

The Efficacy of High-Intensity Focused Ultrasound (HIFU) in Advanced Pancreatic Cancer

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OBJECTIVE To observe the efficacy of high-intensity focused ultrasound (HIFU) in the treatment of late-stage pancreatic cancer.

METHODS Sixteen patients with advanced pancreatic cancer received HIFU therapy. Evaluation of efficacy was made on the basis of changes in clinical symptoms and variations in the tumor echo and size.

RESULTS Clinical symptoms such as pain were significantly alleviated, echo of the tumor was enhanced with B-US and the quality of life such as eating, sleeping and mental status was markedly improved; no serious complications were observed.

CONCLUSION The use of HIFU in the treatment of advanced pancreatic cancer is feasible and safe. It is effective in killing the carcinoma cells and alleviating pain. This technique may offer non-invasive therapy for the treatment of patients with late-stage pancreatic cancer.

KEY WORDS: high-intensity focused ultrasound, pancreatic cancer, pain, treatment.

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Introduction

Pancreatic cancer is one of the most common malignancies in the world and 80% of the patients are unsuitable candidates for surgery. The survival time for advanced pancreatic cancer patients is about 4 months. Moreover, these patients generally suffer serious abdominal pain, significantly harming their quality of life. Chemotherapy and radiotherapy are the most common methods to treat these patients, but these therapies are not well tolerated, their efficacy is poor and the rate of pain relief is very low.

High-intensity focused ultrasound (HIFU) has considerable potential as a non-invasive surgical technique for the local treatment of tumors. It can penetrate tissues and focus on the target region of the tumor. This produces a thermal effect and cavitation at high peak intensities, making it possible to destroy a target region of the tumor without damaging overlying tissue. In this study, 16 patients were treated with HIFU. We evaluated the clinical benefits including pain relief and the improvement of the patients' quality of life.

Materials and Methods

Clinical materials

Sixteen advanced pancreatic cancer patients, with an average age of 46.6 years (range 26~81), including 10 men and 6 women, who were treated with HIFU from July 2006 to March 2007, participated in this study. Three of the cases were confirmed by pathology and the others

were diagnosed by CT or PET/CT and serum analysis. All of the patients had poor general health and suffered from lumbago, backache, or abdominal pain. Eight patients were jaundiced, one had pancreatitis, and two suffered from vomiting. The average performance status score was 57.5 and the lowest 40. Among the patients, 7 had undergone chemotherapy without success, 7 could not tolerate chemotherapy and 9 refused chemotherapy.

Instruments

The HIFUNIT9000 tumor therapy equipment was made by the Shanghai Aishen Science and Technology Development Co. The ultrasound wave frequency was 1.0 MHz. This instrument consists of 3 systems: a microcomputer-based control, positioning, and treatment. The main parameters of the equipment include: maximum output power, 600 W; effective therapy depth, 17 cm; focused sphere, $3 \times 3 \times 8$ mm; treatment time (t 1): 0.1–0.4 s; intermission time (t 2), t 1/t 2 = 2:1; all of the parameters can be adjusted according to the different depth and size of tumors. In this study, the main parameters were: output power, 200–300 W; t 1: 0.1–0.2 s; t 2: 0.2–0.4 s, and the number of times of emission per lattice (N): 6–8.

Treatment procedure

B-mode sonography (B-US), CT, MRI, or PET/CT should be performed first to determine the position, size and morphological aspects of the tumor, and to see how adjacent blood vessels and organs are affected. Depending on the patients' conditions, preparations were routinely conducted. For example, the jaundiced, or the pancreatitis patients should be managed before application of HIFU. For the treatment, the patient lay on the bed, so the tumor could be localized primarily using external B-US and marked by a laser lamp. Then the re-localization of the therapy area was completed through the built-in detecting head of the instrument. The B-US monitoring system was started and the treatment range defined according to the image, by ascertaining the treatment levels and power. Subsequently the treatment focus was moved following the X, Y and Z axes in terms of the planned procedure to cover the target regions. All HIFU administrations were performed percutaneously using real-time US guidance.

Observation index

The efficacy of HIFU was evaluated as the change in clinical symptoms such as abdominal pain, fatigue, difficulty in sleeping, and loss of appetite and weight. The tumor size and echo transformation, complications, and amylase changes were also recorded.

Results

Sixteen patients received HIFU treatment in 68 cycles.

The average number of cycles was 4.25 (range 2–8), on alternate 1–3 day (s), with beamed time 100–200 ms, intermission time 200–400 ms, and beamed power 300 W. All of the patients' tumors could not be totally resected. CT or MRI showed that their tumors had invaded the contiguous blood vessels such as the abdominal aorta and superior mesenteric artery. The tumor of 5 of the patients had spread to the surround organs such as the liver and stomach.

