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Ultrasound Guided High Intensity Focused Ultrasound for malignant tumors: The Spanish experience of survival advantage in stage III and IV pancreatic cancer

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ABSTRACT

We described the experience of the HIFU Onco Unit of Hospital University Mutua Terrassa (Barcelona, Spain) treating malignant tumors, focusing on results of unresectable pancreatic tumors treated with Ultrasound Guided High Intensity Focused Ultrasound (USgHIFU) hyperthermia ablation in combination with adjuvant chemotherapy.

Materials and methods: From February 2008 to December 2013, we treated 140 malignant cases. Of those, 48 cases of unresectable pancreatic tumors were treated from March 2010 to December 2013, and the first 43 were included in the analysis. All the 43 cases (29 cases of stage III and 14 cases of stage IV) were treated with systemic chemotherapy. Clinical responses (thermical ablation achieved) were measured by image techniques, and complications were also recorded and analyzed.

Results: The majority of the 140 cases treated at our HIFU center were pancreatic and liver tumors, among which 43 cases of pancreatic tumors were analyzed. Clinical responses (ablation obtained) were observed in 82% of the cases, and the responses lasted at 8 weeks post-procedure. We obtained 11 complete responses (25%) at the end of the combined treatment, nine from stage III patients and two from stage IV patients. Major complications included severe pancreatitis with GI bleeding (1), and skin burning of grade III that required plastic surgery (2). The median survival was 13 months (6 months–2.7 years). No deaths were registered during the course of the treatment.

Conclusions: HIFU is a potentially effective and safe modality for the treatment of malignant tumors. HIFU proves to have a survival advantage in treating unresectable pancreatic cancer.

1. Introduction

US-guided HIFU is a validated safe technique with no mortality, low morbidity and promising treatment outcomes. At present, there are several ablation techniques employed to treat tumors in different locations. Radiofrequency, microwaves, cryotherapy, ethanol injection, and embolisation are considered for treating tumors in several locations except pancreas, while there is no reported ablative technique suitable for pancreatic lesions. Ultrasound Guided High Intensity Focused Ultrasound (USgHIFU) is a minimally invasive surgical technique that has proven to improve the local control for different types of tumors. Several studies in animals and humans have shown the efficacy of this technique in causing a coagulative necrosis as the main mechanism of eradicating tumor masses. Reports of the treatment of pancreatic masses using USgHIFU have been published recently, underlining its potential role as a novel concomitant treatment with Gemcitabine based chemotherapy [1,2] .

Hospital University Mutua Terrassa (HUMT) is a 500-bed institution that serves an area of 300,000 people. The HIFU Unit in HUMT was established in 2008, after the acquisition of a HAIFU JC device from HAIFU, Chongqing, China (Fig. 1). The early cases treated at the center were exclusively the benign uterine fibroid tumors with only few cases of malignant tumors. In January 2010, HIFU Surgical Oncology Unit was established, and since then a wide variety of malignant tumors has been treated at our institution.

Despite continuous scientific advances in the field of oncology, pancreatic cancer remains to have a poor prognosis. A significant part of the cases are considered unresectable at diagnosis due to

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Fig. 1. The US-guided HIFU System: Haifu JC Chongqing, China. Image of the HIFU device with detail of the transducer.

late detection of the disease or invasion of great vessels surrounding the tumor [1]. Therefore, treatments with chemotherapy and low-grade radiotherapy are the only means suitable for the patients with locally advanced lesion [2]. Overall survival is around 6–10 months in stage III patients and only 3–6 months in stage IV patients [1].

The purpose of this paper was to share our experience in treating malignant tumors with HIFU during a 5-year period and to evaluate retrospectively the results of HIFU treatment in a group of advanced pancreatic cancer patients treated at our institution.

