

# Clinical analysis for the application of endoscopic ultrasonography in the diagnosis of patients with a retroperitoneal space-occupying lesion

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## ABSTRACT

**الأهداف:** تقييم مدى الخبرة التي تملكها في تحديد الحاجة لتطبيق صور الإيكو عبر التنظير أثناء التشخيص الكيفي للآفات الكبيرة خلف الصفاق.

**الطريقة:** شملت هذه الدراسة 26 مريض مصاب بآفات كبيرة خلف الصفاق والتي ثبتت من خلال الأشعة المقطعية وأشعة الرنين المغناطيسي. لقد خضع كافة المرضى لتصوير الإيكو عبر التنظير باستخدام الرشف بالإبرة وذلك في قسم أمراض الجهاز الهضمي، مستشفى أكسيانغ المركزي، مقاطعة هيوي، الصين خلال الفترة من أغسطس 2009م إلى أغسطس 2011م. لقد قمنا بتقييم مجموعة من المقاييس والمتمثلة بالتالي: المضاعفات الناتجة عن الرشف بالإبرة، ونسبة التشخيص المرضي المحدد، وأسباب المرض لكافة العينات.

**النتائج:** أشارت نتائج الدراسة إلى أن من أصل 26 مريض فقد كان 24 مريض مصاب بالتشخيص المرضي، فيما كانت نسبة التشخيص الهيستولوجي 92.3%. ولم يترتب على عملية الرشف بالإبرة أي من المضاعفات مثل: النزيف، أو الالتهاب، أو إصابة الأحشاء البطنية. وأظهرت النتائج إصابة 8 مرضى بالأورام الحميدة وذلك بنسبة 33.3%، وإصابة 16 مريض بالأورام الخبيثة وبنسبة 66.7%. ولم يتعين إصابة مريضين بالتشخيص المرضي المحدد وذلك بسبب قصر العينة النسيجية. كما لم يخضع 8 مرضى للعملية بسبب إصابتهم بالأورام الحميدة.

**خاتمة:** لقد كان للرشف بالإبرة الفضل في تقليل المضاعفات المترتبة، وزيادة نسبة التشخيص الذي يمكن الحصول عليه في التشخيص الكيفي للآفات الجسدية خلف الصفاق.

**Objectives:** To report our experience and to evaluate the application of endoscopic ultrasonography (EUS) in the qualitative diagnosis of retroperitoneal space-occupying lesions.

**Methods:** Twenty-six patients with retroperitoneal space-occupying lesions confirmed by CT or MRI were studied. All the patients underwent endoscopic ultrasonography guided fine needle aspiration (EUS-FNA) at the Department of Gastroenterology, Xiangyang Central Hospital, Hubei Province, China from August 2009 to August 2011. Different parameters were evaluated, such as complications of EUS-FNA, the ratio of definite pathological diagnosis, and the pathologic types of all the specimens.

**Results:** Of the 26 patients, 24 had definite pathological diagnosis; the ratio of histodiagnosis was 92.3%. There were no complications such as hemorrhage, infection, or injury to the abdominal viscera in the process of EUS-FNA. Eight patients had benign tumors, with a ratio of 33.3%, and 16 patients had malignant tumors, with a ratio of 66.7%. Two patients had no definite pathological diagnosis because of the shortness of tissue sample. Eight patients did not undergo operation due to the diagnosis of benign tumors.

**Conclusions:** The EUS-FNA has the advantage of lower complications, and higher diagnostic ratio, which is valuable in the qualitative diagnosis of retroperitoneal space-occupying lesions.

