

Malignancy Rates for Bethesda IV Thyroid Nodules

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Introduction & Objectives

The Bethesda system for reporting thyroid cytopathology (BSRTC) has established a standardized reporting system to categorize thyroid nodules.¹ Intermediate category lesions (Bethesda III and IV) carry a variable rate of malignancy. Our institution and others have previously examined rates of malignancy for Bethesda III, atypia of undetermined significance and follicular lesion of undetermined significance (AUS/FLUS) and found higher than expected malignancy rates.² While there is recognition of institutional variability in malignancy rates for AUS/FLUS, there remains a dearth of evidence for Bethesda IV – follicular neoplasm or suspicious for follicular neoplasm (FN/SFN) biopsies. The goal of this study is to examine the rate of malignancy and cytopathological features associated with FN/SFN biopsies over a period of full implementation of the BSRTC at our institution. Our objectives were to determine the rate of malignancy with Bethesda IV (FN/SFN) nodules and assess for histopathologic and pathologic features associated with benign and malignant diagnoses.

	Benign	Malignant	p-value
N	46	31	
Average Age at Surgery (Min-Max)	51.0 (26-76)	50.7 (25-75)	0.92
Gender: F:M (% Female)	39:7 (84.8)	20:11 (64.5)	0.07
Histopathological Findings (%)			
- Hurthle cells	43 (93.5)	18 (58.1)	<0.001
- Microfollicular groups	5 (10.8)	16 (51.6)	<0.001
- Follicular cells	6 (13.0)	21 (67.7)	<0.001
- Powdery chromatin	1	9	<0.001
- Nuclear grooves	6 (13.0)	12 (38.7)	0.02
- Micronucleoli	4	8	0.08
- Colloid	27 (58.7)	11 (35.4)	0.08
- Hemosidern laden macrophages	16	4	0.94
Pathologic Findings (%)			
- Lymphocytic thyroiditis	17 (36.9)	6 (19.4)	0.16
- Incidental microPTC	16 (34.7)	6 (19.3)	0.22

Table 1. Demographic data, Histopathological, and Pathological Associations

Methods

A retrospective review of thyroid nodule cytopathology from a tertiary center between the dates of January 1, 2010 and October 31, 2018 was performed. The rate of FN/SFN was determined. FN/SFN pathologies were linked to histopathology in surgical cases. Upper and lower boundary estimates were calculate using previously described methods.³ Histopathological and pathological findings that were found in at least 10 patients were assessed for association with benign and malignant diagnosis (**Table 1**). Statistical analysis using paired t-test and chi square was performed.

