

# Prevalence of Extra-Hepatic Incidental Findings on Ultrasound Screening for Hepatocellular Carcinoma

Allison Forrest (✉ [allison.forrest@uvmhealth.org](mailto:allison.forrest@uvmhealth.org))

University of Vermont Medical Center <https://orcid.org/0000-0003-0416-0805>

Sam Afshari

University of Vermont Medical Center

Nathan Franssen

University of Vermont Medical Center

Naiim Ali

University of Vermont Medical Center

---

## Research Article

**Keywords:** incidental findings, ultrasound, HCC screening

**Posted Date:** June 22nd, 2022

**DOI:** <https://doi.org/10.21203/rs.3.rs-1735453/v1>

**License:** © ⓘ This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

---

# Abstract

**Purpose:** Abdominal ultrasound is a cost-effective method for screening for hepatocellular carcinoma (HCC) in high-risk individuals. Currently, at many institutions the protocol for obtaining HCC screening ultrasounds includes a traditional examination of the right upper quadrant, including the pancreas and right kidney. There is no consensus on the role of imaging of extra-hepatic structures and there is limited data describing the frequency and clinical significance of incidental findings discovered during HCC screening. The purpose of this retrospective study is to assess the prevalence and significance of extra-hepatic incidental findings during HCC screening ultrasounds.

**Methods:** A single-center retrospective review of all right upper quadrant HCC screening ultrasounds identified 432 HCC screening ultrasounds performed on 294 adults over a 2.5-year period. Findings in all organs evaluated were recorded. Any incidental finding was classified as minor, moderate, or major clinical significance. LI-RADS category and visualization score were also documented.

**Results:** At least one extrahepatic finding was documented in 56.5% of examinations. The most common extra-hepatic findings occurred in the gallbladder (40.3%), most commonly gallstones (25.4%). Four moderate clinically significant incidental findings were recorded (0.9%). Only one of these incidental findings required specific imaging follow up (0.2%). No major clinical significance incidental findings were identified.

**Conclusions:** Potentially clinically significant incidental findings during HCC screenings are rare. Given the low rates of significant incidental findings identified on HCC screening ultrasound, these data support a more limited HCC screening ultrasound protocol.

## Introduction

Abdominal ultrasound is a cost-effective, noninvasive method for screening for hepatocellular carcinoma (HCC) in high-risk individuals with cirrhosis and/or chronic hepatitis B [1, 2]. Current guidelines recommend screening every 6 months in order to identify early-stage malignancy [3]. The Ultrasound Liver Reporting & Data System (US LI-RADS), first published in 2017, is a standardized approach to imaging, interpretation, and reporting of screening ultrasounds [4]. The US LI-RADS technical recommendations include obtaining longitudinal and transverse images of the liver, with inclusion of the gallbladder, pancreatic head, right kidney, bile ducts, aorta, and inferior vena cava when adjacent to the liver [5]. Despite these recommendations, there is no consensus regarding imaging of these extra-hepatic structures. Currently, at many institutions the protocol for obtaining HCC screening ultrasounds includes a traditional examination of the right upper quadrant, including the pancreas and right kidney. When a traditional right upper quadrant examination is performed for HCC screening, extra-hepatic abnormalities may be identified.

The American College of Radiology defines an incidental finding as “an incidentally discovered mass or lesion, detected by CT, MRI, or other imaging modality performed for an unrelated reason” [6]. Extensive

literature and guidelines have been published regarding incidental findings on imaging [7]. Incidental findings may identify clinically significant findings which require further treatment and evaluation. However, the identification of incidental finding may also lead to unnecessary imaging tests and intervention, increased costs, and patient anxiety [8]. There is limited data describing the frequency and clinical significance of incidental findings discovered on ultrasound. In particular, no studies to date have published data on incidental sonographic findings in patients with cirrhosis and/or hepatitis B undergoing screening for HCC.

The purpose of this retrospective study is to assess the prevalence and significance of extra-hepatic incidental findings during HCC screening ultrasounds in order to further elucidate if imaging these structures during screening examinations is necessary. This evaluation will ultimately guide the creation of a tailored protocol for HCC screening ultrasounds, in order to gain the most relevant clinical information during the examination.

