is more complex, but it has higher sensitivity, specificity and accuracy.[2]

In this study, we compared the 3-point checklist and CASH algorithm to analyze different melanocytic pigmented lesions. Based on preliminary results, we proposed a new modified algorithm, called the 4-point checklist, whose accuracy is comparable with CASH algorithm and whose simplicity is similar to the 3-point checklist.

CASE REPORT

This study included 125 pigmented melanocytic lesion images randomly recruited from two different dermatology units of northern Italy from February to December 2014. Digital images were obtained by dermoscopic analysis with a ×20 magnification and acquired with a camera (SONY-alpha 77II; Sony, Tokyo, Japan). To minimize recall bias, the operator had no prior knowledge of the macroscopic image of the lesion. All lesions were randomly assessed by two independent dermatologists, with over 7 years of experience in dermoscopy. All lesions were excised and independently analyzed by two dermatopathologists. Lesions that did not meet at least two consents were excluded. Other exclusion criteria were low-quality images, and acral and mucosal lesions. Histopathological diagnoses were divided into melanocytic nevi, dysplastic nevi and thin melanomas (<1 mm). The diagnosis of dysplastic nevus was based on the histopathological diagnostic criteria set by the World Health Organization Melanoma Programme.[3] It was considered as a benign lesion. Each dermoscopic image was assessed using the following diagnostic algorithms: CASH algorithm,[4] the 3-point checklist,[5] and one self-made modified version of the 3-point checklist, namely, the 4-point checklist.

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The CASH algorithm has four criteria: color, architectural disorder, symmetry and homo/heterogeneity. Color parameter was evaluated as 1 point (light-brown, dark-brown, black, red, white, blue). Architectural disorder describes non-uniformity of structures and their disposition into the lesion. We attributed 0 points to absence or mild presence, 1 to moderate presence and 2 points for marked presence of architectural disorders. Asymmetry was evaluated as 1 point if the lesion was monoaxial and 2 points if it was biaxial. Homo/heterogeneity was established by the presence of the following dermoscopic features: pigmented network, streaks/pseudopods, globules/dots, blue-whitish veil, blotches, polymorphous blood vessels and regression structures (scarring, blue-gray areas with or without peppering). The presence of each of the previous features was evaluated as 1 point. A CASH total score higher than 7 has been considered suggestive of suspicious lesion. The 3-point checklist is based on three criteria: asymmetry in color and/or structures in one or two axes, pigmented network with thickened lines and irregular distribution, and any blue and/or white structure within the lesion. The concurrent presence of two or more criteria addresses a diagnosis of suspicious lesion. From the 3-point checklist, we developed the 4-point checklist doubling all three criteria of the 3-point checklist and choosing the one which confers more sensitivity, specificity and accuracy. Therefore, the 4-point checklist was developed starting from the 3-point checklist by doubling only the symmetry parameter as shown in Table 1. A total score higher than 2 points was used as cut-off for suspicious pigmented lesion. Dermatoscopic findings were later correlated with the histopathological diagnoses. The performance of the different algorithms was assessed by receiver–operator curve (ROC) analysis. Values of $P < 0.05$ were considered statistically significant and P-values ranging 0.05–0.08 were considered borderline and used to highlight a tendency. Statistical analyses were performed with the Stata/SE-12 software package (StataCorp, College Station, TX, USA).

One hundred and twenty-five lesions belonging to 125 patients (61 men, 64 women; mean age, 44.6 and 50.0 years, respectively) were examined in this study. Lesions, after histopathological examinations, were grouped into thin melanomas ($n = 32$), dysplastic nevi ($n = 50$) and melanocytic nevi ($n = 43$). We compared the group of "thin melanoma" versus "dysplastic nevi and melanocytic nevi" using the CASH algorithm, the 3-point checklist and the 4-point checklist. Areas under the ROC (AUC) were 0.90, 0.77 and 0.84, respectively. The CASH algorithm was more accurate than the 3-point checklist ($P < 0.00001$) and also more accurate than the 4-point checklist ($P = 0.01$), which prevails over the 3-point checklist ($P = 0.006$ as shown in Fig. 1a). By comparing the group of "thin melanoma" versus "melanocytic nevi", we increased the AUC of all the analyzed algorithms as shown in Figure 1(b). Therefore, THE CASH algorithm was significantly different from the 3-point checklist ($P \leq 0.005$) as well as the 4-point checklist from the 3-point checklist ($P \leq 0.01$). CASH and the 4-point checklist were not statistically different ($P = 0.2$). Although the AUC for CASH and the 4-point checklist were not statistically different ($P = 0.2$), CASH was more accurate than the 4-point checklist as evidenced by the ROC for CASH, which was clearly closer to the upper left corner (1, 1–100% specificity, 100% sensitivity), (Fig. 1b). Sensitivity and specificity of the compared algorithms at the defined cut-off were: CASH (cut-off, >7), 100% sensitivity and 76% specificity; 3-point checklist (cut-off, >2), 60% sensitivity and 89% specificity; and 4-point checklist (cut-off, >2), 83% sensitivity and 82% specificity.

Table 1. Description of 4-point checklist

Variable doubling	
Asymmetry of color and structure 1st axis	1 point
Asymmetry of color and structure 2nd axis	1 point
Thick pigmented network	1 point
Irregular pigmented network	1 point
Blue structure	1 point
White structure	1 point
4-point checklist	
Asymmetry of color and structure 1st axis	1 point
Asymmetry of color and structure 2nd axis	1 point
Irregular or thick pigmented network	1 point
Blue-white structure	1 point
Total score >2 points for suspicious lesions	

Choice of variable was made by evaluating the increment of area under the receiver–operator curve for the inclusion of one split variable per time. The resulting 4-point checklist is described.

