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# Medullary thyroid carcinoma in Hong Kong Chinese patients

## 香港華籍髓質性甲狀腺癌病人

**Objective.** To study the clinical parameters and treatment outcome of medullary thyroid carcinoma in Hong Kong Chinese patients.

**Design.** Retrospective study.

**Setting.** Regional oncology unit, Hong Kong.

**Patients.** Patients with medullary thyroid carcinoma who were identified among 1656 patients with thyroid malignancies seen in a single institute in Hong Kong from January 1960 to June 2003.

**Main outcome measures.** Ten-year cause-specific survival, locoregional failure-free survival, and distant metastasis failure-free survival.

**Results.** Twenty-two (1.3%) patients with medullary thyroid carcinoma were identified. The mean age at diagnosis was 43.7 (standard deviation, 16.5) years. The sex ratio was 1:1. The 10-year cause-specific survival, locoregional failure-free survival, and distant metastasis failure-free survival were 75.4%, 82.0%, and 62.4%, respectively. Lymph node metastasis was present in seven (31.8%) patients at diagnosis. Distant metastasis developed in nine (40.9%) patients: lung, 3 (13.6%); bone, 5 (22.7%); liver, 2 (9.1%); mediastinum, 4 (18.2%). Seven (31.8%) patients died of distant metastasis. Mediastinal (n=3) and bone metastases (n=3) were important causes of death. Genetic study confirmed multiple endocrine neoplasia type 2A in 3 (25.0%) of 12 patients who all had bilateral and multifocal diseases. Younger age (<45 years) was associated with better survival, better locoregional control, and less distant metastasis. Patients with pT1N0 disease (n=3) had an excellent prognosis: all were disease-free following total thyroidectomy. Among eight patients who received external radiation therapy, seven achieved good locoregional control. In seven patients with lymph node metastasis, external radiation therapy gave 100% (4/4) locoregional control compared with 33.3% (1/3) in those without external radiation therapy. Chemotherapy using dacarbazine and 5-fluorouracil was tried in three patients with poor response.

**Conclusions.** Early stage (T1N0) medullary thyroid carcinoma is associated with a very good prognosis. Postoperative external radiation therapy can achieve good locoregional control in patients with lymph node metastasis or locally advanced disease.

### Key words:

Carcinoma, medullary;  
 Multiple endocrine neoplasia;  
 Radiotherapy;  
 Thyroid neoplasms

### 關鍵詞：

癌，髓質性的；  
 多發性內分泌瘤；  
 放射治療；  
 甲狀腺瘤

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**目的：**研究香港華籍髓質性甲狀腺癌病人的臨床參數及治療結果。

**設計：**回顧研究。

**安排：**地區腫瘤科部門，香港。

**患者：**1960年1月至2003年6月期間，從1656名被香港單一醫療機構診斷患有甲狀腺惡性腫瘤的病人中，證實患上髓質性甲狀腺癌的病人。

**主要結果測量：**十年特定病因存活率、局部再患病前存活率和遠處擴散前存活率。

**結果：**22名病人 (1.3%) 被診斷出患上髓質性甲狀腺癌。他們接受診斷時平均年齡為43.7歲 (標準差為16.5歲)，男女比例相同。十年特定病因存活率、局部再患病前存活率和遠處擴散前存活率分別為75.4%、82.0%和62.4%。7名病人 (31.8%) 在接受診斷時有淋巴結擴散情況，而9名病人 (40.9%) 出現遠處擴散：擴散至肺部有3人 (13.6%)、骨骼5人 (22.7%)、肝臟2人 (9.1%)，以及縱膈腔4人 (18.2%)。7名病人 (31.8%) 因遠處擴散而死亡，當中以擴散至縱膈腔 (3人) 和骨骼 (3人) 為最主要致死原因。基因研究確定12名病人中有3人 (25.0%) 患有2A型多發性內分泌瘤病，他們同時出現雙側疾病和多源疾病。年齡較輕者 (少於45歲) 有較高存活率、較好局部控制率和較低遠處擴散率。3名患有pT1N0的病人預後效果顯著，他們在切除整個甲狀腺後沒有再發病。8名接受過外部放射治療的病人，7人有良好的局部控制率。7個淋巴結擴散的病人中，接受外部放射治療的能做到100% (4/4) 的局部控制率，沒接受外部放射治療的則只有33.3% (1/3)。對外部放射治療反應欠佳的3名病人，則以達卡巴嗪和5-氟尿嘧啶進行化學治療。

