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ORIGINAL RESEARCH

Importance of the patient's clinical questionnaire for the diagnosis of skin cancer through teledermatology in remote areas of Brazil

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ABSTRACT

Introduction: Skin cancer is the most common cancer worldwide and in Brazil represents 25% of cases of cancer. Brazil is a developing country with a large territorial dimension and not many people have access to information and healthcare providers. Teledermatology is already being used in programs for cancer prevention in a mobile unit at Barretos Cancer Hospital. The aim of this study was to assess the incremental value of the use of a clinical questionnaire added to digital photography to improve the screening of skin cancer.
Methods: A total of 623 patients were included. In the first phase of the study, 436 patients were screened for skin malignancy from February 2010 to July 2011. In the second phase, 186 patients were screened between June and July 2012. All patients had their skin lesions photographed. In the second phase of the study, information on medical and family history, physical characteristics of the lesion and risk factors was collected. Photographs and clinical information from the second phase only were sent to the Barretos Cancer Hospital for diagnosis by medical specialists. Sensitivity, specificity, positive and negative predictive values and accuracy of observers were analysed, using the pathology diagnosis as the gold standard.
Results: The majority of lesions in the first and second phases (68.3% and 64%, respectively), were classified as basocellular carcinoma, and melanoma represented 1.4% and 2.2%, respectively, of skin cancers. The specificity and positive predictive values in the first and second phases of the study regarding observers 1 and 2 changed significantly with the addition of a clinical

questionnaire (observer 1: p=0.003; observer 2: p=0.002). Moreover, there was a significant increase in receiver operating characteristic curve for the observers, comparing the two phases when the clinical questionnaire for diagnosis is implemented.
Conclusions: The clinical questionnaire combined with digital photography has increased the performance of observers for skin cancer diagnosis in an opportunistic screening scenario.

Key words: accuracy, Brazil, diagnosis, public health, questionnaire, skin cancer, teledermatology.

Introduction

Skin tumors are the most frequent malignancy worldwide among all malignant neoplasms. Between 2 and 3 million new cases of non-melanoma skin cancers and 132 000 new cases of melanoma are diagnosed annually[1]. According to the Brazilian National Cancer Institute, 175 760 new cases of non-melanoma skin cancers are expected in 2016[2].

Among the tumors of the skin, non-melanoma represents more than 90% of cases. Most of these lesions are associated with low mortality rates, but they can cause disfigurement and sequelae due to the treatment, since the lesions predominantly appear in skin areas exposed to the sun, like the face, neck and arms[3,4]. However, when detected at an early stage, the therapeutic approach is accessible and inexpensive, with low morbidity[3,5].

Usually the skin tumors do not invade lymphatic vessels and the metastasis rates are less than 1%. However, if undiagnosed and untreated for a long period of time these lesions can invade areas such as eyes, peripheral muscle, nerves, bone and cartilage[6-8]. In contrast, melanoma has a lower incidence (2–5% of skin cancers), but is responsible for most deaths due to its high metastatic potential and drug refractory characteristic[9] ; also, its prognosis is closely related to the clinical stage at diagnosis[10,11]. Although skin cancer is the most common neoplasm in tropical countries[12], there is no population screening for skin cancer in Brazil. For an efficient skin cancer screening, an examination of the all of the skin on the body is expected[2,13]. Moreover, the cost-effectiveness of skin cancer screening programs in decreasing morbidity or mortality is still controversial[2,14,15].
Dermatology as well as radiology and pathology specialties have been using telemedicine[16], among other things, for health care in remote areas and in populations with limited access to healthcare providers[17]. Early in 1995, dermatologists started to use telemedicine resources in a rural area of the state of Oregon in the USA[18].

When used as a tool in the identification and monitoring lesions in large populations, teledermatology has proved to be potentially important in reduction of medical costs and in reducing the time taken to identify suspicious lesions[19,20]. Reports based on the use of digital photography of skin lesions remotely scanned and sent to specialized medical centers, where qualified professionals evaluated them, showed very impressive results in the diagnosis of skin cancer[21,22].

