

**UNDERSTANDING THE EFFECT OF MORPHINE ON THE ACCURACY OF NUCLEAR  
HEPATOBILIARY IMAGING THROUGH A CASE STUDY**

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## Abstract

Many patients present with upper abdominal pain and receive some type of pain-relieving therapy prior to gallbladder imaging. The physiologic effect of morphine and other analgesics on gallbladder function has been well-studied. What hasn't been studied as much are the implications on clinical practice and the decision about whether morphine is the best option to use in suspected chronic gallbladder disease. This case study serves to illustrate the influence of morphine in a patient who underwent both inpatient and outpatient hepatobiliary scintigraphy with dramatically different results. This case study perfectly shows the considerations that must be taken when using morphine because it eliminates many confounding variables; the only difference in the patient at the time of initial and subsequent presentation was the presence of morphine.

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## Case Presentation

This patient was a 54 year old male with hypertension and surgical history of two abdominal hernia repairs with mesh in 1974 and 1995 who presented complaining of epigastric and right upper quadrant abdominal pain. He had been having intermittent sharp right upper quadrant abdominal pain for four months, often having three to four episodes per day lasting up to four hours at a time. Episodes at work were disabling, causing the patient to double over. His symptoms were unrelated to meals and he denied fatty food intolerance. He used antacids without relief. He denied nausea, vomiting, fever, chills, hematemesis, hematochezia, melena, or diarrhea.

The patient's medications included fenofibrate, metoprolol, pantoprazole, buspirone, sertraline, and zolpidem. He had no allergies and no alcohol, tobacco, or drug use. His physical exam at the time of presentation was significant for a soft, non-distended abdomen with well-healed supraumbilical and infraumbilical midline surgical incisions. There was mild voluntary guarding in the right upper quadrant on deep palpation, no involuntary guarding, and Murphy's sign was negative. No hernias noted, masses palpated, with normoactive bowel sounds.

The patient's initial hepatobiliary scan (HIDA) was performed five days prior to presentation. Upon hospital admission, the patient received morphine and pantoprazole. Abdominal ultrasound showed no cholelithiasis and there was no biliary ductal dilation. HIDA scan demonstrates normal filling of the gallbladder with no measurable response to sincalide.

Five days after the initial presentation the HIDA scan was repeated at an outpatient facility. The only change in the patient's medication was the removal of morphine.

## Introduction

While the effect of morphine on HIDA scans has been well studied, there has been much less research completed on the ability of morphine to provide a false positive result on a HIDA scan for chronic cholecystitis. Morphine is an often utilized option for patients who come in with cholestatic pain, and is often given to patients early in the emergency department. This is because in addition to the central analgesic effect that morphine has, it also reduces inflammatory fluid secretion by mucosa in the gallbladder that helps induce biliary pain (Jivegard). By the time a HIDA scan is done, after an initial ultrasound has been completed, morphine is often being used to control a patient's pain.

A pathophysiological model suggesting morphine as an independent variable for increases in false positive HIDA scans for chronic cholecystitis certainly exists within the literature. A study of 11 patients after cholecystectomy showed morphine-induced increase in resistance of passage of bile from the common duct, forcing an increased amount of bile to accumulate in the gallbladder (Pedersen). A second double-blind, placebo-controlled ultrasonographic study demonstrated constriction of the common bile duct after I.V. morphine administration in surgical patients. Before morphine administration the diameter of the common bile duct was  $9.5 \pm 3.3$  mm and after morphine (4 minutes) it was  $7.2 \pm 2.1$  mm and  $5.8 \pm 2.1$  mm (8 minutes) (Zsigmond). These studies show that even as quickly as a few minutes after administration, morphine can have profound physiologic effects on the ability of bile to empty from the gallbladder.

Later studies showed evidence of imaging supporting the explanation for delayed gallbladder emptying in patients with morphine. A retrospective review in 2002 by Barlas et. al investigated 198 patients in the emergency department who underwent nuclear hepatobiliary imaging. Of these, 56 patients received opioids prior to imaging. Delayed common bile duct visualization occurred in 28.6% of subjects receiving opioids and in 12% of those who did not ( $p < .01$ ) with a relative risk of 4.18 for morphine administration compared to 1.46 for meperidine and 2.38 for other opioids. The investigators concluded that opioid usage resulted

in more hepatobiliary imaging and an increase in false positive results that mimicked pathologic obstruction.

The goal of this case study is to examine a case in which a patient had positive HIDA imaging for chronic cholecystitis while he had morphine present in the body. However, days later when the morphine was out of his system, his HIDA test was negative, positing that morphine may have influenced the false positive result. This has profound implications for clinical practice because it could affect the decision making of which analgesic to use in patients with suspected chronic gallbladder pathology, since morphine may affect efficacy of gallbladder imaging in cases that are not clinically apparent.

