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INTRAOPERATIVE ULTRASONOGRAPHY IN ENDOCRINE PANCREATIC SURGERY: PRELIMINARY RESULTS IN 6 CASES OF INSULINOMA

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Abstract

Intraoperative ultrasonography permitted the accurate localization of endocrine tumor in 5 patients with single pancreatic insulinoma; all were palpable during surgery. Preoperative localization was negative in one case. Intraoperative ultrasonography also permitted to determine the localization of these tumors in relation with intrapancreatic vascular and ductal structures. It excluded multiple localization, eventually confirmed by histopathologic examination. In a patient with a Werner syndrome and multiple pancreatic insulinomas, intraoperative ultrasound showed more endocrine tumors than careful palpation of the pancreas; the mean diameter of the tumors was 10.6 $\pm$ 4.3 mm, as compared with the smallest tumor (4 mm in diameter) detected by intraoperative ultrasound examination.

Key-words: Ultrasound, intraoperative — Pancreas, neoplasms — Pancreas, surgery — Pancreas, ultrasound studies.

Surgery of endocrine pancreatic tumors is rendered difficult by the considerable problem of tumor localization: 7 to 25% of the insulinomas (1) and up to 50% of the gastrinomas (1) are missed at palpation during surgery.

The choice for the best-suited surgical strategy is particularly difficult in the patients with multiple insulinomas, which appear as macroscopic and microscopic lesions.

Lane et al (2) and Sigel et al (3) reviewed the reliability of intraoperative ultrasound examination (IOUS) in the detection of endocrine pancreatic tumors and American (4-6), French (7, 8), and Italian (9) publications recently confirmed their conclusions.

This paper is a report of the preliminary results derived from our IOUS examination of 6 cases of insulinoma among which one polyendocrine syndrome with multiple pancreatic tumors.

Material and methods

Pancreatic imaging was obtained on 2 real-time units: ALOKA SSD-256 (in one case) and TOSHIBA SAL 35 (in 5 cases), with respectively a 5 and a 7.5 MHz transducer. The T-shaped, I-shaped, and rake-shaped probes are specifically designed for intraoperative examination. They are waterproof, easy to sterilize, and have a variable contact surface (56 $\times$ 16 mm for ALOKA probes and 28 $\times$ 6 mm for TOSHIBA).

Following extensive colo-epiploic and duodeno-pancreatic dissection, the pancreas is carefully examined and palpated. Transverse and sagittal scanning is performed with a water-filled balloon (acting as coupling medium) placed between the probe and the surface of the pancreas.

We referred to the examination procedure described by Lane (2). Following identification of the vascular (superior mesenteric artery, splenic vein, porto-mesenteric vein) and ductal structures (Wirsung duct and bile duct), the whole pancreatic parenchyma is systematically scanned.

The echograms obtained can be examined on the ultrasonic scanner screen, displayed on films, or recorded on a video.

Following pancreas examination, we perform intraoperative ultrasonic examination of the liver for evidence of liver metastases. This technique has previously been described (10).

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Table I. — *Pre-, intra- and postoperative findings in 6 cases of insulinoma*

	Preoperative diagnosis				Pre-operative localization	Intraoperative diagnosis					Surgery	Histo-pathologic findings	Follow-up (months)
	US	CT	Angio	PVS		Palpation	Intraoperative US			Artificial pancreas			
Obs. 1	–	–	+	+	head single	head single	head	single	sono-lucent	N.D.	pancreato-duodenectomy	single 10 mm	dead (29) (malignant)
Obs. 2	–	–	–	–	unknown	neck single	neck single	single	sono-lucent	+	distal pancreatectomy	single 14 mm	cured (24)
Obs. 3	–	±	±	+	body single	body single	body	single	sono-lucent	+	distal pancreatectomy	single 9 mm	cured (24)
Obs. 4	–	–	–	+	tail single	tail single	tail	single	sono-lucent	+	distal pancreatectomy	single 10 mm	cured (12)
Obs. 5	–	–	+	N.D.	head single	head single	head	single	sono-lucent	+	pancreato-duodenectomy	single 15 mm	cured (18)
Obs. 6	–	+	+	+	head single	head (1) neck (1) body (1) multiple (3)	head (3) neck (2) body (1)	multiple (6)	sono-lucent	+	enucleations	multiple 17, 16, 9, 7, 6 and 4 mm	cured (3)

US: ultrasound; CT: CT-scan; Angio: angiogram; PVS: transhepatic portal vein sampling; N.D.: not done.

