The advantage of using CEUS time-intensity curves vs. conventional ultrasound in the differential diagnosis of mass pancreatitis and pancreatic cancer

Yanshen Liu¹, Weiming Xu²

¹Department of Ultrasound, The First People’s Hospital of Fuyang Hangzhou, Hangzhou 311400, Zhejiang, China; ²Department of Gastroenterology, The First People’s Hospital of Fuyang Hangzhou, Hangzhou 311400, Zhejiang, China

Received April 22, 2020; Accepted June 23, 2020; Epub November 15, 2020; Published November 30, 2020

Abstract: Objective: This study was designed to explore the advantages of using CEUS time-intensity curves (TIC) vs. conventional ultrasound in the differential diagnosis of mass pancreatitis and pancreatic cancer. Methods: From January 2017 to December 2019, 51 patients with mass pancreatitis and 57 patients with pancreatic cancer were recruited as the study cohorts and examined using CEUS and conventional ultrasound. TIC were used to analyze and calculate the arrival times of the contract medium in the lesion (AT), the times to peak (TTP), the peak intensities (I_{max}), and the transition times (TT). The advantages of using the TIC indices vs. conventional ultrasound in the diagnosis of pancreatic cancer were compared. Results: (1) The AT was significantly shorter and the I_{max} was significantly higher in the patients with mass pancreatitis (P<0.05), but no significant differences in the TTP or TT were observed (P>0.05). (2) The accuracy and positive/negative predictive value were significantly higher than the accuracy and positive/negative predictive value of conventional ultrasound when pancreatic cancer was diagnosed according to the criteria of AT ≥ 9.45 s, I_{max} ≤ 72.14%, AT ≥ 9.45 s or I_{max} ≤ 72.14%, AT ≥ 9.45 s and I_{max} ≤ 72.14%. The sensitivity was significantly higher than the sensitivity obtained using conventional ultrasound when the criteria of AT ≥ 9.45 s, I_{max} ≤ 72.14%, AT ≥ 9.45 s or I_{max} ≤ 72.14%, AT ≥ 9.45 s and I_{max} ≤ 72.14% were followed in the diagnosis. The specificity yielded when the diagnostic criteria of AT ≥ 9.45 s, I_{max} ≤ 72.14%, AT ≥ 9.45 s or I_{max} ≤ 72.14% were referenced in the diagnosis of pancreatic cancer was significantly higher than it was when using conventional ultrasound, especially the highest accuracy and sensitivity when AT ≥ 9.45 s or I_{max} ≤ 72.14% was used. Conclusion: Compared with conventional ultrasound, TIC was better at differentiating mass pancreatitis from pancreatic cancer; in particular, its higher accuracy when AT ≥ 9.45 s or I_{max} ≤ 72.14% was adopted as the diagnostic criterion.

Keywords: CEUS, TIC, conventional ultrasound, mass pancreatitis, pancreatic cancer

Introduction

Because it is chronic and a risk factor for pancreatic cancer [1, 2], mass pancreatitis is related to the pathological changes of chronic inflammatory cell infiltration and progressive fibrous hyperplasia. Pancreatic cancer is a common and severe malignant tumor of the digestive tract with a poor prognosis that is often lethal [3, 4], as shown by its 5-year survival rate of only 6%. Both mass pancreatitis and pancreatic cancer are focal lesions in the pancreas, which lies at a shallow place behind the peritoneum, resulting in un conspicuous clinical symptoms and signs when it experiences pathological changes, making early diagnosis difficult [5], as the organ is often attacked insidiously. Clinical therapies for mass pancreatitis and pancreatic cancer are entirely different. If pancreatic cancer is mistaken as mass pancreatitis, the patients may suffer from treatment delays that threaten their lives. Therefore, the early and correct differential diagnoses of mass pancreatitis and pancreatic cancer are particularly important.

In the clinic, CT, MRI, and ultrasound are generally used to differentially diagnose mass pancreatitis and pancreatic cancer. However, the first two options are expensive and not suitable for patients with a renal inadequacy, so their clinical applications are limited [6]. Ultrasound
The advantages of using CEUS TIC vs. conventional ultrasound

is invasive, affordable, reproducible, and radiation free, and it is often used in the clinical differentiation of mass pancreatitis and pancreatic cancer [7]. The ultrasonic images of mass pancreatitis and pancreatic cancer may be similar, as both diseases are local lesions in the pancreas, and they may be subject to interference from factors such as the subject's body shape and gas in the abdomen. Therefore, conventional ultrasound is limited to differentiating mass pancreatitis and pancreatic cancer.