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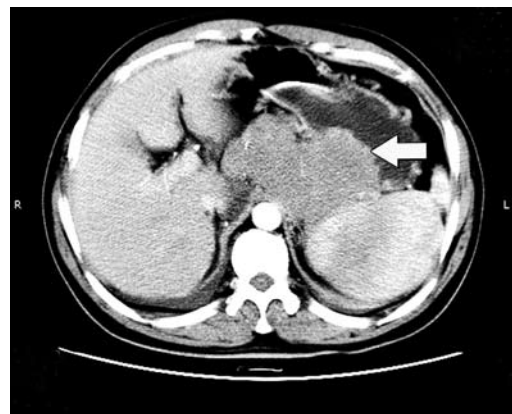
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The retroperitoneal space has looser tissues, and stronger adaptability for the growth of tumors. Therefore, tumors in this part can grow cryptically for a long time without detection, and without any apparent clinical symptoms in the early stages.<sup>1</sup> A palpable mass can only be found when the tumor becomes large and invades neighboring tissues and organs, which can lead to the symptoms of pain, abdominal distention, and anorexia. Then it can generally be detected by medical history, physical examination, and necessary imaging examinations. It was previously believed that most primary retroperitoneal tumors (PRT) were malignant, and most of them were insensitive to radiotherapy and chemotherapy, so complete excision was the preferred treatment method.<sup>2</sup> However, the retroperitoneal tumor has the characteristic of complicated histological classification, and many of them are unsuitable for surgical treatment. For instance, compared with liposarcoma and leiomyosarcoma, malignant lymphoma and neuroblastoma have distinctly different therapeutic methods, the latter that often extensively infiltrate surrounding structures, cannot be excised completely, and are sensitive to radiotherapy and chemotherapy.<sup>3</sup> Therefore, a multimodality treatment such as radiotherapy and chemotherapy is more suitable for the treatment of such diseases. However, most of the metastatic tumors located in the retroperitoneal space are unsuitable for surgical treatment. As various retroperitoneal space-occupying lesions have similar clinical manifestation and imaging appearances, it is difficult to obtain a qualitative diagnosis pre-operation. If surgical exploration is carried out without histological diagnosis, it could definitely cause unnecessary surgical trauma in many patients, delay treatment, and even lead to dissemination of the tumor. The common method of obtaining a histological diagnosis of retroperitoneal space-occupying lesions is by fine needle biopsy guided by ultrasound or CT.<sup>4</sup> However, due to the shortness of tissue sample resulting in unreliable pathological diagnosis, repeated punctures several times should be performed to obtain the preferable result. Meanwhile, most retroperitoneal space-occupying lesions have a close relationship with many tissues and organs, such as the liver, spleen, kidneys, and principal blood vessels, so repeated punctures may cause complications of bleeding and visceral injuries.<sup>5</sup> In this study, we report our experience with the use of endoscopic ultrasonography guided fine needle aspiration (EUS-FNA) in the diagnosis of a retroperitoneal space-occupying lesion.

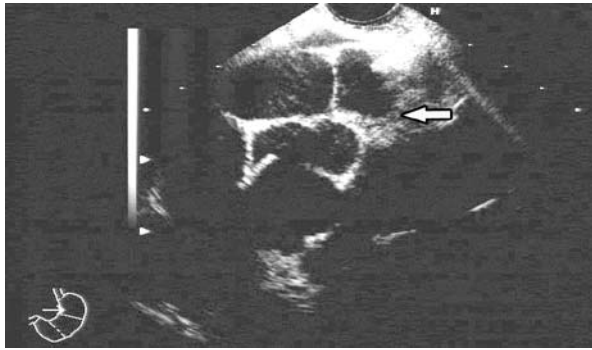
**Methods.** From August 2009 to August 2011, 26 consecutive patients with retroperitoneal space-occupying lesions at the Department of Gastroenterology, Xiangyang Central Hospital, Hubei Province, China,

