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# Gallbladder motility in patients with hepatic cirrhosis before and after portal azygous disconnection

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## Abstract

**AIM:** To determine and compare the effect of vagus nerve on gallbladder motility in patients with hepatic cirrhosis before and after portal azygous disconnection (PAD).

**METHODS:** PAD operation (or Hassab's operation) was performed on 18 patients with portal hypertension, and anterior and posterior vagal trunks were cut. On d 3 before operation and d 10 after operation,  $^{99m}\text{Tc}$ -EHIDA 185 MBq was administered intravenously to the patients, and scintigraphy was performed at 0.25 min/frame. A standard fat meal was administered 30 min after scintigraphy, and dynamic imaging was performed 60 min after the fat meal. Following appearance of the region of interest (ROI) in gallbladder, the time-activity curve of ROI was established. The following seven parameters were used: radioactivity at 30 min after injection of  $^{99m}\text{Tc}$ -EHIDA (RC 30min), bile emptying fraction (EF), bile emptying period (EP), emptying rate (ER), latent period (LP), latent period radiocounting increment (LI), and latent period radiocounting increment rate (LR).

**RESULTS:** The RC 30 min decreased significantly after operation, compared with that before operation ( $2\,693.6 \pm 2\,406.9$  vs  $5\,606.8 \pm 2\,625.4$ ,  $P < 0.05$ ). The radiocounting of gallbladder increased gradually during LP. LP after operation was significantly longer than that before operation ( $13.36 \pm 5.92$  vs  $2.24 \pm 1.48$ ,  $P < 0.01$ ). LI and LR after operation were significantly higher than those before operation ( $2\,861.62 \pm 208.3$  vs  $331.21 \pm 421.02$ , and  $113.42 \pm 49.52$  vs  $7.57 \pm 10.75$ , respectively, both  $P < 0.01$ ). EP after operation was significantly shorter than that before operation ( $18.5 \pm 6.3$  vs  $24.1 \pm 6.4$ ,  $P < 0.05$ ). EF and ER after operation were significantly lower than those before operation ( $13.1 \pm 5.4$  vs  $32.3 \pm 16.3$ , and  $0.7 \pm 0.3$  vs  $1.4 \pm 0.8$ , respectively, both  $P < 0.01$ ).

**CONCLUSION:** PAD operation is a good clinical model in studying the effect of vagus on gallbladder motility. The gallbladder tension after PAD operation decreases significantly

during the interdigestive phase. The latent period of gallbladder contraction prolongs and the motility weakens apparently after a standard fat meal. Human vagus influences the gallbladder motility, and cutting of the nerve inhibits the gallbladder motility.

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## INTRODUCTION

Cholecystolithiasis results from multi-factors<sup>[1-5]</sup>, of which gallbladder motor dysfunction is an important factor<sup>[5,6]</sup>. Gallbladder motility is regulated by nerve system and body fluid<sup>[7]</sup>, especially the vagus<sup>[8-10]</sup>. Because of the complicated interfering factor and its difficulty in control, there were few clinical studies on the gallbladder motility. In this study, vagus nerve effect on gallbladder motility was studied in patients with liver cirrhosis.

## MATERIALS AND METHODS

Eighteen patients with portal hypertension (10 males and 8 females) with an average age of 50 years were included in this study. They had hypersplenotrophy and certain degree of hypersplenism. The esophagogastric varication was confirmed with gastroscop. No biliary abnormalities were found with ultrasonography. Hepatic function was classified as Child A level. Splenectomy (Hassab's operation) was performed, anterior and posterior trunks of vagus were cut off after inferior segment of esophagus was liberated. Aerofluxus was observed 48-96 h after operation. Hepatic function was recovered to Child A level 10 d postoperation.

With empty stomach on d 3 preoperation and d 10 postoperation, respectively,  $^{99m}\text{Tc}$ -labeled diethyl acetyl acid anilide iminodiacetic acid scintigraphy ( $^{99m}\text{Tc}$ -EHIDA) 185 MBq was administered intravenously. American SPECT of GE Company was adopted to perform scintigraphy, 0.25 min/frame. Standard fat meals (ENSURE 250 mL standard solution containing caloric 1046.0 KJ, protein 14%, fattiness 31.5%, carbohydrate 54.5%) was provided for patients after 30 min of continuous displaying. The region of interest (ROI) in gallbladder and the time-activity curve of ROI were established (Figures 3A, B). Then, 7 parameters were used to analyze. the radiocounting of  $^{99m}\text{Tc}$ -EHIDA injected 30 min later (RC 30 min), emptying fraction (EF, %), emptying period (EP min), emptying rate (ER, %/min): EF/EP, latent period (LP, min): the time from having fat meal to the initiation of contraction of gallbladder, latent period radiocounting increment (LI), latent period radiocounting increment rate (LR, %): the increased amount of radioactivity during LP/the initial radioactivity of LP $\times$ 100. The results were expressed as mean $\pm$ SD. SPSS11.0 software was used for analysis.