Patients

A total of 6 patients (among which 4 females) with pancreatic insulinoma were enrolled in this study. Five had single insulinoma (head of the pancreas: 2; neck: 1; body: 1; tail: 1) (table I).

In one case (observation 2), the preoperative examination procedures aiming at localizing the tumor (ultrasound, CT, arteriography, and transhepatic portal vein sampling) failed to locate the lesion. All were palpated during surgery.

Among the six patients, one female, aged 33 (observation 6) presented with Werner polyendocrine syndrome with multiple pancreatic insulinomas. All preoperative investigations for tumor localization (CT, arteriography, transhepatic portal vein sampling) revealed one single 17 mm in diameter tumor of the head of the pancreas (tumor 1). Intraoperative palpation identified the lesion, which was actually localized in the neck of the pancreas, and two additional tumors, respectively 7 and 6 mm in diameter, superficially located in the head (tumor 2) and the body (tumor 3) of the pancreas (fig. 1).

Each time we made use of artificial pancreas (11) during surgery ($n=5$), in our six patients with single insulinoma, we recorded a significant increase in glycemia levels, confirming the complete excision of an hypoglycemic tumor in 2 cases of duodenopancreatectomy, 3 cases of distal splenopancreatectomy and multiple enucleations in the patient with polyendocrine syndrome.

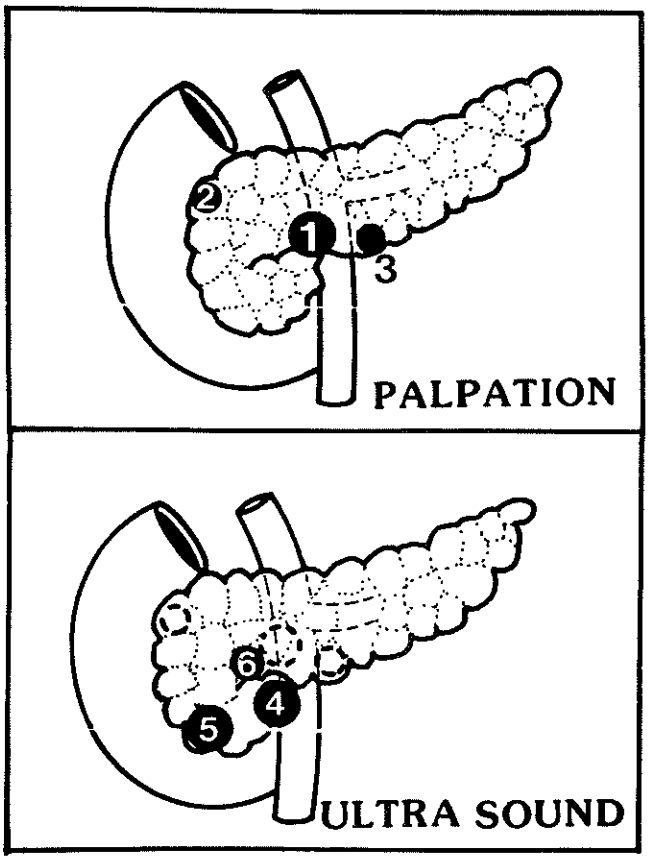

Fig. 1. — Anatomic localization of multiple insulinomas (case 6) in a Werner syndrome patient. *At palpation:* tumor 1 (neck, 17 × 15 mm); tumor 2 (head, genu superius, 7 × 6 mm) and tumor 3 (body, 6 × 4 mm). *At ultrasound,* three additional tumors: tumor 4 (uncinate process, 16 × 11 mm); tumor 5 (head, genu inferius, 4 × 3 mm) and tumor 6 (neck, deep, 9 × 7 mm).

In our series, the mean diameter of the insulinomas was 10.6 ± 4.3 mm. For the patients with benign insulinoma ($n=5$), the follow-up period was 16.2 ± 8.9 months; during this course, all showed normal glycemia values. The patient with malignant insulinoma died 29 months later of a generalized lymphoma without pancreatic recurrence.

