THE ROLE OF CONVENTIONAL ECHOENDOSCOPY (EUS) IN THERAPEUTIC DECISIONS IN PATIENTS WITH NEUROENDOCRINE GASTROINTESTINAL TUMORS

O papel da ecoendoscopia convencional nas decisões terapêuticas em pacientes com tumores neuroendócrinos gastrointestinais

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ABSTRACT - Background: Gastrointestinal neuroendocrine tumors are rare, usually presented as subepithelial or polypoid tumors. Accurate diagnosis and indication of the type of resection are still challenging. Aim: To determine the effectiveness of echoendoscopy in determining the depth of the lesion (T) identified by endoscopy in order to evaluate surgical and/or endoscopic indication, and to evaluate the results of endoscopic removal in the medium term. Methods: Twenty-seven patients were included, all of whom underwent echoendoscopy for TN tumor staging and the evaluation of possible endoscopic resection. The parameters were: lesion size, origin layer, depth of involvement and identified periloesional adenopathies. The inclusion criteria for endoscopic resection were: 1) high surgical risk; 2) those with NET <2 cm; 3) absence of impairment of the muscle itself, and 4) absence of periloesional adenopathies in echoendoscopy and in others without distant metastases. Exclusion criteria were: TNE >2 cm; those with infiltration of the muscle itself with periloesional adenopathies and distant metastases. The techniques used were resection with polypectomy loop; mucosectomy with saline injection; and mucosectomy with ligation with an elastic band. The anatomopathological study of the specimens included evaluation of the margins and immunohistochemistry (chromogranin, synaptophysin and Ki 67) to characterize the tumor. Follow-up was done at 1, 6 and 12 months. Results: Resections with polypectomy loop were performed in 15 patients; mucosectomy in five; mucosectomy and injection with saline in three and the remaining four were referred for surgery. The anatomopathological specimens and immunohistochemical analyzes showed positive chromogranin and synaptophysin, while Ki 67 was less than 5% among all cases. The medium-term follow-up revealed three recurrences. The average size of tumors in the stomach was 7.6 mm and in the duodenum 7.2 mm. Well-demarcated, hyperechoic, homogenous lesions occurred in 75%; mucosal layer in 80%; and the deep and submucosal mucosa in 70%. Conclusions: ECHOENDOSCOPY proved to be a good method for the study of subepithelial lesions, being able to identify the layer affected by the neoplasm, and better indicate the treatment option.

HEADINGS: Endosonography . Carcinoid Tumor. Carcinoma. Neuroendocrine.

RESUMO – Racional: Tumores neuroendócinos gastrointestinais são raros geralmente apresentados como tumores subepiteliais ou polipoides. O diagnóstico preciso e a indicação do tipo de reseção ainda são desafiadores. Objetivo: Determinar a eficácia da ecoendoscopia em determinar a profundidade das lesões (T) identificadas pela endoscopia e objetivos de avaliação do tipo cirúrgico e/ou endoscópico e avaliar os resultados da remoção endoscópica em seguimento em médio prazo. Métodos: Foram incluídos 27 pacientes todos submetidos à ecoendoscopia para estadiamento tumoral TN e à avaliação de possível reseção endoscópica. Os parâmetros estudados foram: tamanho da lesão, camada de origem, profundidade do acometimento e adenopatias periloesionais identificadas. Os critérios de inclusão para reseção endoscópica foram: 1) risco cirúrgico elevado; 2) aqueles com TNE <2 cm; 3) ausência de comprometimento da muscular própria; e 4) ausência de adenopatias periloesionais na ecoendoscopia e em outros sem metástases à distância. Os critérios de exclusão foram TNE >2 cm; aqueles com TNE >2 cm; e aqueles com comprometimento da muscular própria com adenopatias periloesionais e metástases à distância. As técnicas utilizadas foram: reseção com alça de polipectomia; mucosectomia com injeção de solução salina; e mucosectomia após a ligadura com banda elástica. O estudo anatomopatológico dos espécimes inclui avaliação dos margens e imunoistoquímica (cromogranina, sinaptofisina e Ki 67) para caracterizar o tumor. O seguimento foi feito com 1, 6 e 12 meses. Resultados: As reseções com polipectomia foram realizadas em 15 pacientes; mucosectomia em cinco; mucosectomia e ligadura com banda elástica em três e os quatro restantes foram encaminhados para cirurgia. O anatomopatológico dos espécimes e as análises imunoistoquímicas mostraram cromogranina e sinaptofisina positivas, enquanto que o Ki 67 foi menor que 5% em todos os casos. O seguimento em médio prazo revelou três recidivas. A média de tamanho dos tumores no estômago foi de 7,6 mm e no duodeno 7,2 mm. As lesões bem demarcadas, hiperecogênicas, homogêneas ocorreram em 75% da camada mucosa em 80% e da mucosa profunda e submucosa em 70%. Conclusões: A ecoendoscopia mostrou-se um bom método para o estudo de lesões subepiteliais, podendo identificar a camada acometida pela neoplasia, grau de invasão, ecogenicidade, heterogeneidade, tamanho da lesão e acometimento linfonodal periloesional e melhor indicar a opção de tratamento.

