CLINICAL SUMMARY

TissueCypher
Barrett's Esophagus

Pooled analysis from Mayo Clinic

Prediction of progression in Barrett's esophagus using a tissue systems pathology test: A pooled analysis of international multicenter studies

Prasad G. Iyer, MD, MS; D. Chamil Codipilly, MD; Apoorva K. Chandar, MD; Siddharth Agarwal, MD; Kenneth K. Wang, MD, et al. Clin Gastroenterol Hepatol 2022; https://doi.org/10.1016/j.cgh.2022.02.033.

BACKGROUND

Barrett's esophagus (BE) is the only known precursor to esophageal adenocarcinoma (EAC). Progression rates from BE to cancer are relatively low but once a patient has progressed to EAC the 5-year survival rate is < 20%. Predicting patients that are likely to progress is influenced by several factors, but intervention (esophageal eradication) and endoscopic surveillance recommendations are determined almost exclusively based on clinicopathologic factors. This pooled analysis was performed to confirm the utility of the TissueCypher test in predicting progression in BE over clinicopathologic factors alone.

AIMS

- Assess the ability of TissueCypher to predict progression to high-grade dysplasia (HGD) or EAC in patients with BE.
- Develop a progression risk model using only clinicopathologic variables: age, segment length, sex, hiatal hernia, and pathology.
- Evaluate the model's predictive strength in patients with non-dysplastic (NDBE), indefinite for dysplasia (IND), and low-grade dysplasia (LGD) as well as NDBE patients alone.
- Add the TissueCypher risk score to determine if it improves the predictive power of the model.
- Compare performance metrics of various clinicopathologic factors directly with TissueCypher.

METHODS

- Pooled patient-level data from 5 peer-reviewed published studies predicting both incident progression to HGD or EAC, and the combination of incident and prevalent progression.
  - Incident Progression = BE patients progressing to HGD or EAC > 12 months following endoscopy.
  - Prevalent Progression = BE patients diagnosed with HGD/EAC < 12 months following endoscopy.
- Conditional logistical regression analysis was used to compare the risk prediction performance of clinicopathologic factors alone and in combination with TissueCypher.

Access the entire pooled analysis published in Clinical Gastroenterology and Hepatology by scanning the QR code.

Patient Histology

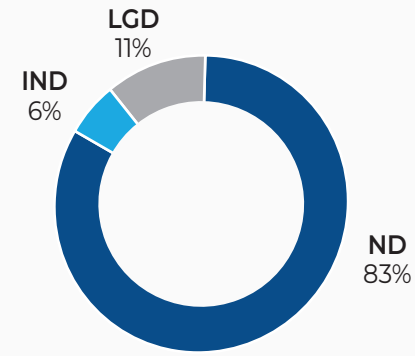

Figure 1. Data included 590 patients that were diagnosed as non-dysplastic (489), indefinite for dysplasia (33), and low-grade dysplasia (68).

Patient Progression

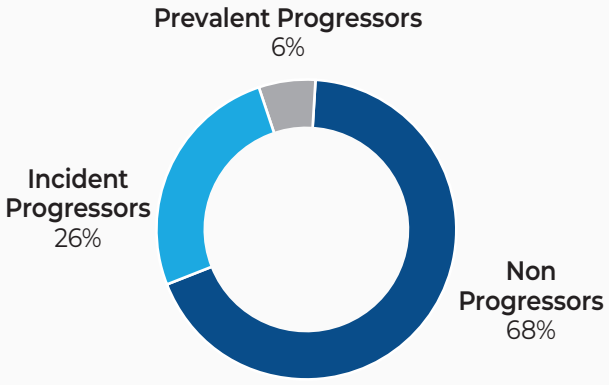

Figure 2. Data included 590 patients that were diagnosed with Barrett's esophagus. 400 patients did not progress during the study, 38 progressed within 12 months, and 152 progressed after 12 months.

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KEY FINDINGS

- Across all analyses, TissueCypher was the strongest and most significant predictor of progression to HGD or EAC.
- Predictive performance of clinicopathologic factors was significantly improved by the inclusion of the TissueCypher risk classes.
- In the NDBE patient cohort, a TissueCypher high-risk score predicted an 18-fold increased risk of progression vs. TissueCypher low-risk score.
- TissueCypher identified 52% of the NDBE progressors, all of whom were missed by the standard of care.

Table 1. Summary of the Odds Ratios (OR) and the C-statistic for models built with and without TissueCypher to predict Incident Progressors (IP) and Incident/Prevalent Progressors (IPP)

	NDBE (Odds Ratio)			NDBE, IND, and LGD (Odds Ratio)		
	IP	IP	IPP	IP	IP	IPP
Age (per year)	1.08*	1.06	1.04	1.08*	1.06	1.03
Hiatal Hernia (yes vs. no)	0.70	0.57	0.51	0.68	0.71	0.77
Segment Length (per cm)	1.17*	1.14	1.15	1.15*	1.13	1.14*
Sex (male vs. female)	2.39	1.05	1.02	3.55	2.95	2.36
Expert diagnosis (IND vs. NDBE)				2.25	2.13	1.87
Expert diagnosis (LGD vs. NDBE)				5.84*	2.92*	3.50*
TissueCypher risk class (intermediate vs. low)		1.69	1.94		1.58	1.81*
TissueCypher risk class (high vs. low)		14.23*	18.07*		6.00*	7.81*
	C-statistic 0.63	C-statistic 0.72	C-statistic 0.72	C-statistic 0.68	C-statistic 0.75	C-statistic 0.76

Strongest predictor of progression in the model * Indicates a significant p value of less than 0.05.

Interpreting C-statistic:

A C-statistic of 0.5 indicates that the model is no better than predicting based on random chance. A C-statistic that exceeds 0.7 is considered a good clinical model.[1]

Interpreting Odd Ratio (OR):

An OR of 1 indicates that the variable does not increase the odds of an occurrence. An OR of 2 indicates that the variable doubles the odds of the outcome.

1 Hosmer et al., Applied Logistic Regression, 3rd Ed, 2013, Wiley Series in Probability and Statistics.

CLINICAL IMPLICATIONS

1. Treatment plans for patients with BE are based upon risk-stratification (risk of progression). TissueCypher was shown to be the most important predictor of progression.
2. TissueCypher has an additive impact on existing clinicopathologic factors; e.g. a high-risk TissueCypher test result in a male BE patient, with 3 cm long NDBE, changes risk of IPP from 4.47x to 22.54x (1.02 + 3.45 + 18.07).
3. Identify high-risk BE patients who are likely to progress and increase endoscopic surveillance or consider endoscopic eradication therapy.
4. Identify low-risk BE patients who are unlikely to progress and extend surveillance intervals or more optimally administer treatment.
5. Use adjunctively to inform key clinical management decisions, allowing upstaging/downstaging based on individual patient risk.

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