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Review

SURGICAL PROCEDURES FOR NEUROENDOCRINE NEOPLASMS OF THE APPENDIX: A CONSENSUS GUIDELINE REVIEW

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Summary

According to the consensus and the recommendations of the European Neuroendocrine Tumor Society (ENETS), the frequency of appendicular neuroendocrine tumors (NETs) is 0.15-0.6/100 000 a year. They are found a little more often in women aged between 40 and 50. Neuroendocrine neoplasms of the appendix are about 30 to 80% of all appendicular tumors. Their evolution is usually asymptomatic. They are diagnosed accidentally during a conventional or laparoscopic appendectomy. In the past, the surgical approach used to depend on the localization of the tumor. Currently, its localization is not a significant factor in the choice of a surgical approach. Our purpose wass to present the consensus guideline and the recommendations of ENETS 2017 for surgical procedures in neuroendocrine neoplasms of the appendix and analyze the difference in the survival rate in different surgical interventions. The literature overview includes studies on surgical treatment of neuroendocrine neoplasms of the appendix and takes into consideration the last consensus guideline of ENETS 2017 on the topic. ENETS recommends a simple appendectomy in well-differentiated appendix tumors smaller than 2 cm, regardless of their localization. Right hemicolectomy is performed for in tumors sized between 1 cm and 2 cm with positive resection lines, with deep mesoappendiceal invasion, high proliferation activity (G2) and vascular invasion. For tumors over larger than 2 cm – right hemicolectomy is recommended. Although current studies have pointed out no significant differences in survival rates between appendectomy for neuroendocrine neoplasms of the appendix and right hemicolectomy, ENETS 2017 suggests that the latest consensus guidelines should be followed.

Key words: neuroendocrine neoplasms of the appendix, surgical procedures

Introduction

Neuroendocrine tumors (NETs) of the appendix represent 30 to 80% of all appendicular neoplasms [1]. The incidence of appendicular neuroendocrine neoplasms is 0.15-0.6/100 000 per year [1]. They are found a little more often in women aged between 40 and 50. Neuroendocrine neoplasms of the appendix are about 30 to 80% of all appendicular tumors. They are also seen in children between 4.5 and 19.5 years.

However, there is no standardized population-based data for this age group. The prognosis of neuroendocrine tumors of the appendix is good. In a series of studies, 5-year survival was 100% or close to 100% in tumors with high differentiation [2, 3]. In large cohort studies, involving tumors of varying degrees of differentiation, the 5-year survival rate is between 70% and 85% [4]. For advanced stages with distant metastases, the 5-year survival is low and ranges from 12% to 28%.

Seventy percent of NETs of the appendix 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 asymptomatically or in the presence of metastasis, and may present with symptoms associated with the localization of metastases. The carcinoid syndrome is rarely observed in case of NETs of the appendix [6]. There are no imaging studies that have highly 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 tumor marker for an advanced disease but is not validated for diagnosis and follow-up of NETs of the appendix.

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 type of surgical therapy. Two surgical techniques are applicable to NETs in the appendix: simple appendectomy and oncological right hemicolectomy [1]. The latest recommendations and consensus guideline of March 2017 set out precise criteria to choose between simple appendectomy and oncological right hemicolectomy.

The purpose of this review was to present the consensus guideline and the recommendations of ENETS 2017 for surgical procedures in neuroendocrine neoplasms of the appendix and analyze the difference in the survival rate after different surgical interventions.

Materials and Methods

The literature overview includes studies on surgical treatment of neuroendocrine neoplasms of the appendix, including the last consensus guideline of ENETS 2017 on the topic.

Discussion

According to ENETS 2017 tumor size, localization, and the tumor cell invasion into the mesoappendix determine the type and extent of surgical intervention. For tumors less than 1 cm (T1 according to ENETS pathological classification), a simple appendectomy is recommended. Studies have shown that simple appendectomy in T1 tumors leads to 100% survival.

Tumors sized between 1 and 2 cm (T2) prove to be a challenge for surgeons because of the risk of metastasis and/or relapse. Metastases occur most often in tumors over 1.5 cm [7]. Tumors above 2 cm (T3) are rare, less than 10% of all appendix NETs. The risk of metastasis in T2 tumors reaches 40% [8, 9]. ENETS recommends oncological right hemicolectomy in T3 tumors. NETs of the appendix emerging from it and infiltrating adjacent structures (T4) require systemic oncological evaluation, including initial right hemicolectomy.

Sixty to 75% of the NETs of the appendix are at the tip of the appendix, 5 to 20% in the middle, and only 10% at the base of the appendix. There is no strict correlation between survival and localization of the tumor, but it is assumed that the tumors at the base of the appendix are more prone to metastasis [10, 11].

Invasion into the mesoapappendix is observed up to 20% in adults, and up to 40% in children [12, 13]. Invasion of more than 3 mm is believed to result in a more aggressive course of the disease.

An oncological right hemicolectomy is recommended if tumors are larger than 2 cm. In T1 tumors, simple appendectomy is sufficient. However, the latter is not enough if the tumor is located at the base, or when it has infiltrated into the mesoepithelium to a depth of more than 3 mm. In T2 tumors, lymph node locations, as well as distant metastases are likely. Therefore, simple appendectomy in such cases is not

always radical, and recurrences are frequent, especially in young people. The risk of relapse increases in tumors of more than1.5 cm in size. In case of any of the following, i.e., moderately differentiated tumor (G2), vascular invasion (V1), lymphatic invasion (L1), and infiltration into the mesoappendix over 3 mm, ENETS recommends oncological right hemicolectomy.

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

ENETS 2017 assumes that if tumors are less than 2 cm in size, appendectomy is sufficient, regardless of the location of the tumor. Right hemicolectomy is justified only in cases of tumors 1 to 2 cm large, with positive or unclear resection lines, invasion into the mesoappendix, high proliferative index, or vascular invasion. Tumors of more than 2 cm should be treated by oncological right hemicolectomy.

Conclusions

Tumors smaller than 1 cm do not require follow-up. For tumors between 1 and 2 cm, follow-up is desirable, but not recommended. For tumors larger than 2 cm, follow-up is mandatory at 6 and 12 months, and then every year, although there is no strictly validated standard yet.

The surgical procedures applied to treat NETs of the appendix are based on specific pathological and clinical criteria developed and recommended by ENETS. Although currently available studies demonstrate lack of significant difference between survival rates following appendectomy for NETs of the appendix and these after right hemicolectomy, ENETS 2017 recommends abidance to the latest consensus established.

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