DISCUSSION

Dermoscopy has become a crucial tool in the diagnostic armamentarium of dermatologists for skin cancer detection. In expert hands, with variable percentages, it increases accuracy, sensitivity and specificity of a single operator, compared with clinical examination.[6] Pattern analysis is the most common method used by expert dermatologists in dermoscopy providing greater diagnostic accuracy for cutaneous pigmented lesion.[7] Dermoscopic experience is not uniform and it requires continuous practice following training in order to learn skills. Simplified algorithms for dermoscopy in melanoma diagnosis were developed to facilitate the use of this technique even by non-experts.[8] Quantitative methods assign a numerical score to pigmented lesions, easily accessible to all dermoscopists for a homogeneous and repeatable interchange of information. The most important simplified semiquantitative algorithms in addition to classical pattern analysis are the ABCD rule,[9] the Menzies method[10] and the 7-point checklist.[11] It is difficult to draw conclusions about the relative efficiency (in terms of diagnostic accuracy, simplicity of use and reproducibility) in comparison with the more complex pattern analysis.[12]

Another limit is represented by application, which is not easy and it is too often mediated by complicated multiplicative factors assigned to each examined parameter. This makes any visit a highly complex exercise for a fast and effective clinical approach. The latest semiquantitative algorithms which have been introduced into clinical practice are the CASH and the 3-point checklist. The first is a valuable tool, which assigns

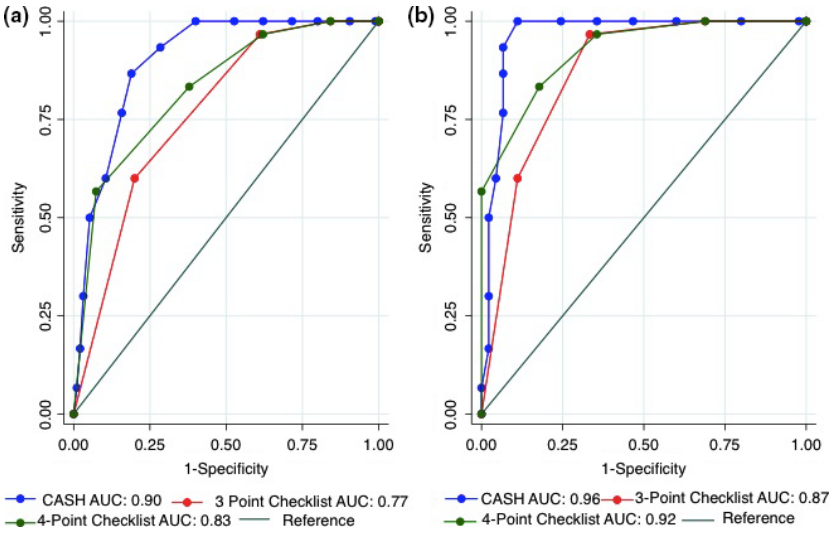

Figure 1. (a) Comparison of three algorithms (CASH, 3-point checklist, 4-point checklist) by receiver–operator curve analysis assessing the group of thin melanoma vs benign lesions (melanocytic nevi and dysplastic nevi). (b) Comparison of three algorithms (CASH, 3 point checklist, 4 point checklist) excluding dysplastic (thin melanoma vs melanocytic nevi). AUC, area under the receiver–operator curve.

Figure 2. A melanocytic nevus scored as suspicious according to the 3-point checklist and non-suspicious according to the 4-point checklist. The lesion shows asymmetry in only one axis (vertical) and an irregular pigmented network.

a numerical value to a qualitative approach, at the cost of a challenging and multiparametric evaluation. The second, conversely, is fast, effective and easily reproducible, but it lacks specificity and accuracy. Moreover, the 3-point checklist was originally introduced also for non-melanocytic lesions including basal cell carcinoma, seborrheic keratosis and solar lentigo.[5]

Our intention was to compare those two algorithms in the differential diagnosis of pigmented melanocytic lesion and in particular between thin melanomas and melanocytic nevi. In agreement with other reports,[3,4,13] CASH appears sensitive and specific, but complex. Contrarily, the 3-point checklist is a quick consultation tool, but it lacks sufficient specificity, even in our cohort.

This study, based on the preliminary results, proposes an amelioration of the 3-point checklist algorithm by doubling the variable "asymmetry". Asymmetry was found to be the variable contributing more highly to the algorithm accuracy. The inclusion of a second perpendicular axis for symmetry confers accuracy to the algorithm, even comparable to CASH. Structure and color asymmetry evaluated on a single axis does not guarantee accurate assessment for several pigmented lesions (Fig. 2). Asymmetry of melanocytic lesions has already been reported as an important indicator of malignancy, substantially contributing to the diagnosis, especially if it is based on semi-quantitative algorithms.[14] Melanomas are significantly more asymmetrical than pigmented and atypical nevi.[15]

In our experience, the 4-point checklist, which can evaluate the two main axes of asymmetry in pigmented skin lesions, can increase the accuracy of the test, ensuring a simpler and rapid assessment even for less expert operators. The cut-off for this new algorithm was 2; therefore, lesions with a score higher than 2 should be considered suspicious and consequently they should be excised. Although the 4-point checklist was found to be accurate and quickly reproducible in the differential diagnosis between melanocytic nevi and thin melanomas, more studies are also needed to assess the usefulness of this new algorithm in the evaluation of non-melanocytic pigmented lesions.

We acknowledge as a limitation of our study the small sample size; therefore, further studies are needed to validate this new quantitative algorithm.

CONFLICT OF INTEREST: None declared.

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