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Original Article

The Role of Prophylactic Parathyroidectomy during Thyroidectomy for MTC in Patients with MEN2A Syndrome

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Abstract

Aim: To define the role of prophylactic parathyroidectomy in the surgical treatment of medullary thyroid carcinoma (MTC) in multiple endocrine neoplasia type IIa (MEN2A) syndrome through a literature review.

Materials and methods: The database of PubMed was searched using the terms "parathyroidectomy" and "medullary" in the fields "Title" and "Abstract", as well as the Google Scholar database. Articles without references to parathyroid management strategies were mainly excluded.

Results: Fourteen articles were reviewed as relevant to this study regarding recommendations for the management of parathyroids during prophylactic thyroidectomy in patients with MTC in MEN2A syndrome. Three of them had the same or similar purpose to our work, and the most recent literature review did not clearly support either one of the two management strategies. References to parathyroid management were found in the rest of the articles, but their purpose was not to determine the appropriate management strategy. The majority of the authors support the preservation of macroscopically normal parathyroid glands, while one study favored routine total parathyroidectomy and autografting.

Conclusions: Although there does not seem to be a gold standard, the strategy of preserving macroscopically normal parathyroid glands with routine lab testing and surgical exploration for hyperparathyroidism during thyroidectomy seems to be a safe and effective strategy.

Keywords

medullary, MEN2A, parathyroidectomy

INTRODUCTION

It is widely accepted that asymptomatic carriers of the RET oncogene need to be treated with prophylactic total thyroidectomy.[1,2] In MEN2B patients, MTC develops in infancy, while in MEN2A, it usually develops later in childhood and early adulthood.[3]

Primary hyperparathyroidism (PHPT) in multiple endocrine neoplasia (MEN) type IIa is rare and occurs in about 20% to 30% of patients.

The concern of most endocrine surgeons after total parathyroidectomy and autotransplantation is postoperative hypoparathyroidism and this is the reason why most of them leave seemingly normal parathyroid glands in situ when performing thyroidectomy in patients with MEN2A syndrome.[4,5] However, patients with MEN2A syndrome run two potential risks. One is the development of hyperparathyroidism after surgery for MTC. If the parathyroid glands are not initially removed, a reoperation will be needed. If autotransplantation is performed, abnormal parathyroid glands can be removed without complications, such as possible recurrent laryngeal nerve damage. Another risk is a recurrence of medullary carcinoma. If the parathyroids are left intact, they are more likely to be removed during reoperation leading to permanent hypoparathyroidism.[5]

AIM

The present work is a narrative review of the respective literature that aims to highlight the role of prophylactic parathyroidectomy in the surgical treatment of patients diagnosed with MTC, which manifests in patients with MEN2A syndrome.

MATERIALS AND METHODS

The literature search included searching the database of the PubMed website, using the terms "parathyroidectomy" and "medullary" in the fields "Title" and "Abstract". The Google Scholar page was utilized too.

Particular emphasis was placed on reviews, systematic reviews, meta-analyses, and articles expressing conclusions about the management of parathyroids during MTC surgery in patients with MEN2A syndrome and the outcome of each approach. We also took into account articles that make suggestions for parathyroid management during therapeutic thyroidectomy for MTC in patients with diagnosed or suspected MEN2A syndrome. Articles not relevant to the aim of our study or articles that are cited by reviews or meta-analyses have been mainly excluded.

RESULTS

Our search yielded a total of 668 articles. Fourteen articles were considered relevant to our study. These articles address recommendations for parathyroid management during prophylactic thyroidectomy in patients with MTC in patients with MEN2A syndrome. Two of them were similar to the current work as considered by title, while three in total were considered similar by their aim. Only one out of these articles was a comparative study between parathyroidectomy with autotransplantation and conservative strategy **(Table 1)**.