The highly safe CEUS supports the dynamic and continuous observation of the microcirculation perfusion at the lesion and plays an important role in the differential diagnosis of mass pancreatitis and pancreatic cancer [8]. When CEUS TIC is used in the quantitative analysis of CEUS images, the microperfusion in the tissues can be observed more accurately and objectively. Therefore, in this study, conventional ultrasound and CEUS examinations were performed on patients with mass pancreatitis and pancreatic cancer. The TIC indices were compared, and the diagnostic advantages of the TIC indices and conventional ultrasound in pancreatic cancer were analyzed in order to provide a supplementary reference for the early differential diagnosis of mass pancreatitis and pancreatic cancer.

Materials and methods

Methods

All the patients received CEUS and conventional ultrasound examinations after fasting for at least 8 hours. The instrument was a LOGIQ E9 high-grade color ultrasound diagnostic apparatus from GE, USA. The probe frequency was set to 2–4 MHz, and the mechanical index was set to 0.08–0.10. During the examination, the patients were required to breathe normally, and the tangent plane selected for imaging was kept unchanged. At the end of CEUS, the dynamic imaging pictures were saved and imported into the SonoLiver. As the lesion and the pancreas area around the lesion (the control) were selected, an ROI sampling box was placed at the selected area with maximal efforts to avoid dilated pancreatic ducts and great vessels. TIC began to calculate the AT, the TTP, the Imax, and the TT, of which, Imax is a relative value expressed as a percentage, expressed as the ratio of echo intensity at the lesion to that of the pancreas area around the lesion. TTP is defined as the time elapsed from the beginning of the echo enhancement at the lesion to Imax, and TT is defined as the time elapsed from the beginning of the echo enhancement to the Imax dropping by 50%. As TTP and TT are related to Imax, the TIC indices are diagnosed with AT and Imax, with AT defined as ≥ 9.45 s and Imax as ≤ 72.14%. The ultrasonic contrast images of mass pancreatitis and pancreatic cancer are shown in Figures 1 and 2.
The advantages of using CEUS TIC vs. conventional ultrasound

Observation indices

The AT, TTP, Imax, and TT were compared between the patients with mass pancreatitis and those with pancreatic cancer. The accuracy, sensitivity, specificity, and positive/negative predictive values of the TIC indices (AT ≥ 9.45 s, Imax ≤ 72.14%, AT ≥ 9.45 s or Imax ≤ 72.14%, AT ≥ 9.45 s and Imax ≤ 72.14%) and of conventional ultrasound in the diagnosis of pancreatic cancer were analyzed.

Statistical analysis

The statistical analysis was performed using SPSS 22.0. The patients’ genders, and their true positive/negative (TP/TN) and false positive/negative (FP/FN) data were expressed as n, and independent-samples X² tests were carried out. The AT, TTP, Imax, and TT were expressed as the means ± standard deviation, and independent-samples t tests were carried out. For all the statistical comparisons, significance was defined as P<0.05.

Results

TIC indices

The AT, Imax, TTP, and TT were (8.44±2.66) s, (86.66±22.41)%, (8.34±2.55) s, and (27.43±9.03) s in the patients with mass pancreatitis and (11.12±3.62) s, (44.37±12.58)%, (8.69±2.47) s, and (27.87±8.81) s in the patients with pancreatic cancer (P<0.05 for AT and Imax, P>0.05 for TTP and TT) (Table 1; Figures 3 and 4).

The advantages of TIC indices and of conventional ultrasound in the diagnosis of pancreatic cancer

The number of TP, FP, FN, and TN cases were 43, 14, 14 and 37 according to AT ≥ 9.45 s, 41, 17, 16, and 34 according to Imax ≤ 72.14%, 53, 20, 4, and 31 according to AT ≥ 9.45 s or Imax ≤ 72.14%, 31, 10, 26, and 11 according to AT ≥ 9.45 s and Imax ≤ 72.14%, and 25, 28, 32, and 23 when done using conventional ultrasound (Table 2).

