



Original research

The use of intraoperative ultrasound for diagnosis and stadiation in pancreatic head neoformations



C. de Werra^{*}, G. Quarto, S. Aloia, S. Perrotta, R. Del Giudice, G. Di Filippo, E. Furino, B. Amato, G. Benassai

University of Naples, A.O.U. Federico II, Italy

ARTICLE INFO

Article history:

Received 12 March 2015
 Received in revised form
 24 March 2015
 Accepted 10 April 2015
 Available online 26 June 2015

Keywords:

Pancreatic cancer
 Intraoperative ultrasound
 Duodeno-cephalo-pancreatectomy (DCP)

ABSTRACT

The intraoperative staging of the pancreatic cancer is important to make a proper treatment. For this reason the intraoperative echography is playing an important role in the right treatment choice. The intraoperative echography, that can be performed with an open or laparoscopic probe, is used to confirm the preoperative diagnosis and assess the pancreatic cancer resectability. The intraoperative echography (IOUS) or laparoscopic intraoperative echography (LIOUS) are useful to identify the patients with a non resectable cancer and perform a faster neoadjuvant treatment. The LIOUS can also avoid an useless laparotomy. The aim of this study is to assess, both in our experience and in the cited literature, the concordance rate between the pancreatic cancer preoperative staging, performed with TC and MRI (when it is available), and intraoperative staging, performed with intraoperative laparotomic or laparoscopic echography.

Material and methods: We have analyzed the treatment management of 34 patients, who were candidate to major surgery for suspected pancreatic head cancer and who underwent to intraoperative LIOUS or IOUS staging from 2001 to 2012.

Results: LIOUS and IOUS have allowed to detect cases in which preoperative diagnosis, proved by CT and MRI, was not agreeing with intraoperative diagnosis (22 patients on 34, 64% discordance rate), avoiding the execution of a demolitive and uneseful surgery in order to guarantee the surveillance and life's quality of patients.

Conclusion: We suggest to perform in every patients undergone to pancreatic surgery an intraoperative ultrasound exam, to detect unresectable and unpredicted lesions.

© 2015 IJS Publishing Group Limited. Published by Elsevier Ltd. All rights reserved.

1. Introduction

The echography is one of the most important diagnostic tool in the abdominal pathologies, and is playing a more important role because of the great technological progress and the development of new and higher performance device. The new intraoperative probes, for both laparoscopic and open surgery, allowed the development of the intraoperative staging of cancers, that for a long time have been only studied by TC and MRI.

The surgeon can directly assess the patient operability by IOUS and LIOUS. With the high frequency probe and direct contact with

the organ targeted it can be obtained high resolution echographic images; so this echographic examination is better than TC or MRI in the pancreatic cancer resectability evaluation. At the beginning the IOUS have been used in the abdominal cavity to diagnose cholelithiasis and choledocholithiasis. During the '80s Lane e Glazer [4] have described the use of IOUS on the "Lancet" as a useful examination to assess the pancreatic pathological lesions. Since then a lot of improvements have been developed to perform the IOUS [31–34]: nowadays we have probes with different forms and frequencies, in a range that goes from 7.5 Mhz to 10 Mhz. The most common intraoperative probes have "I" or "T" shapes and are convex type probes, the linear and sectorial probes are less common. The equipment [27–30] used to perform the exam should be easily sterilizable and easy to use. The standard procedure to perform the intraoperative examination of the pancreatic lesion, requires the opening of the gastro-colic ligament and the access to

^{*} Corresponding author. University of Naples, A.O.U. Federico II, Via Bartolomeo Caracciolo Carafa Nr.3, Italy.

