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# Microsurgical Lymph Node Dissection for Metastatic Asymptomatic C-Cell Carcinoma

Heinz J. Buhr,\* Friedrich Kallinowski,\* Friedhelm Raue,† and Christian Herfarth\*

*In persistent, clinically inapparent medullary thyroid carcinoma, microsurgical dissection of all lymph node compartments of the neck was performed. Between August 1988 and September 1991, 28 cases (mean age 43.3 years) were treated with 38 surgical interventions. Twenty patients had the sporadic form and eight patients the familial form. Unilateral neck dissection resulted in normalization of serum calcitonin (CT) levels even after pentagastrin stimulation in two patients whereas 16 patients exhibited abnormal CT stimulation tests. Eight of ten patients who had bilateral neck dissections had positive pentagastrin test results after surgery. The main postoperative complications included loss of local cutaneous sensation, generally temporary, and unilateral recurrent laryngeal nerve paralysis. (Henry Ford Hosp Med J 1992;40:268-70)*

Approximately 30 new cases of medullary thyroid carcinoma (MTC) are observed per 1 million population in the Federal Republic of Germany. MTC, representing between 5% and 10% of the malignant diseases of the thyroid, is a relatively rare disease. However, it exhibits several unique biological features. The surgical treatment of metastasizing but clinically occult MTC is based on these biological features:

1. Early metastases are noted in regional lymph nodes of the neck and the mediastinal area, followed by a long interval before distant metastases become obvious (1). During family screening, Wells et al (2) detected lymph node metastases in 50% of the patients with elevated basal calcitonin (CT) levels. In patients with clinically detectable tumor masses, this rate increased to 71%.

2. The node status is of prognostic relevance (3-5). The classic data by Woolner et al (6) indicate 10-year survival rates of 85% in patients without lymph node metastases, which is not significantly different from that of an apparently healthy cohort. In patients with lymph node metastases, survival dropped significantly to 42%.

3. MTC is almost radio- and drug-resistant.

The only potentially curative therapeutic modality is the complete surgical removal of tumor tissue including diseased regional lymph nodes. Consequently, Tisell et al (7) introduced the en-bloc-dissection of the lymphatic tissue of the neck and mediastinal area into the therapy of MTC. Using this method and employing microsurgical techniques, all lymph node compartments of the central and lateral neck areas and the mediastinal lymphatic tissue are removed.

## Methods

In our study, all 28 patients exhibited occult metastases in regional neck lymph nodes as demonstrated by abnormal basal or pentagastrin-stimulated CT levels. Imaging techniques (ultra-

sound, computed tomography) failed to visualize the involved lymph nodes. Preoperatively, selective venous catheterization was performed. Using this technique (8), a concentration peak indicative of the site of CT production was obtained suggesting which side of the neck to perform the primary microdissection using Tisell et al's method (7). A complete dissection of all lymphatic tributaries sparing the carotid artery, the jugular vein, and all nerves was achieved with the help of microsurgical techniques. During a single operative session, only one side of the neck was dissected in order to avoid an excessive duration of surgery (9). The mean time required for an operation was 6 hours (range 4 to 8 hours). The anatomical landmarks for the dissection included laterally the edge of the trapezius muscle, proximally the mandible or dorsally the occiput, caudally the subclavian vein, and towards the mediastinum the brachiocephalic vein.

## Patients

Between August 1988 and September 1991, we treated 28 patients (15 males, 13 females) with persistently occult MTC using these techniques. The mean age was approximately 43 years (range 14 to 65 years). A total of 38 neck dissections were performed on these 28 patients. Twenty patients had sporadic MTC and eight had familial MTC (multiple endocrine neoplasia type 2 [MEN 2] syndrome). A total of 28 neck dissections were performed in the 20 patients with the sporadic form (mean age 47 years). The average interval between primary thyroidectomy and the microsurgical lymph node dissection was 1.1 years. The

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eight MEN 2 patients (mean age  $34.5 \pm 6$  years) had 10 surgical interventions with a mean interval between thyroidectomy and lymph node dissection of 6.2 years. A cure is defined as a normal CT value after pentagastrin stimulation.

## Results

### Unilateral neck dissection/sporadic form

One of 12 patients with sporadic MTC was cured. Eleven patients exhibit persistently elevated serum CT values, some basally and some only after pentagastrin stimulation.

### Unilateral neck dissection/MEN 2

One of six MEN 2 patients had a normal CT response after stimulation whereas five patients exhibited a pathological elevation.