**結論：**若在患上髓質性甲狀腺癌的初期 (T1N0) 便被診斷出來，病人會有較好的預後情況。對有淋巴結擴散和局部晚期病的病人，手術後的外部放射治療能達到良好的局部控制率。

## Introduction

Medullary thyroid carcinoma (MTC) is a malignant tumour that shows parafollicular C-cell differentiation. It accounts for 3% to 5% of all thyroid cancers.<sup>1</sup> The histological features are distinctive: sheets and packets of polygonal or plump spindly cells traversed by prominent fibrovascular septa. The tumour cells possess granular cytoplasm, and amyloid deposition is common.<sup>2</sup> The diagnosis can be readily confirmed by immunohistochemical staining for calcitonin and neuroendocrine markers. Medullary thyroid carcinoma is associated with inherited tumour syndromes in approximately 20% of cases: multifocality and bilateral disease is also more common.<sup>3</sup> The tumour syndromes include multiple endocrine neoplasia (MEN) and familial MTC syndrome. Early diagnosis and prompt treatment can result in substantial improvement in clinical outcome. Hereditary forms should thus be recognised and family members screened accordingly.<sup>4</sup> Medullary thyroid carcinoma has rarely been reported in the Chinese population, and there appear to be some epidemiological differences to Caucasian series.<sup>5,6</sup> We present the clinical features and outcomes of 22 Hong Kong Chinese patients seen at our institute.

## Methods

### Patients

Queen Elizabeth Hospital is a tertiary referral hospital in Hong Kong. A retrospective analysis of 1656 patients with thyroid malignancies seen from January 1960 to June 2003 was undertaken by the Department of Clinical Oncology. The distribution of patients with different histology was: differentiated (papillary or follicular carcinomas), 1548; anaplastic, 77; medullary, 22; insular, 5; squamous cell, 3; and mucoepidermoid, 1. Medullary thyroid carcinoma thus accounted for only 1.3% of all thyroid malignancies.

All patients were ethnic Chinese. The diagnostic materials from all except three patients (one patient had surgery in Canada and the other two patients had no slide review arrangement) had been reviewed to confirm the diagnosis. The mean follow-up period was 9.5 years (standard deviation [SD], 7.5 years). Four patients were lost to follow-up after a mean of 10.7 years (SD, 8.8 years). Mean age at diagnosis was 43.7 years (SD, 16.5 years; range, 12.1-80.7 years). The female to male ratio was 1:1.

### Treatment

All patients underwent bilateral thyroidectomy (nine patients underwent completion thyroidectomy after initial hemithyroidectomy). Seven patients who had lymph node (LN) metastasis at diagnosis also underwent LN excision (n=1), selective neck dissection (n=4), or radical neck dissection (n=2). External beam radiation therapy (EBRT) was given to eight patients (four as primary postoperative treatment, and four with locoregional [LR] relapse). It was delivered to the thyroid bed and bilateral cervical lymphatics by either combined photon and electron fields (n=7) or by a minimantle technique (n=1). For the former technique, the treatment was divided into two phases: phase I consisted of a single superiorly tilted anterior cervical field using 4.5-6 MV photons up to 30-36 Gy; phase II consisted of a single superiorly tilted anterior electron field using 12-15 MeV electrons. The irradiated volume covered both sides of the neck from beneath the jaw to the angle of Louis, including both supraclavicular fossae and sternal notch. The upper apices of the lungs were shielded. The spinal cord dose was limited to lower than 45 Gy. For the minimantle technique, an AP-PA field arrangement was employed with heavy anterior weighting and posterior spinal cord shield. Treatment volume covered the neck and superior mediastinum. The patient who had this treatment received 57.5 Gy in 23 fractions over 30 days.

