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16. Medullary thyroid carcinoma

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THE ROLE OF THE RET POLYMORPHIC ALLELE S836S IN THE CLINICAL COURSE OF MEDULLARY THYROID CARCINOMA

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Abstract: A possible role of *RET* variants in modifying the natural course of medullary thyroid carcinoma (MTC) is still a matter of debate. **Objective:** To investigate whether the *RET* variants L769L, S836S, and G691S/S904S influence disease presentation in hereditary or sporadic MTC patients. **Methods:** One-hundred-two patients with hereditary MTC and 67 with sporadic MTC attending our Institution. Sixty-two subjects comprise the control group. **Results:** The frequencies of *RET* polymorphisms in hereditary MTC were as follows: L769L 18.1%, S836S 7.9% and S904S/G691S 18.1%. No associations were observed between these polymorphisms and pheochromocytoma, hyperparathyroidism, lymph-node or distant metastases. However, patients harboring the S836S variant were younger than those without this allele (17 ± 8.2 vs. 28.6 ± 14.4 years, $P=0.01$), suggesting that patients with S836S allele had metastases at young age. Accordingly, the estimated cumulative frequency of local and/or distant metastases by Kaplan-Meier curves showed that lymph-nodes and distant metastases occurred earlier in patients harboring S836S variant ($P=0.002$ and $P=0.024$, respectively). In sporadic MTC patients, the frequency of the *RET* variant S836S was higher when we compared with controls (12.3% vs. 3.2%, $P=0.01$). Similarly to that observed in hereditary MTC, individuals harboring S836S variant were younger (39.8 ± 11.6 vs. 49.2 ± 17.3 years, $P=0.03$) whereas no differences were observed in the rate of local or distant metastasis. Kaplan-Meier estimates of lymph-node and distant metastasis rates yielded distinct curves for patients with or without the S836S allele ($P=0.003$ and $P=0.005$, respectively). Additional analyses using COX regression model showed that the S836S variant was independently associated with metastatic disease [OR 2.95 (95% CI 1.42-6.10), $P=0.04$]. **Conclusion:** The *RET* S836S variant is associated with early onset and increased risk for metastatic disease in patients with hereditary or sporadic MTC.

Disclosure of Interest: None Declared

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