Appropriate Use Criteria for Hepatobiliary Scintigraphy in Abdominal Pain

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EXECUTIVE SUMMARY

^{99m}Tc-labeled hepatobiliary iminodiacetic acid (HIDA) scintigraphy is an important adjunct to the evaluation of patients with abdominal pain. The introduction of radiopharmaceuticals that allowed the performance of these studies in patients with elevated bilirubin levels expanded the clinical use of this important diagnostic imaging technology. The proper use of HIDA scintigraphy requires an understanding of the physiology of the hepatobiliary system in both health and disease states, the metabolism of hepatobiliary radiopharmaceuticals, the sensitivity and specificity of currently used radiopharmaceuticals for biliary collecting system abnormalities during normal and abnormal hepatocellular function, the radiation dosimetry of hepatobiliary radiopharmaceuticals, and the accuracy and risks of alternative diagnostic studies (*1*). Describing the proper use of scintigraphic techniques in the diagnosis of abdominal pain, therefore, requires input from experts in nuclear imaging and in gastroenterology. This document describes the appropriate use of HIDA scintigraphy in patients with abdominal pain and has been constructed with input from expert representatives from the Society of Nuclear Medicine and Molecular Imaging (SNMMI), the European Association of Nuclear Medicine (EANM), and the American Gastroenterological Association (AGA). These experts reviewed the current literature and current practice for the management of patients with abdominal pain and developed this consensus document. The process was performed in accordance with Public Law Number 113–93 (April 1, 2014) (*2*), mandating the development of appropriate use criteria (AUC) for certain diagnostic imaging and nuclear medicine procedures. This AUC is intended to assist referring medical practitioners in the management of patients with abdominal pain, in particular by describing the utility of HIDA scintigraphy.

INTRODUCTION

The present document describes the appropriate use of HIDA scintigraphy in the evaluation of patients with abdominal pain. However, abdominal pain is not managed in isolation from other signs and symptoms; consideration of the entire patient presentation is needed to determine whether or not HIDA scintigraphy is appropriate. In addition, these recommendations do not preclude other testing. This document describes common clinical presentations in patients with abdominal pain in which HIDA scintigraphy may be helpful. Referring providers should consider patient history, physical examination results, and previously acquired test results before considering HIDA scintigraphy. This document is presented to assist the health care practitioner in the appropriate use of HIDA scintigraphy in evaluating patients with abdominal pain but is not intended to replace clinical judgment.

HIDA scintigraphy may be appropriately used in many scenarios not described below; no practice guideline or AUC is able to describe all clinical scenarios for which diagnostic imaging should be used. This document may also be useful for nuclear medicine physicians, radiologists, and technologists, as well as for developers of clinical decision support (CDS) tools who can use it as guidance in validating requests for imaging patients with abdominal pain. Radiology benefits managers and other third party payers could also use this AUC. It is our intention that the AUC be used to help improve the efficiency of the appropriate ordering of HIDA scintigraphy in patients with abdominal pain.

METHODOLOGY

Expert Workgroup Selection

The experts of this AUC workgroup were convened by SNMMI to represent a multidisciplinary panel of health care providers with substantive knowledge of the use of HIDA scintigraphy for abdominal pain. In addition to SNMMI member representation, an international representative from EANM and 2 representatives from AGA were included in the workgroup. Twelve physician members were ultimately selected to participate and contribute to the resulting AUC. A complete list of workgroup participants and external reviewers can be found in Appendix A.

AUC Development

The process for AUC development was modeled after the RAND/UCLA appropriateness method (*3,4*) and included the development of a list of common scenarios in which HIDA scintigraphy can be used, a systematic review of evidence related to these scenarios, and the development of an appropriateness score for each scenario by using a modified Delphi process. This process strove to adhere to the standards of the Institute of Medicine of the National Academies for developing trustworthy clinical guidance (*5*). The process included a systematic synthesis of available evidence, individual and group ratings of the scenarios using a

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formal consensus process, and AUC recommendations based on final group ratings and discussions.

Scope and Development of Clinical Scenarios

To begin this process, the workgroup discussed various potential clinical scenarios for which use of HIDA scintigraphy might be considered (including possible contraindications). The scope of this workgroup was to focus on the appropriate use of HIDA scintigraphy specifically to assess its diagnostic accuracy and effects on treatment decisions and clinical outcomes in adults, children, and infants with abdominal pain who are suspected to have a hepatobiliary condition. For all scenarios, the relevant populations were adults (over 17 y with acute onset of upper abdominal pain or chronic recurrent abdominal pain) or pediatric patients (newborn to 17 y with acute abdominal pain or chronic abdominal pain) of all races or geographic locations (rural, urban, etc.).

The workgroup identified 10 scenarios for the use of HIDA scintigraphy in patients with acute or chronic abdominal pain. The scenarios are intended to be as representative of the relevant patient population as possible for development of this AUC.

The resulting AUC are based on evidence and expert opinion regarding diagnostic accuracy and effects on clinical outcomes and clinical decision making as applied to each scenario. Other factors affecting the AUC recommendations included potential harm—including long-term harm that may be difficult to capture—costs, availability, and patient preferences.

