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Research article

Sonographic features of thoracoabdominal wall metastases of liver cancer after liver transplantation

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ABSTRACT

Objective: Sonographic features are not well-defined in thoracoabdominal wall metastases (TAWM) of liver cancer after liver transplantation (LT), which is one of the most important reasons affecting the long-term survival of transplant recipients. The purpose of this study was to analyze the sonographic features of TAWM from liver cancer after LT and to identify the role of ultrasound (US) in the differential diagnosis between TAWM and benign lesions of the thoracoabdominal wall after LT.

Methods: This retrospective study included 1,999 LT recipients between January 2008 and July 2021. Clinical characteristics and sonographic features of 32 patients with thoracoabdominal wall lesions were analyzed. The types of thoracoabdominal wall lesions were studied, and the US findings of benign and malignant lesions were compared. Whether TAWM from liver cancer after LT exhibited any distinctive sonographic appearance was evaluated.

Results: All seven malignant cases were metastases from liver cancer. The benign group included 13 cases of thoracoabdominal wallencapsulated effusion/hematoma, nine of abdominal incisional hernia, and three of thoracoabdominal wall inflammatory mass. Sonographic features were significantly different between two groups. Compared with the benign group, metastases lesions were frequently located in the parietal peritoneum/pleura (4/7 vs 1/25, $p = 0.009$), fewer lesions were located at abdominal incisions (3/7 vs 23/25, $p = 0.012$), all metastatic lesions were hypoechoic (7/7 vs 5/25, $p = 0.001$), and most lesions had blood flow signals (4/7 vs 3/25, $p = 0.026$). Additionally, most metastatic cases had intrahepatic lesions (4/7 vs 1/25, $p = 0.004$) and multiple extrahepatic solid lesions in the abdomen (6/7 vs 0/25, $p = 0.000$).

Conclusions: Compared with benign lesions, TAWM of liver cancer after LT exhibited unique sonographic features.

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Abbreviations

AFP	alpha-fetoprotein
CEUS	contrast-enhanced ultrasound
CTC	circulating tumor cells
HCC	hepatocellular carcinoma
INR	international normalized ratio
LT	liver lransplantation
MI	mechanical index
PTCD	percutaneous transhepatic cholangiogram
TAWM	thoracoabdominal wall metastases
US	ultrasound

1. Introduction

Primary liver cancer is a significant public health problem worldwide, ranking sixth in incidence and third in mortality [1]. Liver transplantation (LT) is an effective method for patients with primary liver cancer, as it removes the tumor as well as the diseased liver [2,3]. However, the recurrence rate of liver cancer after LT is as high as 20% - 57.8% at 5 years [4–8] and up to 4.3% even if tumors are within the strict Milan criteria [4]. Furthermore, extrahepatic metastases of liver cancer after LT are more common and appear earlier than intrahepatic recurrence [9–12], and significantly reduce the survival rate and quality of life of patients [13]. Thoracoabdominal wall and pleuroperitoneal membrane metastases of hepatocellular carcinoma (HCC) account for 3.6–11% of tumors [14–16], ranking fifth, behind only to metastases of the lung, lymph nodes, bone, and adrenal glands. Thoracoabdominal wall metastases (TAWM) from liver cancer are considered to represent highly advanced disease stage [15,17], however, studies have reported that surgical resection and interventional treatment of TAWM of liver cancer could provide acceptable long-term survival [18–20]. Therefore, it is important to identify TAWM in patients with liver cancer in a timely manner.

Ultrasound (US) is the preferred method for screening and monitoring LT recipients postoperatively. Furthermore, for thoracoabdominal wall masses that are palpable or detected in routine imaging tests, high-frequency ultrasound is more widely available than computed tomography (CT) or magnetic resonance imaging (MRI), given its non-invasiveness, portability, and high spatial resolution for superficial lesions. Only a few studies [21,22] have been reported regarding US manifestations of needle track seeding after biopsy or radiofrequency ablation for HCC. The implanted tumor appears as one or more nodules along the needle track located within the peritoneum, abdominal muscles, pleural surface or subcutaneous and skin tissues, and US displays hypoechoic nodules with intralesional vascularization, smooth and regular margins; however, there was a lack of a control group in these studies. Moreover, compared to needle track seeding tumors, TAWM of liver cancer after LT is more complex and not easily identifiable, because of the surgical procedures and the use of immunosuppressive agents, and metastasis also includes local invasion, lymph node metastasis and hematogenous metastasis, as well as tumor self-seeding caused by circulating tumor cells (CTC) [23,24]. Furthermore, US findings of TAWM of liver cancer after LT have not yet been described. Improving our knowledge about the sonographic characteristics of TAWM of liver cancer after LT so as to achieve early detection and diagnosis, has positive clinical significance.

