Medullary thyroid microcarcinoma survival outcomes; a single institution experience

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ABSTRACT

Background Medullary thyroid carcinoma (MTC) has a propensity for local and distant metastatic spread, with observed metastases in even micro tumors, defined as less than or equal to 1 cm. We review our recent institutional experience with medullary thyroid microcarcinoma.

Methods: Retrospective case series examining patients with micro MTC who underwent at least total thyroidectomy with curative intent.

Results: 27 patients met inclusion criteria. The average age was 44.6 years. The average follow up time was 30.5 months, median 22 months. Twelve patients (44.4%) had a known RET mutation, the remainder of cases were sporadic (13) or untested (2).

25 patients (92.5%) were clinically N0 at presentation, with 2 (7.5%) demonstrating evidence of lateral neck disease (N1b) at presentation. Five patients underwent a central neck dissection, and 3 underwent a lateral neck dissection. Twelve additional patients had non-comprehensive node sampling from the central compartment.

Of 23 patients who had calcitonin checked >60 days post-operatively, 21 (91.3%) achieved biochemical cure. Of those who achieved cure, 5-year biochemical recurrence free survival was 100%. Among all patients, including those with elevated calcitonin, the 5-year disease free survival, defined as no identifiable structural disease locally, regionally nor distant was 94.2%. The 5-year overall survival was 94.5%.

Conclusion: MTC is an infrequent thyroid tumor. Although the majority of microcarcinoma patients do not have evidence of metastatic spread at presentation, there is a significant risk of cervical metastatic disease. Regardless, when compared with non-micro tumors, the rates of biochemical cure and overall survival are excellent.

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INTRODUCTION

Medullary thyroid carcinoma is an uncommon primary thyroid malignancy. Unlike differentiated papillary and follicular tumors, it does not concentrate radioactive iodine and is not considered radiosensitive, so surgical ablation remains the primary treatment modality.

Medullary tumors also have a propensity for local and distant metastatic spread, with observed metastases in even sub-centimeter tumors. However, smaller tumors appear to have more benign behavior, with smaller primary tumor size associated with lower pre-operative calcitonin (Fig 1), higher chance of biochemical cure (Fig 2) and lower risk of neck metastases (Fig 3).

This study reviews our recent institutional experience with micromedullary tumors – those below 1cm in size – to evaluate their natural history and compare them with standard medullary tumors.

METHODS AND MATERIALS

This study was designed as a retrospective chart review. Approval from the Institutional Review Board was obtained. Patients were identified by searching the CCF pathology database from 1997 through 2014. The electronic medical record was reviewed to clarify the clinical history.

Patients were included if they underwent primary treatment at our institution. Primary treatment was defined as at least a total thyroidectomy with curative intent. Patients who underwent primary treatment elsewhere or had incurable disease at presentation were excluded.

Data was collected in Microsoft Excel and analyzed using SAS JMP (SAS, Cary, North Carolina).

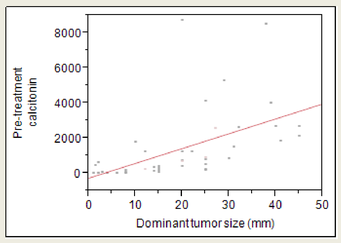


Figure 1. Linear regression of tumor size (mm) vs pre-operative calcitonin (pg/mL). This is a statistically significant relationship ($p < 0.01$), $R^2 = 0.27$. Calcitonin increases by 85 pg/mL for each 1mm increase in size.

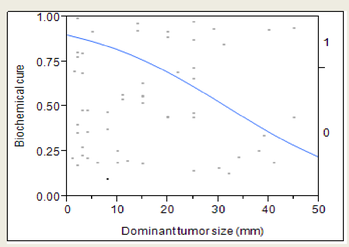


Figure 2. Logistic regression of tumor size in millimeters vs chance of biochemical cure. This is a statistically significant relationship ($p < 0.01$). The chance of cure falls by 0.83 for each 1mm increase in size ($p < 0.01$).

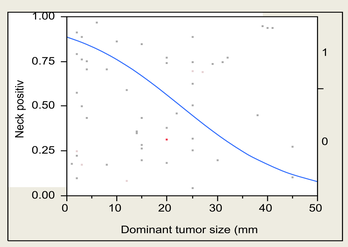


Figure 3. Logistic regression of tumor size in millimeters vs risk of neck metastases (determined by pathology results). This is a statistically significant relationship ($p < 0.01$). The chance of cure falls by 0.91 for each 1mm increase in size ($p < 0.01$).

RESULTS

67 patients received primary treatment for medullary thyroid cancer during the study period. Of this overall group, 27 patients had micromedullary tumors (10mm or less). Average age was 44.6 years, and the population skewed female (67% vs 33% male). Average follow up time was 31 months, with a median follow up of 22 months. 12 patients (44%) had a known RET mutation, the remainder of cases were sporadic (13) or untested (2).

At presentation, 25 (92.5%) had no clinical evidence of neck disease, while 2 (7.5%) were staged N1b. Five patients underwent a central neck dissection, and 3 underwent a lateral neck dissection. Twelve underwent non-comprehensive node sampling from the central compartment. Two clinically-negative patients had pathologically-proven metastases, so 4 of 18 (22.2%) of patients who underwent some form of nodal sampling / dissection had positive neck disease. (See Fig 4a/b)

Four patients were lost to follow up early. Of the 23 remaining patients, 21 (91.3%) achieved biochemical cure (normal calcitonin at first lab check over 60 days after surgery). Of those who achieved cure, 5-year biochemical recurrence free survival (BRFS) was 100%.

