The Surgical Management of Medullary Thyroid Cancer

Alan P.B. Dackiw, MD, PhD

KEYWORDS

• Medullary thyroid cancer • Treatment guidelines
• Evidence-based treatment • Surgical techniques
• DNA testing • Prognosis • Thyroidectomy

Medullary thyroid cancer (MTC), accounts for approximately 5% to 10% of all thyroid cancers and arises from the parafollicular thyroid C cells, neuroendocrine cells that produce calcitonin, and carcinoembryonic antigen. MTC may occur either as a sporadic event (75%) or secondary to a germline mutation of the RET proto-oncogene (25%) with an autosomal dominant pattern of inheritance and almost complete penetrance. Critical to treatment of this disease is complete surgical resection because MTC cells do not take up iodine and thus iodine-131 therapy is ineffective.[1] Total thyroidectomy is the recommended treatment in all patients with MTC. Because lymph node metastases frequently occur in the central compartment of the neck, central neck dissection, defined as removal of all fibrofatty and lymphatic tissue from the hyoid bone to the innominate vessels, between the internal jugular veins is indicated.

Over the last decade, significant advances in the understanding of the biology and clinical outcomes of MTC have been made, culminating most recently in the publication of treatment guidelines by the American Thyroid Association.[2] The MTC expert panel followed an evidence-based approach because the lack of randomized clinical trial data for MTC limits the ability to form strong consensus recommendations on key issues.

Recommendation levels followed by this esteemed panel include;

"A" STRONGLY RECOMMENDS

The recommendation is based on good evidence that the service or intervention can improve important health outcomes. Evidence includes consistent results from well-designed, well-conducted studies in representative populations that directly assess effects on health outcomes.

Division of Endocrine and Oncologic Surgery, Department of Surgery, Section of Endocrine Surgery, Johns Hopkins Hospital, Johns Hopkins University School of Medicine, 600 North Street, Blalock 606, Baltimore, MD 21287, USA
E-mail address: adackiw1@jhmi.edu

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"B" RECOMMENDS

The recommendation is based on fair evidence that the service or intervention can improve important health outcomes. The evidence is sufficient to determine effects on health outcomes, but the strength of the evidence is limited by the number, quality, consistency of the individual studies, generalizability to routine practice, or indirect nature of the evidence on health outcomes.

"C" RECOMMENDS

The recommendation is based on expert opinion alone.

Among the most important, recommendations 61 to 64 address the extent of surgery in typical cases of MTC.

RECOMMENDATION 61

Patients with known or highly suspected MTC with no evidence of advanced local invasion by the primary tumor, no evidence cervical lymph node metastases on physical examination and cervical ultrasound, and no evidence of distant metastases should undergo total thyroidectomy and prophylactic central compartment (level VI) neck dissection (Grade B recommendation).

Prophylactic lateral neck dissection was omitted (Recommendation 61, Grade B). In discussion, the panel recognized a minority view that considers prophylactic ipsilateral modified neck dissection as a possible option. The data supporting this treatment recommendation are discussed later in further detail. Results of preoperative neck ultrasound and biopsy strongly influence the extent of surgery.

RECOMMENDATION 62

Patients who have MTC with suspected limited local metastatic disease to regional lymph nodes in the central compartment (with a normal ultrasound examination of the lateral neck compartments) in the setting of no distant (extracervical) metastases or limited distant metastases should typically undergo a total thyroidectomy and level VI compartmental dissection. A minority of the Task Force favored prophylactic lateral neck dissection when lymph node metastases were present in the adjacent paratracheal central compartment (Grade B recommendation).

Hence, the finding of positive central and negative lateral nodes typically would be treated with total thyroidectomy and level VI dissection only (Recommendation 62, Grade B).

There is some controversy as to the recommended extent of lymph node dissection in patients presenting with a palpable nodule diagnosed on fine needle aspiration (FNA) cytology to be MTC. In a recent report, more than 80% of patients referred with persistent or recurrent MTC were judged to have had an inadequate initial operation.[3] More than 50% of patients have persistently elevated calcitonin levels after initial surgery for MTC.[4,5] As noted earlier, standard surgical treatment for patients diagnosed with MTC is total thyroidectomy and central compartment lymph node dissection. Controversy exists as to the requirement for a unilateral lateral neck lymph node dissection or bilateral lateral neck lymph node dissection.

In general, for patients with familial or sporadic MTC with clinical evidence of regional metastatic disease, compartment-oriented neck dissection in a systematic fashion is advocated.[6] In patients with familial MTC and an elevated basal calcitonin level or a thyroid nodule palpable on physical examination or visualized on ultrasonography, total thyroidectomy with central compartment lymphadenectomy and bilateral