In the 16 sporadic and MEN 2 patients with abnormal postoperative pentagastrin stimulation tests, basal serum CT concentrations were normal in 12 patients (up to  $0.3 \mu\text{g/L}$ ); two patients had values below  $0.1 \mu\text{g/L}$ ; and 10 patients had values between  $0.1$  and  $0.3 \mu\text{g/L}$ . Slightly elevated basal serum CT levels were observed in four patients.

### Bilateral neck dissection/sporadic form

Postoperative serum CT levels of two of eight patients were within normal limits both basally and after pentagastrin stimulation whereas the values of six patients were above the normal range after stimulation.

### Bilateral neck dissection/MEN 2

Both patients exhibit elevated serum CT levels after pentagastrin stimulation.

### Group results

It should be noted that a marked postoperative reduction of the basal and stimulated CT levels was achieved in all patients, even in those eight with persistently abnormal pentagastrin stimulation tests.

The Table lists the lymph node compartments involved in all 38 patients. MTC was detected in the lateral neck and mediastinum in two of four patients with normal postoperative pentagastrin stimulation tests. A high percentage of patients with elevated CT levels had lymph node metastases in the lateral neck and the mediastinal compartments.

Postoperatively, several patients had complications which were mostly transient in nature. Most common were cutaneous nerve lesions which were transient and attributable to the meticulous dissection over a wide distance, compression by retractors, and similar factors. The loss of cutaneous nerve function was only partial; function was generally regained within the first three months after hospital discharge.

The second most common side effect, permanent hypoparathyroidism, was observed in only one patient. Intraoperatively, it was difficult to preserve the vascular pedicle of at least one parathyroid gland due to excessive scarring caused by previous operations. In these cases, the glandular tissue was identified by analysis of frozen sections and replanted into the sterno-

**Table**  
**Lymph Node Compartments Found to be Involved**  
**After 38 Microsurgical Neck Dissections**

Compartment	Calcitonin*	
	Within Normal Limits	Elevated
Central	2	21
Lateral	2	18
Mediastinal	2	15

\*Calcitonin indicates postoperative serum calcitonin concentrations after pentagastrin stimulation.

cleidoid musculature. Transient hypoparathyroidism was usually mild and short-lasting. Ten patients exhibited delayed closure of the wound attributable to a lymphatic fistula in six patients. All fistulae were conservatively treated and closed spontaneously within two weeks. In one patient, excessive postoperative bleeding required surgical intervention. Two patients developed unilateral palsy of the recurrent nerve.

## Discussion

MTC is a rare disease with characteristic biological features. National and international tumor registries facilitate research efforts to expand our knowledge of these biological properties (10,11). However, little experience has been gained in the successful treatment of occult metastatic MTC. There is clear evidence that measurements of the specific tumor marker CT permit the evaluation of the completeness and the success of any surgical intervention (12-16). Elevated basal or pentagastrin-stimulated CT values after primary surgery (thyroidectomy) indicate persistent disease. In most cases, occult metastases undetectable by available imaging techniques are responsible for abnormal CT levels. Selective venous catheterization can aid in the site-selection for further treatment. Elevated postoperative CT levels have been demonstrated to influence the prognosis (5). If it is possible to normalize serum CT concentrations, a favorable outcome can be expected (17). Tisell et al (7) have used microsurgical techniques to achieve complete lymph node dissections. Experience to date suggests that this method holds the greatest potential for cure. Following this rationale, we treated 28 patients with elevated pentagastrin-stimulated CT levels who had already received a total thyroidectomy as the primary therapy. The metastases could not be detected with available imaging techniques. In four of these 28 patients, microsurgical lymph node dissection achieved a biochemical cure as evidenced by the normalization of the pentagastrin stimulation test. The complication rate was not excessive. Cutaneous nerve lesions which comprised the majority of postoperative complications usually disappeared within several months after surgery (18). Further follow-up is necessary to determine whether a potential increase in cure rates by the microsurgical lymph node dissection outweighs the possible complications of surgery. Tisell's technique resulted in normalization of basal and pentagastrin-stimulated CT levels even years after the primary diagnosis of metastatic MTC, and a significant reduction of the tumor burden is

achieved by the extensive microsurgical lymph node dissection. Whether or not we will observe the long-term cures reported by Tisell et al (7) remains to be determined because of the limited postoperative observation period.

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