Among all patients, including those with elevated calcitonin, the 5-year disease free survival, defined as no identifiable structural disease locally, regionally nor distant was 94.2%. The 5-year overall survival was 94.5%.

When compared to the non-micro tumors treated at our institution within the study period (n = 40), micromedullary tumors exhibit favorable pathologic characteristics, with lower rates of extrathyroidal extension (0% vs 33%, $p < 0.01$) and angiolymphatic extension (4.3% vs 79%, $p < 0.01$). When pathologic nodes are examined from microtumors, there is no difference in the rate of extracapsular extension (67% vs 67%, $p = 1.00$).

Micromedullary patients – as expected given prior data, see Fig 2 – have a statistically higher rate of biochemical cure (91.3% vs 57.6%, $p < 0.01$). Direct comparisons between micro and standard tumors are presented in Chart 1. Comparative survival curves are below in Figure 5.

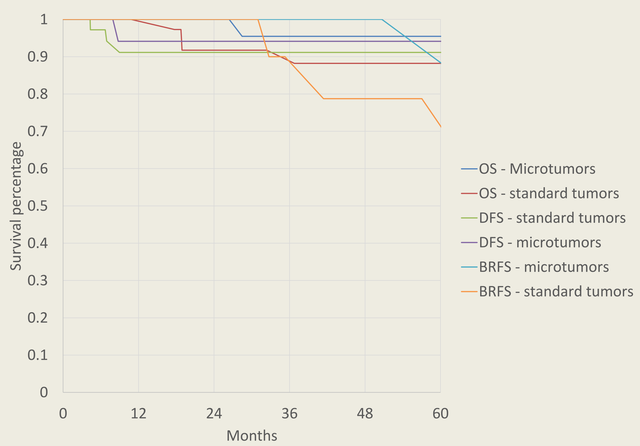
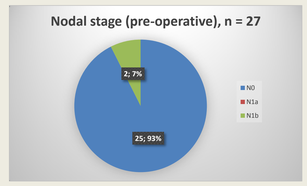


Figure 5. Kaplan-Meier curves with 5 year survival. OS: Overall survival. DFS: Disease free survival (no gross evidence of disease). BRFS: Biochemical recurrence free survival (no abnormal calcitonin after initial normalization).



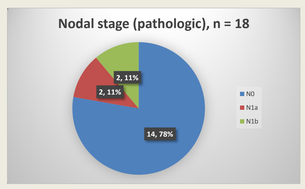


Figure 4a/b. The distribution of nodal stage based on initial clinical staging (top chart) and pathologic findings (bottom chart).

The pathologic N stage (bottom chart) is only reported for those patients who underwent some form of node sampling or neck dissection (n = 18).

Among patients who had positive nodes, the average number was 10.25, although there was a wide range (2-29)

	Micro tumors	Standard tumors
Cervical metastases	22.2%	50%
Extrathyroidal extension	**0%**	**33.3%**
Angiolymphatic invasion	**4.4%**	**79.3%**
Extracapsular extension	66.7%	66.7%
Biochemical cure (initial)	**91.3%**	**57.6%**
Overall survival (5 years)	95.4%	88.2%
Disease free survival (5 years)	94.1%	91.1%
Biochemical recurrence free survival (5 years)	100%	78.8%

Chart 1. Comparisons between microtumors (n = 27) and standard tumors (n = 40) within this patient series. Statistically significant differences are highlighted in bold (threshold $p < 0.05$).

CONCLUSIONS

Medullary thyroid cancer is an infrequent primary thyroid tumor. Primary tumor size is a clear prognostic factor, with tumor size affecting pre-operative calcitonin, risk of cervical metastatic disease and biochemical recurrence.

This study confirms that even micromedullary tumors have a substantial risk of cervical metastases, although not as high as larger tumors. However, high-risk pathologic features such angiolymphatic invasion and extrathyroidal extension are less common. Biochemical cure is more likely, and biochemical survival appears more durable although this is not statistically robust.

Of consideration when interpreting our data is the significantly higher rate of RET mutations in the microtumor cohort; many of these patients underwent prophylactic surgery. Given the excellent 5 year survival outcomes with the micromedullary cohort, we conclude early detection and removal of medullary tumors is important in maximizing patient outcomes.

REFERENCES

Cooper, David S., et al. "Revised American Thyroid Association management guidelines for patients with thyroid nodules and differentiated thyroid cancer: the American Thyroid Association (ATA) guidelines taskforce on thyroid nodules and differentiated thyroid cancer." Thyroid 19.11 (2009): 1167-1214.

Machens, Andreas, et al. "Prospects of remission in medullary thyroid carcinoma according to basal calcitonin level." The Journal of Clinical Endocrinology & Metabolism 90.4 (2005): 2029-2034.

Witt, Robert L. "What is the treatment of the lateral neck in clinically localized sporadic medullary thyroid cancer?." The Laryngoscope 120.7 (2010): 1286-1287.

Noullet, S., et al. "Surgical management of sporadic medullary thyroid cancer." Journal of visceral surgery 148.4 (2011): e244-e249.

Stamatakos, Michael, et al. "Surgical approach to the management of medullary thyroid cancer: when is lymph node dissection needed?." Oncology 84.6 (2013): 350-355.

Nixon, Iain J., and Ashok R. Shaha. "Management of regional nodes in thyroid cancer." Oral oncology 49.7 (2013): 671-675.

Scollo, Claudia, et al. "Rationale for central and bilateral lymph node dissection in sporadic and hereditary medullary thyroid cancer." The Journal of Clinical Endocrinology & Metabolism 88.5 (2003): 2070-2075.