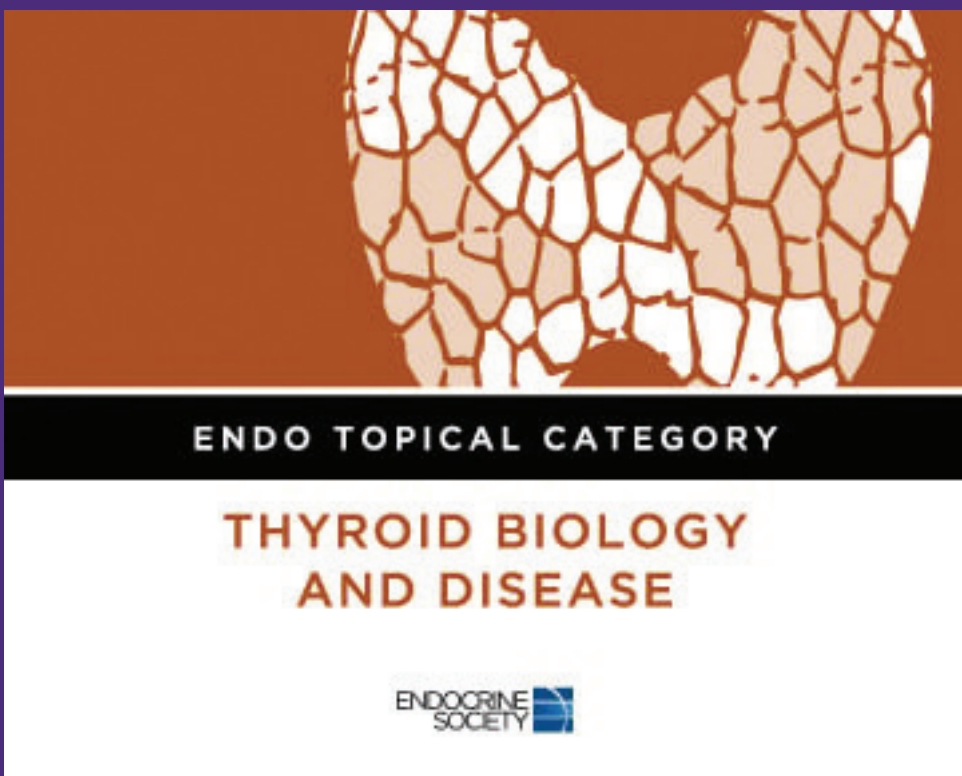




SUN-110

Preoperative Risk Stratification Of Differentiated Thyroid Carcinoma Using A Molecular Cell Cycle Progression Score: Association With American Thyroid Association (ATA) Risk Of Recurrence

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*Potential conflict of interest may exist. Refer to the meeting app.

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INTRODUCTION

- Alterations in cell cycle regulatory genes may lead to abnormal cellular proliferation, tumor development, and malignancy.
- A cell cycle progression (CCP) z-score was derived from the expression of 47 genes identified from The Cancer Genome Atlas (TCGA) Thyroid.
 - High CCP scores were associated with worse clinical outcomes in a TCGA papillary thyroid cancer cohort and higher risk molecular alterations in Afirma Genomic Sequencing Classifier (GSC tested nodules).¹
- The aim of this study was to analyze the correlation of CCP scores to the American Thyroid Association (ATA) risk of structural recurrence in a cohort of Afirma GSC tested patients with differentiated thyroid carcinoma (DTC).

METHODS

- Retrospective cohort study from two medical centers
 - All samples were either (B)ethesda III/IV cytology and Afirma GSC-(S)uspicious or had B V/VI cytology.
- The CCP activity score was correlated with:
 - Bethesda cytology category
 - 2015 ATA risk of recurrence categories
 - The presence of *BRAF*p.V600E mutation
- Statistical analysis utilized the Wilcoxon Rank-Sum Test.

CONCLUSIONS

- The CCP activity score may have an added prognostic role in the pre-operative stratification of cytologically indeterminate—GSC-S and malignant thyroid nodules.
 - The prognostic value is higher in BV/VI vs BIII/IV cytology and is seen in *BRAF*p.V600E+ thyroid cancers.
- Future studies with larger cohorts will be important to determine the broader utility of the CCP score as a preoperative prognostic tool.

