

Background

The International Association for the Study of Lung Cancer (IASLC) recently proposed a three-tiered histologic grading scheme for invasive non-mucinous lung adenocarcinoma. Because of a strong correlation between pattern and other histologic features, only pattern was recommended in the grading system. The aim of this study was to confirm the utility of the IASLC/WHO grading system in an institutional dataset and to compare it to a modification adding other histologic features.

Design

We performed a retrospective review of node-negative, T1-2, non-mucinous lung adenocarcinoma resections from 2004-2018. These were assigned a pattern-based grade using the IASLC criteria and staged using CAP protocol version 4.2.0.0. Mitotic count, presence of spread through airspaces, and nucleolar grade were evaluated by review of H&E-stained slides. Kaplan Meier survival curves were generated with endpoint of tumor recurrence using T stage and WHO pattern grade. WHO grade was modified three ways and analyzed separately by upstaging G1 and G2 each by one grade if mitotic figures > 1/10 HPF; if nucleolar grade 2 or higher (prominent eosinophilic nucleoli), and in the presence of STAS, respectively.

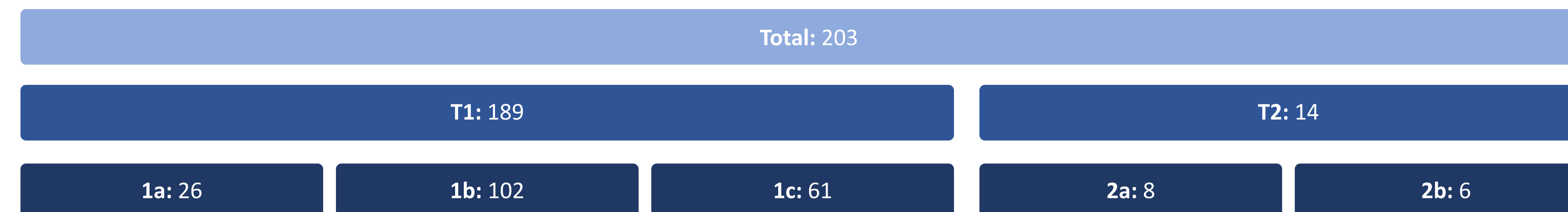


Figure 1: Node-negative, non-mucinous lung adenocarcinoma resections were evaluated.

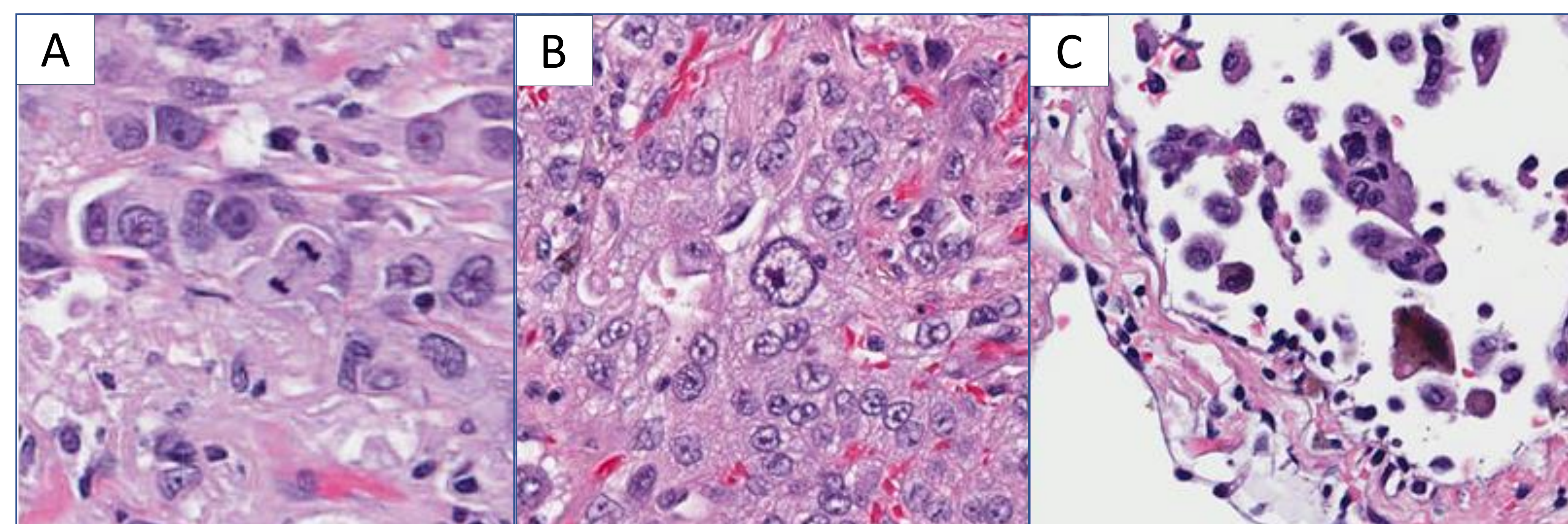


Figure 2: Representative mitotic figure (A), prominent nucleolus (B), and STAS (C).