## Methods

A single-center retrospective review was performed. Institutional review board waiver was obtained. Chart review identified subjects with a medical history of cirrhosis and/or hepatitis B in the medical history or problem list who have been evaluated by abdominal ultrasound from 11/1/2019-4/30/2021. ICD-10 codes included K70.3 "Alcoholic cirrhosis of liver", K74 "Fibrosis and cirrhosis of liver", K74.6 "Other and unspecified cirrhosis of liver," and B18 "Chronic viral hepatitis" [9]. All examinations performed under the order "Limited Abdominal Ultrasound" corresponding to Current Procedural Terminology (CPT) code 76705 were queried [10]. All examinations were reviewed and studies performed for HCC screening were identified. Studies performed for indications other than HCC screening were excluded. Examinations were excluded in patient age less than 18 years. All ultrasound were performed using either a Logic E9 or Logiq E10 ultrasound machine (General Electric Healthcare). There were 10 different reporting radiologists with between 0.5 and 35 years of post-training clinical experience. Twenty different sonographers performed the examinations.

The indication for the exam and availability of prior comparison imaging was documented. Normal and abnormal findings in all organs evaluated were recorded based on original report. Any incidental finding was classified by clinical importance as minor, moderate, or major using criteria outlined by Lumbreras et al [7]. Major findings are those which require follow up or treatment, moderate may require eventual follow up or treatment, and minor significance findings are unlikely to be clinically significant. Incidental findings that were previously known and unchanged based on prior cross-sectional imaging were considered minor significance. Patients who had more than one screening ultrasound in our data set were evaluated, with each ultrasound examination treated as an individual encounter and repeated incidental findings counted as minor significance.

LI-RADS category of negative (US-1), subthreshold (US-2), or positive (US-3) was documented, with follow up of US-2 and US-3 categories recorded. Not all examinations documented a LI-RADS category in the

report, so it was assigned retrospectively based on the findings described in the report if not initially documented. LI-RADS visualization scores of minimal limitations (A), moderate limitations (B), or severe limitations (C) were documented only when reported on the initial report. Incidental findings and any follow up for these findings were recorded.

## Results

Abdominal US exams were identified in patients with a documented medical history of cirrhosis or chronic hepatitis B by chart review. After the initial query, 631 “limited abdominal ultrasound” exams were identified in 463 unique subjects. Of these, 199 were exams which did not include imaging of the liver or were studies for indications other than HCC screening, and were therefore excluded. After initial review, 432 HCC screening ultrasound exams were identified in 294 unique subjects.

Study population was 60.8% male and 39.2% female (Table 1). Average age was 59.8 years ( $\pm$  11.8). Study population was 84.7% white, 8.5% Asian, 2.7% Black or African-American, and 4.1% other. Indications for HCC screening included alcoholic cirrhosis in 37.7%, nonalcoholic steatohepatitis (NASH) cirrhosis in 16.3%, hepatitis C cirrhosis in 20.4%, and hepatitis B (with or without cirrhosis) in 12.2%. The indication was classified as other in 15.3%, including autoimmune hepatitis, primary biliary cirrhosis, and cryptogenic cirrhosis. Some subjects had two types of cirrhosis documented, therefore total percentage is greater than 100%

Table 1  
Demographics of 294 individuals evaluated by ultrasound for HCC screening.

<b>Parameter</b>	<b>Mean (SD) or n (%)</b>
Number of subjects	294
Number of HCC screening exams	432
Age,	59.8 (± 11.8)
Female	115 (39.2%)
Ethnicity	
White	249 (84.7%)
Asian	25 (8.5%)
Black	8 (2.7%)
Other	12 (4.1%)
Indication for Screening	
Alcoholic cirrhosis	111 (37.7%)
Nonalcoholic steatohepatitis (NASH) cirrhosis	48 (16.3%)
Hepatitis C cirrhosis	60 (20.4%)
Hepatitis B (with or without cirrhosis)	36 (12.2%)
Other	45 (15.3%)

The majority of patients had prior right upper quadrant imaging (92.2%). Liver size was normal in 76.2% and enlarged in 23.3%. Hepatic echotexture/echogenicity was normal in 9.7%, increased echogenicity in 34.6%, and coarsened/heterogeneous in 55.6%. Hepatic contour was normal in 35.0% and nodular in 65.0%. Hepatic cysts were identified in 8.2%.

At least one extra-hepatic finding was documented in 56.5% of all exams. Moderate significance incidental findings were identified in 0.9% (Table 2). No major clinical significance incidental findings were identified.

Table 2

Prevalence of minor and moderate incidental finding by organ. No findings of major significance were identified.