In the study of Decker et al.[6], which is a study on the need for autotransplantation of parathyroids in prophylactic surgery for MEN2A syndrome after genetic testing, 36 children (aged 1 month to 12 years) from 4 MEN-IIa kindreds at risk of disease underwent genetic testing. Mutation analysis was performed using a highly sensitive PCR-based denaturation gradient gel electrophoresis technique. Serum parathyroid hormone or calcium concentrations were identified before surgery. Eighteen of these children were tested positive for the MEN-IIa mutation. Of these, 11 underwent prophylactic thyroidectomy at the age of 2 to 12 years (average 7.5 years). In any case, no preoperative biochemical signs of hypercalcemia were found and all parathyroid glands were identified as completely normal upon examination. The glands were carefully preserved and left intact. Postoperatively, 10 of the 11 children retained normal serum calcium, allowing discharge within 24 to 36 hours. The authors concluded that although total thyroidectomy is the indicative treatment, the need for routine parathyroidectomy and autotransplantation as previously described in these asymptomatic children is to be questioned, especially given the low incidence of hyperparathyroidism in MEN-IIa (10%-20%). They concluded also that the alternative method of in situ preservation of the parathyroid glands was a safe choice and could be achieved without compromising the completeness of the thyroidectomy. This conservative approach is considered to prevent the potential morbidity associated with total parathyroidectomy and autotransplantation. However, this study was not comparative.

A study of the long-term function of parathyroid glands after total parathyroidectomy and autotransplantation was performed by Yoshida et al.[5] Between 1994 and 2006, twelve patients with MEN2A syndrome underwent therapeutic total or complementary thyroidectomy and lymph node dissection at least in the central compartment for medullary thyroid carcinoma. Total or complementary parathyroidectomy with autotransplantation was performed with the aforementioned operation. The patients were all adults over the age of 25, with a median age of 48.5 years. They consisted of 5 males and 7 females from 8 families. The mean number of self-transplanted parathyroid glands per patient was 3. Serum calcium and parathormone levels remained stable at a 107-month follow-up in all patients except for one who died of advanced medullary carcinoma of the thyroid the following year. The authors concluded that total parathyroidectomy with autotransplantation at the time of initial surgery for medullary carcinoma (total thyroidectomy with bilateral central neck exploration) was a feasible approach to the management of hyperparathyroidism. This is perhaps the only systematic study that, while not comparative, supports routine parathyroidectomy and parathyroid gland autotransplantation. However, it consisted of a sample of twelve patients and there was no comparison of results with a parathyroid conservation group.

Moley et al.[3] conducted a comparative parathyroid management study after prophylactic thyroidectomy for medullary carcinoma of the thyroid in patients with ME-

Table 1. Articles relative to our study

ARTICLE TITLE	TYPE	SUPPORTS
Fitzpatrick LA.[7] Hypercalcemia in the multiple endocrine neoplasia syndromes. 1989	Review	individualization
Block MA.[8] Surgical treatment of medullary carcinoma of the thyroid. 1990	Review	preservation
Raue et al.[9] Primary hyperparathyroidism in multiple endocrine neoplasia type 2A. 1995	Retrospective study/ Review	preservation
Kraimps et al.[16] Primary hyperparathyroidism in multiple endocrine neoplasia type IIa: retrospective French multicentric study. 1996	Retrospective multicentric study	preservation
Decker et al.[6] Prophylactic surgery for multiple endocrine neoplasia type IIa after genetic diagnosis: is parathyroid transplantation indicated? 1996	**Prospective study**	**preservation**
Arts et al.[17] Prophylactic total thyroidectomy in childhood for multiple endocrine neoplasia type 2A: preliminary results. 1999	Retrospective study	preservation
Brandi et al.[18] Consensus: guidelines for diagnosis and therapy of MEN type 1 and type 2. 2001	Review	individualization/preservation
Szinai et al.[19] Review of multiple endocrine neoplasia type 2A in children: therapeutic results of early thyroidectomy and prognostic value of codon analysis. 2003	Meta-analysis	not mentioned - probably preservation
Akerstrom et al.[20] Surgical management of MEN-1 and 2: state of the art. 2009	Review	preservation
Zhou et al.[24] Diagnosis and surgical treatment of multiple endocrine neoplasia. 2009	Retrospective study	individualization/ preservation
Yoshida et al.[5] Long-term parathyroid function following total parathyroidectomy with autotransplantation in adult patients with MEN2A. 2009	**Prospective study**	**parathyroidectomy**
Moley et al.[3] Management of the parathyroid glands during preventive thyroidectomy in patients with multiple endocrine neoplasia type 2. 2015	**Comparative study**	**inconclusive**
Tonelli et al.[25] Surgery in MEN 2A patients older than 5 years with micro-MTC: outcome at long-term follow-up. 2016	Retrospective study	preservation
Iacobone et al.[26] Surgical approaches in hereditary endocrine tumors. 2017[26]	Review	preservation