## RESULTS

Each of the paired pre- and post-operative parameters was proved in normal distribution by normality test (Table 1).

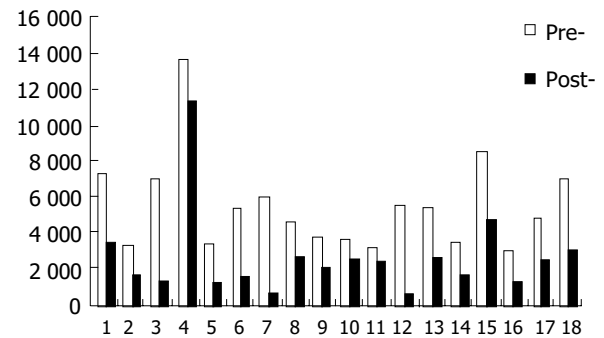
**Table 1** Comparison of gallbladder contractive function (mean±SD)

Parameters	Pre-surgery	Post-surgery
RC30 min	5 606.8±2 625.4	2 693.6±2 406.9 <sup>a</sup>
LP (min)	2.24±1.48	13.36±5.92 <sup>b</sup>
LI	331.21±421.02	2 861.6±2 028.3 <sup>b</sup>
LR (%)	7.57±10.75	113.42±49.52 <sup>b</sup>
EP (min)	24.1±6.4	18.5±6.3 <sup>a</sup>
EF (%)	32.3±16.3	13.1±5.4 <sup>b</sup>
ER (%/min)	1.4±0.8	0.7±0.3 <sup>b</sup>

<sup>a</sup> $P<0.05$ , <sup>b</sup> $P<0.01$ , vs pre-operation.

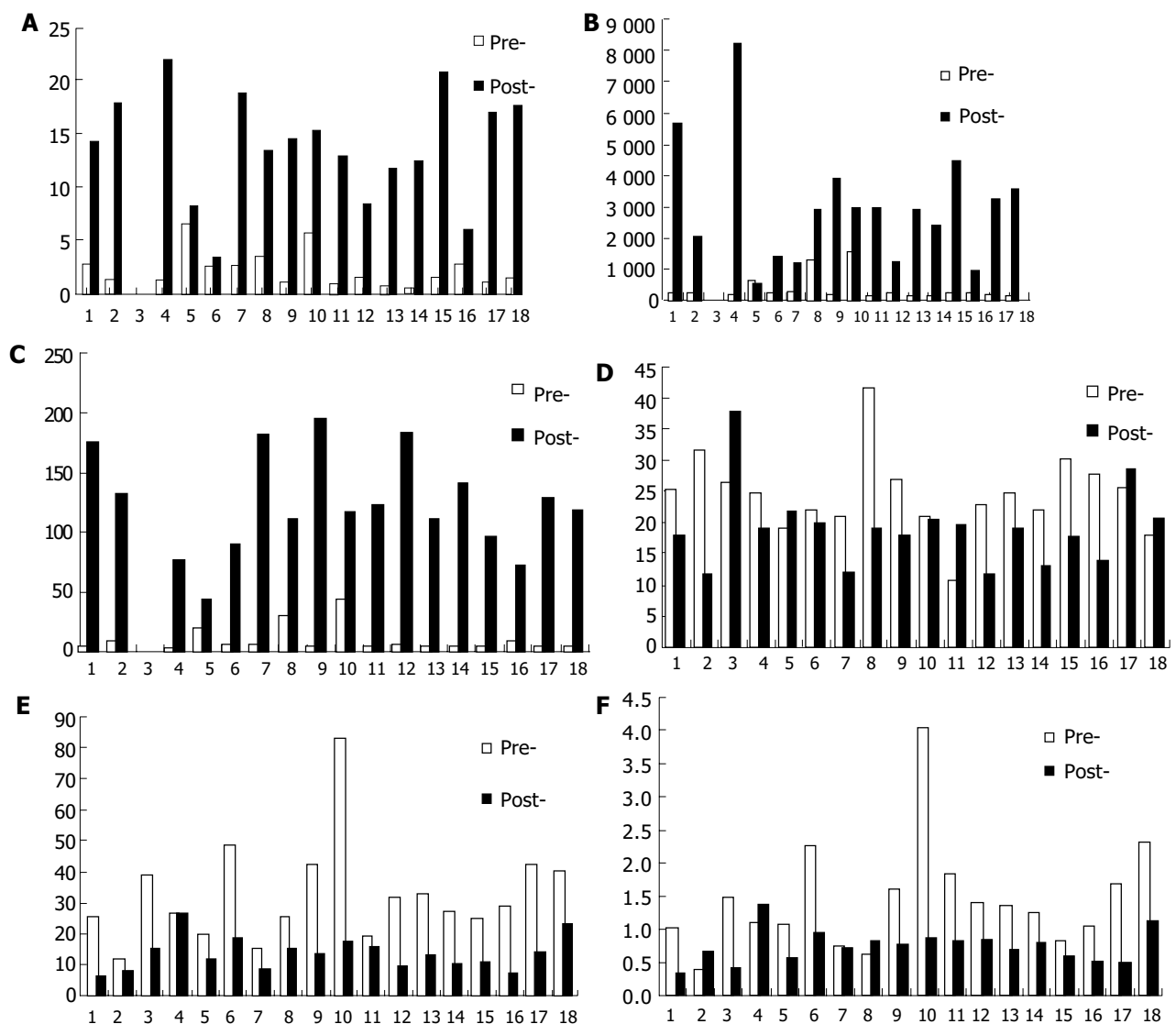
Serum <sup>99m</sup>Tc-EHIDA in blood was rapidly taken by liver, egested to biliary system, stored and concentrated in gallbladder. Thirty min after injecting <sup>99m</sup>Tc-EHIDA, the radioactivity in gallbladder could reflect the bile quantity entered to gallbladder during interdigestive phase. The RC 30 min postoperation decreased obviously than that preoperation (2693.6±2406.9 vs