RESULTS

- 170 samples (Table 1)
 - 95 BIII, 45 BIV, 30 BV/VI
 - ATA risk: 149 (L)ow, 20 (I)ntermediate, 1 (High)
 - ATA I and H cancers were combined when comparing CCP scores against ATA L.
- There was no difference in the CCP score of samples with indeterminate (B III/IV) vs malignant (B V/VI) cytology (Figure 1).
- The CCP score is significantly higher in ATA I-H vs L cancers (Figure 2).
- The CCP score is more prognostic of ATA cancer risk in B V/VI nodules compared to B III/IV (Figure 3).
- The CCP can help distinguish ATA risk categories in samples that are *BRAF*p.V600E+ (Figure 4).

TABLE 1.
Distribution of Bethesda cytology and ATA risk by cohort

	Cohort 1	Cohort 2
Total	108	62
Bethesda		
III	79 (73.1%)	16 (25.8%)
IV	29 (26.9%)	16 (25.8%)
V/VI	0	30 (48.4%)
ATA risk		
High	0	1 (1.6%)
Intermediate	3 (2.8%)	17 (27.4%)
Low	105 (97.2%)	44 (71%)
BRAFp.V600E		
Positive	9 (8.3%)	20 (32.2%)

Reference

1. Athanasios Bikas, Emma Su, Himanshu Patankar, Mohammed Alshalalfa, Yangyang Hao, Joshua Paul Klover, Theodora Pappa, MON-380 Development of a Prognostic Cell Cycle Progression Score in Preoperative Thyroid Tumor Samples to Predict Prognosis, Journal of the Endocrine Society, Volume 9, Issue Supplement_1, October-November 2025