Organ	Prevalence of Minor Significance Incidental Findings, n (%)	Prevalence of Moderate Significance Incidental Findings, % (n)
Pancreas	13 (3.0%)	1 (0.2%)
Gallbladder	174 (40.3%)	0
Bile ducts	23 (5.3%)	1 (0.2%)
Right Kidney	84 (19.4%)	2 (0.5%)
Aorta	5 (1.2%)	0
Inferior Vena Cava	0	0
Any Organ	244 (56.5%)	4 (0.9%)

Minor significance incidental findings in the pancreas were identified in 3.0%, with findings including stable dilated caliber of the main pancreatic duct and stable sub-centimeter cystic lesions. A focal hypoechoic lesion in the pancreatic head was identified, characterized as a moderate significance incidental finding. This was further evaluated with contrast-enhanced MRI and CT, with the lesion determined to be a side-branch intraductal papillary mucinous neoplasm.

The most common extra-hepatic findings occurred in the gallbladder, with 40.3% of exams documenting a minor significance incidental gallbladder finding, most commonly gallstones (25.4%). The gallbladder wall was thickened in 10.4%, all of which were attributed to hepatic dysfunction. Other gallbladder findings included sludge in 4.4%, polyps in 6.9%, and adenomyomatosis in 3.1%. No moderate or major significance incidental findings were identified in the gallbladder. The bile ducts were abnormal in 5.3% due to extrahepatic dilatation, all of which was a chronic finding and therefore a minor significance finding except one instance. In that patient, increasing common bile duct caliber from 4 mm to 8 mm was a moderate significance incidental finding, which was followed up on subsequent screening ultrasound and resolved.

Minor significance incidental findings in the right kidney occurred in 19.4%, with renal cysts being the most common finding, occurring in 15.3%. Renal atrophy/cortical thinning was identified in 1.9%. All other findings, including renal calculi and hydronephrosis were documented in < 1% of exams. No complexity was identified in any renal cyst. New mild hydronephrosis was a moderate significance finding identified in one patient who was lost to follow-up. An enlarging right perinephric hematoma was identified in a patient after renal biopsy and subsequent CT imaging, which was being managed conservatively, therefore characterized as a moderate significance incidental finding given increase in size.

The aorta was documented abnormal in 1.1% due to minor significance findings of atherosclerotic plaque or known aneurysmal dilatation. No incidental findings were identified in the IVC. Incidental note of a right pleural effusion was identified in 1.6%, characterized as a minor finding given likely sequela of portal hypertension. Known right adrenal lesion was identified in one exam, previously characterized as a benign adrenal adenoma on single-phase contrast enhanced CT, therefore categorized as a minor significance finding.

Although not included in the reporting template, the presence or absence of ascites was mentioned in 22.2% of reports. Ascites in the RUQ was reported in 14.8% of cases. The presence or absence of varices or recanalized paraumbilical vein was mentioned in 10.4% of reports. One or more of these findings was reported in 8.3% of reports. Although not included in the RUQ protocol, the spleen was mentioned in 4.7% of reports and reported to be enlarged in 2.3%.

LI-RADS category was US-1 in 91.4%, US-2 in 5.4%, and US-3 in 3.3% (Table 3). This was retrospectively assigned based on described findings in 60.9% of cases. At the time of retrospective review of the 14 subjects assigned US-3, follow up US and/or MRI was performed in 100%. After follow up, 57.1% of these lesions were characterized as LR-1 or LR-2 on MRI (definitely or probably benign) with recommendation to resume US screening. Another 35.7% were characterized as LR-4 or LR-5 (possible or definite HCC), and 7.1% were characterized as LR-M (probably or definitely malignant but without specific features for HCC) by MRI.

Table 3  
LI-RADS category and visualization scores of HCC screening examinations. CT/MRI follow up for US-3 observations.

Parameter	n (%)
LI-RADS Category	
US-1	391 (91.4%)
US-2	23 (5.4%)
US-3	14 (3.3%)
LI-RADS Visualization	
A	111 (65.7%)
B	52 (30.8%)
C	6 (3.6%)
LI-RADS US-3 CT/MRI Follow Up (n = 14)	
LIRADS-1	7 (50.0%)
LIRADS-2	1 (7.1%)
LIRADS-3	0
LIRADS-4	2 (14.3%)
LIRADS-5	3 (21.4%)
LIRADS-M	1 (7.1%)

LI-RADS visualization score was documented in 39.1% of cases. Of those documented, the visualization score was A in 65.7%, B in 30.8%, and C in 3.6% (Table 3).

