

Screening for Barrett's Esophagus in Patients with Cirrhosis Using WATS^{3D}

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INTRODUCTION

Barrett's esophagus (BE) is a premalignant condition that arises from longstanding gastroesophageal reflux disease (GERD). It can lead to esophageal adenocarcinoma (EAC), a cancer with incidence rates that continue to rise in the Western world.¹ The gold standard for screening for BE requires endoscopic evaluation and 4-quadrant esophageal forceps biopsy (Seattle protocol).² However, endoscopists have a higher tendency to refrain from performing forceps biopsies (FB) in patients with an increased risk of bleeding such as patients with cirrhosis.³

Wide-area transepithelial sampling with three-dimensional computer-assisted analysis (WATS^{3D}) is an abrasive cytology brush capable of taking full transepithelial samples and is able to cover a wide circumferential area of esophageal mucosa.^{4,5} Compared to forceps biopsies, WATS^{3D} covers a wider surface area of the esophagus and acquires deep mucosal tissue where pre-malignant cells develop without reaching the submucosal veins. In this case series, seven patients with cirrhosis and GERD are reported that underwent routine surveillance for BE using WATS^{3D} with no post-procedural complications.

CASE REPORT

Seven patients with cirrhosis had risk factors associated with bleeding (Table 1) and underwent screening for BE by upper endoscopy using WATS^{3D}. The first patient was a 70-year-old female with a history of cirrhosis secondary to autoimmune hepatitis along with portal hypertension and gastropathy. She underwent a liver and kidney transplant three years prior to presentation. Given her longstanding history of GERD, she was scheduled for routine surveillance of BE by upper endoscopy. A BE segment (C1 M3) was biopsied per Seattle protocol using traditional forceps and sampled using WATS^{3D} as well. No varices were noted during the procedure. Both modalities revealed intestinal metaplasia and were negative for dysplasia.

The second patient was a 65-year-old male with a history of alcoholic cirrhosis, grade 1 esophageal varices, and portal hypertensive gastropathy. He also had a history of GERD and was due for variceal surveillance. During the procedure, grade 2 esophageal varices and a BE segment (C1 M2) were noted. WATS^{3D} brushing alone was obtained since the patient was at high risk of bleeding. Pathology was consistent with intestinal metaplasia and was negative for dysplasia. The patient was treated with a daily proton pump inhibitor. The patient underwent repeat esophagogastroduodenoscopy (EGD) one year later. Sampling was repeated with WATS^{3D} only and yielded the same results.

The third patient was a 69-year-old male with a history of cirrhosis due to untreated hepatitis C and alcoholism. He also had a history of GERD and BE and was due for variceal surveillance. His procedure

revealed a salmon-colored segment (C0 M6), congestive gastropathy, and grade 1 esophageal varices. WATS^{3D} sampling of the segment was consistent with goblet cell metaplasia and low-grade dysplasia. FB was not done due to concerns for bleeding. Subsequently, he was initiated on a daily proton pump inhibitor. EGD with WATS^{3D} sampling was repeated six months later and yielded the same results.

The fourth patient was a 61-year-old male with a history of alcoholic cirrhosis who was discharged recently from the hospital following a gastrointestinal bleed. An emergent EGD revealed bleeding esophageal varices (Grade 3) that were banded and ultimately required a transjugular intrahepatic portosystemic shunt for management of varices. Upper endoscopy was repeated eight weeks later and showed grade 1 esophageal varices and a distal island of salmon colored mucosa. Sampling of the distal esophagus with WATS^{3D} yielded columnar epithelium with no evidence of BE.

The fifth patient was a 49-year-old male with a history of alcoholic cirrhosis. His previous two EGDs showed portal hypertensive gastropathy and grade 1 esophageal varices. He also had a salmon-colored mucosal segment in the distal esophagus, consistent with Prague class C0 M2 BE. However, no biopsies were taken owing to concerns for hemorrhagic complications. During his most recent endoscopy, the segment and esophageal varices were unchanged. Sampling was performed with both modalities and revealed intestinal metaplasia without evidence of dysplasia. He was prescribed a daily proton pump inhibitor.

The sixth patient was a 63-year-old male known to have celiac sprue and alcoholic cirrhosis. His previous EGD showed portal hypertensive gastropathy and grade 2 esophageal varices. During his variceal surveillance endoscopy, a BE segment (C0 M2) was noted in addition to grade 2 esophageal varices. Sampling was done with WATS^{3D} only. Pathology revealed intestinal metaplasia without evidence of dysplasia, which prompted treatment with daily proton-pump inhibition therapy.