E-mail address: dewerra@unina.it (C. de Werra).

the epiploon retrocavity, so it can be possible to have a direct contact between the probe and the pancreatic head. When it is not possible to reach a direct contact to the pancreatic head, the examination can be performed through the acoustic window of the left liver lobe or pushing the gastric wall with the probe. Placing the probe laterally to the duodenal wall and putting the ultrasound waves in the direction of the portal vein to assess its direction, calibre and eventual infiltration is useful to value the cancer resectability. Moreover the hepatic peduncle and its elements, the gallbladder, the spleen and splenic vessels, the great abdominal vessels and their nearest lymph-nodes are scanned. During IOUS examination, the pancreas [22–26] appear a little more echogenic than the sane hepatic parenchyma. Nevertheless the echogenity pattern of the pancreas can change during the growth or because of chronic alcohol assumption [19–21]. Also the inflammatory chronic diseases of the organ can increase the echogenity pattern of the organ (caused by the deposition and the increasing of the fibrotic tissue) and often decrease the visible part of parenchyma. The patient's body composition is important to guarantee the effectiveness of the IOUS, indeed the presence of a great quote of retro-peritoneal adipose tissue and its infiltration in the pancreas, can sometimes cause a bad valuation of the organ. The IOUS can also help to perform a cytological or biotical examination of ambiguous pancreatic lesions, like the cystic lesions with liquid or partially solid content or the pancreatic head lesions caused by pancreatitis [19–21].

2. Materials and methods

From 2001 to 2012 we have analyzed 34 cases of patients came to Our observation with a neofomation of pancreas' head and elegeble to Duodeno-cephalo-pancreatotomy. Our strategy to treat pancreatic lesions leads, when possible, an intraoperative ultrasound exam performed through laparotomy (IOUS) or laparoscopy. In our study we considered 19 females and 15 males, with an average age of 68 years old (maximum age 75 and 65 minimum). The BMI in females group was 24.5, while in the males one was 25.5. Patients were recruited in Our ambulatory of General HBP Surgery, associated with the Operative Unit of U.H. Federico II, in Naples. Every patients selected for the surgery were undergone to CT or MRI (when it was necessary) in order to stage the grade of their disease. Moreover we evaluated principal tumoral markers: Ca 19.9, Ca 125.5, CEA, AFP. The intraoperative ultrasound exam with probe for open surgery or laparoscopic ultrasound probe was performed by the same surgeon who has an over twenty years of experience in ultrasound field. The ultrasound device used during Our study was an Esaote MyLab 40[®] with a standard linear probe frequencing at 7.5 Mhz and 10 Mhz, and linear laparoscopic probe frequencing 7.5 Mhz and 10 Mhz. Probes were sterilized using a solution for cleaning surgical tools non autoclavable (Barrycidal 30 Plus[®]); when was used the standard linear probe we used a sterilize plastic bag for the laparoscopic optical viewer. Executing the LIOUS was used a trocar of 10 mm for the laparoscopic optic viewer placed on umbilicus scar, a trocar of 10 mm on the right side between the junction of emiclavear line and transumbelicar one and a trocar of 5 mm on the left side and in specular position of the former. To perform IOUS was used a median laparotomy xypho-pubic to access at the abdominal cavity; both in laparoscopy and in open surgery was completely opened the gastro-colic ligament in order to access to epiploon's cavity and perform the exam. Before to set the probe directly on the organ was used a sterilized isotonic solution on pancreas' surface in order to improve ultrasounds transmission. The exam was performed and evaluated always by the same physician, comparing images acquired in surgery with the others acquired through CT or MRI, when available. Criteria to not

perform the surgery were: encroach of superior mesenterical vessels, portal encroachment, farness lymphnodes invasion, peritoneal carcinosis. Moreover was performed a Doppler exam about target vessels. When patients were not eligible for a LIOUS exam due to a severe comorbidity status (heart failure or respiratory diseases) we proceeded with an IOUS. In every patients that after intraoperative exams were not elegeble to resective surgery, we proceeded to a bioptical exam (omental or peritoneal metastasis) or microbiopsy with Tru-Cut[®] needle on the lesion, in order to set the histological grade and, after that lead them to neoadjuvant chemotherapy. When the cancer results resecable, during the intraoperative exam (IOUS or LIOUS), we performed a Duodeno-cephalo-pancreatotomy (DCP) with reconstruction on loop according to Roux.