Developing countries, in which there are huge areas with an important deficit of physicians, could benefit from teledermatology, because it would allow early diagnosis of malignant lesions of the skin by training nurses to identify likely malignant lesions and send the skin photographic images to an experienced dermatologist[23-26] for evaluation.

A clinical questionnaire for patients in addition to medical images is an accepted way to improve the reading of images by radiologists[27-29]. Similarly, telemedicine is used in cardiology: electrocardiogram images are sent with clinical data for remote medical assistance[29].

In 1970, a study in England showed that in 80% of outpatients the isolated clinical questionnaire was responsible for 82.5% of diagnoses, clinical examination for more than 8.75% and additional tests for more than 8.75%[30]. Several other studies showed that the main diagnostic tool of the physician is a clinical questionnaire and physical examination[31,32].

A movement began in the 1990s for the implementation of a rigorous scientific methodology for diagnostic studies. This initiative states that the clinical questionnaire and physical examination give the doctor all the necessary tools for diagnosis, diagnostic hypotheses, and to identify patients in the early stages of diseases that could lead to death[33].

Developing countries with large geographical areas usually have insufficient medical assistance as well as an imbalanced distribution of doctors. The use of teledermatology could be of benefit for the remote regions of these countries, allowing early diagnosis of skin cancer in this population. One possible strategy is to train local healthcare providers to take pictures of suspicious skin lesions and send the images for remote diagnosis by experienced dermatologists[34,35].

The aim of this study was to evaluate the importance of the increment of a clinical patient questionnaire to digital photography for the diagnosis of skin cancer via teledermatology in distant and rural areas of Brazilian territory using mobile units.

Methods

The Cancer Prevention Department (CDP) and the Department of Skin Cancer at Barretos Cancer Hospital (BCH, Barretos, Brazil), performed the skin cancer screening. The program is based on the use of Mobile Unit (MU) of Cancer Prevention that regularly visits the remote areas of Brazil. This MU is fully equipped to perform clinical procedures and small surgical procedures; regarding skin lesions, the team is able to perform 40 clinical dermatology examinations or procedures per day, including cryotherapy and surgery. One well-trained medical doctor is in charge of skin lesion examination by visual inspection.

A nurse from the local municipality who was trained previously at BCH screened all patients examined at the MU. A more detailed description of the MU concept has been published previously[36]. Such local nurses are trained to identify suspicious lesions for skin cancer by BCH nurses and by a physician from BCH with experience in skin cancer screening. A day of training is offered specifically to exemplify the different types of the more frequent skin lesions, and didactic materials (eg image CDs, banners, leaflets and brochures) are given to support the educational training. The nurses and physician from BCH are also responsible for speaking with the clinicians in the municipalities to convince them about the importance of their participation in the prevention activities and also for closely assisting the local nurses' triage. In addition, they are encouraged to principally invite the underprivileged people that live in the suburbs or in rural areas and to inform them that all of the procedures related to the cancer prevention and treatment are free[36].

Study participants

A total of 623 patients referred to the MU appointment participated in the study; 436 were part of the first phase of the study and 186 in the second phase as described below.

First phase: A nurse from a location that MU would visit screened patients for skin malignancy from February 2010 to July 2011. At the MU appointment, clinical assessment, diagnosis (benign or malignant), all the photography and biopsies of lesions in cases of suspected of skin malignancy were performed by a medical doctor. At this point, nurses were present to assist the medical procedures. All the biological material collected (biopsies or surgical specimen) was properly identified, stored in bottles with 10% formalin and sent to the BCH pathology department for analysis.

The photographic images were obtained from a distance of approximately 60 cm from the skin lesion in order to assess the topographic localization of the lesion, and a second image was captured as close as possible to assess the details of the lesion. If the visual inspection suggested a neoplastic lesion, the medical doctor performed the excision of the lesions.