## Discussion

At least one extra-hepatic finding was documented in 56.5% of exams, the vast majority of which were determined to be minor significance incidental findings. The most common extra-hepatic findings occur in the gallbladder, with 39.9% of exams document an incidental gallbladder finding, most commonly gallstones (24.4%). Gallstones are very common, with vast majority asymptomatic, although approximately 10–15% will become symptomatic over a period of 10 to 15 years [11]. Although the presence of gallstones may be clinically relevant in the future, no patients with acute gallbladder disease were identified in this study. Further, the majority of patients had prior right upper quadrant imaging (92.2%), including prior ultrasound, so the presence of cholelithiasis was likely already known in the vast majority of subjects. The gallbladder was thickened in 10.3%, all of which were attributed to hepatic

dysfunction, although multiple radiology reports suggested clinical correlation for right upper quadrant pain if there was suspicion of acute cholecystitis.

Following the gallbladder, the second most frequent incidental findings were identified in the right kidney, most commonly renal cysts, all of which were anechoic and demonstrated no complexity, therefore requiring no follow up [12].

Potentially clinically significant incidental findings during HCC screenings in our patient population are rare, with only four moderate clinically significant incidental findings identified (0.9%). No major clinical significance findings were identified. Only one incidental finding identified required specific additional evaluation (0.2%).

There is limited available data describing the prevalence of incidental findings on ultrasound, however our data are similar to rates of incidental findings described in the literature. Orme et al reviewed incidental findings discovered during imaging research, with 9.2% ultrasounds identifying incidental findings, compared to 39.8% on all modalities [13]. In their study, none of the incidental findings were determined to be clinically significant, compared to 2.5% of all modalities. Our reported rate of clinically significant incidental findings is similar to the study by Orme et al, which identified no clinically significant findings. However, that study reviewed examinations performed for research purposes and likely was conducted in a much healthier population compared to this study population.

Incidence of incidental findings has been studied in a different patient population undergoing screening imaging studies, namely CT colonography for screening of colon cancer [14]. A retrospective review of extra-colonic findings on CT colonography by Pooler et al identified that 88.3% of screening exams are normal or identify benign or unimportant incidental findings, such as simple renal cysts or cholelithiasis. In that study, 2.2% of all patients had a clinically significant incidental finding which required treatment or surveillance, suggesting that CT imaging may identify more clinically significant incidental findings than right upper quadrant US.

Given the low rates of significant incidental findings identified on HCC screening ultrasound, these data support a more limited HCC screening ultrasound protocol. Therefore, we recommend the ultrasound protocol be limited to the liver, gallbladder, and biliary tree, with partial inclusion of the pancreatic head, right kidney, aorta, and inferior vena cava on liver images, but with no dedicated evaluation necessary.

Further, a targeted exam may increase sensitivity for nodule detection, as shown in a study by da Silva et al [15]. This prospective study evaluated liver nodule detection in patients evaluated by a targeted liver ultrasound compared to a complete upper abdominal ultrasound protocol. A significantly higher frequency of nodules was detected when a dedicated protocol was used, possibly due the more dedicated time focusing on relevant liver findings [15].

Many institutions currently use protocols which do not specifically include the spleen, lower quadrants, main portal vein spectral waveform, or color Doppler evaluation of the portal and hepatic veins, which are

optional per the US LI-RADS guidelines [5]. Routine imaging of the hepatic vasculature, spleen, and evaluation for ascites may provide added value for screening studies, including suggesting the presence of portal hypertension [16].

In our study, LI-RADS category was US-1 in 91.4%, US-2 in 5.4%, and US-3 in 3.3%. Our rates of LI-RADS categories are similar to the rates reported by Millet et al, which reported US-1 in 90.4%, US-2 in 4.6%, and US-3 4.9% [17]. Evaluation of the outcomes of the US-3 exams in our study is limited by small sample size. Compared to a study by Sevco et al, follow up of US-3 observations identified no abnormality or benign observation (LR-1 or LR-2) in 57.1% of our cases vs 73.9% in the Sevco study, 0% LR-3 vs. 5.5%, 35.7% LR- 4 or LR-5 vs. 18.8%, and 7.1% LR-M vs. 1.8% [18].

There are multiple limitations to this study. Sample size included a 2.5-year period of studies with a relatively small sample size of 432 exams in 294 patients. Therefore, it is probable that very rare significant incidental findings may have not been included in the evaluated data set. Further, patients were identified by chart review which required a documented diagnosis of cirrhosis or chronic hepatitis B in the medical chart, which may not be present in all patients undergoing HCC screening.