Systematic Review

To inform the workgroup, a systematic review of the relevant evidence was commissioned by an independent group, the Pacific Northwest Evidence-Based Practice Center of Oregon Health and Science University (*6*). The primary purpose of the systematic review was to assess the diagnostic accuracy of cholescintigraphy for acute or chronic right upper quadrant abdominal pain, as well as the effects of cholescintigraphy versus no cholescintigraphy on treatment decisions and the use of diagnostic tests and clinical health outcomes, in order to help inform the development of the AUC.

The key research questions used to guide the systematic review were as follows: What is the diagnostic accuracy of cholescintigraphy for the evaluation of acute or chronic abdominal pain in adults, infants, and children? What are the effects of cholescintigraphy versus no cholescintigraphy for the evaluation of acute or chronic abdominal pain on treatment decisions and the use of diagnostic tests in adults, infants, and children? What are the effects of cholescintigraphy versus no cholescintigraphy for the evaluation of acute or chronic abdominal pain on clinical outcomes in adults, infants, and children?

The inclusion and exclusion criteria for this review were based on the study parameters established by the workgroup, using the PICOTS (population, intervention, comparisons, outcomes, timing, and setting) approach. Searches were conducted on the following databases: the Cochrane Central Register of Controlled Trials, the Cochrane Database of Systematic Reviews, and Ovid MEDLINE (from 1946 through June 2015). These searches were supplemented by reviewing the reference lists of relevant publications.

Two reviewers independently assessed abstracts and full-text articles for inclusion and rated study quality as defined by the established PICOTS parameters. The quality (based on the risk of bias) of each study was categorized as "good," "fair," or "poor" by using Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) for diagnostic accuracy studies (*7*) and Assessment of Multiple Systematic Reviews (AMSTAR) for systematic reviews (*8–10*). The strength of the overall evidence was graded as high, moderate, low, or very low using methods based on quality of evidence, consistency, directness, precision, and reporting bias.

Literature searches resulted in 691 potentially relevant articles. After a dual review of the abstracts and titles, 157 articles were selected for full-text review. One systematic review (of 40 studies) and an additional 32 unique publications were determined to meet inclusion criteria and were included in this review.

Rating and Scoring Process

In developing these AUC for HIDA scintigraphy, the workgroup used the following definition of appropriateness to guide their considerations and group discussions: "The concept of appropriateness, as applied to health care, balances risk and benefit of a treatment, test, or procedure in the context of available resources for an individual patient with specific characteristics" (*11*).

On reviewing the evidence summary of the systematic review, the workgroup further refined its draft clinical scenarios to ensure their accuracy and to facilitate consistent interpretation when scoring each indication for appropriateness. Using the evidence summary, workgroup members were first asked individually to assess the benefits and risks of HIDA scintigraphy for each of the identified clinical scenarios and to provide an appropriateness score for each scenario. Workgroup members then convened in a group setting via webinar to discuss each scenario and its associated scores from the first round of individual scoring. After deliberate discussion, each member independently provided a second round of scores for each scenario. For each indication, the mode numeric score was determined and then assigned to the associated appropriate use category. For this scoring round, the group members were requested to include their expert opinion in addition to the available evidence in determining their scores. All members contributed to the final discussion, and no one was forced into consensus. After the rating process was completed, the final appropriate use ratings were summarized in a format similar to that outlined in the RAND/UCLA appropriateness method.

The workgroup scored each clinical scenario as "appropriate," "may be appropriate," or "rarely appropriate" on a scale from 1 to 9. Scores 7–9 indicate that the use of the procedure is appropriate for the specific scenario and is generally considered acceptable. Scores 4–6 indicate that the use of the procedure may be appropriate for the specific scenario. This implies that more research is needed to classify the scenario definitively. Scores 1–3 indicate that the use of the procedure is rarely appropriate for the specific scenario and is generally not considered acceptable.

As stated by other societies that develop AUC, the division of these scores into 3 general levels of appropriateness is partially arbitrary, and the numeric designations should be viewed as a continuum. Additionally, if there was a difference in clinical opinion about a particular clinical scenario such that workgroup members could not agree on a common score, that clinical scenario was given a score of 5 to indicate a lack of agreement on appropriateness based on the available literature and their collective clinical opinion, indicating the need for additional research.

CLINICAL SCENARIOS AND AUC SCORES

Clinical scenarios for the use of HIDA scintigraphy and final AUC scores for abdominal pain are presented in Table 1 [**Table 1**]

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TABLE 1
Clinical Scenarios for HIDA Scintigraphy in Abdominal Pain

Scenario no.	Description	Appropriateness	Score
1	Patients presenting with suspected acute cholecystitis or acute cystic duct obstruction	Appropriate	9
2	Patients presenting with acute upper abdominal pain	Appropriate	7
3	Patients presenting with chronic upper abdominal pain	May be appropriate	5
4	Patients presenting with functional biliary pain syndrome caused by chronic acalculous gallbladder disease	Appropriate	7
5	Patients suspected of having chronic cholecystitis	Appropriate	7
6	Patients suspected of having biliary obstruction	Appropriate	7
7	Patients presenting with functional biliary pain syndrome caused by chronic acalculous biliary disease, including sphincter of Oddi dysfunction	May be appropriate	5
8	Patients presenting with abdominal pain after surgery with an afferent loop	May be appropriate	4
9	Patients presenting with abdominal pain after surgery or from trauma with suspected bile leakage	Appropriate	8
10	Patients presenting with abdominal pain with suspected enterogastric reflux	Rarely appropriate	3