FIGURE 1.
CCP score by cytology groups in the pooled cohort

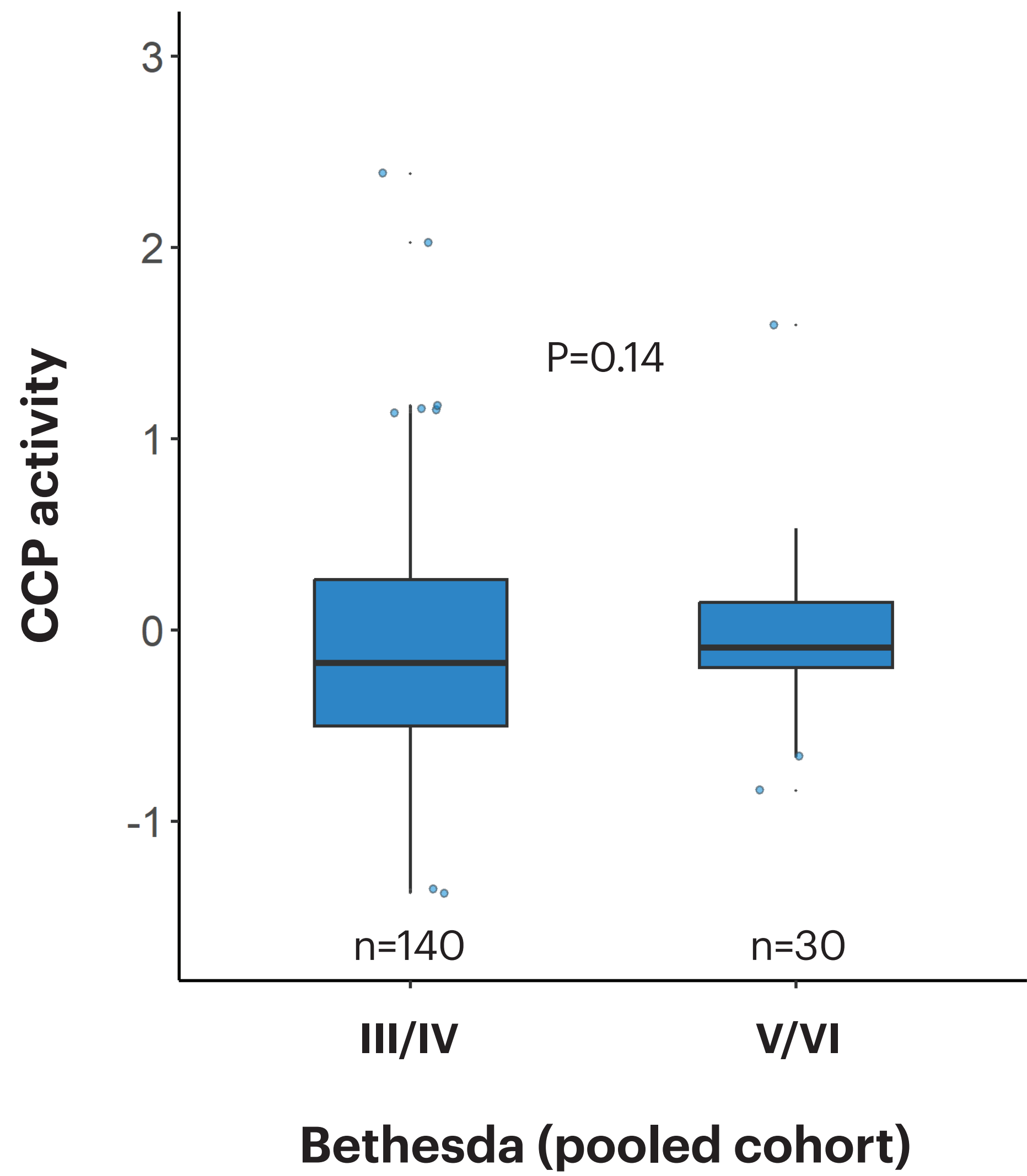


FIGURE 3.
CCP prognostic value by Bethesda category in the pooled cohort

