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High Grade Medullary Thyroid Carcinoma Predicts Greater Lymph Node Burden in the Ipsilateral Lateral Neck

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BACKGROUND

The International Medullary Thyroid Carcinoma Grading System (IMTCGS) is a newly established grading system for medullary thyroid carcinoma and is predictive of disease-specific outcomes. When compared to low-grade tumor patients, patients with high-grade tumors have worse locoregional recurrence rates and overall survival. We aimed to investigate how tumor grade impacts neck lymph node burden and post-resection recurrence patterns in MTC.

METHODS

A retrospective cohort analysis was performed at a single tertiary care cancer center (Memorial Sloan Kettering Cancer Center, New York, NY) between 1/1/1986 to 12/31/2017. Thyroid specimens were categorized as high-grade if they on pathologic review were found to have: a mitotic index ≥ 5 per 2mm², Ki67 $\geq 5\%$, and/or necrosis present. Competing risk modelling was used to analyze post-resection local recurrence, distant recurrence, and survival. Significance was set at a p-value < 0.05 .

RESULTS

Amongst 122 patients, 98 (80.3%) low-grade and 24 (19.7%) high-grade patients were evaluated. A similar proportion of low-grade (73%) and high-grade (75%) patients underwent central neck dissection ($p=0.2$), although the median number of involved lymph nodes in the central neck was greater in high-grade patients (4.5, IQR 0.3-11.2 vs 1.0, 0-2.0; $p<0.05$). Ipsilateral lateral neck dissection (ILND) was performed in a significantly greater proportion of high-grade patients (71%) than low-grade patients (45%; $p<0.05$) owing to regional disease identified preoperatively. Amongst patients who underwent ipsilateral lateral neck dissection, the median number of involved lymph nodes was significantly greater in high-grade patients (6.0, 4.0-19.0) than low-grade patients (4.0, 1.0-6.0; $p<0.05$). Competing risk modelling was subsequently performed to compare disease-specific outcomes between high- and low-grade patients who underwent ILND (Table 1). High-grade patients who underwent ILND had observed worse local recurrence (5yr incidence: 56% vs 19%), distant recurrence (5yr incidence: 38% vs 0%), and overall survival (60% vs 97%) when compared to low-grade patients.

Table 1. Cumulative Incidence at 5 Years of Local and Distant Recurrence Amongst Patients Who Underwent Ipsilateral Lateral Neck Dissection Stratified by Grade

Outcome	ILND for Any Reason			ILND for Known Disease		
	Cumulative Incidence at 5 years	95% CI		Cumulative Incidence at 5 years	95% CI	
		Low	High		Low	High
Local Recurrence						
Low Grade	14%	6%	27%	19%	8%	35%
High Grade	56%	27%	77%	56%	28%	77%
Distant Recurrence						
Low Grade	3.2%	0%	14%	0%	-	-
High Grade	37%	13%	62%	38%	13%	62%

CONCLUSIONS

Patients with high-grade MTC demonstrate worse initial lymph node burden in the central and ipsilateral lateral neck compartments. Despite lymph node dissection in patients with known regional disease, high-grade patients experience worse disease recurrence and survival compared to low-grade patients. Tumor grading remains an important factor in the evaluation of MTC patients that undergo surgical resection and can guide postoperative surveillance strategies.

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