Scenario 1: Patients presenting with suspected acute cholecystitis or acute cystic duct obstruction (Score: 9 – appropriate)

This indication was considered appropriate by unanimous agreement of the panel. From the systematic review of the literature, the pooled sensitivity and specificity of HIDA scintigraphy for the detection of acute cholecystitis was determined to be 96% (range 78%–100%) and 90% (range 50%–100%), respectively (*12–51*). In those studies, in which patients had surgical confirmation, all or nearly all had acute or chronic cholecystitis.

A negative study was found to greatly reduce the odds (by 25-fold) of a diagnosis of acute cholecystitis, whereas a positive study greatly increased the odds (by 10-fold) of this diagnosis. On the basis of the pooled data, HIDA scintigraphy had greater diagnostic accuracy than did ultrasound, CT, or MRI (*12*).

Although fewer studies specifically evaluated acute acalculous cholecystitis, the sensitivity and specificity are generally considered slightly lower (67%–100% and 58%–88%, respectively) than they are with acute calculous cholecystitis (*52–55*).

The SNMMI Procedure Standard for Hepatobiliary Scintigraphy (V 4.0) emphasizes the need to correl ate scintigraphy findings with clinical information and other relevant modalities to arrive at the correct diagnosis (*56*). Adjunctive pharmacologic intervention may also enhance the diagnostic utility of the hepatobiliary study and decrease the time needed to make the diagnosis.

Gallstones are much less common in the pediatric population except in some subgroups, such as patients with hemolytic anemias. Acalculous disease is therefore a relatively more common cause of cholecystitis in children. Although the number of high-quality, pediatric-specific studies on the role of HIDA scintigraphy are limited, such an examination would be expected to have similar diagnostic performance in calculus cholecystitis but to perform less well in children than adults overall because of the prevalence of acalculous disease.

Scenario 2: Patients presenting with acute upper abdominal pain (Score: 7 – appropriate)

The imaging workup of patients presenting with acute upper abdominal pain is variable, as this is a nonspecific symptom. HIDA scintigraphy is usually indicated when a gallbladder or biliary cause is suspected. However, it may not be the first study ordered. If there is a history of gallstones documented by either ultrasound or CT and the clinical setting indicates acute cholecystitis, then HIDA can play a pivotal role in the management of the patient. This is because HIDA has a high sensitivity and specificity for acute cholecystitis. A review of the literature cited in this document showed a pooled sensitivity and specificity for the detection of acute cholecystitis of 96% (range 78%–100%) and 90% (range 50%–100%), respectively (*13–51,57*).

Ultrasound is highly sensitive for the detection of gallstones. However, based on pooled estimates of diagnostic accuracy, the sensitivity was 81% (95% confidence interval [CI], 75%–87%) and the specificity was 83% for acute cholecystitis. MRI was less sensitive and specific, with a reported sensitivity of 85% (95% CI, 66%–95%) and a specificity of 81% (95% CI, 69%–90%). Cholescintigraphy was superior to ultrasound in studies that directly compared the 2 modalities. Based on 11 head-to-head studies, the sensitivity was 94% (95% CI, 90%–97%) for cholescintigraphy versus 80% (95% CI, 71%–87%) for ultrasound, and the specificity was 89% (95% CI, 84%–92%) versus 75% (95% CI, 67%–82%), respectively (*6*).

The accuracy of HIDA scintigraphy for the detection of acute acalculous cholecystitis is more limited, with the reported sensitivity of cholescintigraphy ranging from 67% to 100% and the specificity from 58% to 88% based on 4 studies of critically ill patients (*52–55*). The data for diagnosing common bile duct obstruction were variable, with one study reporting sensitivity of 67% and specificity of 85% (*58*) and another reporting sensitivity of 93% and specificity of 64% (*59*).

Overall, cholescintigraphy is indicated in patients presenting with acute upper abdominal pain if there is a clinical suspicion for a hepatobiliary cause. Hepatobiliary disease is less commonly a cause

of acute abdominal pain in children than in adults, likely because of the lower prevalence of cholelithiasis. For this reason and because techniques such as ultrasound and MRI do not involve exposure to ionizing radiation, scintigraphy is less commonly used in children. Scintigraphy may still be appropriate in the pediatric population and should be considered if there is reasonable suspicion for cholecystitis as a cause of pain. Otherwise, other modalities such as ultrasound, MRI, or CT are generally more appropriate.

Scenario 3: Patients presenting with chronic upper abdominal pain (Score: 5 – may Be appropriate)

Patients who may benefit from cholescintigraphy include those in whom a functional gallbladder disorder caused by a primary gallbladder motility disturbance is suspected as the cause of chronic upper abdominal pain.