Results

In the five patients with single insulinoma, intraoperative ultrasound examination each time visualized the tumor as a sonolucent mass with clearcut limit, and ruled out other parenchymal localization. This was confirmed by histologic examination of the pathology specimen and long-term clinical course. IOUS also enabled the accurate localization of these lesions within the pancreatic parenchyma in relation with the portal vein (fig. 2), the superior mesenteric artery, the common bile duct, and the Wirsung duct (fig. 2). The distance between the tumor and both the vascular and ductal structures (fig. 2), and the pancreatic surface was measured.

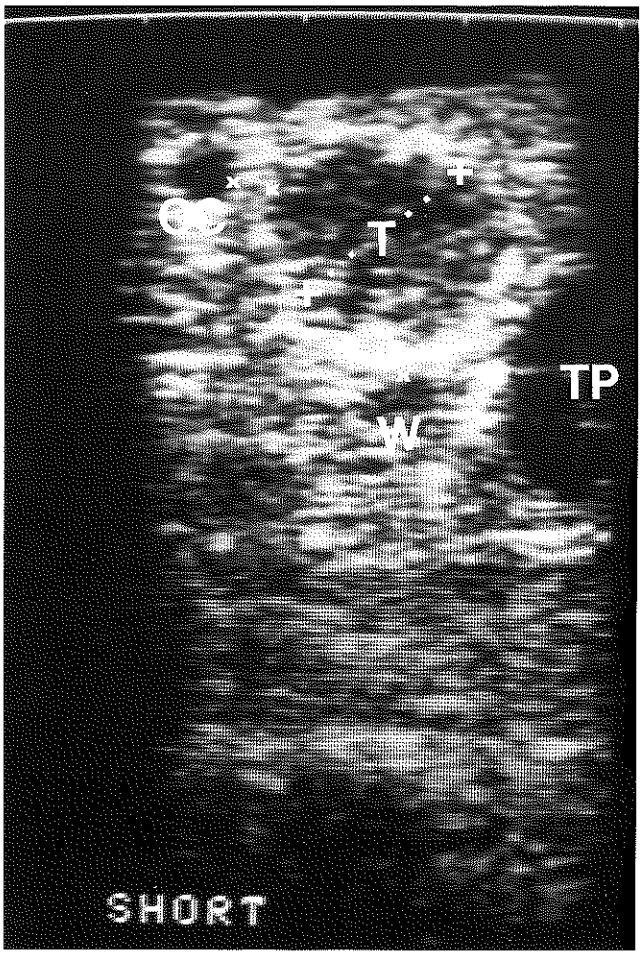

Fig. 2. — Patient with single cephalic insulinoma (case 5). Transverse scan (TOSHIBA) of the pancreas: sonolucent tumor (15 mm diameter), on the right side of the portal vein (TP), at 3 mm of the intrapancreatic common bile duct (CC) and at 3 mm of the Wirsung duct (W).

In the patient with multiple insulinomas, all palpable lesions (tumors 1, 2, 3) were visualized on the intraoperative echograms as a well-circumscribed sonolucent area in comparison with the adjacent pancreatic parenchyma (fig. 3A). Besides, IOUS enabled us to detect 3 additional lesions that could not be palpated (fig. 1): one was 16 mm in diameter and located in the uncinate process (tumor 4), to the right of the superior mesenteric vein, and the other was 4 mm in diameter (tumor 5) and located in the genu inferius (fig. 4). Finally, the last lesion (9 mm in diameter) (tumor 6) was embedded in the pancreatic parenchyma, at the level of the neck of the pancreas, beneath an adjacent superficial lesion (tumor 1) (fig. 3B, 3C). In this patient, the localization of the lesion deep within the parenchyma and near the Wirsung duct did not allow enucleation, and accordingly we did not decide to perform a total pancreatectomy on the patient.

Discussion

A recent survey carried out by the "Association Française de Chirurgie" team (1) reports that all intraoperative procedures for tumor localization altogether detected 62% of the insulinomas and 31% of the gastrinomas. This leaves 38% of the insulinomas undetected preoperatively and 1/3 of these tumors are not palpated during surgery (1).

The occurrence rate of these tumors, called occult tumors, varies from 7 to 25% (1, 12-18). In 10% of the cases, these insulinomas correspond to multiple adenomas (1, 12, 13, 19-22) and in 5% to hyperplasia (1, 12, 23).