3. Results

Among 34 patients dragged in our study, 31 have been exposed to a LIOUS; 3 patients have only been exposed to an IOUS due to an high risk to perform a pneumoperitoneum (ASA IV with right heart failure). In 65% of cases the average value of Ca19.9 was elevated. Among 34 patients in Our study: nine refered only unvolunteer weight loss during the last year; eight patients had obstructive jaundice; three reported dyspepsia; four of them suffered only of typical pancreatic pain; in seven patients only two of these symptoms were evidentiabile and finally three patients present all the above symptoms and signs. Actually in Our clinical records, after the performance of intraoperative ultrasound exam, only twelve patients were eligible to perform a DCP; two patients submitted to IOUS and ten patients exposed to LIOUS. In one of patients exposed to IOUS the preoperative diagnosis performed with CT did not agree with intraoperative ultrasound exam, due to an ignored peritoneal carcinosis with neoplastic peritoneum lesions. On the contrary in patients undergone to a LIOUS exam, the preoperative diagnosis acquired with CT plus MRI (when it is available) was different in 21 cases; so we had an average discordance rate of 64%, it was obtained adding the 21 patients undergone a LIOUS to 1 patient undergone an IOUS both with disagreeing diagnosis. Specifically patients with a different intraoperative diagnosis undergone a LIOUS exposed: five cases with an increasing volume and unclear structure of pancreatic head, which following to microbiopsy exam did with Tru-Cut Biopsy Needle[®], has been identified as chronic pancreatitis.

Other patients, who had a conflicting preoperatory diagnosis, had the following features: 5 of them had omental metastasis (confirmed by extemporary histological exam on the located lesions); in one patient there was a tumoral encroachment of the portal vein carrefour; 2 patients had farness neoplastic lymph-nodes; 2 of them showed a tumoral encroachment of the superior mesenteric vein with signs of omental cancer; 6 patients had some regional suspicious lymph-nodes which, after ultrasound exam, reminded a tumoral encroachment; moreover they also manifested clear signs of encroachment of the principal vessels (mesenteric and portal veins) and omental cancer.

All 22 patients, who were not eligible to surgery excision, were addressed to neoadjuvant therapy and, eventually, treated with surgery only to correct those symptoms associated with development of the disease. In 12 patients, when IOUS and LIOUS exams were agreeing with intraoperatory imaging exam and there were no contraindications to the surgery (valutated after abdominal exploration), we have proceed to surgery doing DCP standard with R1 lymph-nodes resection and restoring the intestinal motility through loop according Roux and closing of pancreatic residue releasing GLUBRAN[®] directly in Wirsung. This type of re-build has been selected because of the average age of patients.

There were no cases of intraoperative deaths.

We have found a morbidity of the 40%, among which: 3 cases of pancreatic fistula, 1 case of postoperative bleeding and 1 case of abdominal infection. All these postoperative complications were treated in conservative way with a correct pharmacological therapy and nutritional support directly in the hospital. Twelve patients, who undergone to DCP surgery, showed the pathologic staging as summarized in [Table 1](#). An average of 13 lymph-nodes were excised. Patients which had 5 years disease free after surgery are 5; 4 patients died in 36 months since surgery and 3 patients died before 24 months since surgery. All our results are summarized in [Table 2](#).