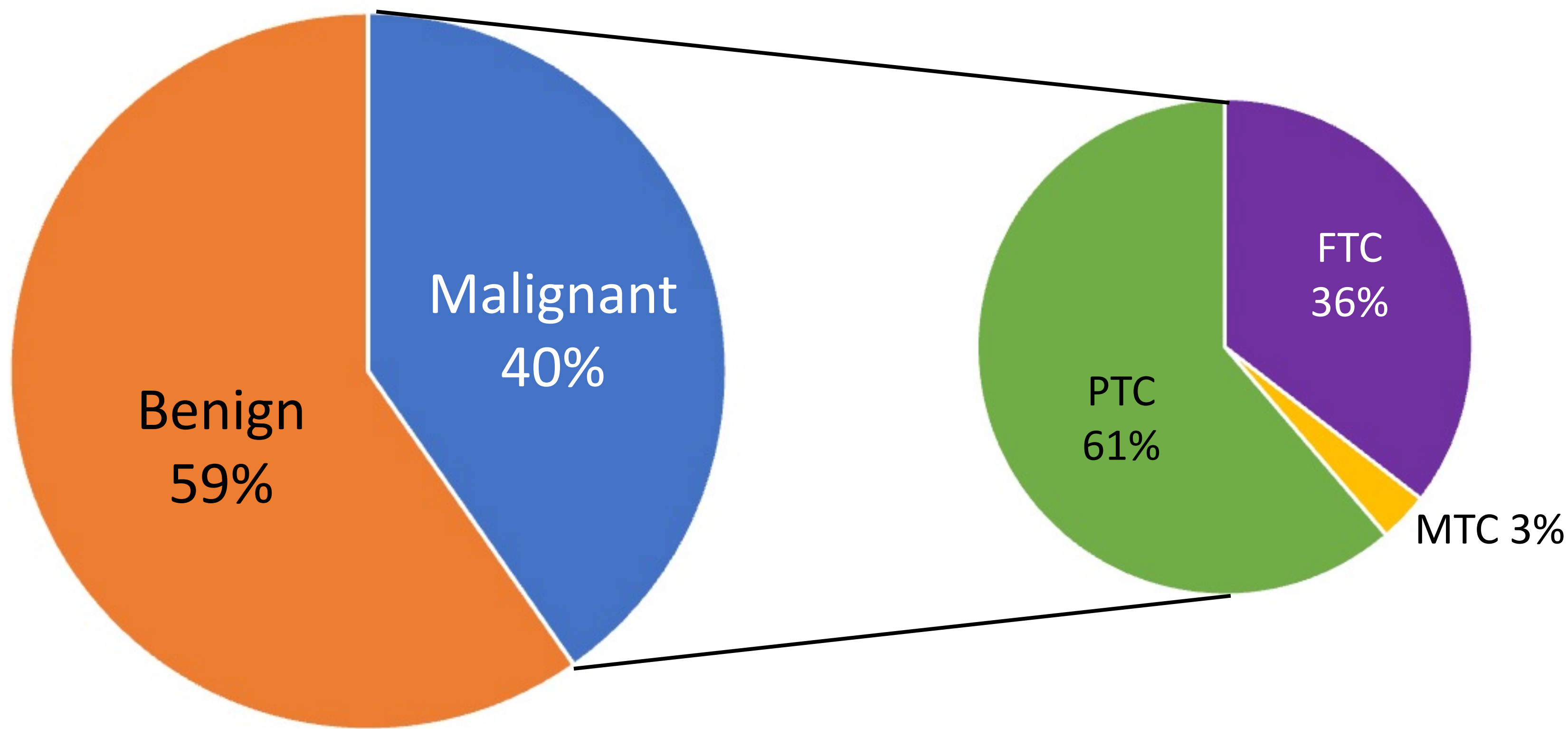


Figure 1. Malignancy Rate and Type of Malignancy

FN/SFN Cohort	Operative Rate	Cohort Malignancy Rate
245 (1.9%)	78 (31.8%)	41.0% (32/78) UBE
		12.7% (31/245) LBE

Table 2. Rate of Bethesda IV Diagnosis and Malignancy Rate

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Results

11,380 biopsies were performed during the study period. 268 FN/SFN biopsies of 247 nodules from 245 patients were identified. From this cohort, 78 patients (31.8%) underwent surgery. The operative rate and and cohort results are shown in **Table 2**. 1 lesion which could not be categorized as malignant or benign and was excluded from further analysis, but included in UBE estimate. Benign pathology was represented by adenomas or multiple adenomatous nodules. The following malignant pathologies were seen: papillary thyroid cancer (61.3%), follicular thyroid cancer (35.5%), and medullary thyroid cancer (3.2%). Papillary carcinoma variants included: follicular (16), oncocytic (2), classical with extensive follicular growth (1). Follicular carcinoma variants included: oncocytic (9), poorly differentiated (1), and unspecified (1). The upper and lower boundary estimates of malignancy were 41.0% and 12.6% respectively. Presence of Hurthle cells was significantly associated with benign pathology, while microfollicular groups, follicular cells, powdery chromatin, and nuclear grooves were significantly associated with malignancy. No significant association was seen with thyroiditis or incidental micropapillary carcinoma.

Discussion & Conclusion

The true malignancy rate of FN/SFN is difficult to determine due to the uncommon finding on cytopathology and due to many patients being managed non-operatively. Our institutional rate of malignancy for FN/SFN nodules is higher than that reported by other institutions 23.6-28.4%, but in keeping with 2017 BSRTC which estimates a 25-40% risk of malignancy.^{1,4-6} This is likely due to clinical factors that selected patients for surgery and were not captured. The lower boundary estimate of malignancy is likely underestimated given the low operative rate in this cohort. Furthermore the majority of these tumors are follicular thyroid cancers (FTC) or follicular variants of papillary thyroid cancer (PTC). Our study is limited by a low rate of FN/SFN cytopathology and a low operative rate. While this prevents us from drawing definitive conclusions the association of particular histopathologic findings with benign and malignant diagnoses has not previously been described and warrants further investigation. Finally, institution specific rates of malignancy remain important when discussing surgical options or considering molecular testing for patients.