ABSTRACT
BACKGROUND: Melanoma has one of the fastest rising incidence rates of any cancer. It accounts for a small percentage of skin cancer cases but is responsible for the majority of skin cancer deaths. Early detection and treatment is key to improving survival; however, anxiety around missing early cases needs to be balanced against appropriate levels of referral and excision of benign lesions. Used in conjunction with clinical or dermoscopic suspicion of malignancy, or both, reflectance confocal microscopy (RCM) may reduce unnecessary excisions without missing melanoma cases.
OBJECTIVES: To determine the diagnostic accuracy of reflectance confocal microscopy for the detection of cutaneous invasive melanoma and atypical intraepidermal melanocytic variants in adults with any lesion suspicious for melanoma and lesions that are difficult to diagnose, and to compare its accuracy with that of dermoscopy.
METHODS: We undertook a comprehensive search of the following databases from inception up to August 2016: Cochrane Central Register of Controlled Trials; MEDLINE; Embase; and seven other databases. We studied reference lists and published systematic review articles.
SELECTION CRITERIA: Studies of any design that evaluated RCM alone, or RCM in comparison to dermoscopy, in adults with lesions suspicious for melanoma or atypical intraepidermal melanocytic variants, compared with a reference standard of either histological confirmation or clinical follow-up.
DATA COLLECTION AND ANALYSIS: Two review authors independently extracted all data using a standardised data extraction and quality assessment form (based on QUADAS-2). We contacted authors of included studies where information related to the target condition or diagnostic threshold were missing. We estimated summary sensitivities and specificities per algorithm and threshold using the bivariate hierarchical model. To compare RCM with dermoscopy, we grouped studies by population (defined by difficulty of lesion diagnosis) and combined data using hierarchical summary receiver operating characteristic (SROC) methods. Analysis of studies allowing direct comparison between tests was undertaken. To facilitate interpretation of results, we computed values of specificity at the point on the SROC curve with 90% sensitivity as this value lies within the estimates for the majority of analyses. We investigated the impact of using a purposely developed RCM algorithm and in-person test interpretation.
MAIN RESULTS: The search identified 18 publications reporting on 19 study cohorts with 2838 lesions (including 658 with melanoma), which provided 67 datasets for RCM and seven for dermoscopy. Studies were generally at high or unclear risk of bias across almost all domains and of high or unclear concern regarding applicability of the evidence. Selective participant recruitment, lack of blinding of the reference test to the RCM result, and differential verification were particularly problematic. Studies may not be representative of populations eligible for RCM, and test interpretation was often undertaken remotely from the patient and blinded to clinical information. Meta-analysis found RCM to be more accurate than dermoscopy in studies of participants with any lesion suspicious for melanoma and in participants with lesions that were more difficult to diagnose (equivocal lesion populations). Assuming a fixed sensitivity of 90% for both tests, specificities were 82% for RCM and 42% for dermoscopy for any lesion suspicious for melanoma (9 RCM datasets; 1452 lesions and 370 melanomas). For a hypothetical population of 1000 lesions at the median observed melanoma prevalence of 30%, this equated to a reduction in unnecessary excisions with RCM of 280 compared to dermoscopy, with 30 melanomas missed by both tests. For studies in equivocal lesions, specificities of 86% would be observed for RCM and 49% for dermoscopy (7 RCM datasets; 1177 lesions...
and 180 melanomas). At the median observed melanoma prevalence of 20%, this reduced unnecessary excisions by 296 with RCM compared with dermoscopy, with 20 melanomas missed by both tests. Across all populations, algorithms and thresholds assessed, the sensitivity and specificity of the Pellacani RCM score at a threshold of three or greater were estimated at 92% (95% confidence interval (CI) 87 to 95) for RCM and 72% (95% CI 62 to 81) for dermoscopy. AUTHORS’ CONCLUSIONS: RCM may have a potential role in clinical practice, particularly for the assessment of lesions that are difficult to diagnose using visual inspection and dermoscopy alone, where the evidence suggests that RCM may be both more sensitive and specific in comparison to dermoscopy. Given the paucity of data to allow comparison with dermoscopy, the results presented require further confirmation in prospective studies comparing RCM with dermoscopy in a real-world setting in a representative population.

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