**Table 1. Clinical characteristics, treatment, and outcome of the Hong Kong Chinese patients with medullary thyroid carcinoma**

Medullary thyroid carcinoma, n=22*	
Mean follow-up period (SD, range) [years]	9.5 (7.5, 0.15-27.20)
Mean age (SD, range) [years]	43.7 (16.5, 12.1-80.7)
Female:male	1:1
Mean size of primary tumour (SD) [cm]	3.2 (2.1)
Extrathyroidal extension	9 (40.9)
Multifocal disease	7 (31.8)
Bilateral disease	5 (22.7)
Lymph node metastasis at diagnosis	7 (31.8)
Distant metastasis at diagnosis	1 (4.5)
Staging by AJCC <sup>†</sup> in 1997 <sup>7</sup>	
I	3 (13.6)
II	11 (50.0)
III	6 (27.3)
IV	1 (4.5)
Not known	1 (4.5)
Treatment	
Total thyroidectomy	18 (81.8)
Total thyroidectomy and external radiation therapy	4 (18.2)
Lymph node surgery	
Nil	15 (68.2)
Excision	1 (4.5)
Selective neck dissection	4 (18.2)
Radical neck dissection	2 (9.1)
Status at last follow-up	
Alive with no disease	12 (54.4)
Alive with locoregional disease	1 (4.5)
Alive with distant metastasis	1 (4.5)
Died of disease	7 (31.8)
Died of unrelated disease	1 (4.5)

\* Data are shown in No. (%), unless otherwise stated

† AJCC American Joint Committee on Cancer

### Endpoints

Locoregional disease was defined as clinically detectable disease in the thyroid bed or cervical LNs. Distant metastases (DM) were defined as clinically or radiologically detectable disease outside the thyroid bed or cervical LNs.

### Statistical analyses

Statistical Package for the Social Sciences (Windows version 10.0; SPSS Inc, Chicago [IL], United States) was used in data analyses. The survival curves were generated according to the Kaplan-Meier method. The impact of various factors was analysed by Chi squared tests, Fisher's exact tests, and log-rank tests. Results were summarised by P values and those less than 0.05 were considered statistically significant.

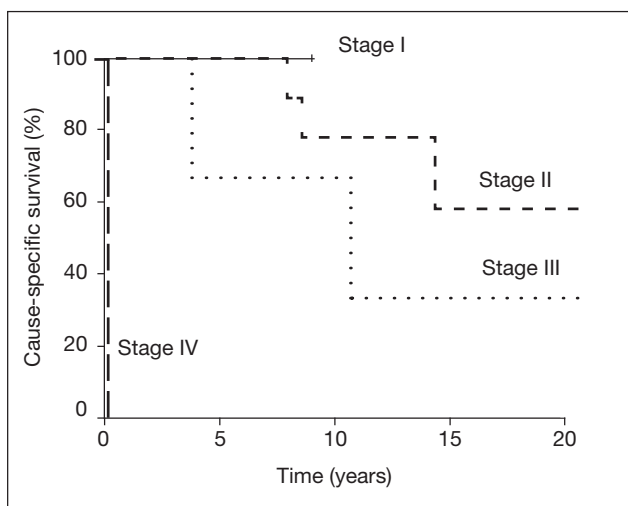
### Results

Most (15/22, 68.2%) patients presented with an anterior neck mass or cervical LN enlargement, while two were detected incidentally, one at diagnosis of nasopharyngeal carcinoma, and the other one during surgery for multinodular goitre. One patient was