DESCRIPTORES: Endossenografía . Tumor carcinoide. Carcinoma Neuroendocrino.

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Mensagem central
Gastrointestinal neuroendocrine tumors have been “overtreated” in the recent past, and as such, there is a current trend towards directing more conservative treatments, such as polypectomies and/or mucosectomies. Many studies have shown that the successful removal of small tumors with mucosectomy does not have a frequent recurrence in long-term follow-up. This study shows that more minimally invasive and endoscopic procedures is likely to occur in near future with the use of echoendoscopy.

Perspective
The role of conventional echoendoscopy (EUS) in therapeutic decisions in patients with neuroendocrine gastrointestinal tumors. ABCD Arq Bras Cir Dig 2020;33(2):e1512. DOI: /10.1590/0102-67202019001e1512

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INTRODUCTION

The non-functioning neuroendocrine tumor (NET) is the most frequent of all neuroendocrine tumors of the digestive system (73.7%) and occurs in the stomach/duodenum in 25%, in the rectum in 14%, appendix in 12% and pancreas in lower frequency. They are being more diagnosed and American epidemiological surveillance data have shown that in the past 35 years their number in the small intestine has increased by about 300-500%.

Gastric NET (NETg) type I tends to be benign, with a low risk of progression or metastasis. Thus, the purpose of surveillance and treatment is a matter of debate. They make up 7% of all gastrointestinal NETs and 2% of all excised gastric polyps. Those in the small intestine, especially those in the duodenum, are increasingly seen in early stages and are easily treated (with a diameter < 10 mm). They are generally non-functioning and found during upper digestive endoscopy, which is being performed for other reasons. In case he has hormonal hypersecretion, the situation is different, more delicate and rare. Functional duodenal NETs (NEDs) usually metastasize at the time of diagnosis. Probably NETg and NETd have been "overtreated" in the recent past, and as such, there is a current trend in directing more conservative treatments such as polypectomies and/or mucosectomies, in addition to endoscopic monitoring and surveillance. NETs < 1 cm are resected by endoscopy, with endoscopic follow-up every six or 12 months. Many studies have shown that the successful removal of small NETg with mucosectomy does not have a frequent recurrence in long-term follow-up.

Endoscopic resection must remove the tumor completely (R0 resection). To date, no recurrence has been observed after polypectomy/mucosectomy that affects the prognosis. Echendoendoscopy (EUS) has been increasingly used to assess the invasion of these tumors and to identify the presence of lymphatic metastases, in addition to determining the appropriate stage of the lesion. Few studies assess its role with the intention of determining which are the best candidates for endoscopic resection.

The objective of this study was to determine the effectiveness of EUS in staging subepithelial lesions identified by endoscopy in order to indicate the better form of treatment, endoscopic and/or surgical, and to evaluate the results of endoscopic removal in a medium-term follow-up.

METHODS

This study was approved by the Ethics and Research Committee of Evangelical Faculty of Paraná, Curitiba, PR, Brazil, and all patients were previously informed about it and signed the informed consent used by the Endoscopy Department of 9 de Julho Hospital, São Paulo, SP, Brazil and the Section of Endoscopy of Hospital das Clínicas, Faculty of Medicine of Ribeirão Preto, University of São Paulo, Ribeirão Preto, SP, Brazil.

Twenty-seven patients with suspected NETs were treated in the cited services and submitted to EUS for TN tumors, TN staging and evaluation of the possibility of endoscopic resection, immediately after. All had subepithelial lesions identified by upper gastrointestinal endoscopy and/or biopsy with NET and underwent radial, sectorial or miniprobes EUS in the frequencies of 5.0, 7.5, 10 and 12 MHz. The examinations were performed with deep sedation using propofol with individual doses for each patient at the discretion of the anesthesiologist.

The EUS studied parameters were: size, layer of origin, depth of involvement (uT1 = mucosa, uT1 = submucosa, uT2 = own muscle and uT3=serous affected) and perilesional adenopathies.

Those who met the following criteria were included for endoscopic resection: 1) high surgical risk; 2) NET < 2 cm; 3) absence of impairment of the muscle itself; and 4) absence of perilesional adenopathies on the examination of EUS and ultrasound, tomography and resonance without distant metastases. NETs > 2 cm were excluded.