Second phase: Patients were screened (by a nurse) between June and July 2012 in the same manner as for the first phase; however, a specific questionnaire (not applied in the first phase) was applied after the medical visit and the photography was performed.

The two photos of each lesion were done in the following way: the first was taken from a long distance; the second was taken near the injury using the macro function in the same way as in the first phase. Briefly, the clinical information collected were race, previous history of skin cancer, previous history of familial cancer, previous or current history of skin disease, physical characteristics of the lesion, duration of the symptoms and evolution (growing and/or changing aspect), anatomical localization of the skin lesion, macroscopic characteristics of the lesion (pigmented, elevated, ulcerated, infiltrative, cutaneous horn-like, edges regular or irregular), if the lesion is recurrent, if the patient was previously submitted to radiotherapy at the site of the skin lesion, if the patient had been or still was in contact with risk factors at work (chemical, sunlight exposition), use of sunscreen, history of tanning, use of immunosuppressive drugs, type of skin phototype recorded (A (I and II), B (III and IV), C (V and VI)).

Digital photography

The camera used was a Sony Cybershot DSC-S780, of resolution 8.1 megapixels. The lighting photography place was a clinic room and four fluorescent lamps of 54 V each were used to illuminate the photographic field. The camera used was the same between the first and second phases in order to avoid any bias of image resolution.

All photos were stored in JPEG format, and they were properly identified and sent blindly, via internet, to two BCH medical doctors with at least 10 years of experience in diagnosis and treatment of skin cancer.

The clinical questionnaire was sent with the photos in the second phase of the study.

Evaluation of photographs

Physicians assessed the photos independently and made the diagnosis classifying them as **(1)** lesion suspicious for malignancy (e.g. carcinoma, Bowen's disease, keratoacanthomas), **(2)** lesion with benign features (such as simple warts, ringworm, simple nevi and other skin conditions that do not need to be referred to a cancer hospital) or **(3)** not evaluated lesion (due to insufficient image for diagnosis – photograph of poor quality (low light, high reflection or out of focus) or ill-defined lesion). Teledermatology non-concordant lesions were invited for new clinical evaluation and submitted to surgery (when necessary).

The same doctor was present in the two phases of the study. Figure 1 presents a flowchart of the process of this study.

Statistic evaluation

The gold standard to calculate the sensitivity, specificity, positive and negative predictive values and accuracy of observers was the pathology report. These results were compared and submitted to descriptive statistical analysis and accuracy, and a receiver operating characteristic (ROC) curve was constructed. For this, the Statistical Package for the Social Sciences v19.0 (IBM Corporation; http://www.spss.com) and R v3.2.3 were used (https://www.r-project.org/). The R package pROC (http://web.expasy.org/pROC/) was used to compute the DeLong's test for two ROC curves comparison. Statistical significance (p value) adopted was 0.05.

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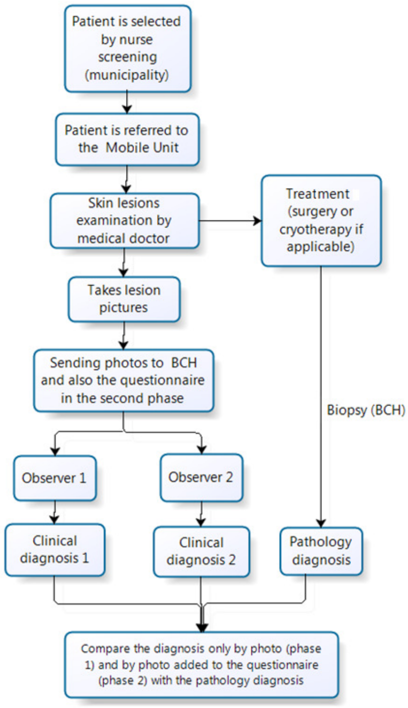

Figure 1: Flowchart of the study.