## Methods

A case study using hepatobiliary iminodiacetic acid scan (HIDA) was performed with a single patient from the Scottsdale Medical Imaging practice as a retrospective review. The HIDA scan results of the patient were utilized to provide the results to the case theory. The HIDA scan has two components. First, the radiotracer Tc99m mebrofenin is injected, and then transported to the liver bound to serum albumin. After arriving at the hepatic perisinusoidal space, these tracers then dissociate from albumin and are extracted by hepatocytes. These tracers are secreted into the biliary calculi unchanged. Initial imaging is done during this time, and if the gallbladder does not fill normally, it can be a sign of acute cholecystitis. Secondly, sincalide, a synthetic analogue for cholecystokinin (CCK), is administered intravenously as a continuous infusion to simulate physiologic CCK release in the body. In response, the gallbladder should empty over time with an EF of  $\geq 38\%$  to be considered normal. This was the test that was performed in order to determine if the patient was suffering from chronic cholecystitis.

## Results

The patient's initial HIDA was performed on admission at the hospital. The HIDA scan demonstrated normal filling of the gallbladder with no measurable response to sincalide. Figure 1 shows the HIDA scan completed at the initial presentation of the patient. Sincalide was administered in a continuous 60 minute infusion with imaging performed throughout. It can be clearly seen that the gallbladder does not empty over time, and the emptying is read as undefined, or 0%.

Five days after the initial presentation the HIDA scan was repeated at an outpatient facility. The only change in the patient's medication was the removal of morphine. Figure 2 shows the HIDA scan 5 days after initial presentation at SMIL. Imaging shows that the gallbladder empties quickly and washes out into bowel, showing completely normal function and 100% emptying. The graph of activity vs. time shows clear emptying and activity change.

## Discussion and Conclusions

The differences between the imaging of the patient from admission with morphine and five days later without morphine clearly indicate a discrepancy in gallbladder emptying. In the initial presentation, it is easy to see that the gallbladder does not empty in response to sincalide, while in the subsequent presentation it does. A very clear difference in activity vs. time plotted in the imaging graphs confirms this as well.

The only difference in this patient's condition from the first to the second set of imaging was the presence of morphine in the patient's system. There are no other variables or medical conditions that play a role and explain the mechanism of morphine contributing to a delay in gallbladder emptying. Morphine is well-known to constrict the sphincter of Oddi, leading to increased pressure in the biliary tree. While this quality is helpful in identifying acute calculous cholecystitis and assessing the patency of the cystic duct, it is problematic for the subsequent investigation of chronic cholecystitis disease in patients. This case illustrates the clinical judgment that must be utilized when making pain control decisions for patients with acute vs. chronic cholecystitis, with the implications for possible future hepatobiliary nuclear imaging considered.

