

## Morphine-augmented cholescintigraphy enhances duodenogastric reflux

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Morphine intervention in cholescintigraphy decreases imaging time to diagnose acute cholecystitis. Not infrequently we observe duodenogastric reflux during scintigraphy with and without morphine intervention. To evaluate occurrence of duodenogastric reflux related to morphine, we reviewed 55 patients who underwent cholescintigraphy with (32) and without (23) morphine intervention. Morphine was injected when there was bowel activity with non-visualization of the gallbladder at 60 min. Duodenogastric reflux was identified by the appearance of activity in the area just below or immediately adjacent to the tip of the left hepatic lobe laterally. Among 32 patients with morphine intervention, 19 had acute cholecystitis and 13 chronic cholecystitis. Eleven of 19 (58%) with acute cholecystitis had duodenogastric reflux and 6 of 13 (46%) had duodenogastric reflux in chronic cholecystitis. The total of duodenogastric reflux in the group with morphine injection was 53%. Two patients' duodenogastric reflux occurred before morphine injection and was more apparent after morphine was given. In the without morphine group, 3 had acute cholecystitis and 20 had chronic cholecystitis; 2 (one acute and one chronic cholecystitis) of these 23 (9%) had duodenogastric reflux. Our results indicate: (1) occurrence of DG reflux in morphine augmented cholescintigraphy is not significantly different in cholecystitis from that in chronic cholecystitis; (2) duodenogastric reflux in morphine augmentation occurs significantly more often than without morphine intervention ( $p < 0.001$ ). We conclude that cholescintigraphy with morphine enhances duodenogastric reflux. The degree of duodenogastric reflux in the acute cholecystitis patients has been more severe than in the chronic cholecystitis patients.

**Key words:** cholescintigraphy, duodenogastric reflux, morphine, acute cholecystitis, chronic cholecystitis, Tc-99m BRIDA, sphincter of Oddi

### INTRODUCTION

NONVISUALIZATION of the gallbladder in hepatobiliary scintigraphy is a hallmark of acute cholecystitis. Presumably cystic duct obstruction is almost always associated with acute cholecystitis and non-visualization of the gallbladder reflects obstruction of the cystic duct. Morphine intervention in cholescintigraphy decreases imaging time to diagnose acute cholecystitis.<sup>1</sup> With intravenous injection of a smaller dose of morphine sulfate contraction of the

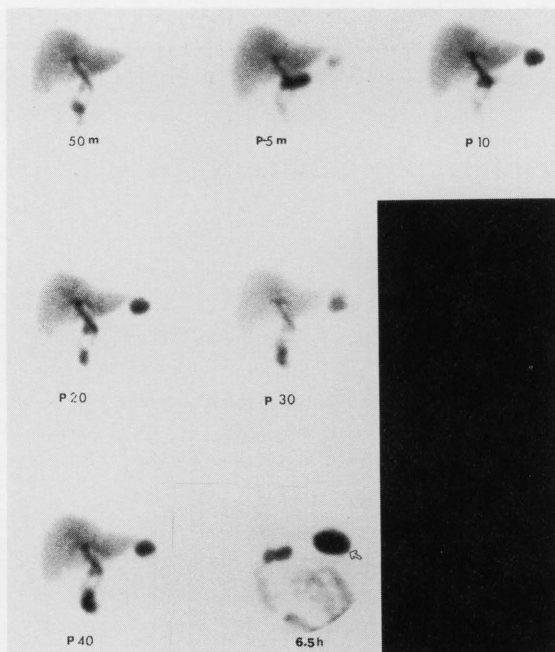
sphincter of Oddi results in increased intraluminal pressure in the common bile duct, and promotes bile flow through a patent cystic duct.<sup>1</sup> Not infrequently we observe duodenogastric reflux during hepatobiliary imaging after the morphine injection. Oates and Achong<sup>2</sup> studied 114 patients with morphine-augmented cholescintigraphy and concluded that a majority of patients with acute and chronic cholecystitis experienced gastric reflux.<sup>2</sup> We studied the patients undergoing cholescintigraphy with and without morphine intervention to assess morphine-related duodenogastric reflux.