Ethics approval

The study was approved by the Research Ethics Committee of BCH, with protocol number 377/2010, in accordance with the ethical standards by the initial 1964 Declaration of Helsinki and including its later amendments. Consent was obtained before starting the study.

All patients undergoing surgical procedures, cases of extensive lesions or anatomical areas of difficult surgical access were referred to BCH for the appropriate procedures (such as surgery and/or radiotherapy). Patients with benign lesions were referred for dermatological treatment in the municipality.

Results

The mean age was 63.1 years (standard deviation=13.1) and 61.7 years (standard deviation=14.2) for patients of phase 1 and 2 respectively. In both phases, most patients had clear skin, skin type (according to Fitzpatrick Scale[37]) I and II (77.2% and 61.2%), most malignant lesions were located in the region of the face and head and neck (70.3% and 63.7%). The vast majority of lesions were diagnosed at an early stage, 0 or 1 (89.5% and 84.1%). The majority of lesions, were classified as basocellular carcinoma (68.3% and 64%), and melanoma represented 1.4% and 2.2%, respectively, of skin cancers. The pathological results of the first and second phases are shown in Table 1.

The photographs of skin lesions were assessed by medical doctors of BCH (observer 1 and 2) for diagnosis. The sensitivity, specificity, positive and negative predictive values and accuracy are shown in Table 2.

Comparison of the two phases shows that the ROC curves for the observers increased significantly (observer 1: p=0.003; observer 2: p=0.002) (Figs 2,3).

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Table 1: Pathological results for phases 1 and 2

Histopathology	Phase 1		Phase 2	
	n	%	*n*	%
Basocellular carcinoma	298	68.3	119	64.0
Squamous cell carcinoma	59	13.5	26	14.0
Melanoma	6	1.4	4	2.2
Tricoepitelioma maligno	8	1.8	1	0.5
Dermatofibrosarcoma	0	0.0	1	0.5
Squamous cell carcinoma in situ	6	1.4	5	2.7
Metatypical lesion	0	0.0	3	1.6
Benign	59	13.5	27	14.5

Table 2: Observer's performance for phases 1 and 2

Phase 1	Sensitivity % (CI)	Specificity % (CI)	PPV % (CI)	NPV % (CI)	Accuracy % (CI)	AUC (CI)
Observer 1	89.3% (0.857–0.921)	38.5% (0.452–0.771)	91.0% (0.876–0.936)	33.9% (0.231–0.466)	82.9% (0.790–0.862)	0.64 (0.515–0.697)
Observer 2	96.2% (0.936–0.977)	25.0% (0.152–0.382)	90.0% (0.866–0.926)	48.1% (0.307–0.660)	87.3% (0.837–0.901)	0.61 (0.549–0.728)
Phase 2	**Sensitivity % (CI)**	**Specificity % (CI)**	**PPV % (CI)**	**NPV % (CI)**	**Accuracy % (CI)**	**AUC (CI)**
Observer 1	81.5% (0.747–0.868)	77.3% (0.566–0.899)	96.2% (0.645–0.776)	37.0% (0.245–0.514)	81.0% (0.746–0.861)	0.79 (0.697–0.901)
Observer 2	89.2% (0.833–0.931)	59.1% (0.387–0.767)	94.0% (0.889–0.968)	43.3% (0.274–0.608)	85.47% (0.796–0.899)	0.76 (0.670–0.858)

AUC, area under curve. CI, confidence interval. NPV, negative predictive value. PPV, positive predictive value.