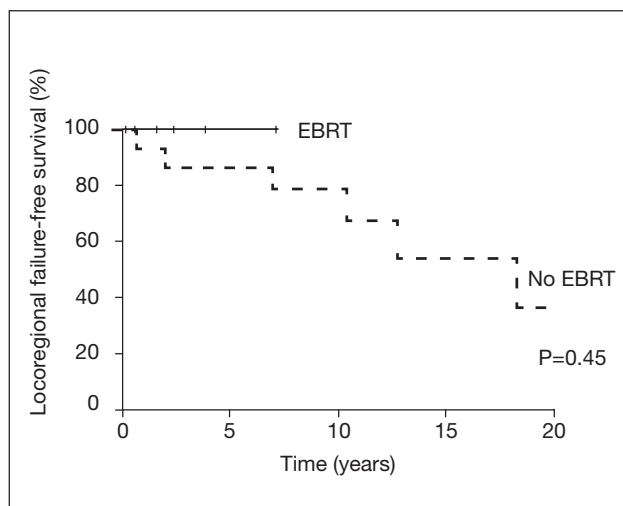
diagnosed by screening after two siblings were confirmed with MEN2A. In two patients, hospital notes recorded no details of initial presentation. Table 1 shows the clinical features, primary treatment, and outcome of the patients. The stage distribution was based on the American Joint Committee on Cancer in 1997.<sup>7</sup> Mean size of tumour was 3.2 cm. Multifocality was found in 31.8% and bilaterality in 22.7% of patients. Extrathyroidal extension was found in 40.9%. The LN metastasis rate at presentation (7/22, 31.8%) was probably underestimated because these were the only patients who underwent initial lymphadenectomy. Only one patient had DM to the lungs and bones at diagnosis. At the last follow-up, 12 patients were alive with no clinical disease. The 10-year cause-specific survival (CSS), locoregional failure-free survival (LRFFS), and distant metastasis failure-free survival (DMFFS) were 75.4%, 82.0%, and 62.4%, respectively. Figure 1 depicts the CSS of patients diagnosed at different stages.

### Prognostic factors

In this small series, only univariate analyses were employed to identify prognostic factors. Younger age



**Fig 1. Cause-specific survival of patients with medullary thyroid carcinoma**

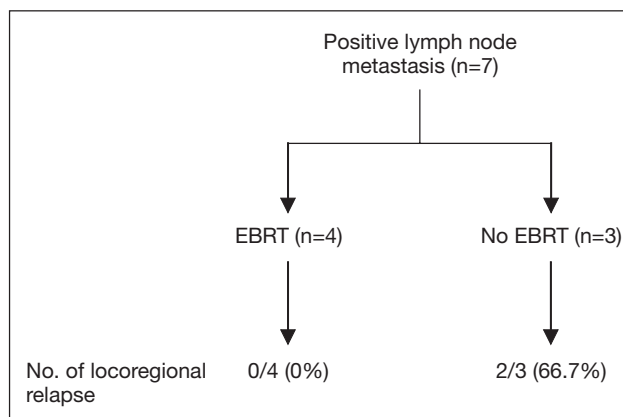


**Fig 2. Locoregional control after postoperative external beam radiation therapy (EBRT)**

(≤45 years) was associated with better CSS (P=0.0006), LRFSS (P=0.01), and DMFFS (P=0.01). Distant metastases occurred in 62.5% (5/8) of older patients (>45 years) compared with 28.6% (4/14) of the younger age-group. Sex, size of tumour (≤ or >1 cm), and LN metastasis did not have a significant effect on survival. Lymph node metastasis was associated with multifocal disease in the primary tumour. Positive LN metastasis was found in 57.1% (4/7) of patients with multifocal disease compared with 21.4% (3/14) of patients with unifocal disease (excluding one patient with incomplete pathological information). A higher incidence of DM was noted in patients with LN metastasis (4/7, 57.1%) than those without (4/12, 28.6%).

**Locoregional control and external beam radiation therapy**

All 22 patients underwent total thyroidectomy (nine had completion thyroidectomy after hemithyroidectomy). Postoperative EBRT was administered to four patients—none had LR relapse following treatment, whereas seven (39%) of 18 patients who did not receive EBRT had LR relapses at 0.9 to 21.3 years (mean, 10 years). Figure 2 shows the LRFSS after primary surgery with or without EBRT. In the seven patients who had LR relapses, two received only palliative treatment because of the presence of DM, and one underwent multiple operations. The four remaining patients had surgery and EBRT; three had LR control at last follow-up. Among the patients who underwent EBRT, 87.5% (7/8) achieved LR control. In patients with positive LN metastasis, EBRT achieved 100% (4/4) LR control.



**Fig 3. Locoregional relapse after external beam radiation therapy (EBRT)**

For the remaining three patients with no EBRT, two (66.7%) had LR relapse (Fig 3).