In this study, we retrospectively reviewed 1,999 LT recipients at our center and analyzed the data on thoracoabdominal wall lesions. We aimed to analyze the sonographic features of TAWM from liver cancer after LT and to identify the role of US in the differential diagnosis between TAWM and benign lesions of the thoracoabdominal wall after LT.

2. Materials and methods

2.1. Patients

This retrospective study was approved by the our Institutional Ethics Review Board (ID: [2022]02-218-01). Informed consent was waived by the board. From January 2008 to July 2021, 1,999 consecutive patients had received 20,670 US examinations after LT, with no restrictions on gender and age, among which 38 patients had thoracoabdominal wall masses that were palpable or detected on imaging tests. Eight patients were excluded for the following reasons: (1) incomplete US imaging data or (2) masses could not be confirmed.

The criteria for the clinical diagnosis of malignant lesions of the thoracoabdominal wall included: (1) primary disease was histopathologically confirmed to be a malignant tumor, (2) thoracoabdominal wall malignant lesions were diagnosed via imaging studies (enhanced CT/MRI/PET-CT), and (3) the size of the masses notably increased [15] during the 3-month follow-up period. The criteria for the clinical diagnosis of benign lesions of the thoracoabdominal wall were as follows: (1) the lesion was observed by imaging (US, enhanced CT/MRI) without obvious malignant manifestations, and (2) reduction, remission, or no malignant progression of the mass without antitumor treatment over a follow-up period of more than 1 year.

One case of liver cancer metastasis obtained a definitive pathological diagnosis, while 31 cases were enrolled for clinical diagnosis, including six cases of liver cancer metastases, thirteen cases of thoracoabdominal wall encapsulated effusion/hematoma, nine cases of abdominal incisional hernia, and three cases of thoracoabdominal wall inflammatory masses. A total of 32 cases were enrolled in this

study. The enrollment flow chart is shown in Fig. 1.

2.2. US examination

Conventional US and contrast-enhanced US (CEUS) were performed using an Aloka Prosound α10, Toshiba Aplio500, and GE LOGIQ E9. A 3.5–5.5 MHz convex probe was initially used for routine grey-scale and color Doppler scans of the liver, perihilar, abdominal cavity, and thoracoabdominal wall lesions, followed by a 7.0–10.0 MHz linear probe to accurately study the sonographic features of the thoracoabdominal wall masses. The relationship between the lesion site and the surgical scar (surgical incision or percutaneous puncture site) was observed and recorded. For CEUS, an appropriate probe was selected according to the size and depth of the lesion. CEUS examinations were performed using a convex probe with a low mechanical index (MI: 0.07–0.08) and a high-frequency linear array probe with a low mechanical index (MI: 0.12). A bolus injection (2.4–4.8 mL) of the contrast medium (Sonovue; Bracco Company, Italy) was administered via the antecubital vein, followed by a 5 mL saline flush. Contrast enhancement was continuously observed for at least 3 min after injection of the contrast agent. The images were then stored. The contrast enhancement was categorized in the early phase (<30 s after injection) and the late phase (30–180 s after injection).

2.3. Image analysis

The US images were analyzed by two doctors with at least eight years of experience in abdominal US in consensus. During the