N2A syndrome. Between 1993 and 2000, prophylactic thyroidectomies were performed on 50 patients with MEN2A (group A). All patients underwent CND in combination with total parathyroidectomy and autotransplantation of parathyroid fragments in the non-dominant forearm or the neck. From 2003 to 2015, when the study was published, 102 prophylactic thyroidectomies had been performed in an attempt to preserve the parathyroid glands with an intact vascular stem (group B). Individual parathyroid fragments were self-transplanted only in the case that they could not be preserved intact. Central cervical exploration was performed only if serum calcitonin was greater than 40 pg/mL, as data indicate that central lymph node metastases are unlikely in patients with basal calcitonin levels below 40 pg/mL and due to hypoparathyroidism in 6% of group A children. This strategy was effective in preventing hypoparathyroidism in most patients of group B patients. Permanent hypoparathyroidism occurred in 3 (6%) of the 50 group A patients, compared to 1 (1%) of the 102 group B patients (p=0.1). After total thyroidectomy, no patient in either group developed hyperparathyroidism. Immediate postoperative levels of serum calcitonin were found within the normal range (<5 pg/ml) in 100 of the 102 patients in group B. None of the patients in either group died. The conclusion was that in patients with MEN2A who had been treated with preventive total thyroidectomy, routine total parathyroidectomy with autotransplantation and central lymph node dissection gave excellent long-term results. However, maintaining parathyroids in situ during prophylactic thyroidectomy in combination with selective central lymph node clearance based on preoperative serum calcitonin levels is an effective and safe alternative that leads to a very low incidence of hypoparathyroidism. Therefore, none of the two strategies is favored over the other.

Other studies have also mentioned parathyroid management; however, their main purpose was not to determine the appropriate strategy and there was heterogeneity of their methods that are described.

A Fitzpatrick[7] review of hypercalcemia in multiple endocrine neoplasms suggests that hyperparathyroidism approach in MEN-2 (2A) should be individualized during surgery for MTC, while the review of MA Block[8] for the treatment of MTC individually or in the context of MEN syndromes concludes that subtotal parathyroidectomy is usually required if there is obvious clinical hyperparathyroidism, while it is unjustifiable in normocalcemic patients. During thyroidectomy, attention should be paid to the preservation of normal parathyroid glands and removal of hyperplastic glands.

Raue et al.[9] conducted a retrospective study of primary hyperparathyroidism between 1972 and 1993, acknowledging that the low incidence of MEN 2A-related PHPTs has not allowed the establishment of a well-defined treatment strategy for the treatment of this condition. When referring to the management of the parathyroid glands during thyroidectomy for medullary carcinoma in patients with MEN2A syndrome, they also referred to opinions from previous studies. Specifically, some researchers have suggested total parathyroidectomy with autotransplantation to all patients with MEN2A syndrome who are about to undergo thyroidectomy for medullary carcinoma.[10,11] This recommendation[11] was based on the incidence of parathyroid hyperplasia and the risk of permanent hypoparathyroidism after total thyroidectomy. According to Raue et al., this comes in contrast to the conclusions of Gagel et al.[12], who investigated affected relatives in the first two decades of life compared to early-stage medullary thyroid cancer, and did not find any evidence of parathyroid hyperplasia, or PHPT development in a 10-year follow-up. They also mention that routine excision of one or more parathyroid glands at the time of thyroidectomy is possible to have delayed the onset of clinically apparent hyperparathyroidism. Based on the results of this and other studies, they conclude that annual monitoring of serum calcium and serum PTH levels (if serum calcium is elevated) are sufficient for early diagnosis of parathyroid adenoma in MEN2A syndrome, citing also Calmettes et al.'s study.[13] This is also recommended for patients who underwent a total thyroidectomy for possible medullary carcinoma. Without any biochemical or clinical evidence of parathyroid adenoma, routine subtotal parathyroidectomy is unnecessary. If the diagnosis is made preoperatively, every parathyroid gland should be identified and the abnormal parathyroid glands should be removed. However, regular subtotal resection is considered not necessary because of low rates of recurrence. The majority of patients with MEN 2-associated parathyroid adenoma have mild disease and serum calcium levels below 3 $mmol^{-1}$ and no renal impairment. It is reported that they could be classified as asymptomatic based on the NIH Consensus Conference on the Diagnosis and Management of Asymptomatic PHPT.[14] These patients can be safely monitored without a need for operation. This is considered to be particularly important in patients over 50 years of age with persistent medullary carcinoma. Therefore, a more conservative approach is justified by selective resection of only abnormal parathyroids. Other authors, according to Raue et al., have suggested that the surgical approach should be individualized.[15]