4. Discussion and conclusions

IOUS and LIOUS techniques are useful, and may help the surgeon to decide the correct approach to pancreatic lesions and moreover [1–3]. Nowadays these techniques are very used to distinguish gallbladder cancer and biliary tract [4,5]. An important element of evaluation is the analysis of lymph nodes and their system, both intraperitoneal and retroperitoneal [5,6]. The use of intraoperative ultrasound can lead, according with some authors, a swing in the operative strategy in about 38–49% of cases [1,5,7]. In the pancreatic surgery ultrasound has a dominant role. Actually it is essential for the type differentiation of lesions (cystic, solid, inflammatory, endocrine, intraductal) [6,8–11]. May be very useful in the evaluation of islet pancreatic cancer and endocrine tumor including inactive ones [2,8,12]. The intraoperative ultrasound exam, during a laparoscopy or laparotomy, helped by a biopsy and cytology, has allowed to reach high level of sensibility and specificity in the determination of resectionability of lesions, indeed in the literature is reported a sensibility of 92–93% and specificity of 95% [1,5,8,9]; while CT results reach lowest values of sensibility (71.4–90%) [1,8,13]. Moreover the intraoperative exam results able to detect enlarged lymph nodes which sometimes, due to a local inflammatory state or plenty of abdominal fat, are difficult to reveal with CT [1,14]. Usually the intraoperative exam is very useful to reveal hepatic lesions less than 5 mm diameter [15,16], reaching an average sensibility of 94% against 86.7% reached by the MRI in the scanning of these lesions [1,8]; to reach these higher value of sensibility we need to execute very carefully IOUS and LIOUS, keeping attention to push the probe with adequate pressure on the liver's capsule and to explore the entire organ. In Our experience the rate of concordance between preoperative staging and further resectability of pancreas head cancer has been of the 35% for patients undergone to IOUS or LIOUS, it depends probably from the small number of patients which has been analyzed. The intraoperative ultrasound exam, with an accurate direct exploration of the all abdominal cavity, has allowed the detection of 22 patients not eligible for surgery resection. These patients, without an ultrasound intraoperative exam, would probably have suffered by an unjustified over-treatment, unable to guarantee improvements in terms of survivor rate and quality of life, beyond to have an higher impact on the financial balance of the hospital; so we suggest to every surgeon dedicate to pancreatic surgery to perform always an intraoperative ultrasound exam. Moreover we reached to obtain an histological diagnosis on microbiopsy with Tru-Cut Biopsy Needle® in five 5 doubtful cases, in which an enlargement of the head of pancreas, with uncertain levels of Ca19.9, which could not obtain to make an

Table 1
Number of patients for each pathological stages detected.

Group A	5 patients	T1N0M0
Group B	4 patients	T2N0M0
Group C	3 patients	T2N1M0

Table 2

Patient Surveillance rate in relation with pathological stage.

Patients with 5 years disease free	4 A; 1 B
Surveillance at least 36 months	3 B; 1 A
Surveillance equal or less than 24 months	3 C

exact preoperative diagnosis. In cases in which the diagnosis was confirmed by the ultrasound exam we obtained a good survivor rate as shown in the [Tables 1 and 2](#). This high survival rate [17,18] depends of the correct diagnostic identification reached by intraoperative ultrasound, which has allowed to select patients with cancer really resectable, obtaining an unexpected surveillance in relationship with this pathology.

Conflict of interests

I declare that All Authors have no conflict of interests.

Source of funding

I declare that All Authors have no source of funding.

Ethical approval

Ethical approval was requested and obtained from the “Azienda Universitaria Federico II” ethical committee.

Author contribution

De Werra C: Participated substantially in conception, design, and execution of the study and in the analysis and interpretation of data; also participated substantially in the drafting and editing of the manuscript.

Quarto G: Participated substantially in conception, design, and execution of the study and in the analysis and interpretation of data.

Aloia S: Participated substantially in conception, design, and execution of the study and in the analysis and interpretation of data.

Perrotta S: Participated substantially in conception, design, and execution of the study and in the analysis and interpretation of data.

Del Giudice R: Participated substantially in conception, design, and execution of the study and in the analysis and interpretation of data.

Di Filippo G: Participated substantially in conception, design, and execution of the study and in the analysis and interpretation of data.

Furino E: Participated substantially in conception, design, and execution of the study and in the analysis and interpretation of data.

Amato B: Participated substantially in conception, design, and execution of the study and in the analysis and interpretation of data.

Benassai G: Participated substantially in conception, design, and execution of the study and in the analysis and interpretation of data; also participated substantially in the drafting and editing of the manuscript.

References

- [1] M. D'Onofrio, F. Vecchiato, N. Faccioli, et al., Ultrasonography of the pancreas. 7. Intraoperative imaging, *Abdom. Imaging* 32 (2007) 200–206.
- [2] J.S. Hiramoto, V.A. Feldstein, J.M. LeBerge, et al., Intraoperative ultrasound and preoperative localization detects all occult insulinomas, *Arch. Surg.* 136 (2001)