were included in this study. The experiment was performed after obtaining patient informed consent, and ethical approval from the Ethics Committee of Xiangyang Central Hospital. This study was carried out according to the principles of the Helsinki Declaration. Our inclusion criteria were patients with retroperitoneal space-occupying lesions confirmed by CT or MRI (Figure 1). The exclusion criteria were that the patients had been diagnosed with malignant tumor or cachexia, or complicated with severe cardiopulmonary disease. Cases with a retroperitoneal space-occupying lesion with a diameter of less than 2 centimeter were also excluded. Before EUS-FNA, 12 cases were examined by CT and 16 cases were examined by MRI. Overall 26 patients underwent EUS-FNA. The ultrasound endoscope used in this study was a Pentax EG-3830UT (Hoya Joint-stock Corporation, Tokyo, Japan), which is a longitudinal-axis linear endoscopic color Doppler ultrasonography (ECDUS) machine. This can perform a sector scan parallel to the long axis of the scope with the maximum angle reaching up to 135 degrees. The EUS has the function of fine needle puncture and the ultra wide range linear-array transducer has a frequency of 5-10 MHz. The endoscopic was PENTAX 3500, and the ultrasonic was HITACHI 5500, which can be used for observing blood vessels and blood stream by color Doppler ultrasonogram. The Olympus NA-10J-1, NA-200H-8022 or COOK ECHO-1-22 (Cook Corporation, Bloomington, Indiana, USA) were adopted as the 22G puncture needle.

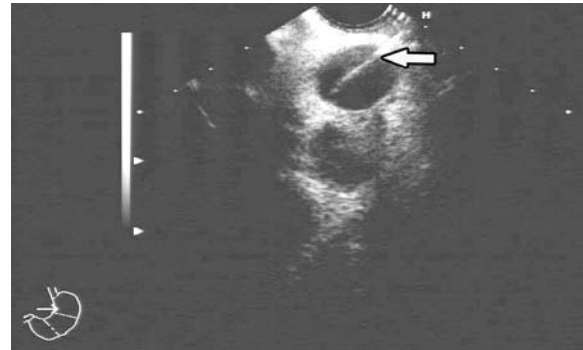
**Preoperative protocol.** All patients were confirmed to have no contraindications to endoscopy or puncture by preoperative assessment. Examination of routine bloods, coagulation function test, hepatitis B virus surface antigen test, and electrocardiogram were performed. A detailed introduction on the purpose, approach, and process of the puncture technique, as well as the



**Figure 1** - A 58-year-old male patient with a retroperitoneal occupying lesion (arrow) was diagnosed with pancreatic carcinoma by CT.



**Figure 2** - The same patient underwent EUS-FNA. This image shows the lesion (arrow) observed under EUS. EUS-FNA - endoscopic ultrasonography-fine needle aspiration

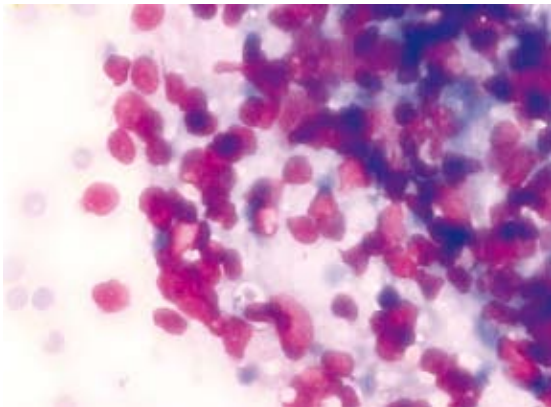


**Figure 3** - The patient underwent EUS-FNA (arrow) as shown. EUS-FNA - endoscopic ultrasonography-fine needle aspiration

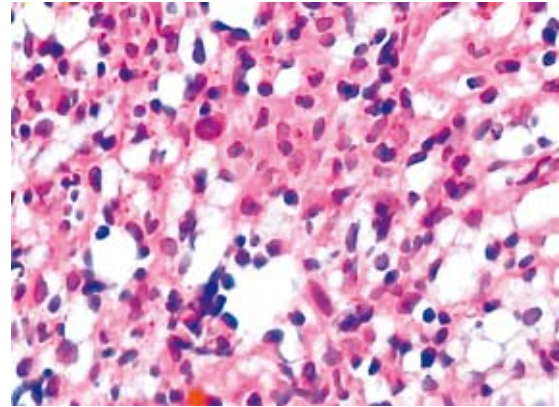
potential complications and treatment measures was given to the patients.