All patients had abdominal pain or/and backache before HIFU treatment, with the effective rate of pain relief reaching 87.5% (14/16 cases): 5 patients (25%) were entirely pain free and the other 9 patients had reduced pain levels. Twelve of the patients had taken pain medication prior to treatment, after which 3 needed no pain medication, while the other 9 took less. Appetite, sleeping and mental status was markedly improved in most of the patients.

The pathway of the tumor focus was measured on the basis of B-US and CT images in order to calculate the volume of each tumor. Our results indicated that the tumor size shrunk in 4 patients, 11 showed no change, and one patient's tumor was larger. US showed that the tumor echo was enhanced significantly in 15 patients. The following changes were generally observed after treatment (Fig.1). The blood supply of 4 patients' tumor was decreased and necrosis was found in the tumors after HIFU as confirmed by CT (Fig.2).

A few complications were observed. One of the patients had slight skin burn, however after 3 days this condition was improved with medication. Ten patients experienced a prickly sensation on their skin, but this feeling disappeared after treatment was stopped. A patient, whose jaundice was aggravated one week after HIFU and had refused a surgical biliary bypass before treatment, was remedied by cholecystojejunostomy. No serious complications such as acute pancreatitis, tumor rupture and bleeding, or damage to the stomach or intestines were observed. One of the patients who had acute pancreatitis before HIFU, received pancreatitis treatment and was cured. He showed no alteration of amylase levels after HIFU treatment.

Discussion

Pancreatic carcinoma is a common malignancy that is increasing in frequency, and advanced pancreatic cancer is resistant to radiation and chemotherapy. Although, gemcitabine therapy is the gold standard for advanced pancreatic cancer, the response to this drug is only about 12%. There is no effective therapy to improve the survive time of advanced pancreatic cancer patients, so the clinical benefit response is used to evaluate the efficacy of treatment in these cases. Pain relief is important for these patients, especially for those who cannot endure chemotherapy or radiotherapy as controlling pain greatly improves their quality of life.

High-intensity focused ultrasound has emerged re-

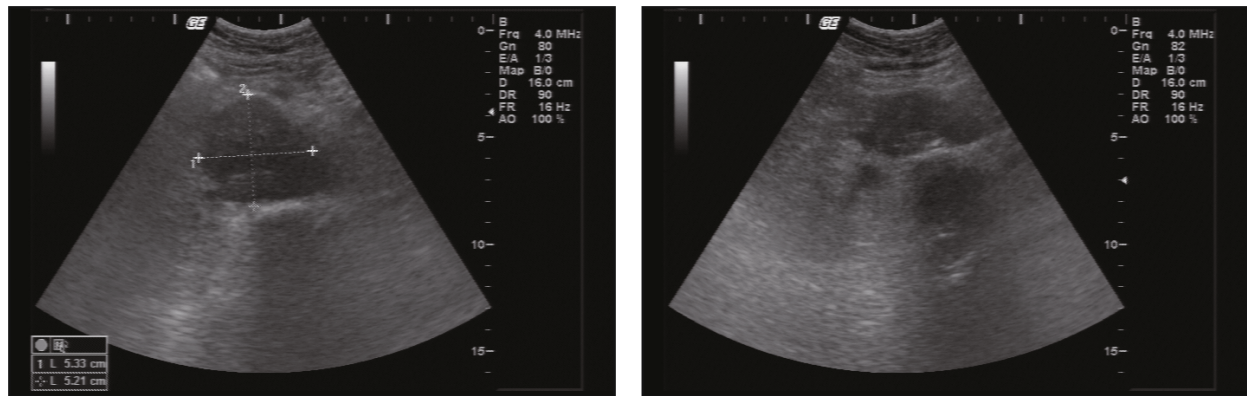


Fig.1. A 46-year-old woman with pancreatic cancer. A, US showed that the tumor size was 5.33 × 5.21 cm before HIFU ablation; B, One month after HIFU ablation, B-US showed the tumor size was 3.5 × 3.0 cm and the echo of the tumor was enhanced.

