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Colposcopy combined with dynamic spectral imaging. A prospective clinical study

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ABSTRACT

Objective: To analyze the value of dynamic spectral imaging (DSI) compared to, and as an adjunct to, conventional colposcopy (CC) in the diagnosis of cervical intraepithelial neoplasia (CIN).
Study design: Four hundred seventy-nine women referred for colposcopy after an abnormal Pap-smear (≥ASC-US) to the Low Genital Tract Unit of the San Carlos Clinical Hospital in Madrid, Spain during the years 2012–2014 were examined simultaneously by CC and DSI. Thirty-six cases (8.1%) were excluded because the DSI map was not calculated. The gold standard for comparisons was the final histological diagnosis performed by punch biopsy or LEEP.
Results: Out of the 443 cases, 293 were found to be negative for CIN, 109 had CIN1 and 41 were found with CIN2+. The sensitivity of CC to detect those with CIN2+ lesions was 73.2% and the specificity 92.3%. Using the DSI map as an adjunct, led to a statistically significant increase of the sensitivity to 87.8% with a concomitant drop in specificity to 85.6%. The adjunctive use of DSI increased the sensitivity for CIN2+ also in the high-risk group of the 65 cases with an identified HPV16/18 infection; CC had a sensitivity of 88.9%, which increased to 100%. The specificity dropped from 91.1% to 87.5%.
Conclusions: Combining conventional colposcopy with DSI mapping improves the capability to detect cervical lesions.

Introduction

Cervical cancer is the third malignant neoplasm in women over the world [1]. Using the Pap-smear for cervical cancer screening has achieved a significant reduction in incidence and mortality, although its overall sensitivity is slightly above 50% [2,3]. The recent incorporation of DNA-HPV as primary test in a cervical cancer screening setting has increased the detection rate for CIN2+ as compared with the traditional Pap smear [4].

Colposcopy with acetic acid 3% (conventional colposcopy) is recommended after an abnormal Pap smear test result, an HPV 16/18-DNA test positive with negative Pap smear, or for presence of a palpably or visually abnormal cervix, vagina, or vulva. However, conventional colposcopy (CC) has a moderate sensitivity and is a subjective technique that should be performed by trained personnel [3,5]. Despite the efforts to improve the accuracy of colposcopy, the sensitivity is lower than 70% [6], and the final histological diagnosis depends on the experience and the ability of the colposcopist to identify the best sites for biopsies [7–9].

The dynamic spectral imaging system (DySIS™, by DySIS Medical Ltd, Livingston, UK), is a new colposcopic system that has been demonstrated to increase the sensitivity of colposcopy in detecting patients with high-grade lesions and improving the selection of cervical biopsy sites [10,11]. It is a digital colposcope that allows physicians to perform CC and also measure the dynamic color changes occurring on the cervix after the application of acetic acid. During the examination, the software that is embedded in the device, measures these dynamic color changes in a standardized way and then calculates and displays a color-coded dynamic spectral imaging (DSI) map that is based on the intensity and time-evolution of the acetowhitening. The DSI map represents the localization of acetowhitening, and also reflects a prediction on the severity of the cervical lesion, indicating options for biopsies [11,12]. Additionally, it was recently demonstrated that assessing the DSI map is a procedure easy to perform, especially among less experienced colposcopists [13].

The aim of this study was to further analyze the impact of using the DSI map combined with CC vs. CC alone in diagnosing cervical intraepithelial neoplasm (CIN) in a prospective and consecutive

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series of patients referred to colposcopy because of abnormal screening result in a single colposcopic office, expecting to observe an increase in sensitivity.

Materials and methods

Between March 2012 and February 2014, 479 consecutive women who were referred for colposcopy to a single colposcopic office at Hospital Clinico San Carlos in Madrid, Spain, and met the inclusion criteria (need for colposcopy and aged 18 or more years) were invited to participate in the study. None refused to participate. The study followed the ethical principles of the Helsinki declaration and was approved by the Institutional Review Board (C.I. 13/314-E).

All patients were examined by the same colposcopist (PJC), who recruited them, collected the consent, used the colposcope to perform CC and DSI mapping, and collected the cervical biopsies. This colposcopist has been accredited as an expert colposcopist by the Spanish Society of Cervical Pathology and Colposcopy (SSCPC).

Women were referred and managed following the guidelines of primary and secondary prevention of cervical cancer of the Spanish Society of Obstetrics and Gynecology and the SSCPC [14]. Following these recommendations, an HPV DNA-test was used for screening of women older than 30 years, after a previous Pap-smear of ASC-US/AGC in women older than 21 years or LSIL/ASC-H in women older than 50 years. The DNA-HPV test was performed with CLART® HPV2 which can detect and genotype 35 different types HPV using multiplex PCR [15]. Besides 16 and 18, the 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68 genotypes were considered as high-risk [16].

