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Summary

DECONVOLVING THE PATTERNS OF COPY NUMBER ALTERATIONS IN BARRETT'S ESOPHAGUS PROGRESSION FROM MULTI-REGIONAL SEQUENCING

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Oesophagus

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Multi-regional longitudinal sequencing of Barrett's Esophagus reveals copy number alteration evolutionary patterns that predict dysplasia with high accuracy and may improve risk stratification.

KEY POINTS

- A random forest model based on copy number alteration risk scores predicted dysplasia with AUC 0.89 (sensitivity 80.6%, specificity 95.7%) in the discovery cohort and AUC 0.84 (sensitivity 73.1%, specificity 93.9%) in the validation cohort.
- Early-stage copy number alterations in non-progressing Barrett's Esophagus showed specific chromosomal gains and losses, whereas later-stage alterations in dysplasia were more widespread and less commonly shared.
- SMAD4 losses and CCND3/GATA4 gains were linked to dysplasia through risk scoring of known drivers.
- The study analyzed 777 samples from 88 patients in the discovery cohort and 256 samples from 95 patients in the validation cohort using shallow whole-genome sequencing and phylogenetic tree analysis.
- Copy number alteration-based risk scores offer a promising tool for lesion risk stratification in Barrett's Esophagus surveillance.

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