**Distant metastasis**

Overall, nine (40.9%) patients had DM. Common sites included lungs (n=3), bone (n=5), liver (n=2), and mediastinum (n=4). The mean time to detection of first DM was 7.8 years (lungs, 2.6; bone, 7.5; liver, 12.3; and mediastinum, 12.3 years). Distant metastasis was the cause of death in all seven patients who died of MTC (mediastinum, 3; bone, 3; liver, 1). Mediastinal metastasis was a significant cause of death (3/7, 42.9%). Among the four patients diagnosed with mediastinal metastasis, three had prior cervical LN relapse. Among the six patients who had LN relapse after primary treatment, three (50%) developed mediastinal metastasis afterwards.

**Table 2. Comparison of clinical characteristics of familial medullary thyroid carcinomas and sporadic medullary thyroid carcinomas**

	Familial (all MEN* 2A)	Sporadic
No. of patients	3 <sup>†</sup>	19
Sex (F:M)	1:2	10:9
Mean age (years)	29.3	46.1
Mean size (cm)	1.4	3.0
Multifocality	100%	21.1%
Bilaterality	100%	10.5%
Lymph node metastasis	33.3%	31.6%

\* MEN multiple endocrine neoplasia

† One detected on family screening

### Chemotherapy

Dacarbazine (DTIC) and 5-fluorouracil (5FU) combination chemotherapy was tried unsuccessfully in three patients with DM. One patient with mediastinal metastasis underwent chemotherapy, but the mediastinal tumour did not shrink. This was followed by EBRT to the mediastinum, then by thoracotomy and excision of the residual mediastinal mass. Although chest X-rays showed a right paratracheal mass and lung fibrosis, the patient remained asymptomatic for 7 years before dying a short time after diagnosis of stage IV diffuse large cell lymphoma.

### RET protooncogene mutation study and multiple endocrine neoplasia 2A syndrome

RET protooncogene mutation study was performed in 12 patients. A germline mutation at codon 634 and MEN2A was confirmed in three patients from two families: two brothers (aged 19 and 27 years at diagnosis), and a woman aged 40 years. All three patients had multifocal and bilateral primary thyroid tumours (Table 2). Lymph node metastasis was found in one patient. At the last follow-up, all were alive: one brother had liver metastasis and the other had neck disease. The female patient underwent postoperative EBRT and remained clinically free of disease at 2.4 years of follow-up. Her son was an asymptomatic carrier of mutated RET gene (diagnosed at 8 years of age and currently 13 years), but the family refused prophylactic thyroidectomy.

### Stage I or pT1N0M0 disease

Lymph node metastasis was present in only one of four patients with tumour size of 1 cm or smaller. The three patients with stage I disease underwent total thyroidectomy without LN dissection. All remained free of relapse both clinically and serologically (with normal serum calcitonin).

### Postoperative serum calcitonin during follow-up

Serum calcitonin assay was not available for patients

in this series until 1990. Among nine patients who had serum calcitonin testing during the disease course, four had elevated levels of above 1000 pmol/L; three patients eventually died of disease while one was lost to follow-up. At the last follow-up, four patients had a slightly raised calcitonin (9.7-384 pmol/L; reference level, <400 pmol/L) but no evidence of clinical or radiological disease at a mean of 9.5 years (range, 1.6-21.3 years) after primary treatment. One patient had normal serum calcitonin after primary total thyroidectomy.

### Discussion

Medullary thyroid carcinoma is a rare type of thyroid cancer in Hong Kong Chinese patients (only 1.3% of all thyroid carcinomas). Similar findings have been reported in a Taiwanese population (2.8%).<sup>6</sup> In Caucasian populations, the figure is around 3% to 5%.<sup>8</sup> The relatively low prevalence in the Chinese population may be related to geographical factors, racial differences, or a low frequency of familial case clusters. According to the literature, the hereditary form accounts for 17% to 42.7% of all MTCs.<sup>3,4,9-13</sup> It accounted for only 13.6% in our series (25% of those who had molecular test), and only 5.3% in a study of Taiwan Chinese.<sup>5</sup>

