

# SURGICAL PROCEDURES FOR NEUROENDOCRINE NEOPLASMS OF THE APPENDIX - A CONSENSUS GUIDELINE

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## ABSTRACT

**INTRODUCTION:** According to the consensus and the recommendations of the European Neuroendocrine Tumor Society (ENETS), the annual incidence rate of neuroendocrine appendicular tumours is 0.15-0.6/100000. They are little more common in women aged between 40 and 50 years. These neoplasms amount to 30-80% of all appendicular tumours. Their evolution is, usually, asymptomatic and they are diagnosed accidentally during conventional or laparoscopic appendectomy. In the past, the surgical approach used to depend on tumour localization. At present, this localization is not a decisive factor in the choice of a surgical approach. Our purpose was to demonstrate the consensus guideline and the recommendations of ENETS 2017 for surgical procedures in neuroendocrine appendicular neoplasms and to analyze the difference in the survival rate following various surgical interventions.

**MATERIAL AND METHODS:** Literature overview included studies dealing with the surgical treatment of the neuroendocrine appendicular neoplasms including the most recent consensus guideline of ENETS 2017 on the topic.

**RESULTS:** Our analysis revealed that according to ENETS 2017, tumour size, localization and tumour cell invasion into the mesoappendix determined the type and volume of surgical intervention. For tumours less than 1 cm (T1 according to ENETS pathological classification), a simple appendectomy was recommended. In T1 tumours, this surgical procedure resulted in 100% survival rate.

**CONCLUSION:** ENETS 2017 recommends to observe the last established consensus guideline despite the fact that the studies up-to-now do not show any significant difference in the survival rate after appendectomy because of a neuroendocrine tumour of the appendix and right hemicolectomy. *Scr Sci Med* 2017;49(3):11-14

**Keywords:** *neuroendocrine appendicular neoplasms, ENETS consensus guideline, appendectomy, right hemicolectomy*

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**Received:** July 21, 2017

**Accepted:** September 15, 2017

## INTRODUCTION

The annual incidence rate of neuroendocrine appendicular tumours is 0.15-0.6/100000 (1). They represent 30 to 80% of all appendicular neoplasms (1). They are little more common in women aged between 40 and 50 years. They are also observed in children aged between 4.5 and 19.5 years, however, there is no standardized population-based data for this age group yet. The prognosis of these neoplasms is good. In a series of studies, five-year survival rate

is 100% or close to 100% in highly-differentiated tumours (2,3). In large cohort studies involving tumours of varying degrees of differentiation, this rate is between 70% and 85% (4). However, it is much lower in patients at advanced stage of the disease and presenting with distant metastases. In such cases, it ranges from 12% to 28%.

Seventy percent of neuroendocrine appendicular tumours are located at the tip of the appendix (1). Their evolution is, usually, asymptomatic and they are diagnosed accidentally during conventional or laparoscopic appendectomy (5). They persist either asymptotically, or in the presence of metastasis. Besides they may exhibit symptoms associated with the localization of the metastases. Carcinoid syndrome is rarely observed with these neoplasms (6). There are no imaging studies characterized by high informative and specific probative value.

Somatostatin receptor imaging and positron emission tomography can be used to prove distant metastases. Chromogranin A is used as a laboratory tumour marker for an advanced disease, however, it is not validated for diagnosis and follow-up of these neoplasms yet.

According to consensus decisions and recommendations from the European Neuroendocrine Tumor Society (ENETS) 2011 and 2017, the size, localization and the tumor cell invasion into the mesoappendix determine the surgical therapy. Two surgical techniques are applicable to these tumours: simple appendectomy and oncological right hemicolectomy (1). The most recent recommendations and consensus guideline of March 2017 set out precise selection criteria for specific surgery which is the most appropriate one for these patients.

Our purpose is to present the consensus guideline and the recommendations of ENETS 2017 for surgical procedures in neuroendocrine appendicular neoplasms and to analyze the difference in the survival rate following various surgical interventions.

## **MATERIAL AND METHODS**

Literature overview includes studies about surgical treatment of neuroendocrine neoplasms of the appendix including the last consensus guideline of ENETS 2017 on the topic.

## **RESULTS**

Our analysis reveals that according to ENETS 2017, tumour size, localization and tumour cell invasion into the mesoappendix determine the type and volume of surgical intervention. For tumours less than 1 cm (T1 according to ENETS pathological classification), a simple appendectomy is recommended. In T1 tumours, this surgical procedure leads to 100% survival rate.

## **DISCUSSION**

Tumours sized between 1 and 2 cm (T2) prove to be a challenge for surgeons because of the risk of metastasis and/or relapse. Most often, metastases occur in tumours larger than 1.5 cm (7). Tumours sized above 2 cm (T3) are rare, less than 10% of all the neuroendocrine appendicular neoplasms. The risk of metastasis in T2 tumours reaches up to 40% (8,9). The European Neuroendocrine Tumors Society recommends oncological right hemicolectomy in T3 tumors. The tumours emerging from the appendix and infiltrating adjacent structures (T4) require systemic oncological evaluation including initial right hemicolectomy.

Sixty to 75% of the neuroendocrine appendicular neoplasms are located at the tip, 5 to 20% of them are placed in the middle, and only 10% of them are at the base of the appendix. There is no strict correlation between survival rate and tumour localization, however, it is assumed that the tumours at the appendicular base are more prone to metastasis (10,11).

An invasion into the mesoappendix is observed in up to 20% of adults and in up to 40% in children (12,13). An invasion of more than 3 mm results in a more aggressive course of the disease.

The oncological right hemicolectomy is recommended for tumours sized above 2 cm. In T1 tumours, the simple appendectomy is sufficient. However, this intervention is not sufficient in cases either when the tumour is located at the appendicular base, or when it infiltrates the mesoepithelium at a depth of more than 3 mm. In T2 tumours, lymph node locations as well as distant metastases are likely. Therefore, the simple appendectomy in these tumours is not always radical and the recurrence is common, especially in young subjects. The risk of relapse increases in tumours sized above 1.5 cm.

ENETS recommends oncological right hemicolectomy if one of the following criteria exists:

- ◆ moderately differentiated tumour (G2)
- ◆ vascular invasion (V1)
- ◆ lymphatic invasion (L1), and
- ◆ infiltration into the mesoappendix deeper than 3 mm.

In T3 tumours, oncological right hemicolectomy is performed either as an initial surgical intervention, or as a second intervention after initial appendectomy. The neuroendocrine appendicular carcinomas (G3) are treated as adenocarcinomas.

ENETS 2017 assumes that in tumours less than 2 cm, the appendectomy is sufficient, regardless of tumour location. Right hemicolectomy is justified only in cases of tumours sized 1 to 2 cm with positive or unclear resection margins, invasion into the mesoappendix, high proliferative index, or vascular invasion. Tumours sized more than 2 cm should be treated by oncological right hemicolectomy.

## CONCLUSION

Well-sized neuroendocrine appendicular tumours smaller than 1 cm do not require any follow-up. For tumours sized between 1 and 2 cm, follow-up is desirable, but not recommended. For tumours sized over 2 cm, mandatory follow-up at 6 and 12 months and then once yearly is recommended, although there is no strictly validated standard yet.

The neuroendocrine appendicular tumour is based on specific pathological and clinical criteria developed and recommended by the European Neuroendocrine Tumor Society. Despite currently available studies demonstrating the lack of significant difference in survival rates after appendectomy compared to right hemicolectomy, ENETS 2017 recommends to strictly observe the most recent established consensus.

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