—Original Article—

Diagnostic yield of endoscopic ultrasound in patients with hypoglicemia and insulinoma suspected

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ABSTRACT

Background and Objectives: Noninvasive imaging techniques have shown limitations to identify insulinomas. In few studies reported so far, endoscopic ultrasound (EUS) has proven to be able to locate lesions. The aim of this study was to compare the performance of computed tomography versus EUS for the detection of insulinomas. **Materials and Methods:** In a retrospective manner prospectively collected data were analyzed. Patients with hypoglucemia and hyperinsulinemia were included. Diagnostic yield was measured in relationship to sensitivity, specificity, positive predictive value, negative predictive value and accuracy. Surgical specimens were considered the gold standard. **Results:** Sensitivity, positive predictive value, and accuracy of EUS was 100%, 95.4% and 95.4%, respectively. In the case of CT the sensitivity was 60%, specificity 100%, positive predictive value 100%, negative predictive value 7%, and accuracy were 68%. **Conclusions:** EUS is useful in the preoperative assessment of patients with hypoglycemia and serum hyperinsulinemia.

Key words: Endoscopic ultrasound, insulinoma, pancreatic neuroendocrine tumors

INTRODUCTION

Neuroendocrine tumors of the gastrointestinal tract pancreas represent about 2% of all tumors of this organ.[1] Of these, the most insulinomas are tumors of the islet cells. The diagnosis of insulinoma can be difficult as the clinical picture may be diverted to other causes, especially in patients with psychiatric and neurological diseases. If the diagnosis was confirmed biochemically, imaging study is important for the timely location of lesions before any surgical procedure, since resection achieves cure.[2]

Access this article online

Quick Response Code:

Website: www.eusjournal.com

DOI: 10.4103/2303-9027.151349

We used multiple imaging enables visualization of pancreatic lesions, including transabdominal ultrasound (US), computed tomography (CT), magnetic resonance imaging (MRI), which have shown limitations to identify small lesions.[3-5] In the few studies reported so far, endoscopic US (EUS) has proven to be able to locate lesions in 81% of cases.[5]

The aim of this study was to compare the performance of CT versus EUS for the detection of insulinomas.

MATERIALS AND METHODS

A retrospective analysis was conducted of patients whose indication of an EUS study was hypoglycemia (glucose <50 mg/dL) and hyperinsulinemia at the National Institute of Medical Sciences and Nutrition Salvador Zubirán from September 2005 to June 2013. Insulinoma was suspected by the presence of

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Received: 2014-07-03; **Accepted:** 2014-07-28

Whipple's triad (low blood glucose levels, symptoms of hypoglycemia and immediate resolution after administration of glucose) and abnormal laboratory tests (fasting test and insulin curve). Other causes of hyperinsulinism and hypoglycemia were discarded. CT and biopsy by fine-needle aspiration guided by EUS (EUS-FNA) in some of the patients was performed. Studies CT and EUS were performed in the same institute. All patients gave their informed consent.

Two experienced endoscopists performed all studies EUS. The procedures were performed under sedation with midazolam, fentanyl and propofol by an anesthesiologist. A linear echoendoscope EG-530UT (Fujifilm) was used with a console SU-8000 (Tokyo, Japan) and a tracking endosonographic frequency of 5 MHz (SU-8000, Tokyo, Japan). An insulinoma was considered when hypoechoic, homogeneous, hypervasculadas, edges regular, well-defined lesions were observed unltrasonographically. When FNA was performed using a 19 or 22 standard needle (Cook Medical, Winstom Salem, PA, USA) the aspirated material was immediately transferred to a glass container and fixed in formalin. All samples obtained by EUS-FNA were sent to pathology for evaluation with stains for chromogranin, synaptophysin or other as proinsulin and insulin. All patients were hospitalized after the procedure EUS for at least 2 h for observation.

CT studies were performed with a multidetector CT scanner cuts 16-64. Images were obtained with the pancreas protocol with cuts every 3-5 mm with a reconstruction interval of 2-2.5 mm. Lesions were considered compatible with insulinomas were those in their arterial phase refuerzaron with the dye; while in its parenchymal phase was homogeneous enhancement with regular contours.