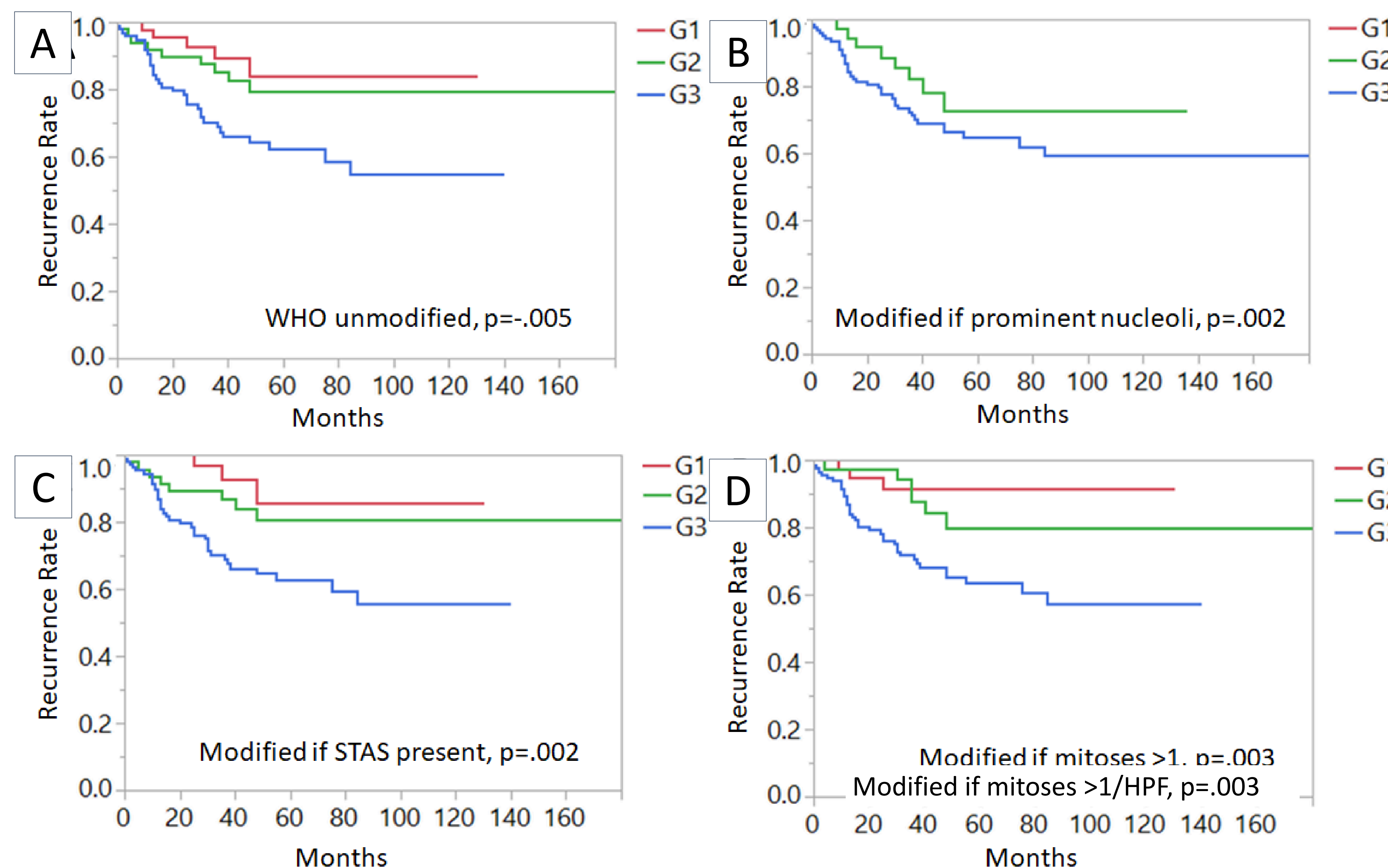


Figure 3: Recurrence rates by grade with no modifications (A), including prominent nucleoli (B), including STAS (C), and including mitoses >1/10 HPF (D).

Results

203 cases were identified, 113 female, (65 ± 10 y), and 83 male, (67 ± 8 y) with an average follow-up interval of 49 months. There were 26 stage 1a, 102 1b, 61 1c, 8 2a, and 6 2b tumors. 62% of patients were recurrence-free during the time of follow-up. There was no significant difference in time to recurrence by T stage. Recurrence rate increased with IASLC/WHO grade ($p=.005$). Upgrading with mitotic figures resulted in a p value of .003; modified by upgrading with STAS and nucleolar grade result in p values each of .002. No patient with G1 tumor by nucleolar upgrade developed recurrence.

Conclusions

Grading of lung cancers by WHO system greatly improves prognostication over T-stage alone. There is a marginal increase in efficacy adding additional histologic variables. In our patient set, no G1 tumor with bland nucleoli developed recurrence.

References

WHO Classification of Tumours Editorial Board. *Thoracic Tumours*. 5th ed. International Agency for Research on Cancer, Lyon, France 2021