Another limitation was the retrospective nature of the study and reliance on the original clinical report for identification of incidental findings. There were 10 different reporting radiologists who had 0.5 to 35 years post-training clinical experience. This may have resulted in differences in rates of reporting incidental findings when present. Finally, a high percentage of reports did not include visualization score or document LI-RADS categories (60.8%), likely a reflection of known slow adoption of standardized reporting in radiology [19].

## Declarations

**Funding:** No funding was received for this study.

**Conflict of Interest:** The authors declare no conflict of interest.

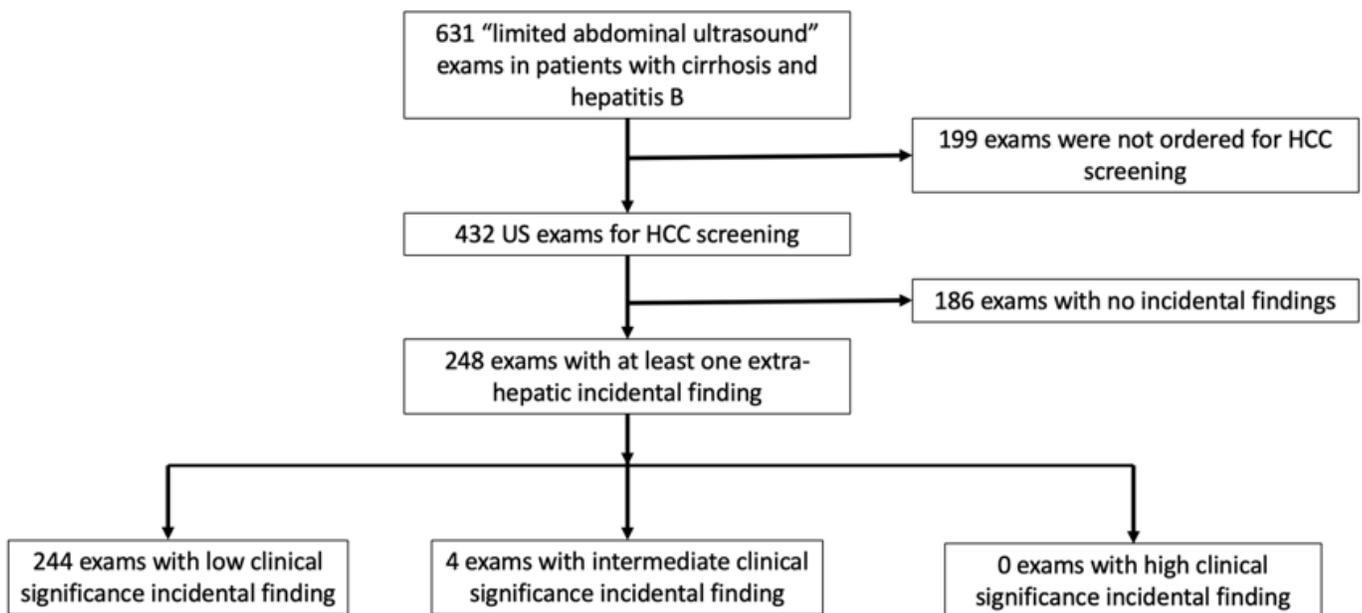
## References

1. Zhang BH, Yang BH, Tang ZY (2004) Randomized controlled trial of screening for hepatocellular carcinoma. *J Cancer Res Clin Oncol* 130:417–422. doi:10.1007/s00432-004-0552-0.
2. Cucchetti A, Trevisani F, Cescon M, Ercolani G, Farinati F, Poggio PD, Rapaccini G, Nolfo MAD, et al. (2012) Cost-effectiveness of semi-annual surveillance for hepatocellular carcinoma in cirrhotic patients of the Italian Liver Cancer population. *J Hepatol* 56:1089–1096. doi:10.1016/j.jhep.2011.11.022.
3. Marrero JA, Kulik LM, Sirlin CB, Zhu AX, Finn RS, Abecassis MM, Roberts LR, Heimbach JK (2018) Diagnosis, Staging, and Management of Hepatocellular Carcinoma: 2018 Practice Guidance by the