- 1020–1026.
- [3] J. Machi, B. Sigel, H.A. Zaren, et al., Operative ultrasonography during hepato-biliary and pancreatic surgery, *World J. Surg.* 17 (1993) 640–645.
- [4] R.J. Lane, G. Glazer, Intra-operative B-mode ultrasound scanning of the extra hepatic biliary system and pancreas, *Lancet* 2 (1980) 334–337.
- [5] R. Kolecki, B. Schirmer, Intra-operative and laparoscopic ultrasound, *Surg. Clin. North Am.* 78 (1998) 251–271.
- [6] J. Kulig, P. Kolodziejczyk, M. Sierzega, Ultrasonografia laparoskopowa I srodoperacyjna, *Ultrasonografia* 35 (2008) 9–12.
- [7] R.A. Kane, Intraoperative ultrasonography: history, current state of the art, and future directions, *J. Ultrasound Med.* 23 (2004) 1407–1420.
- [8] E.E. Long, J. Van Dam, S. Weinstein, et al., Computed tomography, endoscopic, laparoscopic, and intra-operative sonography for assessing respectability of pancreatic cancer, *Surg. Oncol.* 14 (2005) 105–113.
- [9] M.R.M. Sun, D.D. Brennan, J.B. Kruskal, et al., Intraoperative Ultrasonogr. *Pancreas Radiogr.* 30 (2010) 1935–1953.
- [10] E.M. Merkle, I. Gorich, Imaging of acute pancreatitis, *Eur. Radiol.* 12 (2002) 1979–1992.
- [11] T. Kaneko, A. Nakao, S. Inoue, et al., Intraoperative ultrasonography by high-resolution annular array transducer for intraductal papillary mucinous tumors of the pancreas, *Surgery* 129 (2001) 55–65.
- [12] J.A. Norton, Intraoperative methods to stage and localize pancreatic and duodenal tumors, *Ann. Oncol.* 10 (Suppl. 4) (1999) 182–184.
- [13] R. Vargas, M. Nino-Murcia, W. Trueblood, et al., MDCT in pancreatic adenocarcinoma: prediction of vascular invasion and respectability using a multiphasic technique with curved planar reformations, *AJR* 182 (2004) 419–425.
- [14] C. Niederau, J.H. Grendell, Diagnosis of pancreatic carcinoma. Imaging techniques and tumor markers, *Pancreas* 7 (1992) 66–86.
- [15] B. Kaczmarek, R. Kostyrka, M.I. Wojcicki, Wsp: srodoperacyjna ultrasonografia w chirurgii raka trzustki, *Pol. Prz. Chir.* 72 (2000) 37–41.
- [16] M.D. Benson, M.R. Gandhi, Ultrasound of the hepatobiliary-pancreatic system, *World J. Surg.* 24 (2000) 166–170.
- [17] G. Benassai, M. Mastrorilli, G. Quarto, A. Cappiello, U. Giani, G. Mosella, Survival after pancreaticoduodenectomy for ductal adenocarcinoma of the head of the pancreas, *Chir. Ital.* 52 (3) (May 2000) 263–270.
- [18] G. Benassai, M. Mastrorilli, G. Quarto, A. Cappiello, U. Giani, P. Forestieri, F. Mazzeo, Factors influencing survival after resection for ductal adenocarcinoma of the head of the pancreas, *J. Surg. Oncol.* 73 (4) (2000) 212–218.
- [19] R. Pezzilli, G. Uomo, A. Gabbriellini, A. Zerbi, L. Frulloni, P. De Rai, et al., A prospective multicentre survey on the treatment of acute pancreatitis in Italy, *Dig. Liver Dis.* 39 (9) (September 2007) 838–846.
- [20] L. Castoldi, P. De Rai, A. Zerbi, et al., Long term outcome of acute pancreatitis in Italy: results of a multicentre study, *Dig. Liver Dis.* 45 (10) (October 2013) 827–832.
- [21] G. Benassai, M. Mastrorilli, G. Quarto, A. Cappiello, U. Giani, P. Forestieri, F. Mazzeo, Factors influencing survival after resection for ductal adenocarcinoma of the head of the pancreas, *J. Surg. Oncol.* 73 (4) (2000) 212–218.