Initial clinical management should include documentation of the history and character of pain in the epigastrium or right upper quadrant, recurrent episodes of pain, pain that interferes with daily activities, and pain that is not relieved by antacids or bowel movements. Other reasons for chronic upper abdominal pain such as reflux, functional dyspepsia, or cardiac disease should be excluded.

Laboratory study findings, including from pancreatic and liver blood tests and bilirubin, should be normal. Ultrasound of the gallbladder should be obtained to exclude gallstones, microlithiasis, sludge, or polyps and to exclude biliary dilatation.

When patient presentation suggests a biliary cause of chronic upper abdominal pain with negative laboratory test and ultrasound results, cholecystokinin (CCK)-stimulated cholescintigraphy with gallbladder ejection fraction (GBEF) calculation may aid in diagnosis and lead to a change in management, including possible cholecystectomy. For these patients, refer to scenarios 5 and 6.

Young adult patients may present with chronic upper abdominal pain similar to that in adult patients. Although the data specific to the use of HIDA scintigraphy in this population are limited, most studies include some young adult subjects. The utility of HIDA scintigraphy in pediatric and young adult patients with suspected functional gallbladder disorder from primary motility disturbance should be similar to that in adult populations.

Scenario 4: Patients presenting with functional biliary pain syndrome caused by chronic acalculous gallbladder disease (CAGBD) (Score: 7 – appropriate)

The consensus of this multispecialty group of physicians on AUC for HIDA imaging in CAGBD is that CCK cholescintigraphy is a valuable time-proven test used by clinicians and surgeons for over 3 decades, and they give it an overall AUC score of 7.

Patients with CAGBD present clinically with symptoms of recurrent biliary colic that are similar to those of patients with calculous chronic cholecystitis, except that patients with CAGBD do not have evidence of gallstones. Other names used for this entity include gallbladder dyskinesia and functional gallbladder disorder. When other causes of pain have been excluded, hepatobiliary imaging with calculation of a GBEF may be performed to confirm the diagnosis and determine whether cholecystectomy could potentially alleviate the symptoms. A consensus standardized methodology for CCK cholescintigraphy has been published (*60,61*). First, a 60-min HIDA study is performed. When the gallbladder is visualized, a standardized dose of sincalide (a CCK analog) is infused over 60 min to stimulate gallbladder contraction. A GBEF of less than 38% is an abnormal finding. Alternatively, fatty meals have been used, for example, whole milk or Ensure Plus, to contract the gallbladder. Poor gallbladder contraction suggests CAGBD in the proper clinical setting.

The evidence for the clinical utility of a GBEF to determine whether the patient has CAGBD and will respond to cholecystectomy is not as strong as might be suspected from the number of publications advocating it. A prospective randomized controlled study by Yap et al. (*62*) convincingly demonstrated the utility of this technique. Ninety-two percent of the patients with a low GBEF experienced resolution of their symptoms after cholecystectomy. Most of the numerous publications in the literature, over 30, are retrospective and not as well controlled (*63*). The vast majority of investigations found CCK cholescintigraphy to be valuable for confirming the diagnosis and relieving patient symptoms. Review articles and meta-analyses have concluded that a large, well-controlled multicenter prospective study is needed to confirm its utility (*64*). However, CCK cholescintigraphy is presently considered by most surgeons to be part of the standard preoperative workup of patients suspected of having acalculous chronic cholecystitis.

Some of the adult studies reviewed above included young adult patients. Few pediatric-specific studies are available, however, on the role of HIDA scintigraphy in patients with functional biliary pain syndrome caused by CAGBD, as such studies are similarly limited to adult populations. In general, results of HIDA scintigraphy in children and young adults with functional biliary pain syndrome are similar to those of adult patients (*65*).

Scenario 5: Patients suspected of having chronic cholecystitis (Score: 7 – appropriate)

Eleven studies have reported the utility of cholescintigraphy for the diagnosis of chronic cholecystitis, only 2 of which were determined to be of adequate quality for inclusion in the systematic review because of the absence of a reported definition of positive cholescintigraphic findings. Klingensmith and Turner performed a study that evaluated the diagnostic accuracy of CCK cholescintigraphy in 66 patients for surgically confirmed chronic cholecystitis (*33*). From visualization of the gallbladder after 1 h, 31 of 66 patients were determined to have chronic cholecystitis, leading to a sensitivity of 61% and a specificity of 14% (*33*). An important aspect of this study was that CCK was not used and the study design was focused on the diagnosis of acute cholecystitis, with a subset of patients being determined to have false positive test results for this diagnosis because of chronic cholecystitis. Klieger and O'Mara conducted a study that evaluated the role of CCK cholescintigraphy in the diagnosis of chronic cholecystitis in a cohort of 52 patients (*66*). Based on a case definition of ejection fraction of less than 35% in patients with surgically (79%) or clinically (21%) confirmed cholecystitis, the sensitivity was 90% and the specificity was 95% (*66*). An important finding was that 25 of 28 (89%) patients with a low GBEF had histopathologic evidence of chronic cholecystitis, and 27 of 28 (96%) experienced complete relief of symptoms after surgery. Although a low GBEF of less than 35% may be helpful in confirming chronic cholecystitis, a normal GBEF result does not exclude the diagnosis; a study by Raymond et al. demonstrated that 76% of patients with chronic cholecystitis had GBEFs that were within the reference range (*67*). Nine other studies that evaluated the diagnostic utility of HIDA scintigraphy for acute cholecystitis also reported on patients with chronic cholecystitis, although definitions of a positive test result were not reported, and the range of test characteristics were highly variable (sensitivity 8.3%–71% and specificity 17%–81%) (*14,31,34,37,38,44,48,49,51*). Overall, the available evidence base