### MATERIALS AND METHODS

Fifty-five patients' cholescintigraphies were reviewed,

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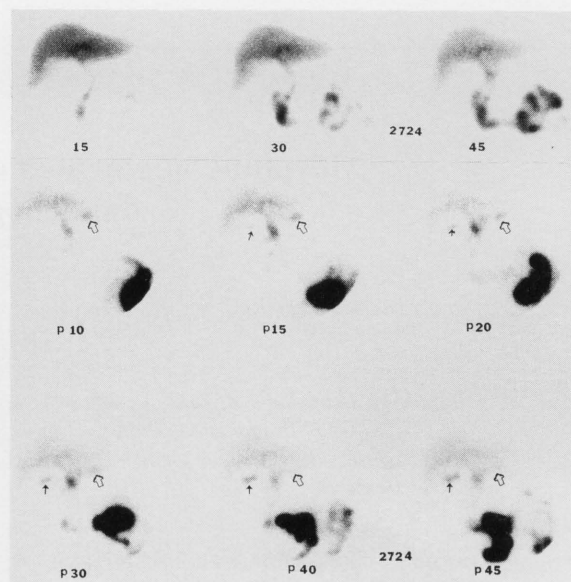


**Fig. 1** Tc-99m mebrofenin hepatobiliary imaging shows presence of bowel activity but no gallbladder activity at 50 min; activity in the gastric region 5 min after morphine IV injection (P-5m), and gradually increased and persistent radioactivity in the gastric region up to 6.5 hr. Open arrow indicates a large amount of duodenogastric reflux at the 6.5 hr image. The gallbladder is not visualized throughout the study, consistent with acute cholecystitis.

and these cholescintigraphies were referred for suspected acute cholecystitis. Cholescintigraphy was performed after intravenous injection of 5–8 mCi (185–296 MBq) of Tc-99m mebrofenin in those patients who had been fasting for at least 4 hours. Sequential 2-, 5-, 10-, 15-, 30-, 45-, and 60 min images were obtained. Morphine sulfate, 0.04 mg/kg usually 2–3 mg, was IV injected when the patient exhibited bowel activity without gallbladder activity usually 45–50 min after radiopharmaceutical administration. Duodenogastric reflux was identified by radioactivity appearance in the area just below or immediately adjacent to the tip of the left hepatic lobe laterally.<sup>3</sup> In those patients without morphine intervention, imaging was performed every 30 min after routine 60 min study up to 4 hrs. Clinical, surgical and/or pathological findings were correlated with scintigraphic results.

## RESULTS

These patients' cholescintigraphies were divided into two categories: cholescintigraphy with morphine intervention (32 patients); and cholescintigraphy without morphine intervention (23 patients). Among the 32 patients with morphine intervention, 19 had non-visualization of the gallbladder (acute cholecystitis), 13 with gallbladder visualization (chronic cholecystitis). All 19 patients with acute cholecystitis underwent cholecystectomy which



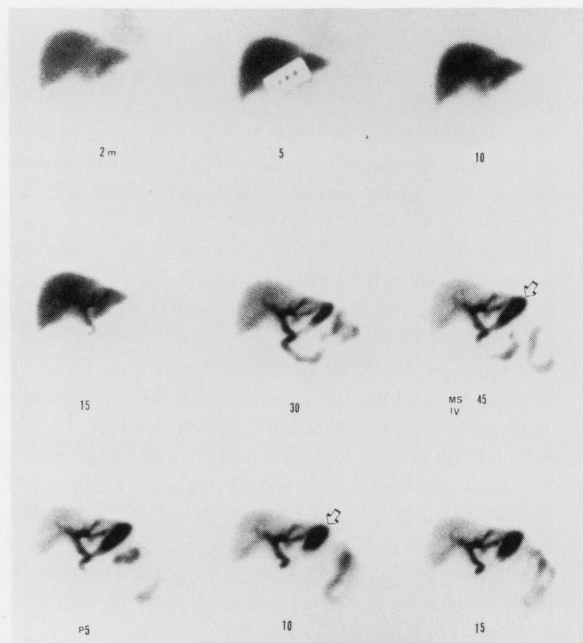
**Fig. 2** Tc-99m mebrofenin hepatobiliary imaging shows no gallbladder activity, presence of bowel activity in the 15-, 30-, and 45 min, visualization of the gallbladder as well as duodenogastric reflux at 10-, 20-, and 30 min after morphine administration. Presence of duodenogastric reflux after 10 min of morphine administration. Visualization of the gallbladder after 15 min of morphine administration. Open arrows indicate duodenogastric reflux; arrows indicates the gallbladder. The gallbladder is visualized after morphine injection indicating chronic cholecystitis.

proved to be acute inflammation by histopathology. Eleven of the 19 (58%) patients with acute cholecystitis had duodenogastric reflux, while 6 of 13 (46%) patients with chronic cholecystitis demonstrated duodenogastric reflux. The amount of duodenogastric reflux (Fig. 1) of the patients with nonvisualization of the gallbladder (acute cholecystitis) is consistently higher than that of the patients with visualization of the gallbladder (chronic cholecystitis) (Fig. 2). The amount of duodenogastric reflux has been estimated by the extent of the area of radioactivity in the gastric region and intensity of the radioactivity.