- [22] F. Rendano, M. Rinaldo, M. Infranzi, C. de Werra, A. Sarno, D. Palimento, L'ecografia intraoperatoria nella chirurgia della via biliare principale, *Il Cardarelli* XXVII (3–4) (1985) 157.
- [23] F. Rendano, M. Rinaldo, C. de Werra, R. Catelli, L'ecografia intraoperatoria nella chirurgia delle vie biliari, in: *Atti dell'VIII Congresso Nazionale Della Sezione Italiana Del Collegium Internationale Chirurgie Digestive*. Bologna, 18–21 maggio 1987, pp. 705–707.
- [24] M. Rinaldo, A. Sarno, C. Borriello, A. De Masi, G. Pezzella, C. de Werra, L'ecografia intraoperatoria nella chirurgia del pancreas, in: *Aggiornamenti in Chirurgia Dell'apparato Digerente Atti Del V Congresso Congiunto SIPAD-AICEB*. Taormina, 12–14/5/1988, pp. 291–292.
- [25] A. Sarno, C. de Werra, M. Rinaldo, C. Borriello, D. Palimento, A. Maresca, F. Rendano, L'ecografia intraoperatoria del fegato, in: *Aggiornamenti in Chirurgia Dell'apparato Digerente Atti Del V Congresso Congiunto SIPAD-AICEB*. Taormina, 12–14/5/1988, pp. 235–238.
- [26] F. Rendano, R. Catelli, C. de Werra, La nostra esperienza in tema di ecografia intraoperatoria del fegato e delle vie biliari, in: *Aggiornamenti in Patologia Dell'apparato Digerente; Atti Del X Congresso Nazionale SIPAD; Folgaria (Tn)*, 2–4/3/1989, pp. 269–278.
- [27] A. Maresca, G. Cammarota, C. Aiello, R. Catelli, C. de Werra, L'ecografia intraoperatoria nella valutazione delle metastasi epatiche sincrone da carcinoma colo rettale, in: *Atti Del Simposio internazionale in Oncologia Medica e Chirurgica*. Milano, 23–25 marzo 1994.
- [28] C. de Werra, A. Maresca, C. Aiello, N. Savino, P. Marra, V. Cerbone, in: *Il Trattamento Chirurgico dell'HCC: Utilità Dell'ecografia Peroperatoria Atti Del Convegno Congiunto SIRM, Eco Italia 1995*, Napoli, 28–30 giugno 1995, pp. 63–64.
- [29] P. Marra, A. Maresca, A. Marano, F. Ciccone, G. Benassai, C. de Werra, in: *L'ecografia Laparoscopica Nella Stadiazione Dei Pazienti Con Neoplasie Del Tratto Gastrointestinale Estratto Dagli Atti del 99° Congresso Della Società Italiana di Chirurgia*. Padova, 19–22 ottobre 1997, p. 116.
- [30] F. Rendano, M. Rinaldo, R. Catelli, S. Canitano, C. de Werra, Peroperative ultrasound in biliary surgery, in: *World Associationn of Hepato-pancreato-biliary Surgery, 1° Congress of the Italian Chapter; Bologna*, 13–15/11/1988, pp. 365–368.
- [31] C. de Werra, P. Marra, L'ecografia intraoperatoria (EIO) nella stadiazione delle neoplasie colo-rettali, in: *Atti Degli Incontri Interregionali di Aggiornamento in Chirurgia, Academy "Cancro del Colon-Retto"*, 1999, pp. 57–61.
- [32] C. de Werra, P. Marra, P. Forestieri, L'ecografia intraoperatoria nell'epatocarcinoma, in: *Da: Collana di Aggiornamento in Chirurgia della Società Polispecialistica dei Giovani Chirurghi: Argomenti di Chirurgia*, vol. 6, FORMA Communications Editore, Roma, 1999, pp. 101–112. Copyright.
- [33] C. de Werra, S. Condurro, F. Ciccone, F. Salvatori, C. Viviano, P. Forestieri, L'Ecografia intraoperatoria relazione dagli atti (relazioni vol. 3°) della 3° settimana chirurgica Italiana, Roma, in: *102° Congresso Nazionale Della Società Italiana di Chirurgia*, 15–20 ottobre 2000, pp. 99–100.
- [34] C. de Werra, P. Marra, F. Rendano, , in coll. G. Con Cammarota, S. Condurro, in: *Francesco Mazzeo (Ed.), Ecografia Intraoperatoria Estratto dal Trattato di Clinica e Terapia Chirurgica*, Piccin (Pd), 2001, pp. 607–617. Cap. 42.