Finally, these tumors are characterized by their small size: under 1.5 cm in 68% of the patients (13, 19-21) and under 1 cm in 39% (12).

In opposition to what was commonly and firmly believed earlier, these hypoglycemic endocrine tumors are not localized preferentially in one pancreatic area (1, 12, 13, 18-21). Therefore, blind left pancreatic excision for occult lesions undetected preoperatively is no longer justified, the more so as such practice scored rather bad results (12, 13, 19).

The use of intraoperative morphologic imaging modalities such as sonography is therefore mandatory in endocrine pancreatic surgery. IOUS is an easy, noninvasive and harmless procedure which enables the accurate identification and localization of a tumor which, in almost all the cases (25 insulinomas are reported in the literature) is visualized as a

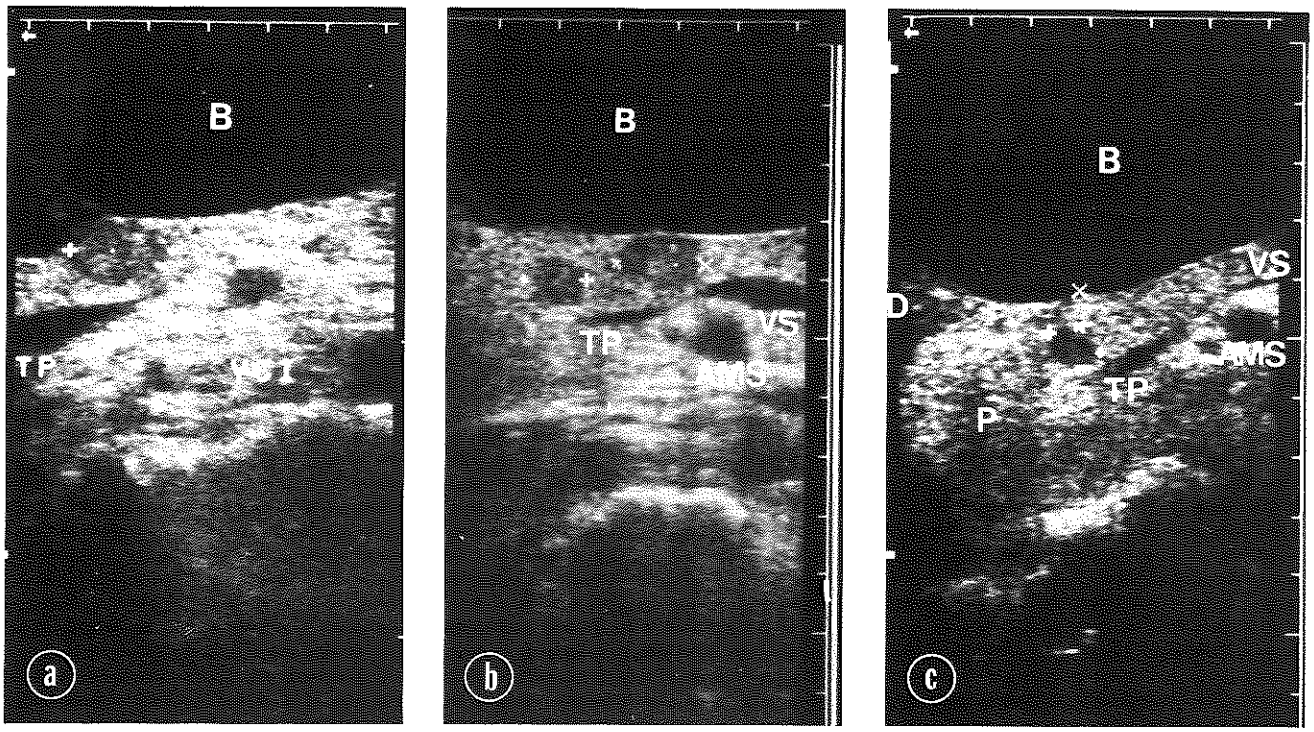

Fig. 3. — Patient with multiple insulinomas (case 6).
A. *Sagittal scan of the pancreas* (ALOKA): superficial sonolucent tumor (tumor 1) of 17 mm diameter, localized in the neck of the pancreas, above the portal vein (TP). The inferior vena cava (VCI) is behind.
B. The same tumor (tumor 1) on *a transverse scan*: presence of a second cephalic tumor (tumor 6), of 9 mm diameter, adjacent to tumor 1. Porto-mesenteric vein (TP) collabed by the probe. Splenic vein (VS). Superior mesenteric artery (AMS) on this transverse scan.
C. Tumor 6 on *a transverse scan* after enucleation of tumor 1, at 6 mm of the pancreatic surface, in the head of the pancreas (P). Duodenum (D).