The sensitivity and specificity of the TIC indices and of conventional ultrasound in diagnosing pancreatic cancer

In diagnosing pancreatic cancer: (1) The accuracies of AT ≥ 9.45 s, Imax ≤ 72.14%, AT ≥ 9.45 s or Imax ≤ 72.14%, AT ≥ 9.45 s and Imax ≤ 72.14%, and conventional ultrasound were 74.07%, 69.44%, 77.78%, 66.67% and 44.44% (P<0.05); and (2) The sensitivities of Imax ≤ 72.14%, AT ≥ 9.45 s or Imax ≤ 72.14%, and conventional ultrasound were 75.44%, 71.93%, 92.98% and 43.86% (P<0.05). In the case of AT ≥ 9.45 s and Imax ≤ 72.14%, the sensitivity was only 54.39% (P>0.05); (3) The specificities of AT ≥ 9.45 s, Imax ≤ 72.14%, AT ≥ 9.45 s and Imax ≤ 72.14%, and conventional ultrasound were 72.55%, 66.67%, 80.39% and 45.10% (P<0.05). In case of AT ≥ 9.45 s or Imax ≤ 72.14%, the specificity dropped to 60.78% (P>0.05); (4) The positive/negative predictive values of AT ≥ 9.45 s, Imax ≤ 72.14%, AT ≥ 9.45 s or Imax ≤ 72.14%, AT ≥ 9.45 s and Imax ≤ 72.14%, and conventional ultrasound were 75.44%/72.55%, 70.69%/68.00%, 72.60%/88.57%, 75.61%/61.19%, and 47.47%/41.82% (P<0.05) (Table 3).

Figure 1. Ultrasonic image of mass pancreatitis.

Figure 2. Ultrasonic image of pancreatic cancer.
The advantages of using CEUS TIC vs. conventional ultrasound

Table 1. A comparison of the TIC indices between mass pancreatitis and pancreatic cancer ($\bar{x} \pm s$)

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>AT (s)</th>
<th>TTP (s)</th>
<th>Imax (%)</th>
<th>TT (s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mass pancreatitis</td>
<td>51</td>
<td>8.44±2.66</td>
<td>8.34±2.55</td>
<td>86.66±22.41</td>
<td>27.43±9.03</td>
</tr>
<tr>
<td>Pancreatic cancer</td>
<td>57</td>
<td>11.12±3.62</td>
<td>8.69±2.47</td>
<td>44.37±12.58</td>
<td>27.87±8.81</td>
</tr>
</tbody>
</table>

| t       | 4.341 | 0.723 | 12.256 | 0.256 |
| P       | <0.001 | 0.471 | <0.001 | 0.798 |

Figure 3. Comparison of the AT between mass pancreatitis and pancreatic cancer. The AT in patients with mass pancreatitis is significantly lower than it is in patients with pancreatic cancer ($P<0.05$). *$P<0.05$ for intergroup comparison.

Figure 4. Comparison of the Imax between mass pancreatitis and pancreatic cancer. The Imax in patients with mass pancreatitis is significantly higher than it is in patients with pancreatic cancer ($P<0.05$). *$P<0.05$ for intergroup comparison.

Discussion

The concealment of pancreatic cancer in the early onset stage results in most patients missing the best treatment window and already being at the middle-to-advanced stage when they are first referred to a specialist. Even after surgical treatment, the 5-year survival is not optimistic [9, 10]. Mass pancreatitis has a long duration and local masses due to long-term tissue fibrosis and inflammatory cell infiltration, and it is a known hazard of pancreatic cancer [11, 12]. Pancreatic cancer is similar to mass pancreatitis in its ultrasonic manifestation, clinical symptoms, and signs. They are difficult to differentiate, and they are treated using entirely different therapies. Therefore, an early differential diagnosis and symptomatic treatment would play a significant role in improving the prognosis.

Conventional ultrasound is usually used for the preliminary screening of pancreatic lesions. However, most pancreatic lesions are manifested as mixed or low echoes. The similarity exerts an influence on the accuracy of this tool in the differential diagnosis of mass pancreatitis and pancreatic cancer [13, 14], while the subject’s body shape and gas in the abdomen also affect its sensitivity. In contrast, CEUS supports pure blood pool imaging by conducting the CEUS medium into the tissue gaps, in order to accurately reflect the low-volume and low-flowrate blood signals in the lesion and to continuously observe the tissues concerned on a real-time basis. In this way, CEUS plays a key role in the differential diagnosis of local pancreatic lesions [15, 16]. However, some studies have pointed out that the visual observation of normal pancreatic tissues and pancreatic lesions for enhancement degrees and reinforcement times may be subjective [17, 18]. Therefore, TIC was adopted in this study to quantitatively analyze mass pancreatitis and pancreatic cancer based their TIC indices, and a comparison was performed between the TIC indices and conventional ultrasound to determine their advantages in the differential diagnosis of the two diseases.