Regarding the retrospective study of Raue et al.[9], it was based on cases recorded by the EUROMEN group (nine participating centers) from 1972 to 1993. PHPT characteristics were examined in 67 patients (41 women, 26 men) with MEN2A. All patients underwent surgical exploration of the neck: parathyroid adenoma was confirmed biochemically and/or histologically. The median age at the time of the diagnosis was 38 years. Parathyroid adenoma and MTC were diagnosed simultaneously in 75% of patients, while in 4%, parathyroid adenoma had been diagnosed earlier. Parathyroid adenoma was diagnosed postoperatively in 18% of patients and after pheochromocytoma was diagnosed in 3% of them. Primary hyperparathyroidism was asymptomatic in 84% of patients, while 15% suffered from kidney stones. Serum calcium was found elevated in 69% (2.9 ± 0.2 $mmol^{-1}$) and normal in 16% of subjects. Forty-two percent of patients underwent a single adenoma resection, 31% received a subtotal parathyroidectomy, and 16% – a total parathyroidectomy with autotransplantation. Regardless of the extent of the resection, treatment was successful in 94% of patients, but 13% of them developed hypoparathyroidism, while hypercalcemia remained in 3% of them, and no information was available about another 3% of the patients. Hypercalcemia recurred in 12% of patients in an 8-year follow-up, although half of them had undergone total or superficial parathyroidectomy. In conclusion, parathyroid adenoma associated with MEN2A syndrome is characterized by a mild and mostly asymptomatic hypercalcemia that is much less aggressive than usual, easily treated, and rarely recurs. Thus, most cases can be treated by a simple resection of the enlarged parathyroid gland. It should be noted that there is no specific reference to the management of parathyroids during thyroidectomy for medullary carcinoma; however, avoiding parathyroidectomy due to a lack of clinical or biochemical indications is indirectly advised as the strategy of choice.

Kraimps et al.[16] conducted a multicentric study on the treatment of primary hyperparathyroidism in patients with MEN2A syndrome, proposing the removal of the enlarged parathyroid glands only due to its low incidence. Specifically, the aim of their work was to evaluate the clinical findings, surgical treatment, and outcomes in 56 patients with parathyroid adenoma affected among 249 MEN2A patients from 84 families by the Groupe d'Etude des Tumeurs á Calcitonine. This retrospective study was based on cases recorded by the GETC (20 participating centers) from 1969 to 1994. PHPT characteristics were examined in 56 patients (31 women, 25 men) with MEN2A. All but two underwent cervical exploration. The median age at diagnosis was 37.6 years. Parathyroid adenoma was diagnosed