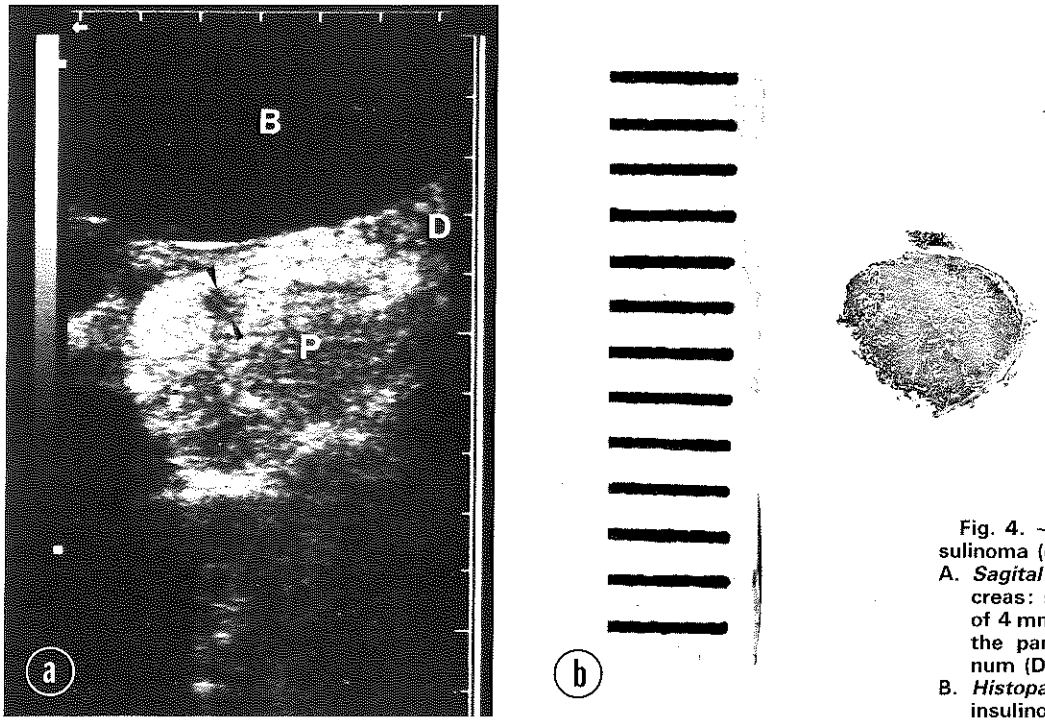

Fig. 4. — Patient with multiple insulinoma (case 6): tumor 5.
A. *Sagital oblique scan* of the pancreas: sonolucent tumor (arrows) of 4 mm diameter, superficially in the pancreatic head (P). Duodenum (D). Water-filled balloon (B).
B. *Histopathologic specimen:* benign insulinoma. Diameter: 4 mm.

sonolucent area easy to delineate within the adjacent pancreatic parenchyma (2-4, 6, 8, 9, 24, 25). However, it must be noted that Angelini reported one case of insulinoma producing hyperechogenic images (9). IOU is particularly reliable for the localization of occult tumors that remained undetected preoperatively and not palpated during surgery (3, 4, 6, 9).

It enables the accurate localization of a tumor in relation with the surrounding vascular structures (splenic vein, porto-mesenteric vein, superior mesenteric artery). Real-time scanning plays a twofold role by identifying and visualizing dynamically the vessels and enabling the localization of the tumors in relation with ductal structures such as the main bile duct in its intrapancreatic course and the Wirsung duct (6, 9). These highly relevant data enable the practician to make the right choice between resection or enucleation. Besides, when enucleation is decided, real-time scanning highly contributes to the determination of the best site for pancreatic exploratory capsulotomy (6, 9). For some practicians, insertion of needles around the tumor under ultrasound control may be of great help for guidance when performing enucleation (2, 6). In this way, IOUS permits to reduce the number of useless and harmful repeated capsulotomies (3).