5606.8±2625.4,  $P<0.05$ ) (Figure 1).

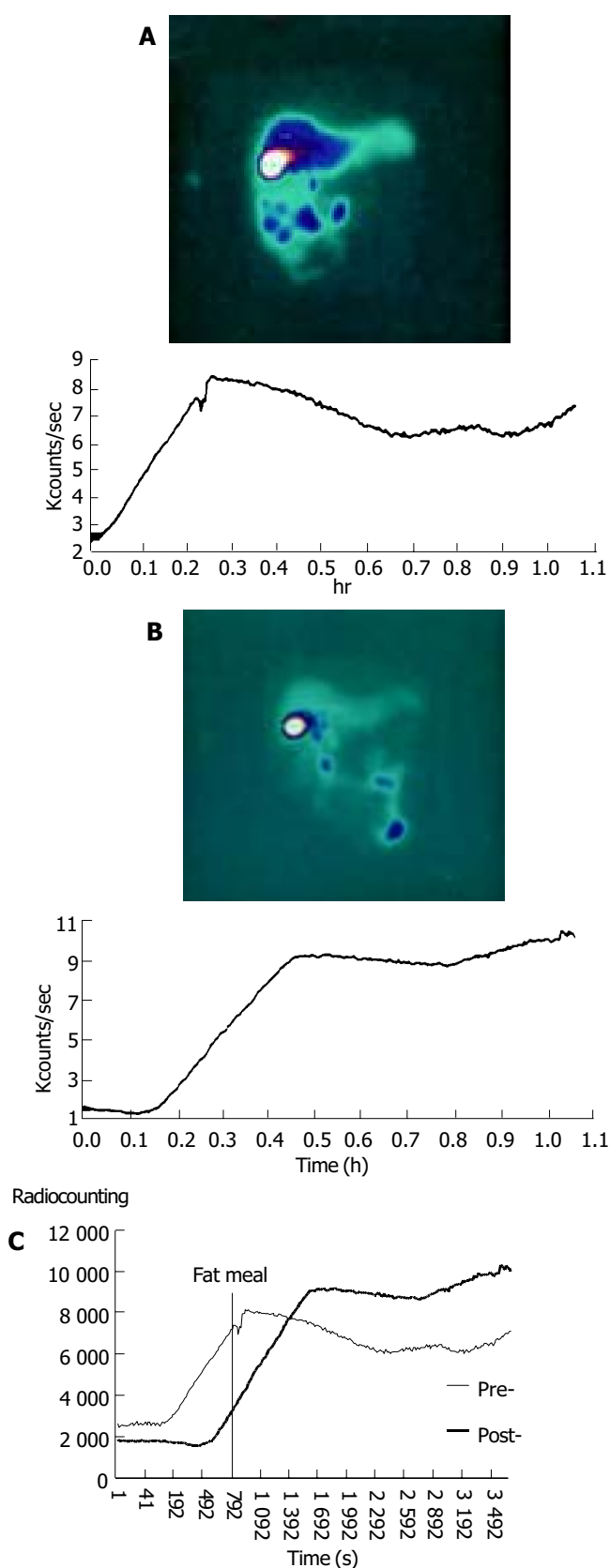


**Figure 1** RC 30 min of gallbladder in pre-PAD and post-PAD.

LP in cirrhotic patients was very short preoperation, and LP prolonged significantly postoperation (13.36±5.92 vs 2.24±1.48,  $P<0.01$ ). The radioactivity in gallbladder in LP increased gradually. LI and LR increased significantly postoperation (2861.6±2028.3 vs 331.21±421.02, 113.42±49.52 vs 7.57±10.75,  $P<0.01$ ) (Figures 2A, B, C). EP in cirrhotic patients was shorter postoperation than that preoperation, EF and ER decreased significantly (13.1±5.4 vs 32.3±16.3, 0.7±0.3 vs 1.4±0.8,  $P<0.01$ ) (Figures 2D, E, F).



**Figure 2** After administration of fat meal, changes in some parameters of gallbladder contraction. A: LP, B: LI, C: LR, D: EP, E: EF and F: ER.



**Figure 3** Time-activity curves of gallbladder in cirrhotic patients before (A) and after portal azygous disconnection (B) as well as their comparison (C).

## DISCUSSION

The Portal azygous disconnection (PAD) is a clinical research model to study the function of human vagus. Most studies on vagus function in gallbladder motility were limited to animal experiments<sup>[9-13]</sup>. Some scholars studied the gallbladder motility after gastrectomy and speculated that human vagus had an

important effect on gallbladder motility<sup>[14-16]</sup>. In PAD anterior and posterior trunks of vagus were cut, while the integrality of alimentary canal was maintained. Therefore, PAD could eliminate many disturbing factors. Although the basic liver function of patients could disturb the research, we reduced the disturbance to the lowest degree by adjusting liver function of every patient to Child A level, and auto-control method was used on same patient pre- and post-operation.

Radioactive nuclide <sup>99m</sup>Tc-EHIDA can be specifically taken by liver cells, then egested with bile and discharged through biliary system to intestinal tract. Dynamic flowing of bile can be displayed accurately by SPECT scintigraphy with a clear picture and a high resolution. It has little radiation damage to the patients, and is a good way to study the motility of gallbladder and biliary system<sup>[17-19]</sup>.