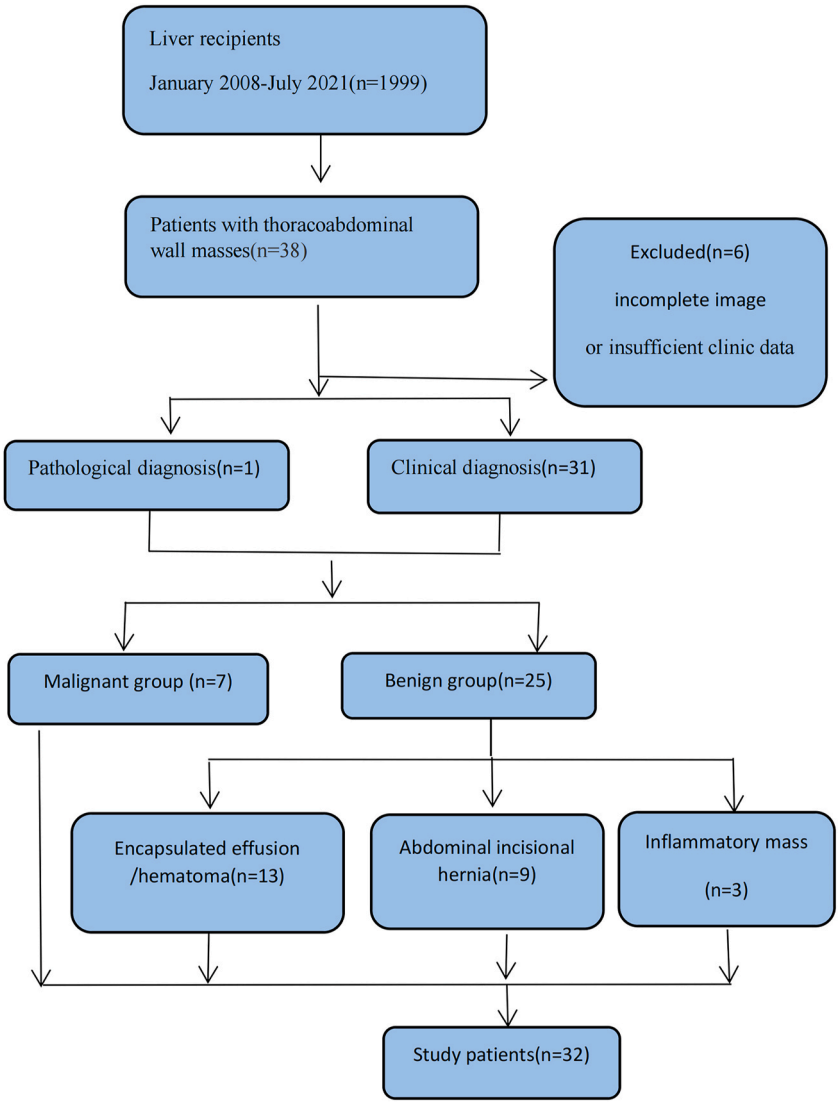

Fig. 1. Enrollment of subjects.

assessment, the doctors were blinded to the patients' history, clinical presentation, laboratory results, and results of previous imaging tests. US findings were evaluated with regard to the lesion location within the thoracoabdominal wall (intradermal/subcutaneous/intramuscular/parietal peritoneum or pleural/multilamellar), number, size, boundary, margin, echogenicity, liquid content, blood flow signal, and whether they were with or without intrahepatic and extrahepatic lesions in the abdomen. The recorded CEUS images were reviewed, and the patterns of CEUS enhancement were classified as no enhancement, peripheral ring-shaped enhancement, homogeneous enhancement, or inhomogeneous enhancement.

2.4. Statistical analysis

Statistical analyses were performed using SPSS version 21.0. Categorical variables were compared using Pearson's chi-square test or Fisher's exact test. Measurement data were compared by Student's t-test for normal distributions, whereas the Wilcoxon rank-sum test was used for non-normal distributions. The tests were performed using an alpha level of 0.05 for statistical significance.

3. Results

3.1. Demographic and clinical data

A total of 1,999 patients who underwent LT from January 2008 to July 2021 were identified, of which 32 patients were enrolled in the study (Fig. 1). Demographic data and clinical findings between the groups were compared. (Table 1). The malignant group was more significantly associated with primary liver cancer than the benign group, as shown in Table 1 (100% vs 32%, $p = 0.025$). Furthermore, to further analyze the relationship between the primary tumor and malignant lesions of the thoracoabdominal wall, the primary tumor characteristics between the two groups were compared, and that tumor growth in the malignant group was more progressive than that in the benign group, but the difference was not statistically significant. There were no significant differences in age, sex, time to detect lesions, palpability, preoperative international normalized ratio (INR), postoperative INR, preoperative Alpha-fetoprotein (AFP), and postoperative AFP between the two groups. Taken together, these results suggest that primary liver cancer plays an important role in malignant lesions of the thoracoabdominal wall after LT.

3.2. Sonographic features

To obtain a greater understanding of the sonographic features of thoracoabdominal wall lesions after LT, the site of lesions and their location within the thoracoabdominal wall, ultrasonographic morphology, and concomitant lesions were compared between the two groups, and the results were as demonstrated in Table 2.

First, the lesion site and location within the thoracoabdominal wall were significantly different between the two groups. Masses were more common at the surgical incision/percutaneous puncture site in the benign group (23/25, 92.0%) than in the malignant group (3/7, 42.8%) ($p = 0.012$). In addition, malignant lesions were more often located deeper in the thoracoabdominal wall; masses in the malignant group in more than half of the cases (4/7, 57.1%) were in the parietal peritoneum/pleura (Fig. 2A,B,C,E and 3A,E); in contrast, masses in the benign group were most commonly located in the multilamellar (Fig. 4A,B,C,D) or subcutaneous/intramuscular region ($p = 0.009$). Second, lesion echogenicity was significantly different between the two groups ($p = 0.001$); all malignant lesions presented as hypoechoic (Figs. 2A and 3A), however, benign cases were mainly characterized by mixed echogenicity, and the internal echo pattern of these masses included thick-walled cystic nodules, partially cystic isohyperechoic nodules, anechoic with punctate weak echoes, and cystic and honeycomb-like patterns of hypoechogenicity. Of note, liquid content was not necessarily present in encapsulated effusion/hematoma. For incisional hernias, hernial contents involved the small bowel, omentum, and even ascites, as

Table 1
Demographic data and clinical findings between the two groups.