The 10-year CSS of 75.4% reported in this series is within the range reported by other series (49-86.5%).<sup>3,4,10-12,14</sup> The prognostic factors that have been identified by multivariate analysis are stage,<sup>4,10</sup> age,<sup>4,10,12</sup> extent of LN metastasis,<sup>12</sup> type of surgery,<sup>12</sup> DM at presentation,<sup>12</sup> postoperative residual disease,<sup>15</sup> extraglandular invasion,<sup>15</sup> and postoperative calcitonin level.<sup>11</sup> It is well recognised that RET protooncogene screening can detect carriers of the mutant gene and hence the presence of a tumour at an earlier stage. This results in an excellent prognosis following prophylactic thyroidectomy or prompt treatment.<sup>4</sup> The tempo of disease progression is generally slow.<sup>4,10,16</sup> Because of the small number of patients in this series, only univariate analyses were performed. Patients younger than 45 years were associated with better CSS, LRFFS, and DMFFS. Stage, size of primary tumour, and LN metastases at presentation were not significant factors, probably because of the small case number.

### Treatment of lymph node

Prophylactic LN dissection is not a routine procedure in Hong Kong, thus the 'actual' prevalence of LN metastasis could not be ascertained in this study. Other series have shown that the incidence of LN metastasis

is high, around 55% to 63%,<sup>9,12</sup> and that LN metastasis occurs early.<sup>9</sup> When microdissection of all four locoregional LN compartments is performed, LN metastasis is almost a universal finding (94%) and upper mediastinal LN metastasis is positive in 36%.<sup>17</sup> A strong association between tumour size and LN metastasis has been reported.<sup>9</sup> Even if the size of tumour is less than 1 cm, LN metastasis is present in 22% to 33%. Biochemical cure (normalisation of calcitonin) after surgery can be achieved in 95% LN-negative patients compared with 32% of patients with LN metastasis.<sup>9</sup> Scollo et al<sup>9</sup> advocate standard LN surgery, irrespective of tumour size and whether or not it is hereditary. Although most guidelines agree total thyroidectomy is an acceptable treatment for a thyroid tumour, the extent of LN surgery is controversial. Joint guidelines produced by the British Thyroid Association and the Royal College of Physicians of London<sup>18</sup> and those from the National Comprehensive Cancer Network<sup>19</sup> recommend central node dissection as part of initial surgery. Nonetheless no agreement was reached by a meeting of experts (mostly endocrinologists) in 1999.<sup>20</sup>

#### **External beam radiation therapy**

External beam radiation therapy effectively improves local control of MTC.<sup>12,14,15,21</sup> Although an earlier study<sup>22</sup> from the same institute showed that EBRT had little effect on the outcome of MTC, a later study<sup>21</sup> observed a benefit in LR control in patients with LN metastasis: 10-year LR control was achieved in 84% after postoperative EBRT—against 24% of those without. An updated study from this institute further substantiated the benefit of EBRT in improving LR control.<sup>16</sup> Similarly, a study of patients considered high risk (defined as microscopic residual disease, extraglandular invasion, or LN metastasis) reported that EBRT improved 10-year LR control to 86%—against 52% in those without.<sup>15</sup> Although EBRT improves LR control, it does not influence survival.<sup>14,15,21,23</sup> It is useful for reducing local relapse in those with elevated postoperative calcitonin.<sup>23</sup> In patients with local relapse, the rate of metastases was significantly higher than in those without local failure.<sup>14</sup> The therapeutic value of EBRT is being increasingly recognised when surgical excision is impossible or incomplete.<sup>24</sup> External beam radiation therapy can also improve LR control in those with an advanced thyroid primary tumour and those with LN metastasis. It should be administered to patients with locally advanced disease, for examples, pT4 disease or positive resection margins, large cervical LN metastasis or multiple LN metastasis. It is hoped that this will improve LR control and reduce the risk of distant failures.

#### **Mediastinal metastasis**

Upper mediastinal metastasis has been reported in 36% of patients if routine four-compartmental LN surgery is performed.<sup>25</sup> This was confirmed by this study: mediastinal metastasis/relapses caused death in 42.8% (3/7) of patients. Mediastinal metastasis occurs late in the clinical course, after a mean interval of 12.3 years after diagnosis. In view of the high (50%) frequency of mediastinal relapse following LN relapse and the high associated fatality rate, good LR control is crucial. Early EBRT may confer a benefit to reduce LR failure and prevent mediastinal metastasis. The volume of coverage should include the superior mediastinum. With advances in radiation planning techniques, eg 3-D conformal technique, intensity-modulated radiation therapy, radiation doses to critical organs, such as the lungs and spinal cord, can be minimised.