**Surgical technique.** The regional gastrointestinal wall was generally observed after the ultrasound endoscope entered the stomach. Then the ultrasound system was started, and the size, shape, location, margin, and echo of the tumor were detected by the ultrasonic probe probing along the fundus, body, and antrum of the stomach, duodenal bulb, and descending duodenum (Figure 2). At the same time, whether the surrounding tissues, portal vein, mesenteric vein, splenic vein, and mesenteric artery had been invaded, as well as the lymph node at the pancreas, greater curvature of stomach, lesser curvature of stomach, celiac artery, cardia and mediastinum were checked. Once the tumor locating at the hypogastrium or pelvic cavity, EUS could be performed through colonoscope and should abide by the same protocol listed above. Ultrasonography of the blood stream and blood vessels were taken by Color Doppler ultrasonography so as to avoid injury to the

blood vessels while puncturing. The endoscope was fixed after the best position had been selected. Then the fine needle was rapidly punctured from the biopsy hole to the focal area of the lesion (Figure 3). It was important that the body of the scope was straightened while puncturing. A 22G 5-12 ml negative pressure puncture needle was adopted in the puncture biopsy. Two punctures were taken at each part, and each puncture included 10 times lifting and thrusting. Once the sample was found with much bloody fluid and fewer line-shape tissues at the first puncturing, the puncture biopsy was performed repeatedly until enough samples were obtained. Each liquid sample was immediately pushed out onto the glass slide by a needle core or injector. Three smears were taken from each slide at once, and sent to the Cell Lab of the Pathology Department immediately after naturally drying. The sample was performed with Wright-Giemsa's Compound Stain and was read after 20 minutes (Figure 4). Each line-shape sample was fixed by formalin, sent to the Pathology Department and was



**Figure 4** - The cytological examination indicated that there was no definite diagnosis for this patient.



**Figure 5** - Histopathological examination revealed that the final diagnosis of this patient was Hodgkin's disease (nodular lymphocyte predominant Hodgkin's lymphoma).



paraffin-embedded. The pathological section was stained with Hematoxylin and Eosin (HE) (Figure 5). Once the quantity of the pathological section was sufficient, the relevant immunohistochemical test according to the origin of the sample and the result of the HE staining was conducted. Both cytologic smears and pathological sections were read by 2 or 3 pathologists, and the final result was the consensus.

**Postoperative protocol.** The outpatients were administered 0.2 g of Levofloxacin orally, the inpatients were administered antibiotics intravenously for several days. The inpatients were followed-up on the first day, third day, and fifth day respectively after operation to find out whether any complications had occurred. The outpatients were given the cell-phone number of the operator, and advised to call in case of any relevant uncomfortable symptoms, and to pay a follow-up visit to the Ultrasound Endoscope Room when receiving the pathological report on the fourth day after the operation. The recorded minor complications included sore throat, slight abdominal pain and abdominal distention, and major complications include pyrexia, massive gastrointestinal bleeding, local hematoma, gastrointestinal perforation, and acute pancreatitis.

Chi-square criterion and fourfold table exact probability were adopted for statistics. The Statistical Package for Social Sciences Version 12.0 (SPSS Inc., Chicago, IL, USA) and Microsoft Excel software were used for the statistical analyses.

**Results.** The demographic characteristics of the patients in our series include a median age of 51 years (range = 10-75 years), and a male:female ratio of 18:8. Among the 12 cases who were examined by MRI, 6 cases obtained an imaging diagnosis in accordance with the final pathological diagnosis, and the conformity rate in this group was 50%. Among the 14 cases who were examined by CT, 6 cases obtained an imaging diagnosis in accordance with the final pathological diagnosis, and the conformity rate in this group was 42.9%. Overall, 26 patients underwent EUS-FNA, 24 cases had a clear pathological diagnosis, and the rate of histodiagnosis in this group was 92.3%. The ratio of histodiagnosis in the EUS-FNA group was significantly higher than that in CT and/or MRI group ( $p=0.0003$ , the 95% confidence interval was 78.37%-83.43% versus 18.72%-23.68%, Table 1).

