Background: The incidence of thyroid cancer has increased over the last three decades, particularly driven by the increased detection of papillary thyroid microcarcinoma (PTMC). Although the majority have excellent prognosis, a subset of PTMC have been shown to harbor aggressive pathologic features that include lymph node [LN] metastasis, extrathyroidal extension [ETE], lymphovascular invasion [LVI], and distant metastasis, which negatively affect survival. Current guidelines for PTMC either recommend thyroid lobectomy or active surveillance for low risk patients without clinically evident metastases or local ETE, and convincing cytologic evidence of aggressive disease that can be only reliably identified on final histopathology following surgical resection. The optimal treatment for PTMC with aggressive pathologic features, however, remains unclear. The aggressive features of PTMC that may affect survival have not been comprehensively delineated in the current literature. This study examines demographics and clinical factors that may affect patient outcome and survival associated with PTMC.

Methods: Adult patients with histologically proven papillary thyroid carcinoma < 1.0 cm who underwent thyroidectomy between 2004-2016 were identified in the National Cancer Database (NCDB). Cox proportional hazards analyses were performed to identify the factors affecting survival while adjusting for variables including patient demographics, comorbidities, stage, grade, LN involvement, ETE, LVI, multifocality, distant metastasis, margin status, extent of operation, and type of treatment institution. Survival was estimated by the Kaplan Meier method and compared using log rank tests. Finally, binary logistic regression analyses were performed to identify advanced features associated with margin status.

Results: Of 13,648 patients with PTMC identified from the NCDB who met the study inclusion criteria, 2676 patients (19.6%) presented with advanced features: LN metastasis (14.8%), ETE (7.2%), LVI (2.9%), and distant metastasis (0.3%). Factors affecting survival of PTMC involved non-modifiable determinants, including age, female sex, presence of ≥ 1 comorbidity, LN involvement, and LVI, as well as modifiable determinants, such as margin positivity, increased length of hospital stay, and treatment at an academic institution. Positive margin status, in particular, was found to be the most significant modifiable risk factor affecting survival (HR 1.576, 95% CI 1.035-2.412, p=0.008). Compared to negative margin status, positive margin status was associated
with statistically significant lower overall survival (155.4 vs. 145.7 months, p=0.031). Finally, total thyroidectomy (OR 0.701, 95% CI 0.503-0.987, p=0.013) and treatment at an academic facility (OR 0.747, 95% CI 0.589-0.947, p=0.016) were the modifiable factors significantly associated with lower odds of margin positivity.

**Conclusion**: The high rates of aggressive features, including LN involvement, ETE, LVI, and distant metastasis, found in a subset of PTMC reflect its insidious nature that may negatively affect prognosis. Among the various risk factors identified, positive margin status is the most significant modifiable determinant that affects patient survival for PTMC. Furthermore, total thyroidectomy and treatment at academic centers are associated with lower odds of margin positivity and may improve survival in this subset of PTMC patients with aggressive pathologic features.