Patient characteristics	Malignant group (N = 7)	Benign group (N = 25)	*p*
Sex (male/female)	7/0	19/6	0.296
Age (years; mean, range)	50.29 ± 7.11 (46–64)	53.88 ± 11.47 (22–68)	0.44
Time to detect lesions (month, median, range)	5.9 (2.8–33)	1.5 (0.03–72)	0.283
Palpable/nonpalpable	4/3	23/2	0.057
Preoperative INR (mean, range)	1.51 ± 0.77	1.95 ± 0.94	0.276
Postoperative INR (mean, range)	1.18 ± 0.09	1.14 ± 0.18	0.574
Preoperative AFP (normal/abnormal)	3/4	14/11	0.678
Postoperative AFP (normal/abnormal)	2/5	18/7	0.073
Primary disease (liver cancer/liver failure)	7/0	8/17	0.025
Primary liver cancer characteristics	N = 7	N = 8	
Differentiation (poor/moderate/well)	0/7/0	1/6/1	1.000
Number (1 or 2/multiple)	4/3	1/7	0.119
Size (mm, mean)	88.57 ± 55.35	60.50 ± 28.88	0.259
Vascular invasion (with/without)	6/1	4/4	0.282
Milan criteria (beyond/within)	6/1	7/1	1.000

AFP, alpha-fetoprotein; INR, International Normalized Ratio.

Table 2
Sonographic findings between the two groups.

Patient characteristics	Malignant group (N = 7)	Benign group (N = 25)	*p*
Lesion site (at surgical incision or percutaneous puncture site/not)	3/4	23/2	0.012
Location within the thoracoabdominal wall (intradermal/subcutaneous/intramuscular/parietal peritoneum or pleural/multilamellar)	0/1/1/4/1	0/3/8/1/13	0.009
Size (mm, mean, range)	23.29 ± 14.92 (11–50)	34.88 ± 18.88 (8–85)	0.147
Margin (regular/irregular)	5/2	19/6	1.000
Boundary (distinct/indistinct)	5/2	22/3	0.296
Echogenicity (hypo-/Iso- or hyper-/mix echogenicity)	7/0/0	5/6/14	0.001
Liquid content (with/without)	0/7	11/14	0.066
Blood flow signal (with/without)	4/3	3/22	0.026
Intrahepatic solid lesions (with/without)	4/3	1/24	0.004
Multiple extrahepatic solid lesions in the abdomen (with/without)	6/1	0/25	0.000
CEUS enhancement pattern	N = 4	N = 3	1.000
Inhomogeneous enhancement	2	2	
Peripheral ring-shaped enhancement	2	0	
No enhancement	0	1	