The final diagnosis was based on histological results obtained from the surgical specimen.

Statistical analysis

Descriptive statistics for nonparametric distribution (median and range) was used. Absolute and relative frequencies were also used. Sensitivity, specificity, predictive values and likelihood ratios for the results obtained with EUS and CT were calculated. The areas under the curve of both studies were compared. $P < 0.05$ was considered as significant $P < 0.05$. All analyzes were performed using SPSS version 20 for Mac.

RESULTS

Thirty-four patients were identified with documented episodes of hypoglycemia, and 10 patients were excluded from the analysis. In nine patients, the results of EUS and CT were reported without the presence of lesions in the pancreas and normal serum levels of insulina; in one patient the lesion suggestive of neuroendocrine tumor was evident during the evaluation of obstructive jaundice.

Of the 24 cases included, 15 (62.5%) patients were female and 9 (37.5%) men, whose median age was 46 (19-74) years. The median time between onset of symptoms and diagnosis was 96 (12-570) weeks. The median number of pancreatic lesions was 1 (1-2). There were four patients who had two lesions each.

Results of endoscopic ultrasound

Twenty-eight lesions in 24 patients were detected. The location was: 15/28 (53.5%) lesions in the body, 10/28 (35.7%) lesions were detected in head, 2/28 (7.1%) lesions tail and 1/28 (3.5%) lesion in uncinate process. The median size of the lesions was 15 (4-40) mm. A total of 8 (32%) patients underwent EUS-FNA in all tissue was obtained for histopathologic evaluation and confirmation was obtained in 6 (75%) cases. Of the two negative, histopathological report was inflammatory material alterations. No complications secondary to EUS were documented.

Results of CT

In 16 (64%) patients underwent CT. Nine pancreatic lesions were noted in nine patients. Among the nine lesions, 6 (66.7%) were located in the pancreatic head, 2 (22.2%) in the body and 1 (11.1%) in tail. The median diameter was 17.5 (11-29) mm. EUS documented all lesions documented by CT. In contrast, the CT not visualized six lesions that EUS did.

Results of surgical procedure

Twenty-four lesions in 22 patients who underwent surgery were removed: 11/22 (50%) patients underwent pancreatectomy laparoscopic distal, 6/22 (25%) patients underwent pancreatectomy open and 5/22 (20.8%) patients distal underwent surgery type Whipple. Postoperative complication in 9 (45%) were documented: 8 pancreatic fistula and 1 with abdominal sepsis. There was no mortality.

Histopathological analysis of 22 surgical specimens indicated that 21 (95.5%) lesions were insulinomas; in

one case, the histopathological report only mentioned normal pancreatic parenchyma. In this particular case, the CT did not report any injury of the pancreas while the EUS did, thus giving a false positive.

Of the patients who were not operated (n = 2), one was diagnosed with reactive hypoglycemia and one was lost to follow-up.

Diagnostic yield

To compare the diagnostic accuracy of EUS and CT in the localization of insulinomas, sensitivity and specificity were calculated for each imaging method [Table 1]. Based on the number of patients who were evaluated with EUS and underwent "gold-standard" surgery, the sensitivity, positive predictive value, and accuracy were 100%, 95% and 95%, respectively. The specificity and negative predictive value were not calculable. In the case of CT the sensitivity, specificity, positive predictive value, negative predictive value and accuracy were 60%, 100%, 100%, 14% and 63%, respectively.

DISCUSSION

In our study, EUS proved useful in patients with suspected hypoglycemia and insulinoma. The diagnostic yield of EUS is superior to that shown by CT.

Almost 30% of neuroendocrine tumors are not located preoperatively by traditional imaging techniques, such as US, CT, or MRI.[5] The introduction of the EUS as a diagnostic technique has been successful, but still are not clear about the values that define its diagnostic impact in this group of patients. According to a recent meta-analysis, in which 13 studies evaluating the diagnostic accuracy of EUS in localizing neuroendocrine tumors were included, insulinomas data mentioned in seven studies.[6] Data from 9 studies with 242 patients with insulinoma showed that pooled sensitivity of EUS in detecting a pancreatic Insulinoma was 87.5% (95% CI: 81.2-92.3) and a pooled specificity of 97.4% (95%CI: 90.8-99.7). Our results are in agreement with some previous reports of higher performance by EUS in the diagnosis of small and large pancreatic neuroendocrine tumors.[5] In our study reported insulinomas that were not visualized by CT and whose tumor was histologically verified after surgery. Results in the same direction were reported by Khashab *et al.* in a recent report where EUS has better detection rate than CT in patients with pancreatic neuroendocrine tumors.[7] Other reports are in agreement with our results[8,9] Despite improved CT detection rate, our results demonstrate a significantly higher sensitivity and incremental benefit of EUS over CT.