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at the same time with MTC or pheochromocytoma in 43 patients (77%), while it was asymptomatic in 68% of them. Serum calcium levels ranged from 2.20 to 3.70 mmol/L (mean 2.82 mmol/L, normal 2.10–2.60 mmol/L). The number of parathyroid glands removed was 0 (n=2), 1 (n=24), 2 (n=5), >2 (n=12), and 4 (n=11). The findings of histopathological examinations (in the initial surgery) consisted of 24 adenomas, 4 double adenomas, and 25 hyperplasias. Treatment after initial surgery was achieved in 89%, with an incidence of hypoparathyroidism in 22%. There were 6 cases (11%) with persistent adenoma. In a median 6.4-year follow-up, five patients (9%) had recurrent parathyroid adenoma. The results of this study also suggest that MEN2A syndrome-associated parathyroid adenoma is generally associated with mild, often asymptomatic, hypercalcemia. In spite of the recurrences observed 5 to 15 years after the first cervical exploration, resection of only macroscopically enlarged glands appears to be generally sufficient. According to the authors, the routine subtotal or total parathyroidectomy with autotransplantation is associated with a higher rate of hypoparathyroidism. In the study, there is no specific reference to the management of parathyroids during thyroidectomy for medullary thyroid carcinoma; however, the maintenance of macroscopically normal parathyroids in patients with MEN2A syndrome is suggested once again.

The study of Arts et al.[17] for prophylactic total thyroidectomy in childhood was aimed at evaluating prophylactic total thyroidectomy at MEN2A gene vectors. This is a retrospective study on 14 carriers of the MEN2A gene who underwent prophylactic thyroidectomy (7 boys and 7 girls, median age 9.1 years, range: 4.8–14.7) from June 1993 to July 1997 at the Pediatric Surgery Department of the Wilhelmina Children's Hospital in the Netherlands. The median time between genetic testing and surgery was 5.5 months (range: 2–35). The parathyroid glands were identified and left intact as much as possible, while self-transplantation was performed twice due to doubts about viability. Outpatient follow-up was done every 3 to 6 months. One of the patients (a 13.4-year-old) developed macroscopic thyroid carcinoma, while the other 13 developed microscopic multifocal medullary thyroid carcinoma. In 11 of them, the carcinoma was bilateral and in 3, the surgical incisions were tumor-free. There was one case of temporary voice hoarseness, three cases of temporary hypocalcemia and two cases of permanent hypoparathyroidism. There was no hypocalcemia after the autotransplantation. The median follow-up was 3.2 years (range: 1 month–4.0 years). Mild psychological problems were observed in 4 patients and psychiatric problems in one patient. In conclusion, the authors recommended prophylactic total thyroidectomy during the first decade, while additional lymph node dissection and total parathyroidectomy were considered not necessary. To prevent possible postoperative hypoparathyroidism, autotransplantation of at least one parathyroid was recommended. Although the concern of the study was the results of thyroidectomy, total routine parathyroidectomy is suggested to be avoided.

In a review by Brandi et al.[18] aiming at establishing guidelines for the diagnosis and treatment of MEN1 and MEN2 syndromes, most cases of patients with parathyroid adenoma in multiple endocrine neoplasia syndrome had no symptoms, although hypercalciuria and renal stones could occur. It is reported more specifically that the adenoma is milder in MEN2A syndrome than in MEN1. The authors point out that the indications for parathyroid surgery (excision of enlarged glands only, subtotal parathyroidectomy, parathyroidectomy with autotransplantation) should not be different from those in other patients with the possibility of multiple parathyroid tumors. However, they report that during thyroid surgery in a MEN2A patient with normal serum calcium levels, the surgeon may encounter one or more parathyroid tumors and then the operation should be performed as if there is biochemical evidence of mild adenoma.

A meta-analysis by Szinai et al.[19] for multiple endocrine neoplasms type 2A in children analyzes the therapeutic effects of early thyroidectomy and the prognostic value of codon analysis. A 5.6% incidence of hyperparathyroidism is reported, but the management of parathyroid glands is not mentioned. The only element we could take into consideration is the low incidence of adenoma in the context of MEN2A syndrome. This article could have been considered as not relevant to our study, yet it was included as the most relevant meta-analysis,