During the puncture process, most patients had no uncomfortable feelings, and some patients had mild pain. There were no complications such as bleeding, infection, and visceral damage. There was no death in this series. The average size of the tissue samples was 19.5 mm. For patients that obtained an accurate diagnosis, there were 8 benign lesions (33.3%), and 16 malignant

lesions (66.7%). The benign lesions included one case of lipoma, one case of lymphangioma, one case of idiopathic retroperitoneal fibrosis, one case of dermoid cyst, one case of neurofibroma, one case of neurilemoma, and 2 cases of inflammatory pseudotumor. The malignant lesions included 3 cases of liposarcoma, one case of dermoid sarcoma, 2 cases of neurofibrosarcoma, 2 cases of leiomyosarcoma, one case of malignant paraganglioma, 2 cases of malignant lymphoma, 2 cases of pancreatic cancer, one case of neuroblastoma, and 2 cases of lymph node metastasis cancer. There were 2 cases with no definite pathological diagnoses in this group due to insufficient samples, and they were suspected to be diagnosed with malignant lymphoma according to the abdominal enhancement CT. However, the patients refused further checking and treatment, so they were unavailable for follow up. Among the other 24 cases for which we obtained clear pathological diagnosis, 16 cases received surgical treatment, and the accordance ratio of postoperative pathological diagnosis reached 100%. Eight cases did not undergo surgical treatment, including one case of idiopathic retroperitoneal fibrosis, 2 cases of inflammatory pseudotumor, 2 cases of malignant lymphoma, one case of neuroblastoma, and 2 cases of lymph node metastasis cancer.

**Discussion.** The retroperitoneal space is a broad potential interspace between the retroperitoneum, posterior abdominal wall, and pelvic cavity muscles. This space has the characteristic of soft texture, deep anatomical position, and broad scope.<sup>6</sup> Aside from PRT, the space-occupying lesions in the retroperitoneal space also include the tumors of various organs in this space, such as the pancreas, kidney, adrenal gland, great vessels, and so forth.<sup>7</sup> The retroperitoneal metastatic lymph nodes caused by other primary tumors can also be found in this space. Due to the wide growth range and deep location of tumors, and due to the various surrounding organs, complicated histological classification and lack of specific clinical symptoms and signs in the early stage, qualitative diagnosis of these diseases is very difficult.<sup>8</sup>

**Table 1** - The conformity rate of histodiagnosis among EUS-FNA, CT, and MRI investigations in patients with retroperitoneal space-occupying lesions.

Group	n	Conformity	Unconformity	Ratio of conformity (%)
EUS-FNA	26	24	2	92.3*
CT	14	6	8	42.0
MRI	12	6	6	50.0

\*compared with CT and MRI group,  $p=0.0003$ ,  
EUS-FNA - endoscopic ultrasonography-fine needle aspiration

In 1980, Dimagno reported the use of ultrasound combined with routine endoscope in animal experiments.<sup>9</sup> It was the first report of the successful application of EUS, which initiated a new era of endosonography in clinical application. After 30 years of efforts, the application of EUS has grown more widely than ever. Technologies such as EUS-FNA have significantly improved the standards of diagnosing, and interventional treatment for gastrointestinal disease.<sup>10</sup>

The EUS-FNA is the technique of using specific puncture needles to puncture into the target tissue inside or outside the wall of the gastrointestinal tract under real-time ultrasound monitoring;<sup>11</sup> the ultrasonic probe is installed at the end of the endoscope to aspirate the target tissue accurately for cell pathology examination. As an important supplement for EUS examination, EUS-FNA can significantly increase the diagnostic rate of retroperitoneal space-occupying lesions.<sup>12</sup> In recent years, the technique of EUS-FNA has been improved gradually, with the application expanding from diagnosis and treatment of gastrointestinal diseases to mediastinum and lung diseases.<sup>13</sup> Over the last 2 years, we have adopted EUS-FNA to perform the biopsy of retroperitoneal space-occupying lesions detected by CT or MRI for pathological examination, and achieved favorable consummation.