#### **Stage I disease (pT1N0M0)**

Stage I disease is associated with an excellent prognosis, almost 100% following surgery. All three patients with pT1N0/Nx disease in this series underwent total thyroidectomy, and were alive with no disease at the last follow-up. This is in accordance with other studies showing that disease stage is a significant factor in predicting survival.<sup>10,11</sup>

#### **Chemotherapy**

Chemotherapy, such as DTIC, 5FU, and adriamycin, has been used in several studies, but has been unsuccessful in most cases.<sup>11,12,26-28</sup> This was confirmed by this study: no patient showed any clinical or radiological response. The lack of a clinical response and significant toxicity of DTIC and 5FU combination discouraged further trial of these agents in our patients.

#### **Follow-up of patients by serum calcitonin**

The incidence of postoperative hypercalcaemia ranges from 27% to 65%,<sup>9,29,30</sup> and is associated with a higher recurrence rate and decreased survival.<sup>11,31</sup> It can be nonetheless extremely difficult to localise the site of relapse, despite the availability of current imaging modalities like magnetic resonance imaging, computed axial tomography scanning, ultrasonography, and selective venous sampling. Positron emission tomography scanning has been reported useful by some recent case reports.<sup>32</sup> Re-operation by microdissection is advocated by some centres, while a conservative approach adopted by others. The former consider re-operation a safe and helpful means to identify recurrence, with normalisation of basal calcitonin and stimulated calcitonin achieved in 45%<sup>25</sup> and 38%<sup>33</sup> of patients, respectively. The latter base their conserva-

tive approach on the evidence that raised postoperative calcitonin is compatible with long-term survival. In the Mayo Clinic series, re-operation increased complications, and normalisation of calcitonin was achieved in no patients (n=11).<sup>34</sup> Re-operation thus remains a controversial decision. A report from the Royal Marsden Hospital, London, stated that EBRT significantly improved the 20-year local recurrence-free survival from 30% to 66%,<sup>23</sup> but did not improve overall survival and had no consistent effect on serum calcitonin level.

In our series, four patients with mildly raised serum calcitonin (9.7-384 pmol/L) underwent extensive search by imaging studies, and no sites of recurrence could be identified. These patients were alive without disease or symptoms at 1.6 to 21.3 years (mean, 9.5 years) after detection of hypercalcaemia. These patients will continue to be monitored regularly by imaging studies.

#### Screening and prophylactic thyroidectomy

Patients with MTC have an excellent prognosis if diagnosed early and should thus be tested for germline mutation of the *RET* protooncogene so that, if present, family members can be likewise screened. Carriers of *RET* germline mutation warrant close follow-up and prophylactic thyroidectomy. In a study of 207 carriers from 145 families (EUROMEN study),<sup>35</sup> age-related progression from C-cell hyperplasia to MTC and then LN metastasis was observed. For codon 634 mutation, the mean age at surgical diagnosis of C-cell hyperplasia, MTC, and LN metastasis was 6.9, 10.1, and 16.7 years, respectively. No LN metastasis was observed before 14 years old and the risk increased to 42% at 20 years of age. Since LN metastasis adversely affects the prognosis in MTC, prophylactic surgery should be performed before progression to the stage of LN metastasis.

#### Conclusion

Medullary thyroid carcinoma is a rare thyroid malignancy in Hong Kong Chinese patients. Older age (>45 years) is associated with a poorer outcome. Appropriate treatment is total thyroidectomy with consideration for prophylactic LN dissection by expert surgeons. Small-sized tumour following surgery with no LN metastasis (T1N0) shows an excellent prognosis. In patients at high risk of LR relapse (eg large LN metastasis or multiple LN metastasis), extrathyroidal extension, or at high risk of postoperative residual disease (eg pT4 disease and/or positive margins), EBRT can improve LR control.

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