Akerstrom et al.[20] conducted a review on the surgical treatment of MEN1 and MEN2 syndromes. The authors point out that the main concern in patients with MEN2A syndrome is the avoidance of hypoparathyroidism during thyroidectomy in combination with extensive lymph node dissection and that surgical management of parathyroid adenoma should aim to maintain parathyroid function, by citing their own literature review.[21,22] They mention that all parathyroid glands should be identified, but only the enlarged glands should be excised, although this is recommended to patients with the syndrome even if the patient is normocalcemic. When all four glands are enlarged, subtotal parathyroidectomy is performed, which is preferred to total parathyroidectomy with autotransplantation. According to the authors, the strategy during thyroidectomy is generally conservative and consists of leaving the normal parathyroid glands in situ and performing an autotransplantation only of the ischemic glands. If the normal parathyroid glands are unintentionally removed or are at risk during lymph node resection, they should be self-transplanted freely in the forearm in MEN2A cases (and in the sternocleidomastoid muscle in MEN2B cases).[23] They also point out that many cases of parathyroid adenoma develop several years after thyroidectomy as a result of solitary adenoma or polyadenous disease and can then be treated with a conservative strategy, removing only the abnormal glands.[9,23] The cure rate after a conservative approach to parathyroid surgery in MEN2A patients is 97% and 100%, while the recurrence rate is low (3%–5%).[9,21,22]

Zhou et al.[24] performed a retrospective study on the di-

agnosis and surgical treatment of multiple endocrine neoplasia syndromes. The clinical data of 95 MEN cases were analyzed retrospectively. There were 60 cases of MEN2A. Total thyroidectomy with bilateral lymph node dissection was performed in sixteen patients with MEN2A and enucleation of nodules in nine patients with persistently elevated calcitonin levels. At the same time, the enlarged parathyroid glands were resected and the pathological diagnosis was hyperplasia. Although there is no clear suggestion or specific conclusion for the management of the parathyroid glands, the authors chose to resect the macroscopically abnormal parathyroid glands and therefore leave normal parathyroids in situ.

Tonelli et al.[25] performed a retrospective study among patients with MEN2A between 1990 and 2010. It included 17 patients (9 men and 8 women) diagnosed with RET gene mutation after the age of 5 years who underwent surgery and were diagnosed with micro-MTC stage N0. The treatment was total thyroidectomy with central lymph node dissection, while bilateral examination of the parathyroid glands was performed in all cases. Because none of the patients were diagnosed with hyperparathyroidism, the parathyroid glands were preserved in all cases. Two of the patients were found to have temporary hypoparathyroidism, while none experienced permanent hypoparathyroidism or hyperparathyroidism at a mean follow-up of 16.6 years.

A review on surgical approaches to hereditary endocrine tumors was performed by Iacobone et al.[26] In their study, the authors mention that parathyroidectomy, if necessary, should be performed at the time of thyroidectomy for MTC. In patients without obvious parathyroid adenoma at the time of thyroidectomy for medullary carcinoma, prophylactic parathyroidectomy is not recommended, as in this case the main concern is not parathyroid adenoma but postoperative hypoparathyroidism due to parathyroid devascularization after level 6 lymph node dissection.

A retrospective study on prophylactic thyroidectomy in MEN2A syndrome in children was performed by Visier et al.[27] This was a clinical study aiming to describe the complications and long-term effects in patients with multiple endocrine neoplasm syndrome type 2A (MEN2A) who underwent prophylactic thyroidectomy, according to the recommendations of the American Thyroid Association (ATA). This retrospective study included 14 patients with MEN2A who underwent thyroidectomy between 2000 and 2017. Demographic, clinical, and imaging data were reviewed. Postoperative complications and long-term follow-up were analyzed. Eight boys and 6 girls with a mean age of 5 years (range 2–10) were treated. The predominant genetic mutation was due to codon 634 (8/14, 57.14%). All patients underwent total thyroidectomy (TT) without central neck dissection. An upper right parathyroidectomy was performed in a patient due to intraoperatively recognized enlargement. We therefore conclude that the parathyroid conservation strategy has been followed, although there is no specific reference to what management strategy they employ.

DISCUSSION

Our review of the literature did not yield any conclusive findings regarding the best approach to take when treating parathyroid glands during prophylactic thyroidectomy for medullary carcinoma in MEN2A syndrome patients. In fact, sometimes we encounter dichotomies. We acknowledge that the vast majority of surgeons seem to follow the conservative strategy; however, this does not result from randomized controlled trials and so there seems not to be a level 1 evidence-based suggestion. The most recent literature review being the only comparative one[3] does not reach a conclusion as to a suggestion for the ideal management strategy, while it presents both methods, that of total parathyroidectomy with autotransplantation and that of preservation of parathyroids, as equally safe alternatives.