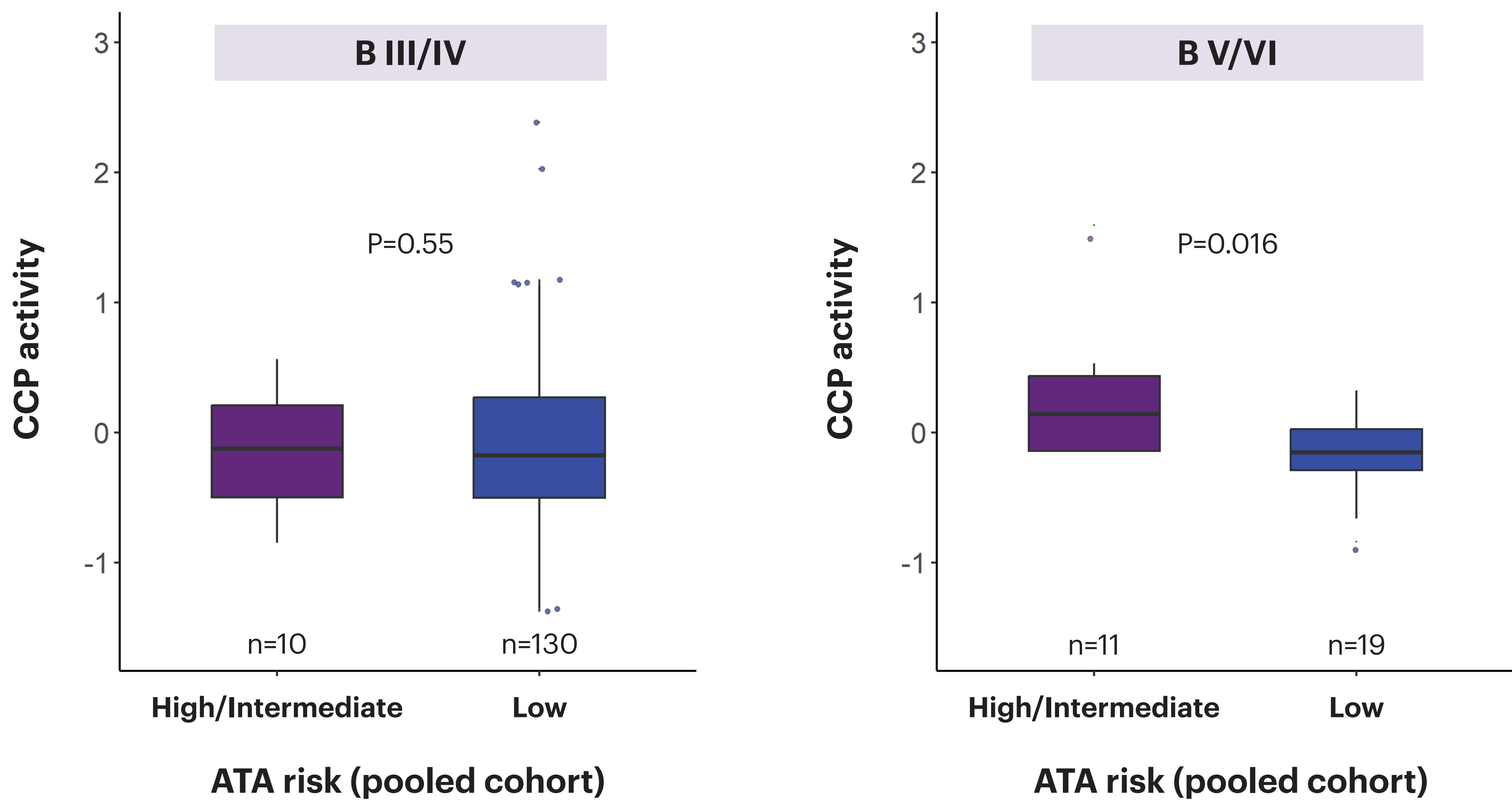


FIGURE 2.
CCP score by ATA risk category in the pooled cohort

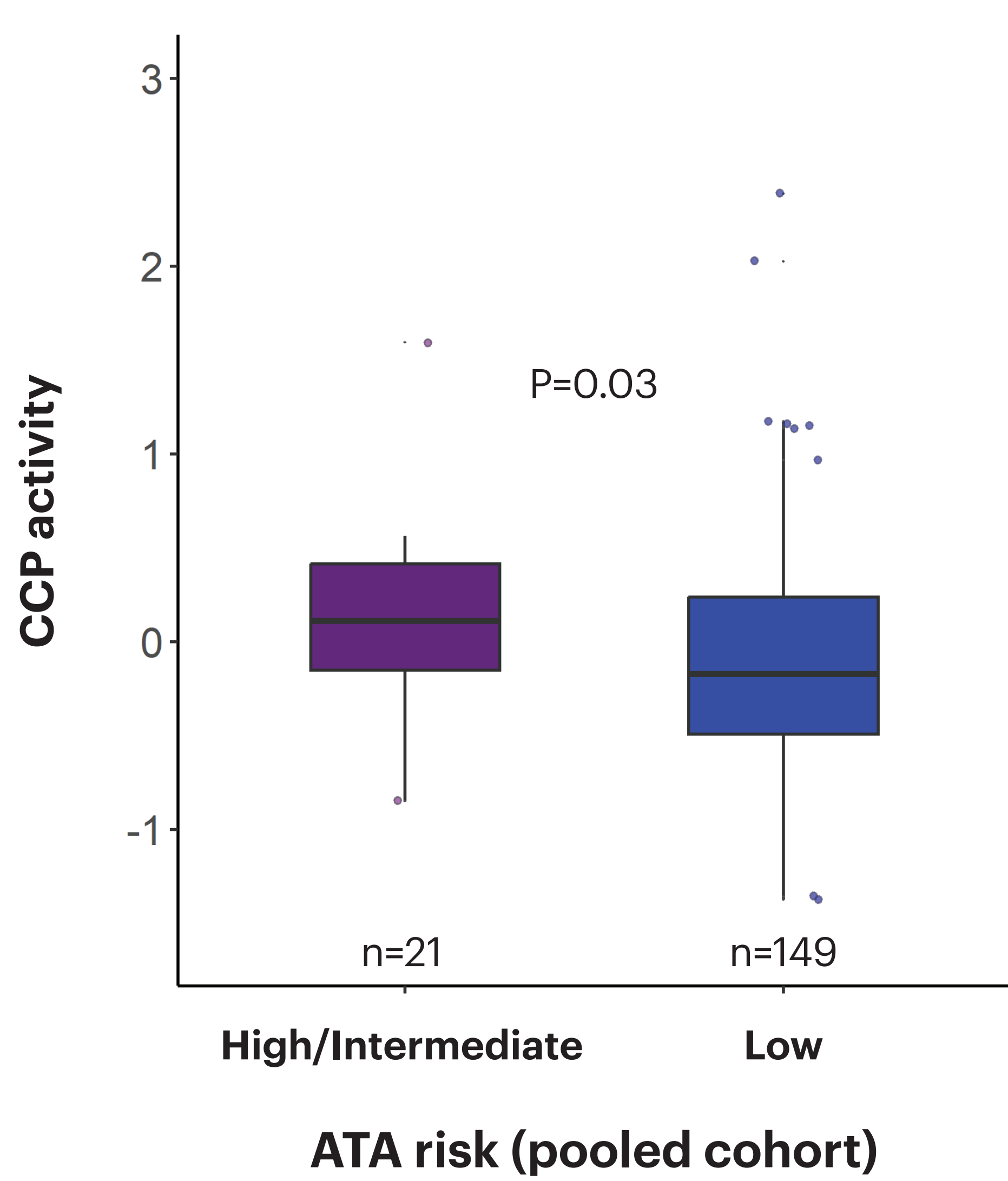


FIGURE 4.
CCP score by ATA risk category in BRAFp.V600E+ tumors

