Characterization of Clinicopathologic Features and Molecular Recurrence Risk Profiles in Patients with Early-Stage NSCLC

ABSTRACT 3708
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BACKGROUND

The National Comprehensive Cancer Network (NCCN) Guidelines recommend that patients with early-stage non-small cell lung cancer (NSCLC) be treated with adjuvant chemotherapy post-surgical resection if they are high-risk.[1] The NCCN notes certain clinicopathologic features as examples of what could be considered as high-risk; however, these clinicopathologic features have never been validated to stratify risk or predict chemotherapy benefit. A CLIA-certified, commercially available 14-gene quantitative PCR expression assay (DetermaRx™) has been extensively validated to assess mortality risk in early-stage non-squamous NSCLC.[2] In a non-randomized single-institution prospective cohort, the 14-gene molecular risk classifier was superior to the NCCN high-risk features in assessing mortality risk, and predicted benefit from chemotherapy in stages I-IIA.[3]

METHODS

Clinical factors, pathology, and molecular risk profiles of all non-squamous NSCLC specimens received for testing with the 14-gene expression assay in a CLIA certified laboratory (Razor Genomics) between 2/3/2020 and 12/21/2020 were reviewed. Pathologic stage and the type and number of NCCN high-risk clinicopathologic features (poorly differentiated tumor, vascular invasion, wedge resection, tumor size >4cm, visceral pleural involvement, unknown lymph node status) were obtained from the pathology reports submitted with the specimens for testing. Inclusion criteria for this analysis were Stage I-IIA tumors in which only one specimen was sent for testing, and for which the status of all NCCN clinicopathologic features were available.

RESULTS

One hundred and forty cases were available for analysis at the time of abstract submission. The analysis has since been expanded to 250 cases. Specimens were sent from a total of 39 community and academic medical centers; 80% of cases were from a community setting. Sixty-five percent of tests were ordered by thoracic surgeons, and 35% by medical oncologists. Sixty-nine (28%) of cases were resulted as molecular high- or intermediate-risk by the 14-gene expression assay. Two-thirds (65%) of all specimens received were stage IA according to AJCC 8th edition staging criteria, and about one-fourth of these stage IA cases were found to be molecular high/intermediate-risk. Molecular high/intermediate-risk cases were more likely to have at least one NCCN high-risk feature compared to molecular low-risk (67% vs. 45%). However, 64% of cases that would have been considered high-risk by NCCN (defined as having at least one high-risk feature) were reclassified as low-risk by the molecular assay, and 19% of cases that had no NCCN high-risk features were reclassified as molecular high or intermediate-risk.

Table 1: Stage by Molecular Risk Results

	Stage IA	Stage IB	Stage IIA	Total
Low	124 *(50%)*	48 *(19%)*	9 *(4%)*	181 *(72%)*
Intermediate	28 *(11%)*	16 *(6%)*	2 *(<1%)*	46 *(18%)*
High	10 *(4%)*	12 *(5%)*	1 *(<1%)*	23 *(9%)*

Table 2: Number NCCN High-Risk Features by Stage

	0	1	2	3+
Stage IA	100 *(40%)*	37 *(15%)*	23 *(9%)*	2 *(<1%)*
Stage IB	21 *(8%)*	32 *(13%)*	16 *(6%)*	7 *(3%)*
Stage IIA	1 *(<1%)*	9 *(4%)*	2 *(<1%)*	0 *(0%)*

Table 3: Number NCCN High-Risk Features by Molecular Risk

	0	1	2	3+
Low	99 *(40%)*	51 *(20%)*	26 *(10%)*	5 *(2%)*
Intermediate	17 *(7%)*	16 *(6%)*	10 *(4%)*	3 *(1%)*
High	6 *(2%)*	11 *(4%)*	5 *(2%)*	1 *(<1%)*

Figure 1: Percent Cases by NCCN High-Risk Feature

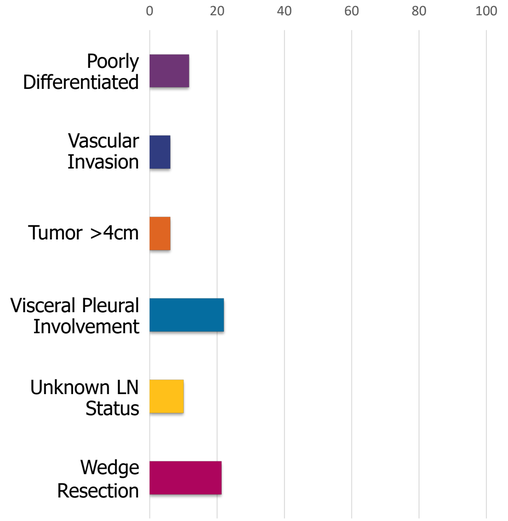
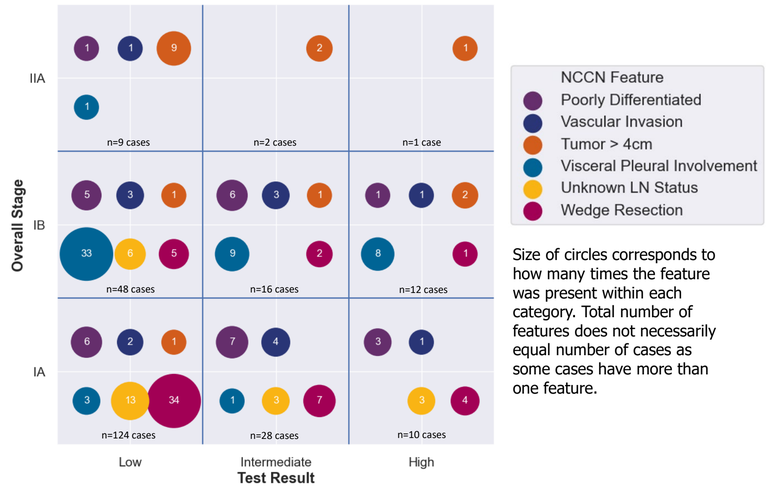


Figure 2: Counts of NCCN High-Risk Features by Stage & Molecular Risk



Size of circles corresponds to how many times the feature was present within each category. Total number of features does not necessarily equal number of cases as some cases have more than one feature.

CONCLUSION

Clinical adoption trends reveal that molecular risk classification is being utilized in the early-stage setting, particularly for stage IA patients. An extensively validated 14-gene expression assay that has previously been demonstrated to outperform NCCN high-risk features in assessing mortality risk reclassifies traditional clinicopathologic feature-based risk for many early-stage patients in the clinical setting.

REFERENCES:
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