2. Materials and methods

During the 5-year period of 2008–2013, we treated 140 malignant tumors. (Table 1), most of which were pancreatic and hepatic tumors: 48 pancreatic tumors, 31 liver metastases, 15 hepatocellular carcinomas, 16 soft tissue tumors, 8 bone metastases, 7 kidney tumors, 4 bile ducts carcinomas, 2 neuroblastomas, 2 lung metastases and 1 lymphoma.

We analyzed forty-three cases of unresectable pancreatic tumors due to locally advanced lesions that were treated with HIFU in our institution from March 2010 to December 2013. Most patients were referred to our hospital from the oncology or surgery departments of different Spanish hospitals, and three of them came from other European institutions. All of them had a pathologically confirmed diagnosis of pancreatic cancer and underwent systemic chemotherapy with a Gemcitabine based combination prior to or after HIFU treatment (Fig. 2). Patient's age ranged from 32 to 79 years, with a median of 63.

Table 1
Cases treated during a 5-year period. Notice pancreatic tumors as the most prevalent in our complete series of oncologic cases. Liver tumors are rated in second place.

	Total	2008	2009	2010	2011	2012	2013
HCC	15	2	3	3	1	1	5
Kidney	7	0	1	4	0	2	0
Pancreas	48	2	4	13	13	9	7
Liver met	31	1	2	14	10	3	1
Bone met	8	1	2	0	2	3	0
Soft tissue T	16	0	0	4	6	3	3
Neuroblastoma	2	0	0	1	0	0	1
Lymphoma	1	0	0	1	0	0	0
Breast T	6	1	1	3	0	1	0
Colangiocarc.	4	0	0	0	1	0	3
Lung met	2	0	0	1	0	0	1
Total	140	7	13	44	33	22	21

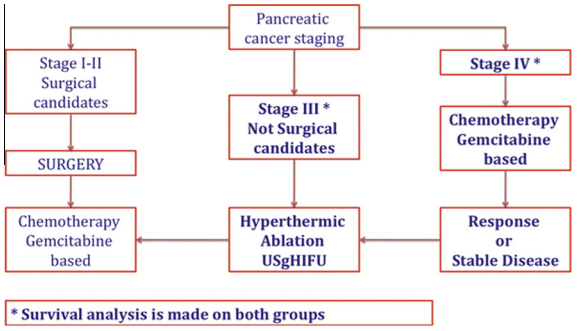

Fig. 2. Clinical pathway for pancreatic cancer. Flow diagram of the design of the study. Notice that patients on stage III enter directly to HIFU treatment. Patients on stage IV need response to chemotherapy.

There were 29 cases of locally advanced stage III and 14 cases of metastatic stage IV based on TNM International classification. HIFU treatment was administered at least 4 weeks after chemotherapy was discontinued. Previous color Doppler ultrasound was obtained and simulation procedure was performed in all cases. Two cases were excluded from the initial selection because ultrasound imaging was not able to obtain a good identification of the tumoral mass and therefore treatment could not be planned and performed.

All patients were treated under general anesthesia to manage the procedure-associated pain and to obtain a better control of the respiration movements during treatment. The whole procedure lasted between 2 and 4 h, of which the exposure time to HIFU lasted between 1500 and 3000 s. In forty patients, HIFU treatment was performed only once, while the treatment was repeated 2 months later to ablate the remaining tumor mass in three patients. The median intensity of treatment was 350 W, which corresponded to a median temperature of 70 °C.

Clinical responses to HIFU ablation were evaluated at 4, 8, 12, and 16 weeks by CT Scans, MRI and PET image techniques at our hospital. A positive response was considered if an ablation of more than 60% of the tumor mass was achieved, and the consensus was reached by two experienced radiologists (Figs. 3 and 4). Patients with poor hematologic conditions, a history of previous radiotherapy treatment or poor Karnofsky index (lower than 60) were excluded from the treatment. Responses obtained were measured under RECIST criteria. The complications were also analyzed.

Fig. 3. CT scan of tumor ablated in pancreas body preserving superior mesenteric artery. CT scan image of a completely ablated tumor in the body of the pancreas: round image in the center with vessel preserved in the middle.