

Clinical and biochemical criteria for the prognosis of small medullary thyroid carcinomas

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Introduction - Aim of the study

- ✓ The prevalence of small medullary thyroid carcinomas (sMTCs, ≤ 1.5 cm) has increased during recent years.
- ✓ They are frequently diagnosed as incidental findings in surgical and occasionally in autopsy specimens.
- ✓ As their clinical course varies, various prognostic risk factors for their biological behaviour have been repeatedly investigated.

We examined whether tumor size is a predictor of clinical behaviour of these tumours.

Patients - Methods

204 MTC patients underwent total thyroidectomy.

119 patients had sMTC (≤ 1.5 cm)

- Mean age at diagnosis 41.33 \pm 17.15 yrs (range 5-78)
- 37% men (n=44)
- Mean time of follow-up: 6.16 \pm 5.9 yrs (range 0.9-34)
- 47.1% familial

Patients were classified according to tumor size (cm) in:

1. group1: 0.1-0.5 (n=25, 24.8%)
2. group2: 0.6-0.8 (n=22, 21.8%)
3. group3: 0.8-1.0 (n=23, 22.8%)
4. group4: 1.1-1.5 (n=31, 30.7%)

Clinical and biochemical parameters at diagnosis and during follow-up were recorded.

Results

- ✓ The demographic characteristics are shown in table 1.
- ✓ Familial cases did not differ from sporadic ones concerning stage at diagnosis or outcome.
- ✓ Cervical lymph node and capsular invasion were more frequent with increasing tumor size (fig 1).
- ✓ No distant metastases at diagnosis were found in the four groups (fig 1).
- ✓ Preoperative and postoperative calcitonin levels were positively associated with tumour size ($p < 0.001$).
- ✓ The stage at diagnosis was more advanced and the outcome less favourable with increasing tumour size ($p < 0.004$, fig 2, 3).
- ✓ Group 1 and 2 patients were more frequently cured (group1: 88%, group2: 86.7%, group3: 72.7%, group4: 51.7%, $p = 0.009$).
- ✓ The 10-year probability of lack of progression of disease according to tumour size did not differ significantly between the 4 groups (group1: 96%, group2: 100%, group3: 100%, group4: 81.5%, $x^2 = 4.61$, $p = 0.2$, Log Rank, fig 4).
- ✓ It differed marginally between patients with tumour 0.1-1.0 and 1.1-1.5cm (98.5%, 81.5%, $x^2 = 4.15$, $p = 0.042$, log rank, fig 5).
- ✓ In the subgroup of microMTCs (≤ 1.0 cm) patients with microMTC ≤ 0.8 had less advanced stage at diagnosis compared to 0.9-1.0cm (stage I&II: 89.4% vs 66.7%, stage III: 8.5% vs 33.3% and stage IV: 2.1% vs 0%, $p = 0.032$, table 2).
- ✓ No differences in the outcome were found between microMTC subgroups.

Table 1. Demographic characteristics according to the tumor size (≤ 1.5 cm)

| | Largest tumor diameter (cm) | | | | P |
|--------------------------------|-----------------------------|----------------------------|----------------------------|----------------------------|-------|
| | Group1 0.1-0.5 n=30 | Group 2 0.6-0.8 n=31 | Group 3 0.9-1.0 n=26 | Group 4 1.1-1.5 n=32 | |
| Age (yrs \pm SD) | 32.83 \pm 17 | 45.84 \pm 14 | 45.08 \pm 18 | 41.88 \pm 16 | 0.011 |
| Sex: males (%) | 40% | 32.3% | 46.2% | 31.3% | 0.6 |
| Family history: sporadic (%) | 29.6% | 54.8% | 52.2% | 46.7% | 0.3 |
| Years of follow up (\pm SD) | 5.0 \pm 5.94 | 3.33 \pm 4.97 | 4.9 \pm 5.12 | 7.05 \pm 6.8 | 0.12 |
| Median (IQR) | 2 (8.5) | 1 (3) | 3 (4) | 5 (9) | |

Fig 1. Clinical and histological characteristics according to the tumour size (≤ 1.5 cm)

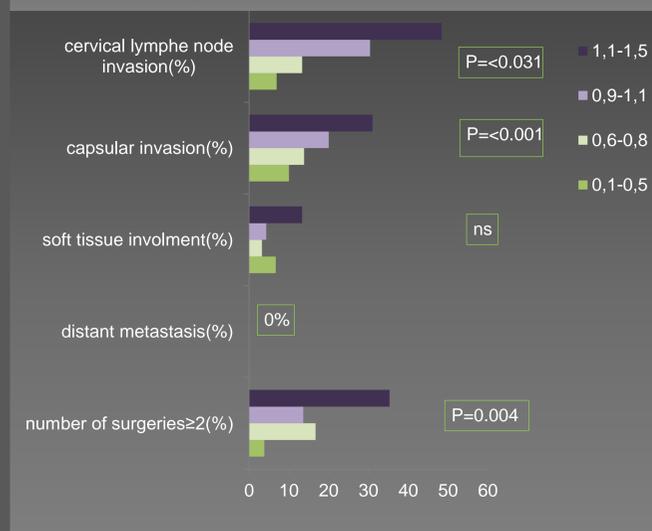


Fig 2. Stage at diagnosis according to the tumor size (≤ 1.5 cm)