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to assess the role of HIDA with or without CCK in the diagnosis of chronic cholecystitis is limited and does not distinguish between acalculous and calculous cholecystitis. Routine HIDA imaging is insensitive and nonspecific for the diagnosis of chronic cholecystitis, but delayed visualization of the gallbladder is suggestive of this diagnosis. CCK cholescintigraphy may be helpful to diagnose chronic cholecystitis in patients with an initial normal HIDA result. On the basis of moderate-level evidence demonstrating the utility of cholescintigraphy in the evaluation of chronic cholecystitis, the guideline panel has deemed HIDA with CCK to be *appropriate in patients with abnormal ultrasound results* and it *may be appropriate in patients with normal ultrasound results*.

There are no high-quality specific studies on the role of HIDA scintigraphy in pediatric patients with suspected chronic cholecystitis. The diagnosis, however, is known to occur in pediatric and young adult populations and the expert panel felt the role of cholescintigraphy should be similar in this population.

Scenario 6: Patients suspected of having biliary obstruction (Score: 7 – appropriate)

This question was addressed in the setting of 2 clinical scenarios: (a) patients suspected of having painful biliary obstruction with negative results on other imaging studies (ultrasound, CT, and MR cholangiopancreatography) and (b) patients suspected of having painful biliary obstruction with positive results on other imaging studies. The question was evaluated in the adult and pediatric population.

The evidence for the diagnostic accuracy of HIDA for suspected biliary obstruction is limited. The 2 studies evaluating the role of HIDA that used endoscopic retrograde cholangiography as the reference standard demonstrated variable rates of sensitivity (67%–93%) and specificity (64%–67%) (*58,59*). The accuracy of HIDA in the setting of acute obstruction has been described in patients presenting with pain of recent onset (24–72 h) (*68–70*). HIDA scintigraphy may also be useful in patients with partial recurrent biliary obstruction with negative imaging study results (*51,58*).

Performance of HIDA scintigraphy in the setting of negative results in other imaging studies was considered appropriate (overall AUC score 7) by the group, given the possibility of biliary obstruction in this clinical scenario in the adult and pediatric populations. However, the expert panel felt that performance of HIDA scintigraphy was rarely appropriate when other imaging studies showed positive results in either population.

Scenario 7: Patients presenting with functional biliary pain syndrome caused by chronic acalculous biliary disease, including sphincter of Oddi dysfunction (Score: 5 – may Be appropriate)

Several institutions use HIDA scintigraphy routinely to screen patients with symptoms suggestive of sphincter of Oddi dysfunction (SOD) to help determine which patients require endoscopic retrograde cholangio-pancreatography to confirm or exclude the diagnosis. However, a review of the literature has not found sufficient evidence to strongly support this indication.

The consensus of the AUC group gave this indication a score of 5. CAGBD or SOD presents as recurrent upper abdominal pain in patients (adult and pediatric) who have had a prior cholecystectomy. SOD is a partial biliary obstruction, not caused by stones, stricture, or tumor. To exclude these entities, endoscopic retrograde cholangiopancreatography is required, which has been associated with a high incidence of adverse effects, including a 20% incidence of pancreatitis. Sphincterotomy is the usual specific therapy for SOD. Several published investigations have found that HIDA scintigraphy was valuable when ultrasound and MR cholangiopancreatography were not informative (*71,72*); however, different methodologies were used in these studies and the findings were inconsistent.

Scenario 8: Patients presenting with abdominal pain After surgery with an afferent loop (Score: 4 – may Be appropriate)

An afferent loop is a postoperative blind loop after a gastrojejunostomy (Billroth II), Roux-en-Y gastric bypass, and pancreaticoduodenectomy (Whipple) (*69*). The afferent loop in a gastrojejunostomy consists of a blind loop of duodenum and proximal jejunum adjacent to the gastrojejunostomy anastomosis that allows for the drainage of biliary and pancreatic secretions into the bowel lumen.

Afferent loop syndrome (ALS) is an infrequent partial or complete mechanical obstruction of the afferent loop after a gastrojejunostomy that accumulates biliary and pancreatic secretions with afferent limb dilatation. Clinical symptoms may be acute or chronic (less than or greater than 7 d postoperatively) manifested as abdominal pain and distention with nausea and severe bilious vomiting, the latter occurring with decompression of the obstructed afferent loop with reflux of afferent loop contents into the stomach (*73*). CT is the diagnostic test of choice and surgical intervention is usually indicated (*74*).