For patients with mass pancreatitis, the AT was significantly shorter than the AT of the patients with pancreatic cancer. The reason is that the vascular density in patients with mass pancreatitis or pancreatic cancer was decreasing, but the tissue reconstruction, necrosis, thrombus, and bleeding produced in the course of chronic inflammation can lead to cicatrix fracture and
The advantages of using CEUS TIC vs. conventional ultrasound

The contraction of the entire gland, so that the contrast medium can rapidly enter the lesions [19, 20]. However, in patients with pancreatic cancer, the tumor tissue was densely enveloped by microvessels, which slowed down the speed of the contrast medium approaching the tumor center [21, 22]. In this study, it was also found that the Imax in patients with mass pancreatitis was significantly higher than it was in patients with pancreatic cancer. The reason lies in the enhanced vasa vasorum in a shape of a strip found in or around the tumor during the arterial phase imaging, and the contrast medium flowed from the periphery to the center [23, 24]. Furthermore, there are fewer microvessels in a cancerized pancreas than there are in a normal one, and the vasa vasorum are generally deployed around the tumor lesion where fibrous tissues proliferate and the vascular density is relatively low. So, the enhancement and the Imax in patients with pancreatic cancer are at a low level [25, 26]. Moreover, no significant differences in TTP (the time elapsed from the beginning of echo enhancement at the lesion to Imax) or in TT (the time elapsed from the beginning of echo enhancement to Imax dropping by 50%) were observed in this study, which may have a possible relevance with their definitions.

Studies have shown that CEUS is of great significance in the diagnosis of thymic tumors and peripheral pulmonary lesions in the elderly, and its diagnostic value is higher than that of conventional ultrasound [27]. In this study, CEUS was applied to the diagnosis of pancreatic cancer through a quantitative analysis, which is different from most previous studies. The results showed that the value of the different indicators of ultrasound TIC in the diagnosis of pancreatic cancer was higher than that of conventional ultrasound. Therefore, $AT \geq 9.45\, s$ or $Imax \leq 72.14\%$ had the highest accuracy and sensitivity in the diagnosis of pancreatic cancer (77.78% and 92.98% respectively), which is consistent with the findings of Fan et al. [28]. Those results proved that TIC quantitative analysis, especially $AT \geq 9.45\, s$ or $Imax \leq 72.14\%$, was more advantageous in the differential diagnosis compared with conventional ultrasound.

To sum up, when compared with patients with pancreatic tumors, patients with mass pancrea-
The advantages of using CEUS TIC vs. conventional ultrasound

...had lower AT and higher Imax values but significant differences in TTP and TT were not observed, indicating that AT and Imax can be used as an important basis for the differential diagnosis of mass pancreatitis and pancreatic cancer. When compared with conventional ultrasound, TIC is better at differentiating mass pancreatitis and pancreatic cancer and has a particularly high accuracy when AT ≥ 9.45 s or Imax ≤ 72.14% is used. Therefore, TIC indices can be used in the objective and accurate differential diagnosis of mass pancreatitis and pancreatic cancer. Nevertheless, there are also limitations to this study: ultrasound examinations will be affected by gastrointestinal gas and a patient’s body shape. The TIC quantitative analysis is subject to factors such as breathing, psychology, and normal pancreatic depth, but this study was relatively limited in terms of the size of the cohorts, so an in-depth study with a large sample size is still needed in the future.

Acknowledgements

The authors received no financial support for the research, authorship, and/or publication of this article.

Disclosure of conflict of interest

None.

Address correspondence to: Yanshen Liu, Department of Ultrasound, The First People’s Hospital of Fuyang Hangzhou, No. 429 Beihuan Road, Fuchun Street, Fuyang District, Hangzhou 311400, Zhejiang, China. Tel: +86-13897657801; E-mail: tt400anen@163.com

References


8583

The advantages of using CEUS TIC vs. conventional ultrasound