The therapeutic endoscopy techniques were: polypectomy loop; mucosectomy with saline injection; and mucosectomy after ligation with an elastic band. In addition, anatomopathological studies were carried out, including evaluation of the margins, and immunohistochemistry with the removed part tested by chromogranin, synaptophysin and Ki 67.

The follow-up of the patients was obtained with imaging exams. Magnetic resonance imaging, computed tomography, digestive endoscopy and EUS at 1, 6 and 12 months were used.

RESULTS

The demographic characteristics of the 27 patients can be seen in Table 1. There were 16 men and 11 women with an average age of 59.4 years (34-78). Sixteen had NETg (Figures 1 and 2), two at the fundus, three in the proximal and middle body, 11 in the distal body. Eleven were NETd, nine in the first and 20 in the second duodenal portion. In this series, endoscopic biopsy diagnosed NET in 26/27 patients (96.2%). The finding of NET was incidental in 89% (n=24) and in 11% (n=3) carcinoid syndrome had been diagnosed only clinically, before endoscopy. The size of the tumors was assessed during this examination, and divided into two groups: less than or equal to 10 mm (52%) and 11-19 mm (48%).

Table 1 - Demographic characteristics and variables evaluated (n=27)

| Variables | Number of patients (%) |
|-----------|------------------------|
| Patients  | 27                     |
| Genre     |                         |
| Male      | 16 (59.3)              |
| Female    | 11 (40.7)              |
| Resected NET | 23 (85.1%)           |
| Number of procedures | 29                 |
| Associated conditions |                  |
| Carcinoid syndrome | 3 (11.1)           |
| Location  |                         |
| Stomach   | 16 (59.2)              |
| Distal body | 11                      |
| Proximal/middle body | 3              |
| Fundus    | 2                      |
| Duodenum  | 11 (40.8)              |
| First portion | 9                      |
| Second portion | 2                      |
| Size      |                         |
| <10 mm    | 14 (52)                |
| 11-19 mm  | 13 (48)                |
| Resection technique |                  |
| Conventional technique - polypectomy loop | 15 (55)        |
| Mucosectomy with elevation (injection) of the submucosa | 5 (34)          |
| Mucosectomy after ligation with elastic band | 3 (11)         |
| Complete resection (free margins) | 23/29 (79.3) |
| Complications |                  |
| Relapse   | 3 (11)                 |
| Abdominal pain | 1 (3.7)           |
| Duodenal perforation | 1* (3.7)         |

* Patient died after several surgical procedures.
the tumor. Tumors can be found in any of the three layers and EUS is quite accurate in differentiating the layers of the wall of the stomach. Instead of endoscopic resection, thus avoiding adverse events. Therefore, some of the patients referred for surgery were managed conservatively and were released in a few days. Other studies have shown that the depth of tumor invasion, especially in cases of NET, is a useful parameter, as it offers additional preoperative information on depth, location, and roughness, which are associated with malignancy and can be expected to affect the overall survival of the patients.

On the other hand, other studies have shown that the depth of tumor invasion, especially in cases of NET, is an important parameter to consider in the differential diagnosis of NET. The association of these parameters with the neoplasm, degree of invasion, echogenicity, heterogeneity, size, location, and perilesional lymph node involvement, making the differential diagnosis of NET a complex task, is crucial in making the best treatment decision. With these indicators it allows to point out the best treatment, whether it is endoscopic treatment or surgical. Therefore, the best treatment for NET is endoscopic resection, such as polypectomy/mucosectomy or surgical. With these indicators it allows to point out the best treatment, whether it is endoscopic treatment or surgical.

The neoplasm, degree of invasion, echogenicity, heterogeneity, size, location, and perilesional lymph node involvement, making the differential diagnosis of NET a complex task, is crucial in making the best treatment decision. With these indicators it allows to point out the best treatment, whether it is endoscopic treatment or surgical.

NETs are rare and most are less than 10 mm in size, have a well-defined margin and are hypoechoic in nature; they are located in the deep mucous and submucous layers. The association of these parameters with the neoplasm, degree of invasion, echogenicity, heterogeneity, size, location, and perilesional lymph node involvement, making the differential diagnosis of NET a complex task, is crucial in making the best treatment decision. With these indicators it allows to point out the best treatment, whether it is endoscopic treatment or surgical.

Previously, most NETs were treated by total gastrectomy, as they have a low risk for the development of lymph node or metastases. However, the role of conventional echoendoscopy (EUS) in therapeutic decisions in patients with neuroendocrine gastrointestinal tumors is an important aspect to consider in the differential diagnosis of NET.

EUS proved to be a good method for studying subepithelial lesions, being able to identify the layer affected by the neoplasm, degree of invasion, echogenicity, heterogeneity, size of the lesion and perilesional lymph node involvement, making endoscopic treatment safe and effective. With these indicators it allows to point out the best treatment, whether it is endoscopic or surgical.

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