# Figures and Tables

Figure 1 - Initial HIDA scan in hospital

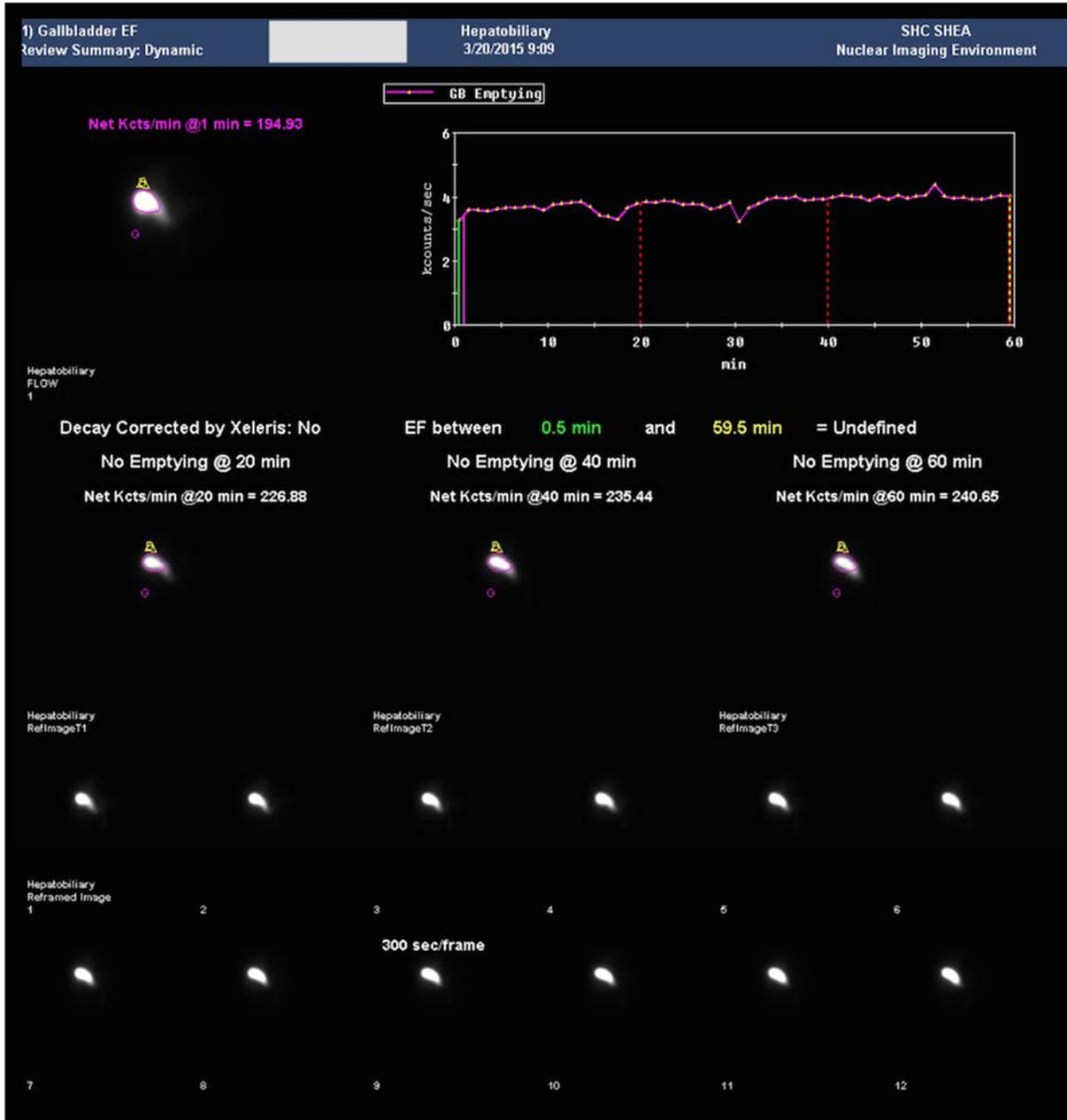
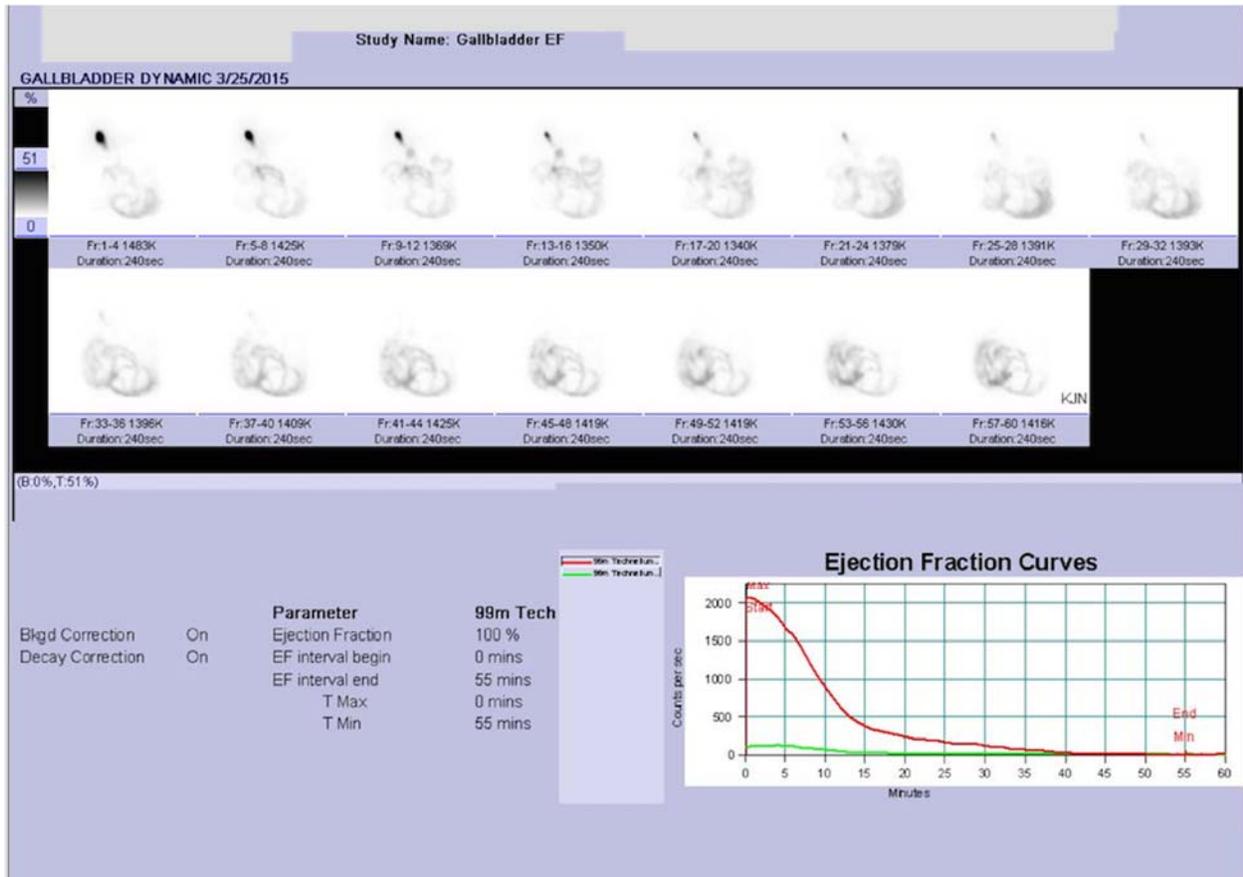


Figure 2 - HIDA scan 5 days after initial presentation at SMIL.



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