HIDA for ALS may be helpful in acute ALS (*75,76*) but is limited in chronic ALS (*74*). Normal HIDA scintigraphy results demonstrate biliary to enteric transit of afferent loop activity into the distal small bowel. Persistent afferent loop activity with nonvisualization of the distal small bowel suggests an afferent loop obstruction. However, the diagnostic usefulness of HIDA in ALS is yet to be determined.

Scenario 9: Patients presenting with abdominal pain After surgery or from trauma with suspected bile leakage (Score: 8 – appropriate)

Cholescintigraphy is commonly used in clinical practice for the determination of bile leaks after surgery and less frequently after trauma. The literature on patients presenting with abdominal pain after surgery (*77–84*) or trauma (*85–89*) with suspected bile leakage is limited and descriptive or retrospective. In general, published papers show that HIDA scintigraphy provides important information about the presence or absence of leaks. In one series of 854 patients undergoing laparoscopic cholecystectomy, 15 had biliary leaks. Eleven of the 15 patients underwent imaging with ^{99m}Tc iminodiacetic acid. All 11 scans had positive results, indicating the presence of the bile leak (*81*). In another small series, all 6 cases of bile leak were detected by cholescintigraphy (*80*).

A few articles made the case that SPECT/CT HIDA scans add value to the evaluation of bile leaks. In one series, 110 patients had positive results for bile leaks by HIDA scanning. Forty-two of these patients underwent SPECT/CT and in 32 of them, it was useful in defining the exact location of the collection, defining the extent of the abnormal collection, characterizing large abdominal collections, characterizing suspected contamination, or identifying other miscellaneous conditions (*90*).

High-quality pediatric-specific studies of the role of HIDA scintigraphy in suspected biliary leak do not exist. The expert panel believes that the role of cholescintigraphy in pediatric patients with bile leak should not be any different than that in adults.

Scenario 10: Patients presenting with abdominal pain with suspected enterogastric reflux (Score: 3 – rarely appropriate)

This recommendation applies to both adult and pediatric patients. Enterogastric reflux (EGR) is bile reflux into the stomach, which can be asymptomatic and a normal finding on cholescintigraphy that rapidly clears (*91,92*), but it may also be symptomatic. Such symptoms include upper abdominal pain ("heartburn" with or without gastroesophageal reflux), nausea, and bile emesis and are occasionally respiratory (e.g., cough, sore throat, hoarseness). Larger and more persistent reflux is more likely to be symptomatic. EGR has been reported to be enhanced with morphine sulfate and CCK (*93–95*) and may persist or develop after cholecystectomy (*95*).

Few studies have been published on EGR, and the clinical significance of this condition is unclear. Two studies found no difference in patients with or without EGR (*96,97*), one reporting discordant anatomic and scintigraphic findings. Two other authors claim EGR may cause alkaline gastritis and mucosal metaplasia (*96,98*).

BENEFITS AND HARMS OF IMPLEMENTING THE AUC GUIDANCE

The goal of this document is to describe the most efficient and cost-effective use of HIDA scintigraphy in the clinical scenarios described earlier. These recommendations are intended to be incorporated into clinical decision support (CDS) tools to educate referring physicians about the most appropriate use of HIDA scintigraphy and to subsequently allow more efficient ordering of HIDA scintigraphy for these indications.

It is not possible, however, to describe the entire spectrum of appropriate use of HIDA scintigraphy. There are instances in which HIDA scintigraphy may be useful for patient management even when no literature is available to support that particular clinical scenario. In these less common indications, the concern is that reliance on CDS tools for ordering HIDA scintigraphy will diminish the proper use of the imaging procedure for clinical scenarios not described in this document. The impact of this diminished use on patient outcomes will be extremely difficult, if not impossible, to measure. The introduction of CDS systems, which use validated AUC, like this one, also means ordering physicians will be under more scrutiny about how they use health care resources, particularly advanced diagnostic imaging studies such as the study described in this AUC. The future impact on patient outcomes of CDS tools that use AUC is unknown for many reasons, including that it is not known how the data generated from the ordering patterns of advanced diagnostic imaging studies will be scrutinized and how it will be used.

QUALIFYING STATEMENTS

After reviewing the available literature for HIDA scintigraphy used in the evaluation of abdominal pain, it is apparent that most articles describing this test are more than a decade old. Although this suggests that the technology is relatively stable, it also raises the issue that much of the available literature is not written with an emphasis on outcomes. Additionally, previous literature describing HIDA scintigraphy was not written to directly evaluate the effect of the study on the clinical management of abdominal pain. For example, some papers describe the accuracy of the study for the diagnosis of acute cholecystitis in patients with surgical or pathologic confirmation, but not how the study influenced the management of abdominal pain, such as whether the test influenced the decision for surgical intervention. Prospective studies to evaluate the effect of HIDA scintigraphy on the management of patients with abdominal pain, with adequate follow-up to determine study value and accuracy, are rare.

Many papers produced in the original literature search were case reports or case series of less than 100 patients that described the diagnostic accuracy of HIDA scintigraphy. Some of these appeared early in the use of HIDA scintigraphy using different formulations of HIDA. More recently, an effort has been made to evaluate the effect of HIDA scintigraphy on management and outcomes. Although outcomes can sometimes be inferred, papers specifically addressing them are rare. Our appropriateness ratings are therefore heavily influenced by the diagnostic accuracy of the study and the experience of our expert panel, including individuals from the imaging community and from the specialties who order and use these studies to evaluate and manage patients with abdominal pain.