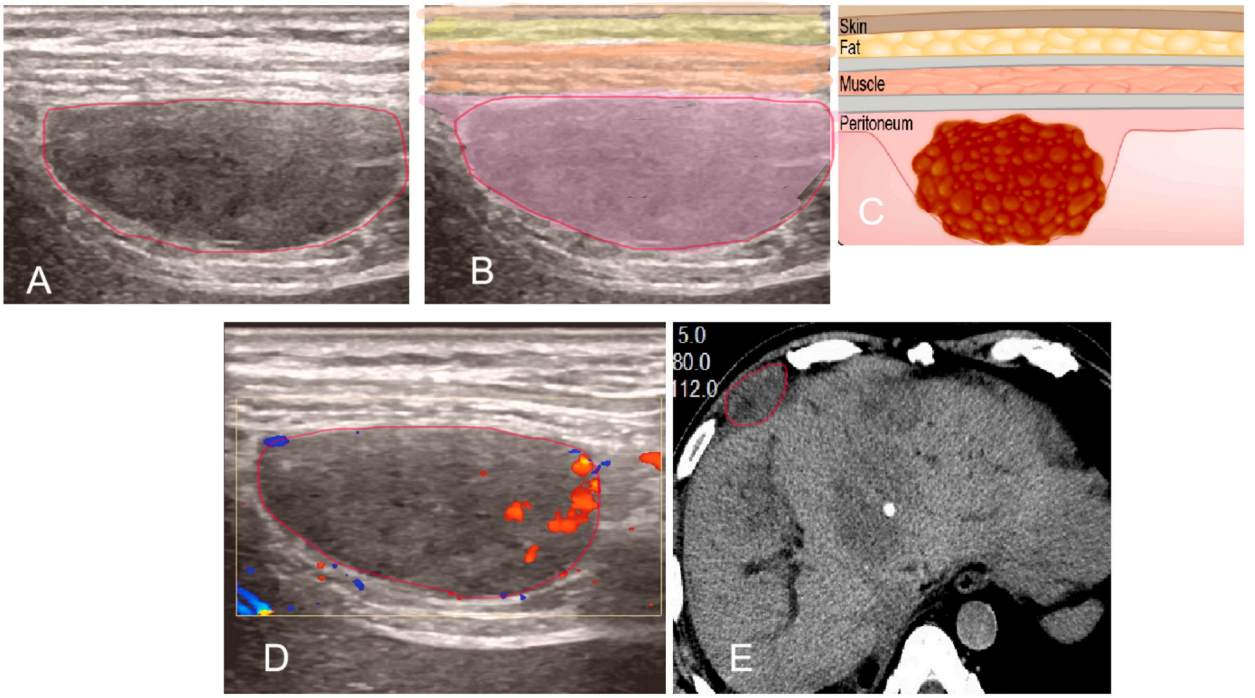

Fig. 2. A 47-year-old male with abdominal wall metastasis of HCC at two years after LT. A: A well-defined, hypoechoic solid mass (red circle, protruding into the liver). B: Four different colors mark the skin, fat, muscle, and parietal peritoneum layers of the abdominal wall and show the mass located in the parietal peritoneum. C. Schematic illustration of the mass location within the abdominal wall. D: Color Doppler flow imaging revealing a mass with rich blood flow signals. E: CT demonstrating right abdominal wall metastasis (red circle) of HCC. Abbreviations: HCC: hepatocellular carcinoma, CT: computed tomography, LT: Liver Transplantation. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

well as mixed echogenicity or liquid content. Inflammatory masses presented as ill-defined, irregular, hypoechoic, or mixed echogenicity masses. Moreover, there were more lesions with blood flow signals (Figs. 2D and 3B) in the malignant group (4/7, 57.1%) than in the benign group (3/25,12.0%, $p = 0.026$). No differences in size, boundary, liquid content and margin were observed between the two groups. CEUS was performed for four cases in the malignant group; two nodules showed inhomogeneous enhancement (Fig. 3D), one nodule demonstrated homogenous enhancement, and the remaining one showed peripheral ring-shaped enhancement. CEUS was performed in a patient with thoracoabdominal wall-encapsulated effusion, and the mass showed no enhancement. CEUS in two patients with inflammatory masses showed inhomogeneous enhancement (Fig. 4E and F). Finally, the proportion of patients with intrahepatic lesions and multiple extrahepatic solid lesions in the abdomen (Fig. 3C) was significantly higher in the malignant group