Gallbladder motility is regulated by nerve system and body fluid factors. Gallbladder emptying after ingestion is affected by multiple factors. Vagus cholinergic fibers could cause gallbladder empty after ingestion, sham feeding could result in gallbladder emptying to 25-56%, and this function could be inhibited by cutting vagus or injection of atropine<sup>[8-11,20,21]</sup>. Acetylcholine and other parasympathomimetic drugs could enhance the gallbladder tension and motility. Stimulating the vagus of dogs with electric current caused contraction of gallbladder, and gallbladder contracted slowly after both sides of the vagus were completely cut<sup>[10]</sup>. In our study, vagus in patients with liver cirrhosis was cut off in PAD to study its effect on gallbladder motility. <sup>99m</sup>Tc-EHIDA scintigraphy was used. Gallbladder motility was compared between pre- and post-PAD. We found that EP was shortened post- PAD ( $P<0.05$ ), EF and ER were significantly reduced, and the motility of gallbladder was obviously weak after meal. Our study showed that human vagus had an important regulatory effect on gallbladder motility after meal.

Vagus is an important factor for maintaining gallbladder tension during interdigestive phase<sup>[11,13,22]</sup>, the gallbladder volume could increase two times if both sides of vagus were completely cut<sup>[10]</sup>. Gallbladder was a weak in situation during interdigestive phase, and appeared rhythmic contraction and relaxation<sup>[11]</sup>. Tenuity bile was continuously excreted by liver exchanges with condensed bile stored in gallbladder<sup>[23-25]</sup>. Our study showed that RC 30 min post-operation was significantly decreased when fasting. The reason might be that cutting the vagus reduced the gallbladder tension during interdigestive phase, and then affected the exchange of bile.

Cholecystolithiasis patients did not contract at once after meal, but had a long latent period<sup>[26]</sup>. In this study, LP post-operation after fat meal was prolonged ( $P<0.01$ ). The gallbladder lost the contractive stimulation in cephalic phase after vagus was cut. The result in our study was similar to that previously described<sup>[27]</sup> (LI2861.6±2028.3, LR 113.42±49.52%). We conclude that bile containing nuclides entering into gallbladder more rapidly results from the heightened pressure of biliary tract. The motility of Oddi's sphincter is adjusted by vagus<sup>[11]</sup>, and the bile excreted by liver is mainly adjusted by body fluid<sup>[28-31]</sup>. Fat meal may increase the bile excreted by liver through humoral regulation, and amputation of the vagus can weaken the contraction of Oddi's sphincter cephalic phase, so the pressure of biliary tract increases. Further study is required for clarifying the mechanism in detail.

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