Wide-area transepithelial sampling of Barrett's epithelium: "WATS" the benefit?

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Regular surveillance of Barrett's esophagus (BE) is recommended by all leading gastroenterology societies worldwide [1, 2]. The rationale for such a strategy is supported by several retrospective studies that have demonstrated reduced esophageal adenocarcinoma (EAC)-related mortality and earlier stage diagnosis of cancer in patients receiving endoscopic monitoring as compared with patients not undergoing surveillance [3].

How should the endoscopic monitoring be performed? Despite the overwhelming technological progress that has been made in the field of endoscopy, to date, the gold standard of BE surveillance relies on a biopsy protocol that was established nearly three decades ago – in the era of fiberoptics! The Seattle protocol involves targeted forceps biopsies (FBs) for any visible lesion, followed by a set of biopsies every 1–2 cm in four quadrants of the BE segment. Unfortunately, this protocol is deemed labor-intensive and time-consuming, resulting in poor compliance among clinicians, especially for long-segment BE and in nonexpert centers [4]. Moreover, only an estimated 4 %–6 % of the BE area is sampled with this technique, which may lead to the inevitable risk of missing focal dysplasia [5]. This caveat also underlies the rate of missed EAC within surveillance cohorts, which can be as high as 14 % [6].

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It is therefore not surprising that new, more efficient, and operator-friendly methods of epithelial sampling in BE are being investigated. One such modality is wide-area transepithelial sampling with computer-assisted analysis (WATS^{3D}; CDx Diagnostics, Suffern, New York, USA), which uses an abrasive brush to sample the deep layers of the glandular epithelium across

large esophageal areas. After appropriate processing, brushing samples are sent to a CDx Diagnostics laboratory, where dedicated pathologists perform a centralized computer-assisted analysis.

Several previous studies have demonstrated the valuable role of WATS^{3D} in the detection of both intestinal metaplasia (IM) and dysplasia within the BE segments. However, all of these studies looked at WATS only as an adjunctive tool rather than as a substitute for FB. A recent meta-analysis, including seven studies on the topic, showed an incremental yield of dysplasia detection with WATS of 7.2 % (95 %CI 3.9 %–11.5 %) when used as such an adjunctive tool with FB [5]. The additional value of the brush to collect more tissue and increase the diagnostic performance of endoscopic surveillance is compelling, but is it practical? Performing the Seattle protocol on its own is already deemed tedious, therefore the addition of further sampling techniques does not seem ideal.

A single randomized trial aimed to compare the efficacy of WATS as an alternative and independent sampling method to FB in IM detection. The study included regular patients undergoing endoscopic evaluation of gastrointestinal symptoms, as well as post-treatment BE patients undergoing surveillance. Overall, no difference was found in either IM detection between WATS and FB (22.7 % vs. 19.6 %; P = 0.2) [7]. However, when looking specifically at individuals with no history of IM who were found to have a visible segment of columnar-lined mucosa in the distal esophagus, WATS^{3D} was able to diagnose twice as many cases of IM as the FB did (32.4 % vs. 15.2 %; P = 0.004). Most of these newly diagnosed BE segments were short and maybe, in such cases, WATS maximizes the likelihood of confirming IM.

Taking a step forward, how does the brush perform as an alternative to FB in detecting BE-related dysplasia?

In this issue of *Endoscopy*, van Munster et al. report on the utility of WATS^{3D} in diagnosing advanced neoplasia (high grade dysplasia [HGD]/EAC) within a selected group of patients with BE and prior dysplasia, without visible lesions [8]. The trial was conducted by a group of recognized experts in the field of BE at 17 referral centers. Patients were randomized to receive endoscopic surveillance using either WATS followed by FB, or vice versa. The primary end point was the concordance for detecting HGD/EAC between the two techniques.

Interestingly, the WATS technique was not found to significantly increase the detection of HGD/EAC compared with the standard FB technique (P = 0.36). Altogether, 21 patients (of the 172 included) had HGD/EAC captured with both modalities. There were an additional 18 cases of HGD/EAC detected by WATS but missed by FB, and 12 other cases detected by FB only, but missed by WATS (notably, > 80 % of patients detected by WATS alone had been diagnosed with low grade dysplasia on FB). Even so, when considering WATS as an adjunct to FB, the absolute increase in HGD/EAC detection amounted to 10 % (95 %CI 6 %–16 %; P < 0.01). Lastly, (and expectedly) the mean procedural time of WATS was shorter than that of the Seattle protocol (4.9 minutes versus 6.6 minutes; P < 0.01).

Taking all these results together, is there a beneficial role of WATS in endoscopic clinical practice?

This trial seems to show that, in the hands of expert endoscopists, WATS is a comparable diagnostic modality to FB. The important question to address is: can WATS help raise the standard of nonexpert endoscopists to the level of more experienced endoscopists? In other words, can WATS compensate for the nonexpert operator in picking up discrete dysplastic areas that would otherwise be missed?

With its ease of use and shorter procedural time, one could see that WATS^{3D} might be a helpful tool for initial screening procedures in at-risk individuals at community-based hospitals to provide a baseline diagnosis. Another advantage, in such a setting, could be the access to the centralized CDx Diagnostics laboratory reading by expert pathologists.

Considering this, while the study by van Munster et al. found no statistically significant difference between the independent use of either WATS or FB in the dysplasia detection rate, it in fact represents a basis for further studies that should be focused on nonexpert centers. This may indeed unveil the hidden benefits of WATS, which for now still remain elusive. Reflecting this, the recently updated ACG guidelines do not recommend the routine use of WATS^{3D} in patients undergoing regular BE surveillance [2].

Competing Interests

The authors declare that they have no conflict of interest.

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