During the colposcopic examination 3% acetic acid was used; Schiller's (iodine) test was used on some of the cases, as deemed clinically necessary. The colposcopic procedure using the DSI colposcope was performed as described previously [11]. Briefly, CC was performed during the 2–3 min that it takes the DSI procedure to complete image acquisition and analysis. During this time, any cervical lesions were identified and graded by the colposcopist, who committed to impression and location of lesions. The new International Federation for Cervical Pathology and Colposcopy terminology classification [17] was used to classify the CC results in suggestion of low-grade (abnormal findings grade I) or high-grade cervical lesions (abnormal findings grade II). At the end of DSI process and before finalizing the biopsy decision and biopsy site selection, the corresponding color-coded DSI map was displayed and evaluated. Blue color of the DSI map was interpreted as indicative of normal tissue, green as low grade lesions and red-yellow-white colors as suggestive of a high-grade (CIN2+) lesion (Fig. 1).

A cervical biopsy was performed with punch forceps when any cervical lesion was detected either by CC or when the colors green, red, yellow or white in the DSI color map were identified. When CC and DSI indicated different sites, a biopsy was taken from both places. An endocervical curettage was performed when the transformation zone was type 3 (squamocolumnar junction not

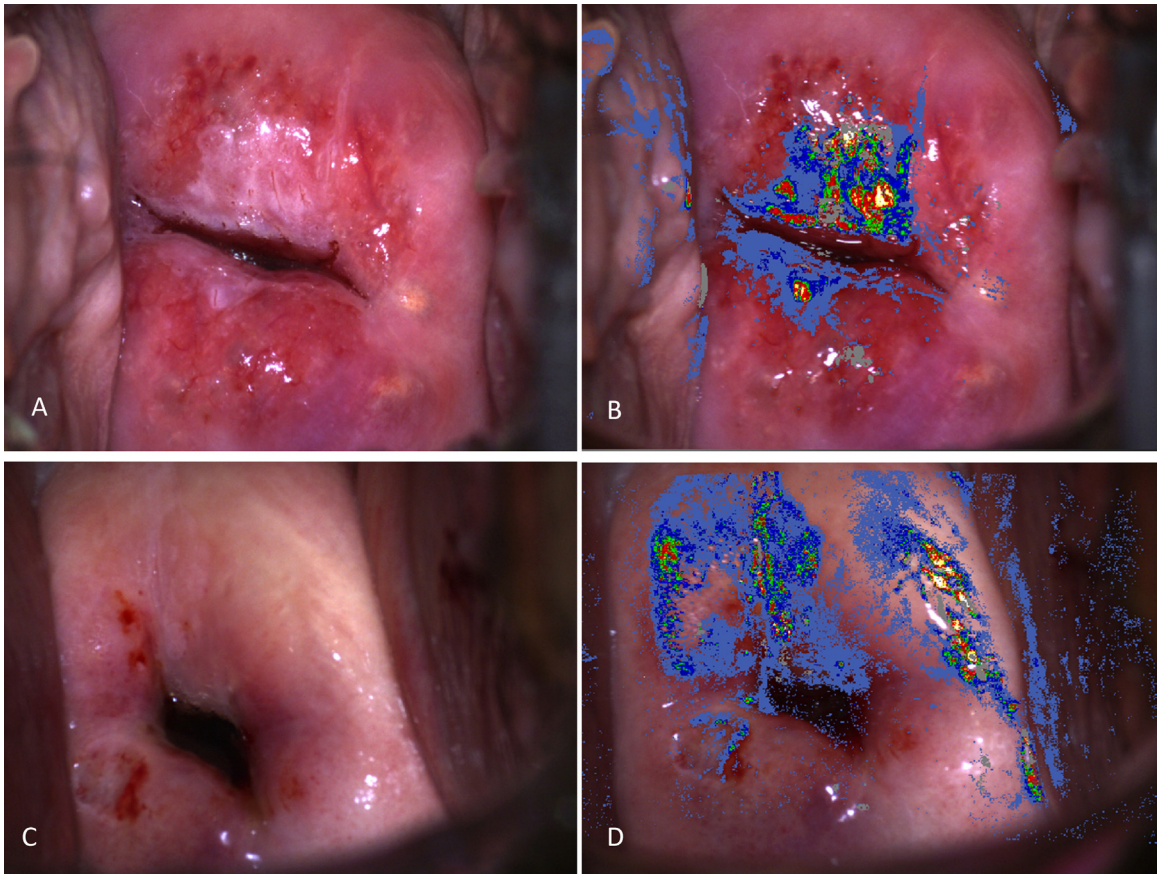

Fig. 1. Cervical images from two cases indicative of conventional colposcopy (CC) and the corresponding dynamic spectral imaging (DSI) maps. Images A/B (case 1), and C/D (case 2) correspond to CC/DSI map, respectively. In case 1, the pathological result was CIN 2–3 both in punch biopsy and LEEP. (A) CC showing abnormal findings grade II. (B) DSI map showing red-yellow-white areas suggesting high grade. In case 2, the punch biopsy result was CIN 3, the LEEP showed microinvasive squamous carcinoma and in hysterectomy the final result was an invasive squamous carcinoma (FIGO stage Ib1). (C) Conventional colposcopy showing abnormal findings grade I with the squamocolumnar junction not completely visible (unsatisfactory colposcopy). (D) DSI map showing red-yellow areas in the lesion observed by CC corresponding to CIN 3, and white areas in the periphery with no lesion in CC. These areas were negative in punch biopsy. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)