Nevertheless, it seems that intraoperative ultrasound scores the best results in the exclusion of multiple adenomatous lesions (25). In one of our patients, for instance, IOUS disclosed 3 additional tumors ignored by intraoperative palpation, whereas preoperative examinations only identified one single tumor, in the head of the pancreas.

Superficial and small-size lesions may escape IOUS (4) but are easily diagnosed by careful intraoperative examination and palpation. Literature reports a 11.3 ± 5.4 mm mean diameter for the lesions detected by operating room sonography, whereas we observed a 10.6 ± 4.3 mm value in our series. Smaller size tumors may also be detected: Sigel (3) identified lesions of 4 mm, and we made the same observation.

Such results could be achieved thanks to the specific technical characteristics of IOUS examination: the probe is directly applied on the surface of the pancreas, excluding intestinal structures interference. Isotonic solution in the operative field—as in Sigel and Lane reports (2, 3, 26)—or a water-filled balloon (10) are used as coupling media. We use higher frequency (5 to 10 MHz) transducers. They have a lower penetration ratio, but this represents little inconvenience since the probe is directly applied on the pancreas; —furthermore, the organ is thin. The resolution power of the probe is definitely higher, reaching 1 mm, even for deeply situated lesions.

Finally, IOUS enables the differential diagnosis between endocrine tumors and chronic pancreatitis, which can be recognized by their specific sonographic characteristics (24).

Since 10 to 15% of the insulinomas are malignant tumors (1, 12, 13, 18-20), IOUS examination of the pancreas must be complemented by thorough IOUS examination of the liver for metastases (10).

Conclusion

Review of approximately 25 cases of insulinoma described in the literature and analysis of our own observations—though on a still limited series—enable us to conclude that IOUS is able to detect even small or multiple endocrine tumors.

On the sonograms, the lesions are visualized as relatively constant sonolucent masses. The role of IOUS in the pre- and intraoperative localization of pancreatic endocrine tumors and its diagnostic value remain to be determined on large scale studies, in particular in the small-size multiple tumors and the lesions not localized before surgery and not palpated during surgical intervention. Progress in technical knowledge, and in particular in the design of transducers better adapted to intraoperative ultrasonic examination will probably contribute in improving its diagnostic value.

IOUS therefore appears to be a prioritary tool for localizing and assessing the lesions during endocrine pancreatic surgery.

Résumé

L'échographie peropératoire (EPO) a permis la localisation précise de la tumeur chez 5 patients porteurs d'une insulinome pancréatique unique, par ailleurs tous palpables à l'intervention. Dans un cas, la localisation préopératoire était restée négative. L'EPO a également permis de situer ces tumeurs par rapport aux structures vasculaires et canalaires du pancréas. Elle a exclu d'autres localisations intraparenchymateuses pancréatiques, ce qui a été confirmé par l'histologie définitive. Enfin, chez une autre patiente porteuse d'un syndrome de Werner avec insulinomes pancréatiques multiples, l'EPO a découvert plus de tumeurs endocrines que la palpation peropératoire du pancréas. Le diamètre moyen de ces tumeurs était de $10,6 \pm 4,3$ mm. La plus petite des tumeurs trouvées avait 4 mm de diamètre.

Samenvatting

De peroperatieve echografie (EPO) heeft een juiste localisatie van het gezwel mogelijk gemaakt bij 5 patiënten die een solitaire pancreas insulinoma hadden, die allen tijdens de interventie tastbaar waren. In één geval is de preoperatieve localisatie negatief gebleven. De peroperatieve echografie heeft ook toegelaten de gezwellen

te localizeren ten opzichte van de vasculaire en canalaire structuren van de pancreas. Ze heeft ook andere localisaties uitgesloten, hetgeen door de histologie bevestigd werd. Bij een andere patient met een Werner syndroom en meervoudige pancreatische insulinoma's toonde de peroperatieve echografie méér gezwellen dan de peroperatieve palpatie van de pancreas. De gemiddelde diameter van deze gezwellen bedroeg $10,6 \pm 4,3$ mm. Het kleinste gezwel dat door peroperatieve echografie gevonden werd had een diameter van 4 mm.

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