Of the group receiving a morphine injection, 53% exhibited D-G reflux. Two patients' duodenogastric reflux which occurred before morphine injection became apparent after morphine was given (Fig. 3).

Among 23 patients without morphine intervention, three patients had acute cholecystitis and 20 had delayed visualization of the gallbladder (chronic cholecystitis); two (one acute and one chronic cholecystitis) of these 23 (9%) had duodenogastric reflux.

Occurrence of duodenogastric reflux in morphine-augmented cholescintigraphy is not a statistically significant difference between acute and chronic cholecystitis ( $p = 0.51$ ); duodenogastric reflux after morphine augmentation occurred at a significantly higher rate than without morphine intervention ( $p < 0.001$ ).



**Fig. 3** Duodenogastric reflux occurring before morphine administration becomes apparent after morphine given; amount of duodenogastric reflux as indicated by open arrows increases immediately after morphine IV injection. The gallbladder is not visualized throughout the study indicating acute cholecystitis. MS, morphine sulfate; IV, intravenous injection.

## DISCUSSION

Normal Tc-99m IDA cholescintigraphy will be obtained if there is integrity of hepatocyte uptake, patent intrahepatic ducts, cystic duct, and common bile duct, normal gallbladder function, and normal function of the sphincter of Oddi. Appearance of radioactivity occurs in the following order: cardiac blood pool, the liver, intrahepatic ducts, gallbladder, and bowel. Cholescintigraphy has been proven a highly efficacious approach to the diagnosis of acute and chronic cholecystitis. Nonvisualization of the gallbladder reflecting cystic duct obstruction is a hallmark of acute cholecystitis.<sup>4</sup> Cholescintigraphy also enables noninvasive identification of duodenogastric reflux.<sup>2,3,5-7</sup> Various etiological factors result in duodenogastric reflux or enterogastric reflux; these include exploratory laparotomy, acute and chronic cholecystitis,<sup>2,3,5,8-13</sup> peptic ulcer disease, and chronic gastritis.<sup>6,7</sup> Our previous study<sup>3</sup> concluded that gallbladder dysfunction or nonfunction is demonstrated more frequently when duodenogastric reflux is present than with normal gallbladder function.<sup>3</sup>

Opioid drugs have several pharmacological effects on the upper gastrointestinal tract. For example, morphine sulfate contracts the sphincter of Oddi and pylorus and also increases the resting tone of the stomach, duodenum, and small intestine, causing periodic, nonpropulsive spasmic contracts in the proximal small bowel, and delayed gastric emptying.<sup>14</sup> Morphine causes constriction of Oddi

with the common bile duct pressure increasing more than 10 fold.<sup>14</sup> The pressure in the bile duct facilitates flow of the intravenous injection of Tc-99m IDA into the gallbladder through the cystic duct during cholescintigraphy. If the gallbladder is not visualized in 45 min when there is bowel activity, typically 0.04 mg/kg<sup>1</sup> or usually 2 mg of IV morphine is administered. Imaging is then continued for another 30 mins; thus morphine intervention has been shown to reduce imaging time from 4-24 hrs to about 90 mins.<sup>1,15</sup>

Our results indicate that the morphine intervention group had enhanced duodenogastric reflux as compared to patients who did not receive morphine intervention in two ways: either by an increase in reflux volume or by the presence of reflux from the absence of reflux. These findings were paradoxical in relation to the pharmacological actions of morphine. This paradoxical finding, entero-gastric reflux after morphine injection, has also been described as occurring in 86% of acute cholecystitis cases and in 80% of chronic cholecystitis cases.<sup>2</sup> Enterogastric reflux increased after morphine given to 57%<sup>2</sup> and 2 of the patients with reflux had increased reflux. Our findings show that the degree of duodenogastric reflux in acute cholecystitis patients was more severe than that of chronic cholecystitis and has not been previously described. The mechanism of this paradoxical finding is unknown. Oates et al. hypothesized as follows: morphine induced intestinal spasms and preexisting duodenal inflammation secondary to adjacent cholecystitis may result in synergically exaggerated retrograde peristalsis. This mechanism requires further investigation.

In summary, duodenogastric reflux or enterogastric reflux on cholescintigraphy has been enhanced by morphine administration. Constriction of the sphincter of Oddi, as an effect of morphine administration, causes radiopharmaceutical already present in the small bowel to be redistributed to the stomach through the pyloric sphincter. Reflux occurred more significantly with morphine intervention than without it; the degree of duodenogastric reflux was more severe in the acute cholecystitis patients than in the chronic cholecystitis patients. Thus duodenogastric or enterogastric reflux on cholescintigraphy was enhanced by morphine administration.

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