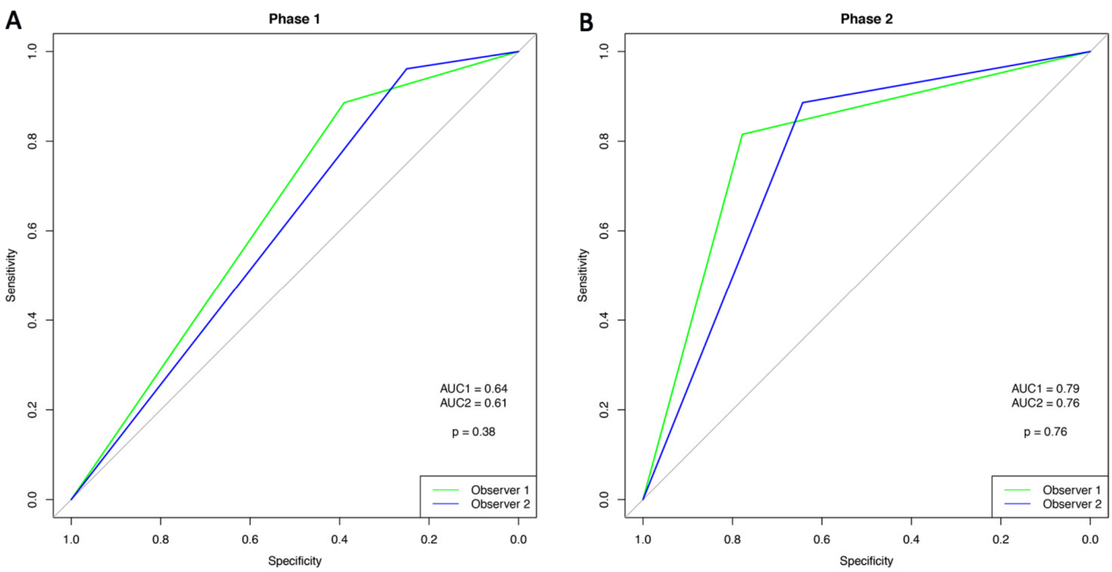

Figure 2: Receiver operating characteristic curve for phase 1 (A) and phase 2 (B).

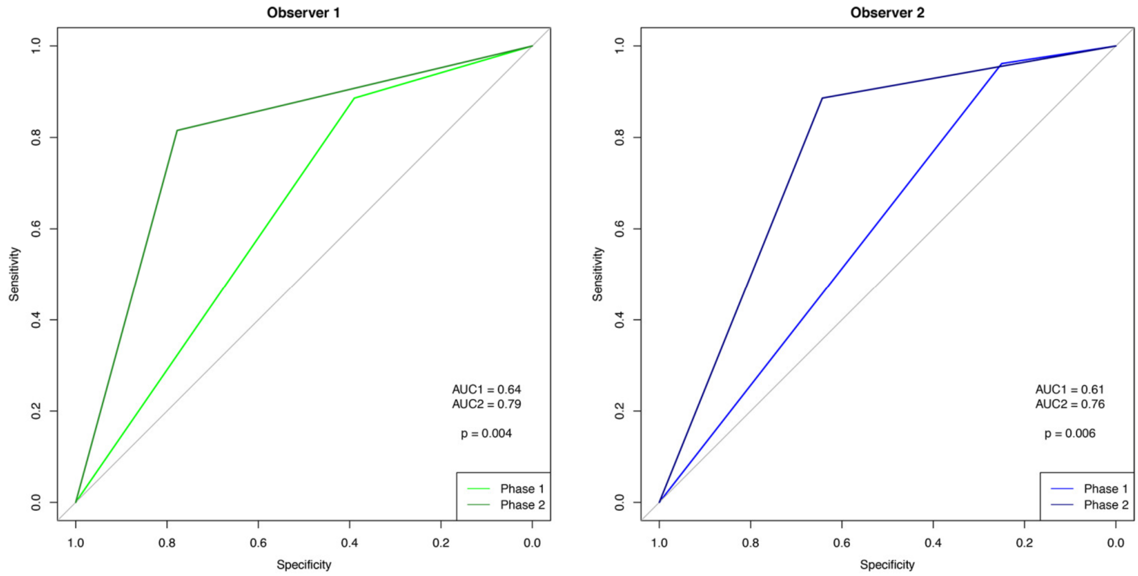

Figure 3: Receiver operating characteristic curve for observers 1 and 2.