It is clear, however, that most authors follow the conservative strategy as a safe alternative in terms of efficacy, given the low incidence of hyperparathyroidism in MEN2A syndrome, and as a strategy to avoid possible postoperative permanent hypoparathyroidism. Nevertheless, there have been studies that have shown that this serious postoperative complication is not so common. Moreover, one of them[5] suggested routine total parathyroidectomy with autotransplantation as the treatment of choice, emphasizing the risk of late onset hyperparathyroidism, in addition to the risk of recurrence of medullary carcinoma of the thyroid gland, which would lead to a reoperation that will make it difficult to further preserve the parathyroid glands.

Finding it challenging to establish a golden rule, we could assume that given the rarity of parathyroid adenoma in MEN2A syndrome, the maintenance of parathyroid glands, but with routine biochemical and operative screening, is an effective and safe strategy for the vast majority of the population. Besides the rarity of the phenomenon, it seems that hyperparathyroidism in MEN2A syndrome is clinically milder.[9,16,18] The identification of enlarged parathyroids during cervical exploration is quite important and equivalent to a biochemical diagnosis of hyperparathyroidism.[18,20] If normal parathyroid glands are unintentionally removed or are in danger during lymph node resection, they should be self-transplanted freely in the forearm in MEN2A cases and in the sternocleidomastoid muscle in MEN2B cases.[20,23] Annual serum calcium levels should be monitored and, if elevated, serum parathyroid hormone levels should also be checked for early diagnosis of hyperparathyroidism.[9,13]

At this point, it is worth mentioning an interesting finding by Castellano et al.[28] about serum calcitonin that can be elevated in some cases of sporadic hyperparathyroidism (a finding in 25 of 290 patients – 8.6%). This study is about sporadic primary parathyroid adenoma not in patients with MEN2A syndrome, but it could be studied as well in that context.

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CONCLUSIONS

Although there does not seem to be a gold standard, the strategy of macroscopically preserving normal parathyroid glands – with routine lab testing and surgical exploration for hyperparathyroidism during thyroidectomy – seems to be a safe and effective strategy. This conclusion is weak because of the heterogeneity of the studied articles. More information could be possibly acquired from randomized controlled trials in order to establish a level 1 evidence-based strategy.

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Competing Interests

The authors have declared that no competing interests exist.

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Роль профилактической паратиреоидэктомии при тиреоидэктомии по поводу МТР у пациентов с синдромом MEN2A

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Резюме

Цель: Определить роль в профилактической паратиреоидэктомии при хирургическом лечении медулярного тиреоидного рака (МТР) при синдроме множественной эндокринной неоплазии типа IIa (MEN2A) путём обзора литературы.

Материалы и методы: Поиск проводился в базе данных PubMed с использованием терминов „паратиреоидэктомия" и „медуллярный" в полях „Название" и „Реферат", а также в базе данных Google Scholar. Статьи без ссылок на стратегии лечения паращитовидной железы в основном исключались.

Результаты: Четырнадцать статей были рассмотрены как имеющие отношение к данному исследованию относительно рекомендаций по лечению паращитовидных желез во время профилактической тиреоидэктомии у пациентов с МТР при синдроме MEN2A. Три из них имели ту же или близкую цель, что и наша работа, и самый последний обзор литературы не подтвердил однозначно ни одну из двух стратегий управления. Ссылки на лечение паращитовидной железы были найдены в остальных статьях, но их целью не было определение соответствующей стратегии лечения. Большинство авторов поддерживают сохранение макроскопически нормальных паращитовидных желез, в то время как одно исследование отдаёт предпочтение рутинной тотальной паратиреоидэктомии и аутотрансплантации.

Заключение: Хотя золотого стандарта не существует, стратегия сохранения макроскопически нормальных паращитовидных желез с помощью рутинных лабораторных исследований и хирургического исследования гиперпаратиреоза во время тиреоидэктомии кажется безопасной и эффективной стратегией.

Ключевые слова

медуллярный, MEN2A, паратиреоидэктомия