Considerations for Pregnant Patients

The use of any nuclear medicine study in pregnant or potentially pregnant patients should be determined with careful consideration of the risk-benefit ratio for the study in that particular patient. In particular, consideration should be given to the effect of the study on patient management. Although radiation exposure from HIDA scintigraphy is small, a conservative approach to radiation exposure of patients is part of medical standard-of-care. The discussion of risks and benefits should involve the patient, with the clinician explaining the value of the potential information obtained from the study and the radiation risks. The process, discussion, and patient consent should be documented in the medical record. The decision to use HIDA scintigraphy should also be affected by the availability and performance of other diagnostic methods (e.g., ultrasound) to achieve diagnosis and define management.

IMPLEMENTATION OF THIS GUIDANCE

To develop broad-based multidisciplinary clinical guidance documents, SNMMI has been working with several other medical specialty societies. This collaboration will foster the acceptance and adoption of this guidance by other specialties.

SNMMI has developed a multipronged approach to disseminate the AUC for HIDA scintigraphy in abdominal pain to all relevant stakeholders—referring physicians, nuclear medicine physicians, and patients. The dissemination and implementation tactics will be a mix of outreach and educational activities and will be targeted to each of these audiences.

SNMMI will create detailed case studies for its members, as well as for referring physicians, and make them available via online modules and webinars. These cases will cover the appropriate clinical scenarios for the use of HIDA, as well as some cases in which the results of HIDA are equivocal.

Related resources such as the systematic review supporting the development of these AUC, a list of upcoming education events on the AUC, factsheets, and other didactic materials will be made available on the SNMMI webpage dedicated to HIDA AUC. Live sessions will be held at the SNMMI annual and midwinter meetings, as well as at the relevant societal meetings of referring physicians to highlight the importance of this AUC.

SNMMI also aims to create a mobile application for the HIDA AUC for both Apple and Android platforms. Mobile applications are becoming increasingly popular in the health care industry and can be used to push updates to all users.

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In addition to these activities, SNMMI will also undertake patient-focused outreach to provide education on how AUC can play an invaluable role in achieving a more accurate diagnosis.

APPENDIX A: WORKGROUP MEMBERS AND EXTERNAL REVIEWERS

WORKGROUP

The members of the workgroup are Gary Dillehay, MD, FACNM, FACR (chair), Northwestern Memorial Hospital, Chicago, IL (SNMMI); Zvi Bar-Sever, MD, Schneider Children's Medical Center of Israel, Petah Tikva, Israel (EANM); Manuel Brown, MD, Henry Ford Health System, Detroit, MI (SNMMI); Richard Brown, MD, University of Michigan Hospital, Ann Arbor, MI (SNMMI); Edward Green, MD, University of Mississippi Medical Center, Ridgeland, MS (SNMMI); Marie Lee, MD, FACR, Virginia Mason Medical Center, Seattle, WA (SNMMI); Joseph Lim, MD, Yale University School of Medicine, New Haven, CT (AGA); Darlene Metter, MD, The University of Texas Health Science Center, San Antonio, TX (SNMMI); Andrew Trout, MD, Cincinnati Children's Hospital, Cincinnati, OH (SNMMI); Robert Wagner, MD, MSMIS, FACR, FACNP, Loyola University Medical Center, Maywood, IL (SNMMI); Sachin Wani, MD, University of Colorado Anschutz Medical Campus, Aurora, CO (AGA); and Harvey Ziessman, MD, The Johns Hopkins Hospital, Baltimore, MD (SNMMI).

EXTERNAL REVIEWERS

The external (peer) reviewers are Chun K. Kim, MD, Brigham and Women's Hospital, Harvard Medical School, Boston, MA; Giuliano Mariani, MD, University of Pisa, Pisa, Italy; Erik Mittra, MD, PhD, Stanford Hospital and Clinics, Stanford, CA; M. Elizabeth Oates, MD, University of Kentucky College of Medicine, Lexington, KY; and S. Ted Treves, MD, FACNM, Brigham and Women's Hospital, Harvard Medical School, Boston, MA.

SNMMI

The supporting staff from SNMMI are Sukhjeet Ahuja, MD, MPH, Director, Evidence & Quality Department and Julie Kauffman, Program Manager, Evidence & Quality Department.

APPENDIX B: DEFINITION OF TERMS AND ACRONYMS

Acalculous cholecystitis: a condition found in 5%–10% of cases of cholecystitis, in which the gallbladder becomes inflamed in the absence of a gallstone. Acalculous cholecystitis is more commonly seen in severely ill people, such as those in intensive care units or in those who have recently undergone major surgery.

