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● *Original Contribution*

CONTRAST-ENHANCED ULTRASONOGRAPHY OF PANCREATIC CARCINOMA: CORRELATION WITH PATHOLOGIC FINDINGS

YANJIE WANG,* KUN YAN,* ZHIHUI FAN,* LI SUN,† WEI WU,* and WEI YANG*

*Key laboratory of Carcinogenesis and Translational Research (Ministry of Education/Beijing), Department of Ultrasound, Peking University Cancer Hospital & Institute, Beijing, China; and †Key Laboratory of Carcinogenesis and Translational Research (Ministry of Education/Beijing), Department of Pathology, Peking University Cancer Hospital & Institute, Beijing, China

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Abstract—We concluded that contrast-enhanced ultrasound (CEUS) has clinical value in identifying the pathologic changes of pancreatic carcinomas. Forty-three patients diagnosed with pancreatic carcinoma through surgery were retrospectively investigated. CEUS examinations were performed on all patients before surgery. Enhancement patterns on CEUS were observed. Time–intensity curves of CEUS were generated for the regions of interest in the pancreas, and quantitative parameters were obtained. Resected cancer specimens were stained with hematoxylin and eosin for histologic analysis, and the microvascular density (MVD) of the specimens was determined by CD34 immunohistochemical staining. Enhancement patterns of CEUS were compared with histopathologic findings in pancreatic carcinomas. Correlations between time–intensity curve parameters and microvascular density were analyzed. Twenty cases manifested centripetal enhancement, and 23 cases, global enhancement. The amount of tumor necrosis or mucus in the centripetally enhanced pancreatic carcinomas was greater than that in the globally enhanced pancreatic carcinomas ($p = 0.027$). Thirty-eight of 43 (88.4%) pancreatic carcinomas manifested hypo-enhancement with a maximum intensity (IMAX) <90%. Contrast arrival time in pancreatic carcinoma was longer than that in adjacent pancreatic tissue ($p < 0.05$). IMAX was positively correlated with microvascular density ($r = 0.577, p < 0.05$). We concluded that CEUS manifestations could reflect the histologic changes of pancreatic carcinomas and CEUS can be used to evaluate blood perfusion of tumors, as IMAX is positively correlated with microvascular density. (E-mail: ydbz@vip.sina.com) © **2016 World Federation for Ultrasound in Medicine & Biology.**

Key Words: **Contrast-enhanced ultrasonography, Pancreatic carcinoma, Pathology, Microvascular density.**

INTRODUCTION

Pancreatic carcinoma is the most common malignant tumor of the pancreas, and its incidence has been increasing in recent years (Kougioumtzopoulou et al. 2014). Although multiple imaging methods, such as contrast enhanced computed tomography (CECT) and magnetic resonance (MR) imaging have been widely applied in the diagnosis of pancreatic carcinoma (Furuhashi et al. 2015; Niu et al. 2014), the differentiation from other pancreatic lesions such as mass-forming pancreatitis can still be difficult. The application of endoscopic ultrasound (EUS)-guided needle biopsy aspiration greatly improved the differentiation of pancreatic lesions (Fritscher-Ravens et al. 2002). Nevertheless, non-invasive methods for detecting this malignancy are still preferred. Ultrasound (US) is a common method used to detect pancreatic lesions; however, it is difficult to determine the nature of lesions with US. In recent years, contrast-enhanced ultrasonography (CEUS) has been found to have important clinical value in the diagnosis of pancreatic lesions as it can non-invasively reflect the blood perfusion of tumor tissues in real time (D'Onofrio et al. 2007a; Fan et al. 2013). The application of CEUS has greatly improved the diagnostic accuracy in differentiating pancreatic carcinoma from other pancreatic lesions, which could exempt patients with benign lesions from unnecessary surgery (D'Onofrio et al. 2014; Hocke et al. 2008; Sofuni et al. 2005). Although hypo-enhancement has been proven to indicate the malignancy of a pancreatic tumor (Dietrich et al. 2008), there are a diversity of

Address correspondence to: Kun Yan, Fucheng Road Number 52, District of Haidian, Beijing, China. E-mail: ydbz@vip.sina.com

enhanced manifestations on CEUS that can be confused with other pancreatic lesions. In this study, the enhancement patterns and time–intensity curve (TIC) parameters of CEUS in pancreatic carcinomas were analyzed. The pathologic changes associated with different CEUS manifestations were explored.

