Barrett’s esophagus (BE) is a precursor to esophageal adenocarcinoma (EAC), and guidelines recommend endoscopic surveillance for early detection and treatment of dysplasia and EAC.\(^1,2\)

- The overall rate of progression from non-dysplastic BE (NDBE) to high grade dysplasia (HGD) and EAC is low (0.63%) years.\(^1\)
- However, patients with NDBE represent 89% of the approx. 490,000 patients undergoing endoscopic surveillance for BE each year in the U.S.\(^4\)
- The high incidence of NDBE indicates that at least 50% of the patients who progress to HGD/EAC each year are diagnosed as NDBE, and can be missed and, therefore, undertreated.

- Current clinical practices that rely on clinicopathologic factors to guide management have limited effectiveness in risk-stratifying NDBE patients.\(^3,5\)

- Objective risk stratification is needed to enable risk-aligned patient management to improve patient health outcomes.

This study evaluated the impact of the commercially available, validated tissue systems pathology test (TissueCypher, TSP-9)\(^7\) in guiding risk-aligned care for patients with NDBE in a minimally invasive gastrointestinal surgery center.

### Methods

- Clinical data and pathologic diagnosis were abstracted from medical records for 3 patients with BE.
- TSP-9 test was ordered to provide individualized risk assessment including risk score, risk class and probability of progression to HGD/EAC within 5 years.
- Risk assessment provided by the TSP-9 test results was used in conjunction with clinical information and pathologic diagnosis to guide shared decision-making by physicians and patients for the clinical management of BE.

### Results

#### TSP-9 test results and clinical information for 3 patients with pathologic diagnosis of NDBE

**Figure 1. 69-year-old male patient with C3M4, no hiatal hernia, and diagnosis of NDBE.**

- The patient had previously undergone neoadjuvant and radiation therapies for EAC but had declined surgery 5 years earlier, and was in ongoing endoscopic surveillance.
- The high-risk result and 14% (95% C.I. 12-15%) probability of progression to HGD/EAC from the TSP-9 test guided upstaging of care from continued endoscopic surveillance to therapeutic intervention with radiofrequency ablation (RFA) to prevent recurrence of EAC.

**Figure 2. 81-year-old male patient with C4M6, 6cm hiatal hernia, and diagnosis of NDBE.**

- The patient was in endoscopic surveillance for NDBE with no history of dysplasia or EAC.
- The intermediate risk result and 7% (95% C.I. 5-9%) probability of progression to HGD/EAC from the TSP-9 test guided upstaging of the management plan from endoscopic surveillance to therapeutic intervention with RFA and anti-reflux surgery to prevent progression to HGD/EAC.

**Figure 3. 71-year-old male patient with C0M2, small hiatal hernia, and diagnosis of NDBE.**

- The patient was in endoscopic surveillance for NDBE with no history of dysplasia or EAC.
- The intermediate risk result and 6% (95% C.I. 4-7%) probability of progression to HGD/EAC from the TSP-9 test guided upstaging of the management plan to therapeutic intervention with RFA and anti-reflux surgery to prevent progression to HGD/EAC.

### Discussion

- Risk stratification by the TSP-9 test identified high/intermediate-risk NDBE patients who could be missed if only clinicopathologic variables were considered. Shared decision-making resulted in upstaging of management to RFA alone or in conjunction with anti-reflux surgery in all three NDBE patients who scored TSP-9 high/intermediate-risk.
- High/intermediate risk scores predicted 5-year risk of progression to HGD/EAC that was similar (range 6-14%) to the published estimates of progression rates in patients with confirmed LGD (8.5%).\(^1,2\)
- This finding is consistent with prior studies that have consistently shown that the TSP-9 test identifies a subset of NDBE patients who progress to HGD/EAC at a similar or higher rate to patients with confirmed LGD.\(^1,2\)
- Guidelines recommend endoscopic eradication therapy such as RFA for patients with confirmed LGD based on the associated risk of progression.
- Identification of NDBE patients with similar progression risk to LGD enables physicians and their patients to consider use of RFA after ruling out missed prevalent HGD/EAC, since RFA has been shown to be 92-99% effective in eradicating BE and preventing development of EAC.\(^1-4\)
- Anti-reflux surgery can reduce the risk of persistent or recurrent BE after RFA, which may prevent development of EAC.\(^1,7\)
- Close surveillance of high/intermediate risk patients may also be appropriate to detect and treat dysplasia and EAC at the earliest possible stage.

### Conclusions

- The TSP-9 test results demonstrated significant clinical utility in NDBE patients by guiding risk-aligned upstaging of care to ablation and/or anti-reflux surgery, which have both been associated with improved health outcomes in BE patients.

### References


### Disclosure

R. Critchley is a full-time employee of and holds stock and stock options in Castle Biosciences. L. Critchley serves on Castle Biosciences' paid speakers bureau to present on the TissueCypher Barrett’s Esophagus test.

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