The seventh patient was a 65-year-old male who was newly diagnosed with cirrhosis due to untreated hepatitis C. Upper endoscopy revealed a BE segment (C20 M21) and a nodularity with ulcerations that were suspicious for high grade dysplasia (HGD) and confirmed by FB and WATS^{3D}. No varices were seen during the procedure. Endoscopic mucosal resection was unsuccessful since the mucosa was tacked down to deeper tissues at the site of ulcerations.

All patients (except for the last patient) followed-up in our gastroenterology clinic multiple times within the first year after the EGD. None had any immediate or delayed post-procedural complications such as bleeding, infections, and perforation. The last patient did not display any early complications, however, was lost to follow-up for further management.

Table I. Patient characteristics.

Patient Number	Age (Years)	Gender	Variceal Grade	Prague Score	Sampling by FB	FB Pathology	Sampling by WATS ^{3D}	WATS Pathology
1	70	F	0	C1 M3	Yes	Non-dysplastic BE	Yes	Non-dysplastic BE
2	65	M	2	C1 M2	No	N/A	Yes	Non-dysplastic BE
3	69	M	1	C0 M6	No	N/A	Yes	LGD + BE
4	61	M	3	N/A	No	N/A	Yes	Columnar mucosa
5	49	M	1	C0 M2	Yes	Non-dysplastic BE	Yes	Non-dysplastic BE
6	63	M	2	C0 M2	No	N/A	Yes	Non-dysplastic BE
7	65	M	0	C20 M21	Yes	HGD + BE	Yes	HGD + BE

Abbreviations: forceps biopsy (FB); Prague criteria Circumferential Barrett's segment (C) and longest tongue of Barrett's (M); High grade dysplasia (HGD); Low grade dysplasia (LGD); Barrett's Esophagus (BE); Not applicable (N/A).

DISCUSSION

GERD is associated with a 10 - 15% risk for developing BE.² The rate of progression to EAC depends on the degree of dysplasia. The annual incidence rate of EAC in patients with HGD is 7% according to the American College of Gastroenterology.² Other randomized studies have shown that this rate can be as high as 19%.³ While GERD is very common in the general population, several studies have demonstrated a higher prevalence of GERD in patients with cirrhosis and an incidence rate of dysplasia ranging from 33% to 64%.⁶⁻¹¹

Studies initially had attributed this association to the presence of esophageal varices (EV) mechanically impeding lower esophageal sphincter (LES) closure and reported no association between GERD and cirrhosis in the absence of EV.^{11,12} However, a more recent study showed that cirrhosis causes GERD in the absence of EV by demonstrating a negative correlation between LES pressures and Child-Pugh scores.⁷ The increased intra-abdominal pressure from ascites and the increased generation of nitrous oxide in advancing liver disease are two of the main contributing factors.^{6,7} We can infer that GERD in patients with liver disease is a progressive outcome and unpreventable. Cirrhotic patients occupy a significant proportion of the total population of patients that require screening for BE. With the increased risk of neoplastic progression in patients with GERD and cirrhosis, it is necessary to adhere to screening guidelines for BE in patients with cirrhosis.

Unfortunately, physicians often refrain from taking biopsies in patients with advanced liver disease due to the anticipated risk of bleeding from esophageal varices and coagulopathy. Consequently, BE may be underdiagnosed in this subpopulation.³ Clinically-significant bleeding following FB in the general population is rare and has an incidence rate of 0.03 to 0.16%.¹³⁻¹⁵ However, no studies have evaluated the risk of bleeding in patients with cirrhosis following esophageal FB.

WATS^{3D} is less traumatic and associated with minimal post-procedural bleeding complications.^{4,16} Studies have demonstrated improved rates of detection of BE when WATS^{3D} is used as an adjuvant to the standard 4-quadrant forceps biopsy protocol by about 18% in community settings and up to 83% in referral centers.^{4,15,17} This provided a significant improvement to standard FB, which has a reported accuracy of 35% to 68% and correlated positively with the number of biopsy samples taken.²

CONCLUSIONS

With the added benefits of WATS^{3D} and no increased risk of bleeding, it would be beneficial to use this modality in patients with cirrhosis. Future studies assessing the risk of bleeding in patients with cirrhosis using WATS^{3D} and FB are needed to establish a clear recommendation as to what modality would be most appropriate to use for screening in this patient population.

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