In this study, the histodiagnosis rate of the patients was 92.3% (24/26). Guided by ultrasound endoscope, all the cases in this group underwent biopsy successfully at only one time; the quality and quantity of puncture samples was higher than fine needle aspiration guided by common ultrasonic probe.<sup>14</sup> The accordance rate of postoperative pathological diagnosis of the 16 cases reached 100%, higher than the diagnostic accordance rate of puncture biopsy reported by the literature.<sup>15</sup> Among 26 patients, 8 cases avoided unnecessary laparotomy, including one case of idiopathic retroperitoneal fibrosis, 2 cases of inflammatory pseudotumor, 2 cases of malignant lymphoma, one case of neuroblastoma, and 2 cases of lymph node metastasis cancer. A 10-year-old child in this group had been diagnosed with neuroblastoma by EUS-FNA, he received comprehensive treatment of systemic chemotherapy combined with radiotherapy, and there was a great reduction in the tumor, so the boy obtained surgical opportunity, preparing him for surgical treatment. Two cases of malignant lymphoma underwent different chemotherapy regimens according to different subtypes and achieved complete remission. For 2 cases of lymph node metastasis cancer, further investigations were performed to look for a primary focus, and one of them was found to be strongly positive for PSA expression by immunohistochemical analysis of the sample, then a prostate needle biopsy was

performed and the pathologic diagnosis was prostate cancer. The retroperitoneal mass disappeared, and complete remission was achieved after castration.

During the process of EUS-FNA, most cases had no discomfort and a few patients felt mild pain. In this group, there were no complications such as bleeding, infection, and visceral damage. The entire process of puncture was guided by the endoscope, which ensured the accuracy of puncturing and helped to avoid the damaging of major vessels and organs surrounding the area of the target tissue. Therefore, EUS-FNA is a diagnostic method for retroperitoneal space-occupying lesions with fewer complications, a higher diagnosis rate, and has advantages such as easy operation, high quality, and quantity of samples, and little discomfort to the patient.

In recent years, more and more researchers have recommended EUS-FNA to be used in the diagnosis of submucosal tumors of the gastrointestinal, for judgment of the stage of malignant tumors of the esophagus and gastric, diagnosis of liver, gall bladder, and pancreas disease, and diagnosis and staging of mediastinum and lung tumors.<sup>16</sup> They also have suggested that new treatment indications for EUS-FNA will continue to emerge.<sup>17</sup> However, it should be noted that the advantage of EUS-FNA lies in qualitative diagnosis, the imaging examination is still needed for diagnostic localization of the retroperitoneal space-occupying lesion, and to look for distant metastases.<sup>18</sup> Meanwhile, an imaging examination can help to select the appropriate channels to entry the ultrasound endoscope. If EUS-FNA could be combined with imaging examination, the diagnostic rate of retroperitoneal space-occupying lesions could be greatly improved.<sup>19</sup> It not only could present a rational basis for subsequent treatment, but would also help to avoid unnecessary surgical treatment for some cases.<sup>20</sup> Our experience shows that EUS-FNA has great value in clinical application for the diagnosis of retroperitoneal space-occupying lesions (Table 1). However, our sample size was too small for the duration of the study, and compared with CT or MRI, the main disadvantage of EUS-FNA is that it is an invasive technique. Further study should include recruitment of more patients to widen the experience of skill, and the protocol of EUS-FNA will also be ameliorated to avoid any major injury in the process of puncture.

In conclusion, EUS-FNA has the advantages of lower complications and higher diagnostic ratio, which are valuable in the qualitative diagnosis of retroperitoneal space-occupying lesions.

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