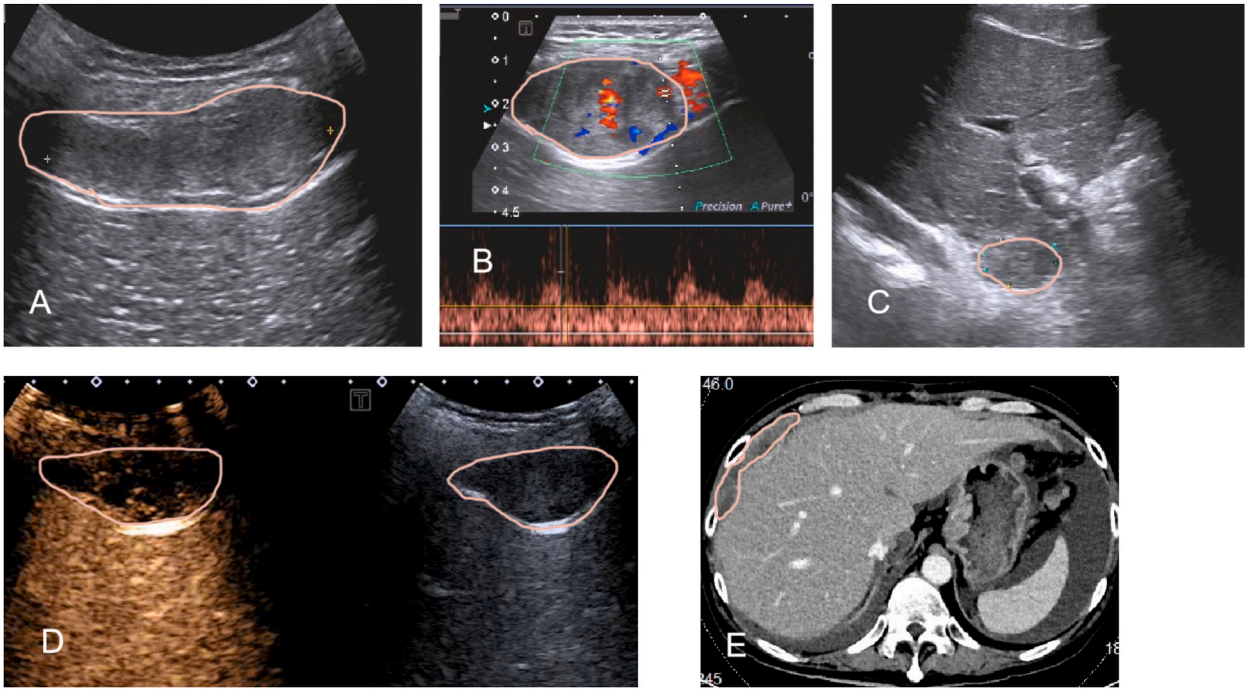

Fig. 3. A 47-year-old male with abdominal wall metastasis of liver cancer at 3 months after LT. A: A well-defined, hypoechoic solid mass (pink circle) located at the parietal peritoneum. B: Color Doppler flow imaging revealing abundant blood flow signals within the mass and pulse-Doppler demonstrating arterial spectrum within the mass. C: Another extrahepatic metastasis (pink circle) in the abdomen. D: CEUS showing inhomogeneous enhancement (pink circle). E: CT showing right abdominal wall metastasis (pink circle) of liver cancer. Abbreviations: CT: computed tomography, CEUS: Contrast-Enhanced Ultrasound, LT: Liver Transplantation. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

than in the benign group ($p = 0.004$ and $p = 0.000$, respectively). In summary, these data suggest that malignant lesions of the thoracoabdominal wall have peculiar US findings. The main sonographic features of malignant and benign lesions are shown in Fig. 5A,B,C,D,E,F.

4. Discussion

TAWM from liver cancer is a rare complication, but severely impacts patient survival and quality of life. It has been reported that the cumulative survival rates of thoracoabdominal wall seeding tumors from HCC were 55.6%, 27.8%, 9.3% at 1, 3, and 5 years, respectively [17]. However, studies have reported that the cumulative 1-, 3-, and 5-year survival rates could reach 82.6%, 73.5%, and 63%, respectively, after appropriate treatment [19]. Therefore, it is important to accurately identify cases of TAWM from liver cancer.

The results of our study indicated that thoracoabdominal wall lesions after LT included encapsulated effusion or hematoma, abdominal incisional hernia, inflammatory masses, and metastases of liver cancer. There were no primary malignant tumors of the thoracoabdominal wall in the present study, and all cases in the malignant group were metastases of liver cancer. Our findings revealed that TAWM of liver cancer have sonographic characteristics different from those of benign lesions.

The most intriguing finding of the current study was that the lesion site and location within the thoracoabdominal wall were significantly different between benign and metastatic lesions. Benign lesions were more common at surgical incision or percutaneous puncture sites than metastatic lesions (92.0% vs 42.8%, $p = 0.012$). This can be explained by the fact that abdominal incisions are the main cause of complications such as infection, pain and incisional hernia [25]. However, one of the possibilities accounting for liver cancer metastasis is micro-metastasis which is difficult to detect preoperatively or from residual protumorigenic factors in the peripheral blood. On the other hand, surgical manipulation by pressing or mobilizing the liver may result in intra-operative tumor rupture and in a greater possibility of tumor dissemination [26,27], and with the increasing use of percutaneous ablative techniques, needle-track recurrence can be found after LT [20,28,29]. Additionally, immunity offered by the liver graft could work against the growth of host liver cancer within the liver, directing the liver cancer to spread systemically [30]. Moreover, the transfer pathways also include local invasion, lymph node metastasis and hematogenous metastasis and tumor self-seeding by CTC [23,24]. Taken together, metastatic lesions were not always at surgical incision or percutaneous puncture sites.

The major strength of our report was the analysis of lesion-specific locations within the thoracoabdominal wall. Our data revealed that most benign nodules were located at the multilamellar (13/25) or subcutaneous/muscular (11/25) layers of the thoracoabdominal wall; in contrast, most of the metastatic lesions (4/7) were located in the parietal peritoneum/pleural layer. All