Discussion

Brazil experiences strong solar radiation in most parts of its vast territory. This constitutes a risk factor for skin cancer. Optimizing the options for skin lesion diagnosis is critical to reduce bad outcomes in populations affected by skin cancer that live and work in rural remote areas. The present study's results have demonstrated that teledermatology has major potential to detect early lesions of skin cancer and also to favor the recognition of a skin lesion.

Currently, melanoma and non-melanoma skin cancer screening programs do not exist in Brazil; consequently, diagnosis is often postponed and the lesions are diagnosed tardily and mainly at an advanced stage. Non-melanoma tumors are associated with extended local resections, which are in turn associated with high morbidity[38]. Skin melanoma has a worse prognosis, leading to potential loss of significant years of life with indirect costs associated with morbidity and premature mortality[39].

Screening of skin cancer has been implemented in several countries, showing the potential to reduce cases of advanced cancers at diagnosis[40].

In Germany a recent study observed that melanoma mortality decreased by 47% among men and 49% among women after implementation of screening for skin cancer, providing significant evidence that screening can prevent a reasonable number of deaths from melanoma. However, despite the strong favorable evidence, the data lack definitive arguments to support the statement that the skin cancer screening program reduced melanoma mortality in the Schleswig-Holstein area[40].

Access to specialized medical services in remote areas or even in the outskirts of large cities is a recurrent problem in many parts of the world. Additionally, there is an evident difficulty in convincing skilled medical doctors to work in rural and remote areas of both developed[36,41,42] and developing countries[43]. For these reasons the authors strongly advocate the use of teledermatology to aid in reducing the distance between patients and medical doctors specialized in dermatology[44], reducing the time to perform the diagnosis and indicate adequate treatment when compared to the traditional healthcare system[24,45,46]. Although there are few studies using teledermatology in screening skin cancer, they showed encouraging results[24,26] . In this context the use of teledermatology in skin cancer prevention looks promising.

The images of the lesions are the main semiotic element of dermatological diagnosis. The effectiveness of teledermatology and dermatological telescreening depends on the quality of the picture, clinical representativeness of the lesion, significance of the lesion aspects inherent in three dimensions, palpation characteristics and dimension of the lesions, as well as notions about the topography of the injuries[47].

Following these premises, the two-dimensional format of the digital images certainly represents limitations regarding the estimated size, topography and palpation consistency of the lesions; however, the present study's results were satisfactory in relation to the histopathological findings, and a clinical questionnaire improved the sensitivity and accuracy of observers.

Due to patients having been previously screened by the physician of the MU there were a small number of negative cases; consequently, specificity and negative predictive values were low in the first and second phases. However, there was a slight increase in the negative predictive value in the second phase. Due to this limitation of the study this result cannot be attributed to the use of the questionnaire; however, the ROC curves for the observers increased significantly between the two study phases.

Conclusions

The study data revealed an exciting perspective for further programs of skin cancer prevention. If the questionnaire had been introduced at the establishment of these activities the results herein may have been more remarkable. Additionally, the design of this study did not permit the evaluation of false negative results.

The clinical questionnaire combined with digital photography has increased the performance of observers in opportunistic skin cancer screening. Teledermatology proved to be an effective tool to improve population screening for patients at high risk of skin cancer.

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Modified on 22 June 2017: the correction "The third author, Adriane Feijó Evangelista, was initially omitted from the article, although she made substantial contributions to the analysis and interpretation of data. This author and her contact details have now been added to the published article.

Also, the name of the tenth author, Adhemar Longatto, has been amended to Adhemar Longatto-Filho".