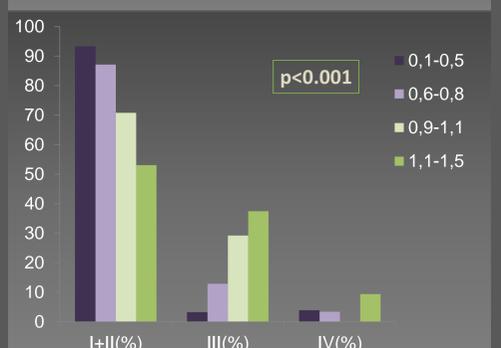


Fig 3. Outcome of the disease according to the tumour size of sMTCs (≤ 1.5 cm)

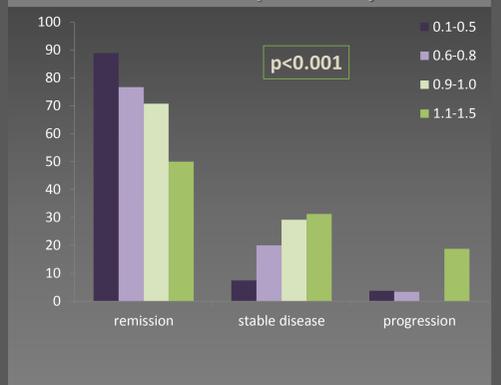


Fig 4. 10-year probability of lack of progression of disease according to the tumour size (0.1-1.5 cm)

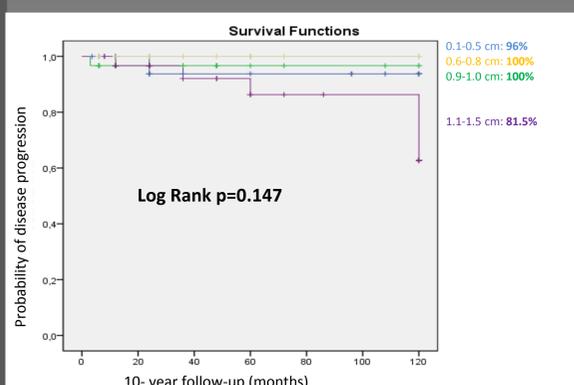


Fig 5. 10-year probability of lack of progression of disease according to the tumour size (0.1-1.0 and 1.1-1.5 cm)

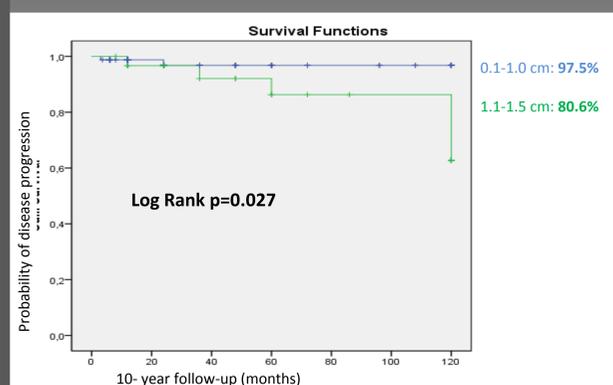


Table 2. Results in the subgroup of patients with micro MTC (≤ 1.0 cm)

| | Largest tumor diameter (cm) | | P |
|---------------------|-----------------------------|------------|------|
| | 0.1-0.8 cm | 0.9-1.0 cm | |
| Stage at diagnosis: | | | |
| I+II | 90.2% | 70.8% | 0.04 |
| III | 8.2% | 29.2% | |
| IV | 1.6% | 0.0% | |
| Outcome : | | | |
| Remission | 82.5% | 66.6% | 0.2 |
| Stable | 14% | 33.3% | |
| Progression | 3.5% | 0.0% | |

Conclusions

- Within the group of small MTCs (≤ 1.5 cm) the probability of 10yr-disease progression slightly increases in those with tumour size > 1.0 cm.
- In the subgroup of microMTCs (≤ 1.0 cm) the stage is less advanced in tumours ≤ 0.8 cm, while the outcome is similar to those with tumour size 0.9-1.0cm.
- Thus tumour size may be of clinical importance for the progression of disease only in patients with MTCs > 1 cm.