METHODS

Patients

From August 2009 to December 2013, 412 patients with pancreatic disease underwent CEUS at our hospital; among these, 206 patients had obtained a pathologic diagnosis based on surgery or biopsy. Forty-three lesions in 43 patients were pathologically diagnosed as pancreatic carcinoma after surgery. The mean diameter of pancreatic carcinomas as determined by US was 3.59 ± 1.08 cm (range: 2.15–5.32 cm). The 43 patients comprised 21 men and 22 women (mean age: 61.23 ± 10.32 y, age range: 28–78 y). Thirty-three lesions were located in the pancreatic head and neck and 10 in the pancreatic body and tail. Thirty-seven cases were dancer antigen-199 (CA-199) positive, and 6 cases CA-199 negative.

Institutional review board approval was obtained, and informed consent forms were signed by all the patients before the study. The work flow of this study is depicted in Figure 1.

Contrast-enhanced ultrasonography technique

All patients were asked to fast for at least 8 h before CEUS. A Logiq E9 ultrasonic unit (GE Healthcare, Milwaukee, WI, USA) was used. Images were obtained with a C1-5 2.5-MHz convex probe. The second-generation ultrasound contrast agent SonoVue (Bracco, Milan, Italy) was used. Lyophilized SonoVue powder was dissolved in 5 mL saline. Two milliliters of the suspension was injected into the antecubital vein *via* a 20-G cannula within 2–3 s, followed by a 5-mL saline flush. After injection of contrast agent, the pancreas was scanned using contrast-enhanced harmonic gray-scale sonography. The mechanical index was set at 0.11, and the transmitted acoustic power was 100%.

Dynamic blood perfusion of tumor tissue and surrounding tissues was observed from baseline to late phase. Then the images were stored. The enhancement phases were divided into early phase (10–30 s after injection) and late phase (30–120 s after injection).

The enhancement patterns of pancreatic lesions were analyzed by two ultrasound doctors with more than 5 y of experience in pancreatic imaging. Enhancement from the periphery to the center was defined as centripetal enhancement. Enhancement of the periphery and the center at the same time was defined as global enhancement. If there was a discrepancy between the two ultrasound doctors, they reached agreement by consensus.

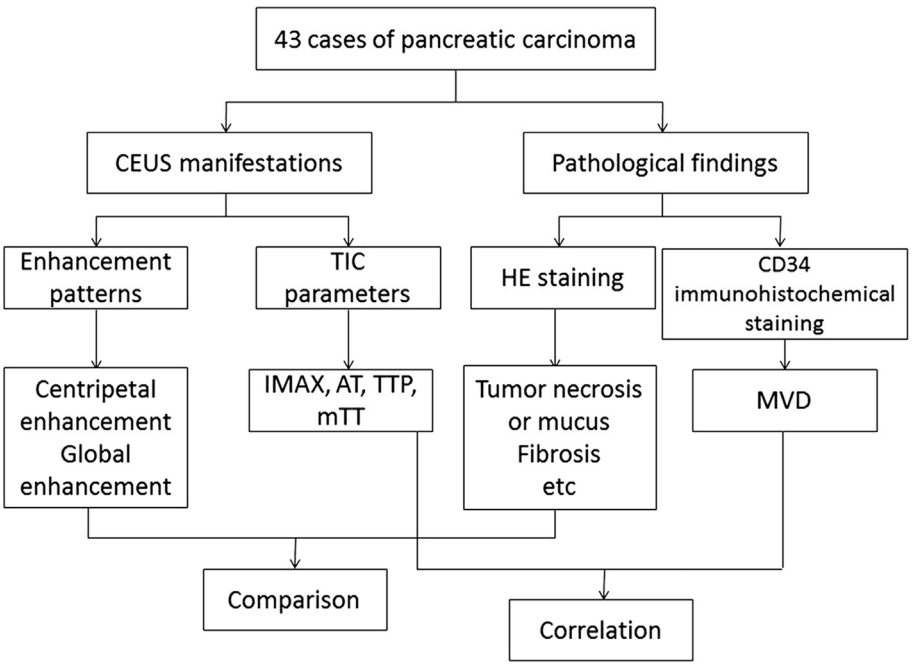

Fig. 1. Work flow of this study. CEUS = contrast-enhanced ultrasound, TIC = time–intensity curve, IMAX = maximum intensity, AT = arrival time: time from beginning of contrast agent injection to beginning of enhancement, TTP = time to peak: time from beginning of enhancement to maximum intensity, mTT = mean transit time: mean time from beginning of enhancement to time when enhancement intensity decreases to half of IMAX.