Acute calculous cholecystitis: occurs in roughly 90% of cases of cholecystitis. It is caused by gallstones blocking the flow of bile in the biliary tree, leading to inflammation of the gallbladder (acute calculous cholecystitis). Blockage of bile flow leads to thickening of bile and bile stasis, which leads to an enlarged, red, and tense gallbladder. The gallbladder is initially sterile but often becomes secondarily infected by bacteria, predominantly by *Escherichia coli*, *Klebsiella*, *Streptococcus*, and *Clostridium* species. Inflammation can spread to the outer covering of the gallbladder, leading to irritation of surrounding structures such as the diaphragm, which leads to referred right shoulder pain.

Afferent loop syndrome (ALS): a purely mechanical complication that infrequently occurs after construction of a gastrojejunostomy. Creation of an anastomosis between the stomach and jejunum leaves a segment of small bowel, most commonly consisting of duodenum and proximal jejunum, lying upstream from the gastrojejunostomy. This limb of intestine conducts bile, pancreatic juices, and other proximal intestinal secretions toward the gastrojejunostomy and is thus termed the afferent loop.

AGA: American Gastroenterological Association.

AUC: appropriate use criteria.

Biliary: having to do with the gallbladder, bile ducts, or bile. The biliary system consists of all 3.

Biliary obstruction: blockage of the common or cystic bile duct, usually caused by one or more gallstones.

Biliary pain: most frequently caused by obstruction of the common *bile* duct or the cystic duct by a gallstone. However, the presence of gallstones is a frequent incidental finding and does not always necessitate *treatment* in the absence of identifiable *disease.*

CAGBD: chronic acalculous gallbladder disease.

CCK: cholecystokinin.

CDS: clinical decision support.

Cholecystitis: inflammation of the gallbladder.

Chronic cholecystitis: occurs after repeated episodes of acute cholecystitis and is almost always due to gallstones. It may be asymptomatic, may present as a more severe case of acute cholecystitis, or may lead to several complications such as gangrene, perforation, or fistula formation.

CI: confidence interval.

CT: CT.

EANM: European Association of Nuclear Medicine.

EGR: enterogastric reflux.

Gastrectomy: surgical removal of all or part of the stomach.

GBEF: gallbladder ejection fraction.

Hepatobiliary iminodiacetic acid (HIDA) scintigraphy: an imaging procedure used to diagnose problems in the liver, gallbladder, and bile ducts. In HIDA scintigraphy, a radiopharmaceutical or tracer is injected into a vein in the patient's arm. The tracer is handled like bile by the liver.

Kidney *stones* (renal lithiasis, nephrolithiasis): small, hard mineral deposits that form inside the kidneys. The stones are made of mineral and acid salts. Kidney stones have many causes and can affect any part of the urinary tract from kidneys to bladder.

MRI: MRI.

PICOTS: population, intervention, comparison, outcome, timing, and setting.

SNMMI: Society of Nuclear Medicine and Molecular Imaging.

SPECT: SPECT.

Sphincter of Oddi (SOD) dysfunction: occurs when the sphincter muscle does not open when it should. This prevents the bile and pancreatic juice from flowing through and causes a backup of digestive juices that can cause bouts of severe pain in the abdomen.

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Stricture: an abnormal narrowing of a body passage, especially a tube or a canal. The stricture may be due to, for example, scar tissue or a tumor. Stricture refers to both the process of narrowing and the narrowed part itself.

APPENDIX C: DISCLOSURES AND CONFLICTS OF INTEREST (COIs)

SNMMI rigorously attempted to avoid any actual, perceived, or potential COIs that might have arisen as a result of an outside relationship or personal interest on the part of the workgroup members or external reviewers. Workgroup members were required to provide disclosure statements of all relationships that might be perceived as real or potential COIs. These statements were reviewed and discussed by the workgroup chair and SNMMI staff and were updated and reviewed by an objective third party at the beginning of every workgroup meeting or teleconference. The disclosures for workgroup members can be found in Table 1C. A COI was defined as a relationship with industry—including consulting, speaking, research, and other nonresearch activities—that exceeds $5,000 in funding over the previous or upcoming 12-mo period. In addition, if an external reviewer was either the principal investigator of a study or another key member of the study personnel, that person's participation in the review was considered likely to present a COI. All reviewers were asked about any potential COI. A COI was also considered likely if an external reviewer or workgroup member was either the principal investigator or a key member of a study directly related to the content of this AUC. All external reviewers were asked about any potential COI.

APPENDIX D: PUBLIC COMMENTARY

The workgroup solicited information from all communities through the SNMMI website and by direct solicitation of SNMMI members. The comments and input helped to shape the development of these AUC on the appropriate use of HIDA scintigraphy for abdominal pain.

TABLE 1C
Relationships with Industry and Other Entities for Task Force Members

Workgroup member	Reported relationships
Zvi Bar-Sever	None
Manuel Brown	ACR accreditation reviews
Richard Brown	None
Gary Dillehay	None
Edward Green	None
Marie Lee	None
Joseph Lim	None
Darlene Metter	None
Andrew Trout	None
Robert Wagner	None
Sachin Wani	Covidien Educational Grant for GI Cook Educational Grant for GI
Harvey Ziessman	Elsevier book royalties

ACR = American College of Radiology; GI = gastrointestinal.

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QUERIES - jnm195602q

[AQ1] There are no queries in this article. Please reply to approve the proof or to make additional corrections.