- American Association for the Study of Liver Diseases. *Hepatology* 68:723–750. doi:10.1002/hep.29913.
4. Rodgers SK, Fetzer DT, Gabriel H, Seow JH, Choi HH, Maturen KE, Wasnik AP, Morgan TA, et al. (2019) Role of US LI-RADS in the LI-RADS Algorithm. *Radiographics* 39:690–708. doi:10.1148/rg.2019180158.
  5. Morgan TA, Maturen KE, Dahiya N, Sun MRM, Kamaya A, American College of Radiology Ultrasound Liver I, Reporting Data System Working G (2018) US LI-RADS: ultrasound liver imaging reporting and data system for screening and surveillance of hepatocellular carcinoma. *Abdom Radiol (NY)* 43:41–55. doi:10.1007/s00261-017-1317-y.
  6. Berland LL (2013) Overview of white papers of the ACR incidental findings committee ii on adnexal, vascular, splenic, nodal, gallbladder, and biliary findings. *J Am Coll Radiol* 10:672–674. doi:10.1016/j.jacr.2013.05.012.
  7. Lumbreras B, Donat L, Hernandez-Aguado I (2010) Incidental findings in imaging diagnostic tests: a systematic review. *Br J Radiol* 83:276–289. doi:10.1259/bjr/98067945.
  8. Samim M, Goss S, Luty S, Weinreb J, Moore C (2015) Incidental findings on CT for suspected renal colic in emergency department patients: prevalence and types in 5,383 consecutive examinations. *J Am Coll Radiol* 12:63–69. doi:10.1016/j.jacr.2014.07.026.
  9. World Health Organization (2004) ICD-10: international statistical classification of diseases and related health problems : tenth revision, 2nd ed.
  10. American Medical Association (2022) CPT 2022 Professional Edition.
  11. Murphy MC, Gibney B, Gillespie C, Hynes J, Bolster F (2020) Gallstones top to toe: what the radiologist needs to know. *Insights Imaging* 11:13. doi:10.1186/s13244-019-0825-4.
  12. Richard PO, Violette PD, Jewett MA, Pouliot F, Leveridge M, So A, Whelan TF, Rendon R, et al. (2017) CUA guideline on the management of cystic renal lesions. *Can Urol Assoc J* 11:E66-E73. doi:10.5489/cuaj.4484.
  13. Orme NM FJ, Siddiki HA, Harmsen WS, O'Byrne MM, Port JD, Tremaine WJ, Pitot HC, McFarland EG, Robinson ME, Koenig BA, King BF, Wolf SM. (2010) Incidental findings in imaging research: evaluating incidence, benefit, and burden. *Arch Intern Med* 170:1525–1532. doi:10.1001/archinternmed.2010.317.
  14. Pooler BD, Kim DH, Pickhardt PJ (2017) Extracolonic Findings at Screening CT Colonography: Prevalence, Benefits, Challenges, and Opportunities. *AJR Am J Roentgenol* 209:94–102. doi:10.2214/AJR.17.17864.
  15. da Silva PH, Gomes MM, de Matos CAL, de Souza ESIS, Gonzalez AM, Torres US, Salazar GMM, D'Ippolito G (2021) HCC Detection on Surveillance US: Comparing Focused Liver Protocol Using US LI-RADS Technical Guidelines to a General Complete Abdominal US Protocol. *J Ultrasound Med* 40:2487–2495. doi:10.1002/jum.15637.
  16. McNaughton DA, Abu-Yousef MM (2011) Doppler US of the Liver Made Simple. *RadioGraphics* 31:161–188. doi: 10.1148/rg.311105093.

17. Millet JD, Kamaya A, Choi HH, Dahiya N, Murphy PM, Naveed MZ, O'Boyle M, Parra LA, et al. (2019) ACR Ultrasound Liver Reporting and Data System: Multicenter Assessment of Clinical Performance at One Year. *J Am Coll Radiol* 16:1656–1662. doi:10.1016/j.jacr.2019.05.020.
18. Sevco TJ, Masch WR, Maturen KE, Mendiratta-Lala M, Wasnik AP, Millet JD (2021) Ultrasound (US) LI-RADS: Outcomes of Category US-3 Observations. *AJR Am J Roentgenol* 217:644–650. doi:10.2214/AJR.20.23447.
19. Langlotz C (2009) Structured radiology reporting: are we there yet? *Radiology* 253:23–25. doi:10.1148/radiol.2531091088.

## Figures



**Figure 1**

Flow chart of the study to determine incidence of incidental findings on HCC screening ultrasound.