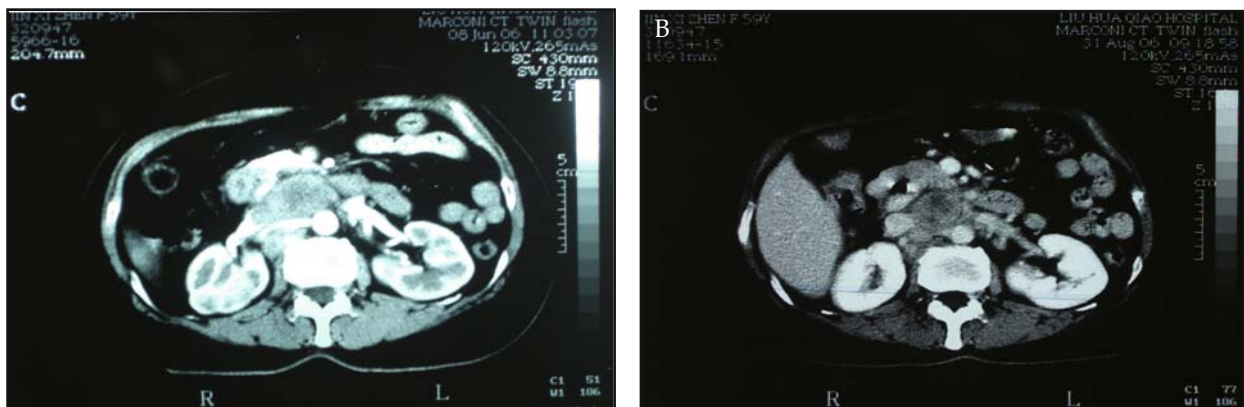


Fig.2. A 60-year-old woman with pancreatic cancer. A, Enhanced CT- scan showed that the enhancing tumor was 3.0 × 4.8 cm before HIFU ablation; B, Two months after HIFU, enhanced CT showed there was necrosis in the tumor and the tumor shrunk to 2.4 × 2.9 cm.

cently as a non-invasive surgical technique for tumor treatment. Theoretical and experimental evidence has shown that HIFU can destroy tumor tissue, kill tumor cells, restrain the proliferation of malignancy^[1-3], and reduce pain from the tumors quickly and safely^[4-7]. It is an optimal method for late-stage pancreatic cancer^[8-11].

Pain is the most common and serious clinical symptom of pancreatic cancer, generally manifested with a dull pain which may radiate to the waist and in some cases the pain is acute. When a late-stage tumor invades the solar plexus, the pain tends to be more intense, affecting sleep and appetite. At present, oral administration of morphine is applied, but complications can arise and it is not always appropriate treatment. HIFU can relieve the pain quickly and safely, and in our study, this was achieved on the second day after HIFU reaching a rate of 87.5%. More anodyne administration was not needed, and their sleeping, eating and mental status was improved.

A 62-year-old female patient with advanced pancreatic cancer had acute lumbago causing her to lay on the bed all day. Her performance status score was 40 before HIFU and it was impossible for her to take chemotherapy or radiotherapy. After the second day of HIFU treat-

ment her lumbago and abdominal pain eased so she was given smaller doses of morphine. After 3 HIFU treatments, her performance status score reached 60 with an improved quality of life. She finished 6 cycles of HIFU and she survived more than 6 months, indicating that HIFU can be effective and feasible for this cancer, especially in severe cases.

The means by which HIFU relieves pain may be: production of high temperatures (70°C~100°C) in the target region, resulting in the destruction of pancreatic carcinoma cells. In addition, the targeted solar plexus may be inactivated preventing transfer of the pain excitation to the brain. At the same time, the pressure on the nerve would be reduced owing to the shrinking of the tumor size.

The chief concern with this procedure is clinical safety. Since this therapy is painless during treatment, no anesthetic is needed, and HIFU treatment can be repeated if follow-up indicates tumor focus growth. No serious complications such as intestinal perforation, vascular damage or bleeding of the tumor, or peritonitis were observed, suggesting that HIFU therapy for pancreatic carcinoma is safe. To prevent complications, one must pay attention to the following: in the first instance,

orientation according to B-US should be confirmed and purging of the intestine is needed because gas and fecal residue in the intestine will interfere with orientation of B-US causing the ultrasound radiation to be scattered rendering the treatment less effective. Therefore food intake should be restricted before treatment. Conditions such as pancreatitis, serious infections, cachexia, jaundice, etc. must be managed before HIFU therapy is given. In this study, one patient had pancreatitis which we treated until his amylase was normalized before HIFU. His amylase did not increase after HIFU. Another patient with jaundice refused to accept a surgical biliary bypass. One week after HIFU the jaundice was serious, although the pain was relieved, showing that patient pre-treatments are of importance.

The echo of the focus was boosted to differing degrees with enhancement in 93.7% of the patients. CT showed necrosis in the tumor and the blood had disappeared in the treated area, indicating that the tumor and undergone necrosis and the vessels had been occluded by HIFU. However, most of the tumors failed to shrink, but pain had decreased. This showed that the size of the tumor is not the only bench mark to evaluate HIFU efficacy in treating pancreatic cancer.

In conclusion, our study indicated that using HIFU treatment in advanced pancreatic carcinoma was effective and safe. Although, HIFU can relieve the pain quickly, this relief can last for only a few days in some patients. Long-term studies with more patients are needed to determine if HIFU can improve the survival rate. Perhaps the optimal method to treat advanced pancreatic cancer is by using HIFU in conjunction with radiotherapy and chemotherapy.

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