Table 1. Data for calculate diagnostic yield of EUS and CT with surgical specimen as gold standard

Imagen technique	Surgical specimen+	Surgical specimen−	Total
EUS+	21	1	22
EUS−	0	0	0
			22
CT+	9	0	9
CT−	6	1	7
			16

EUS: Endoscopic ultrasound, CT: Computed tomography

It's clear that CT has advantages over EUS to detect distant metastases and because of that, we cannot to dispense with this important study in pancreatic patients. We can consider these two imaging modalities as complimentary. Conversely, it is well known that EUS allows small neoplasias (<2cm) to be identified that are not detected by other diagnostic modalities and it also tissue samples for cytology to be obtained.

In our data, due to false positive results by EUS, there was a change of diagnosis after the CT in one patient. However, the EUS correctly detected lesions in six patients despite false negative results by CT.

Limitations of our study are its retrospective design and that all patients come from a single center. At work Puli *et al.*, it can be seen that all the included studies, only three studies have a greater number of patients than the current study, which would put this study in the fourth highest number of insulinomas diagnosed by EUS. Not all patients included in our study were evaluated by CT, but we do not have elements to consider that if we would have the data of remaining patients (n = 7) our results change radically.

CONCLUSION

Endoscopic ultrasound is useful in the preoperative assessment of patients with hypoglycemia and serum hyperinsulinemia. The EUS has adequate diagnostic yield for patients with probable insulinoma.

REFERENCES

1. Frankel WL. Update on pancreatic endocrine tumors. *Arch Pathol Lab Med* 2006;130:963-6.

2. Geoghegan JG, Jackson JE, Lewis MP, *et al.* Localization and surgical management of insulinoma. *Br J Surg* 1994;81:1025-8.
3. Gouya H, Vignaux O, Augui J, *et al.* CT, endoscopic sonography, and a combined protocol for preoperative evaluation of pancreatic insulinomas. *AJR Am J Roentgenol* 2003;181:987-92.
4. Mathur A, Gorden P, Libutti SK. Insulinoma. *Surg Clin North Am* 2009;89:1105-21.
5. Varas Lorenzo MJ, Miquel Collell JM, Maluenda Colomer MD, *et al*. Preoperative detection of gastrointestinal neuroendocrine tumors using endoscopic ultrasonography. *Rev Esp Enferm Dig* 2006;98:828-36.
6. Puli SR, Kalva N, Bechtold ML, *et al.* Diagnostic accuracy of endoscopic ultrasound in pancreatic neuroendocrine tumors: A systematic review and meta-analysis. *World J Gastroenterol* 2013;19:3678-84.
7. Khashab MA, Yong E, Lennon AM, *et al.* EUS is still superior to multidetector computerized tomography for detection of pancreatic neuroendocrine tumors. *Gastrointest Endosc* 2011;73:691-6.
8. Ardengh JC, Rosenbaum P, Ganc AJ, *et al.* Role of EUS in the preoperative localization of insulinomas compared with spiral CT. *Gastrointest Endosc* 2000;51:552-5.
9. Pitre J, Soubrane O, Palazzo L, *et al*. Endoscopic ultrasonography for the preoperative localization of insulinomas. *Pancreas* 1996;13:55-60.

How to cite this article: Téllez-Ávila FI, Acosta-Villavicencio GY, Chan C, Hernández-Calleros J, Uscanga L, Valdovinos-Andraca F, *et al*. Diagnostic yield of endoscopic ultrasound in patients with hypoglicemia and insulinoma suspected. Endosc Ultrasound 2015;4:52-5.

Source of Support: Nil. **Conflict of Interest:** None declared.