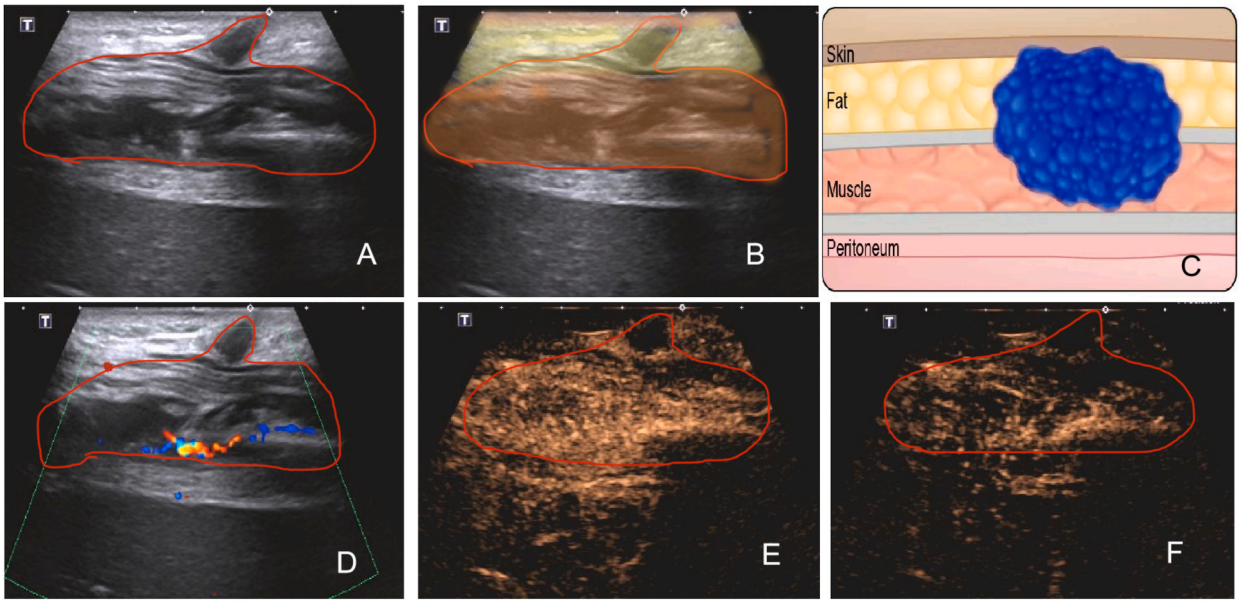

Fig. 4. A 57-year-old male who suffered from pain and had a palpable mass at the PTCD puncture site. The patient was diagnosed with an abdominal wall inflammatory mass at 2 months after LT. A: An ill-defined, irregular, and mixed echogenicity mass (red circle). B: Three different colors mark the skin, fat, and muscle layers, and show the mass infiltrating multiple structures (intradermal, subcutaneous, and muscular) of the abdominal wall. C: Schematic illustration of the mass location within the abdominal wall. D: Color Doppler flow imaging presented a mass with rich blood flow signals. E, F: CEUS showing inhomogeneous enhancement. Abbreviations: PTCD: Percutaneous Transhepatic Cholangiogram, CEUS: Contrast-Enhanced Ultrasound, LT: Liver Transplantation. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

malignant cases were metastases from liver cancer in the present study, and it was presumed that spread could occur via lymphatic, hematogenous, neural, or direct invasion of the peritoneum/pleura. This finding was in line with previous reports on extrahepatic metastatic spread of HCC in the literature. It has been reported that peritoneal and omental metastases of liver cancer rank fifth, behind only to metastases of the lungs, abdominal lymph nodes, bone, and adrenal glands as the most common site of extrahepatic liver cancer, and incidences of liver cancer metastases to the peritoneum and omentum can reach up to 11% [15]. For benign cases, we speculated that an excessively thick fat layer affects the healing of the incision, leading to fat liquefaction and infection of the incision [31]; therefore, most encapsulated effusions and inflammatory masses were typically located in the abdominal wall subcutaneous layer. In contrast, abdominal wall hematomas were typically confined to the muscularis, primarily due to rupture of the epigastric artery and/or tear of rectus abdominis muscle during the surgical procedure. In addition, US findings of abdominal incisional hernia appear as a defect of the muscular or fascial layers, and the small bowel and/or omentum herniate through the abdominal wall defect to the superficial abdominal wall; therefore, incisional hernias were considered as in the multilamellar abdominal wall in our study.

There was a significant difference between the two groups in terms of mass echogenicity and blood flow signals. Most metastatic cases presented as well-defined, regular, hypoechoic, and hypervascular. These US findings were consistent with previous reports of skin metastases and needle track seeding after biopsy or radiofrequency ablation for HCC in the thoracoabdominal wall [21,32,33]. However, there was a lack of a control group in these two studies about thoracoabdominal wall needle track metastasis from HCC [21, 32], and it was easy to identify the needle track. Where our current results differ from previous findings is the characteristic of tumor site and location within the thoracoabdominal wall.

In addition to the sonographic features, we also discussed and compared some clinical features. The factors that contribute to liver cancer recurrence and metastasis include tumor burden (number, size, distribution, within or beyond Milan criteria), tumor biology behavior (differentiation, vascular invasion, and microsatellite lesions), and tumor marker (AFP levels). All these tumor features among the two groups were compared in present study. Different from the previous literature [15], these characteristics did not reach statistical significance due to the small sample size, but tumors in the metastasis group were more progressive than in the benign group. The number of cases of increased postoperative AFP level in the malignant group was higher than that in the benign group, but there was no statistical significance, which might be due to the fact that some benign thoracoabdominal wall lesions, such as incision subcutaneous effusion and hematoma, occurred in the early postoperative period, and the patient' s AFP level had not decreased to the normal range at that time.

Our study had some limitations. First, the study was retrospective, with all the typical inherent limitations of retrospective analyses. Second, clinical and imaging follow-up was used rather than histopathology as the reference standard for thoracoabdominal wall metastases of liver cancer; however, the diagnosis of primary liver cancer relied on typical radiological findings [26,27], and extra-hepatic metastatic liver cancer was diagnosed based on radiological findings, AFP levels, and follow-up [1,16,34]. Third, there were no malignancies other than metastases of liver cancer and no primary benign tumors of the thoracoabdominal wall in this study; the

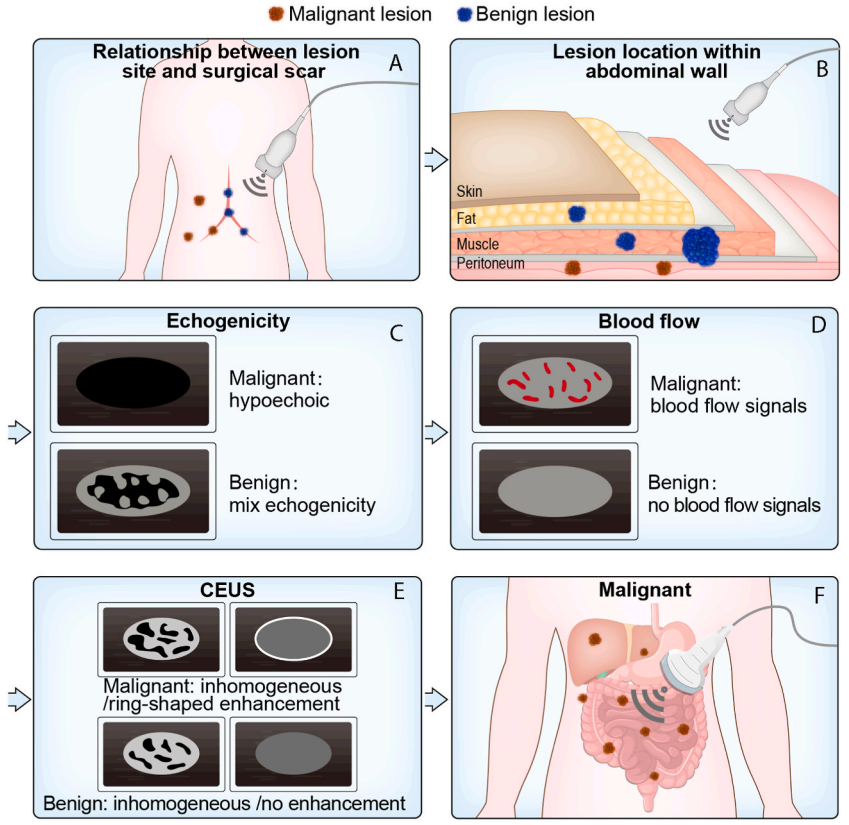

Fig. 5. Schematic illustrations of the main sonographic features of malignant and benign lesions. A:Masses were more common at the surgical incision/percutaneous puncture site in the benign group than in the malignant group. B:Masses in the malignant group were more common in the parietal peritoneum/pleura, while in the benign group were most commonly located in the multilamellar or subcutaneous/intramuscular region. C: Malignant lesions presented as hypoechoic, however, benign cases were mainly characterized by mixed echogenicity. D:There were more lesions with blood flow signals in the malignant group than in the benign group. E:CEUS showed inhomogenous enhancement and peripheral ring-shaped enhancement in malignant lesions, and inhomogeneous enhancement and no enhancement in benign lesions. F:Most malignant cases had intrahepatic lesions and multiple extrahepatic solid lesions in the abdomen.

inclusion of these diseases is a direction that we would like to study further. Fourth, the number of cases was relatively limited, so the diagnostic value of US in TAWM after LT could not be statistically calculated. A future study should include a large sample size, especially of TAWM. Still, our findings provide a basis for the positioning and qualitative diagnosis of thoracoabdominal wall lesions after LT.

In conclusion, TAWM of liver cancer after LT commonly manifested as the primary disease was liver cancer, located at the parietal peritoneum/pleura and not always at the surgical incision. Metastases were well-defined, solid hypoechoic, hypervascular, and accompanied by multiple intrahepatic and extrahepatic lesions. US findings have proven to be useful in the demonstration of benign lesions and metastases of liver cancer in the thoracoabdominal wall after LT. Doctors who perform follow-up US examinations should recognize the clinical and ultrasonographic findings of TAWM from liver cancer after LT.

Declarations

Author contribution statement

Mei Liao: Performed the experiments; Analyzed and interpreted the data; Wrote the paper.
Hongjun Zhang: Performed the experiments; Analyzed and interpreted the data.
Jieyang Jin: Performed the experiments.
Huanyi Guo: Performed the experiments; Contributed reagents, materials, analysis tools or data.
Shuhong Yi: Conceived and designed the experiments; Contributed reagents, materials, analysis tools or data.
Jie Ren: Conceived and designed the experiments; Wrote the paper.

Data availability statement

Data included in article/supplementary material/referenced in article.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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