Title Page

Incidental hepatic steatosis on unenhanced computed tomography performed for suspected renal colic: gaps in reporting and documentation

Short title: Incidental hepatic steatosis on emergency CT

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Note:
Preliminary results of this study were presented by one of the authors (DA) at Abdominal Radiology Groups of Australia and New Zealand (ARGANZ) conference in March 2018, Melbourne, Australia, and won the Mendelson Research Prize.

Conflict of interest:

No authors have conflicts of interest to declare.

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Incidental hepatic steatosis on unenhanced computed tomography performed for suspected renal colic: gaps in reporting and documentation

Abstract

Introduction:

Hepatic steatosis is a common incidental finding on computed tomography (CT) in patients presenting to the emergency department (ED). The aims of our study were to assess prevalence of hepatic steatosis in ED patients with suspected renal colic and to assess documentation in radiology reports and medical charts with correlation to alanine transaminase (ALT) levels.

Methods:

Over 18 months from January 2016 to July 2017, all unenhanced CTs performed for suspected renal colic were reviewed. Quantitative assessment measuring hepatic and splenic attenuation in Hounsfield Units was performed. Hepatic steatosis was defined using multiple CT criteria including liver/spleen (L/S) ratio. Radiology reports, medical charts and ALT levels, if collected within 24 hours of CT, were reviewed.

Results:

A total of 1290 patients were included with a median age 52.5 years (range 16 - 98) and male predominance (835 [64.7%]). A total of 336 (26%) patients had hepatic steatosis measured by L/S ratio of ≤1. Ninety-four patients (28%) had radiology reports noting steatosis. Documentation in medical charts was noted in 18 out of 94 patients (19.1%) for whom steatosis was reported. Liver enzymes were available for 704 (54.6%) patients. There was a significantly higher mean ALT level in patients with hepatic steatosis (42.2 U/L; 95% CI 38.4 – 46.0) compared to patients without (28.8 U/L; 95% CI 25.7 – 31.9) (p<0.0001).

Conclusion:

Our findings highlight multiple gaps in the reporting and evaluation of hepatic steatosis among radiologists and emergency clinicians alike. Recognising and reporting this incidental finding may impact health outcomes.

Keywords:

Alanine Transaminase

Computed Tomography

Fatty Liver

Incidental Findings

Non-alcoholic Fatty Liver Disease

Background:

Hepatic steatosis is a common incidental finding on computed tomography (CT) studies performed for various indications. Detection of hepatic steatosis on unenhanced CT relies on identification of low attenuation of the liver beyond a certain threshold or comparison of hepatic attenuation with other organs such as the spleen. Depending on different attenuation thresholds, the sensitivity and specificity of CT in detection and quantification of hepatic steatosis can be variable.(1-4) There is no recommendation to use imaging as a screening tool for hepatic steatosis in the general population. However, abdominal CT studies already obtained during routine clinical care for other indications can provide additional information in the form of opportunistic screening when hepatic steatosis is incidentally detected.

Non-alcoholic fatty liver disease (NAFLD) represents a spectrum of liver disease ranging from simple hepatic steatosis through to non-alcoholic steatohepatitis (NASH), and in a minority, NASH-related cirrhosis and ultimately hepatocellular carcinoma and/or liver failure. The diagnosis of NAFLD requires evidence of accumulation of fat in the liver confirmed on imaging or biopsy and lack of secondary causes of fat accumulation such as significant alcohol intake.(5) Simple hepatic steatosis on its own is considered a benign non-progressive finding in the majority of patients. However, a proportion of patients with hepatic steatosis may progress to hepatic fibrosis potentially leading to NASH.(6) The prevalence of NASH is estimated to be close to 60% among biopsied NAFLD patients and close to 30% among NAFLD patients without an indication for biopsy.(7) Development of hepatocellular carcinoma has been well demonstrated in NAFLD patients even in the absence of significant fibrosis or cirrhosis(8) and there is growing evidence linking NAFLD with extrahepatic malignancy.(9) Furthermore, the association of NAFLD with subclinical cardiovascular disease, metabolic syndrome and their outcomes beyond traditional risk factors, makes hepatic steatosis an incidental finding of clinical and public health importance.(10) The prevalence of NAFLD in Australian adults remains uncertain due to lack of large imaging-based cohort studies. However, it is likely similar to global prevalence in Western countries and estimated between 20 and 30%.(11, 12)

Emergency physicians are often challenged with time-constrained management of acute presentations for patients with various medical conditions. Multiple previous studies evaluated the prevalence of incidental findings on CT studies performed in the emergency setting. However, documentation, organising work-up and communication of incidental findings to patients has been shown to be suboptimal.(13)

The primary aim of our study was to assess the prevalence of hepatic steatosis in patients presenting to the emergency department (ED) who underwent an unenhanced CT for suspected renal colic. We also assessed whether hepatic steatosis was reported when present. Furthermore, we assessed whether including incidental steatosis in radiology reports resulted in documentation of this finding by referring emergency clinicians in medical charts. Finally, we correlated the presence of hepatic steatosis with abnormal liver tests when present.

Methods:

Patients:

Institutional Review Board approval was obtained for this retrospective study at Austin Health, Melbourne, Australia. We included unenhanced CT studies performed for assessment of suspected renal colic in adult patients presenting to our ED from 1 Jan 2016 to 30 June 2017. For patients with recurrent presentations and multiple CT studies within the study period, we included the first CT study in the analysis. We excluded other indications for unenhanced CT studies to eliminate indication bias. Patients with documented or known chronic liver disease were excluded. Radiology reports were reviewed to identify whether hepatic steatosis was mentioned within the “body” or “findings” section and within the “conclusion” or “impression” section of the report. Presence of urolithiasis was documented. Electronic medical charts and discharge summaries for patients with radiology reports noting hepatic steatosis were reviewed.

Liver function tests (LFTs), if performed within 24 hours of CT, were reviewed for all patients and alanine aminotransferase (ALT) level was recorded. The level of ALT provides a biochemical indicator on hepatic inflammation in NAFLD and also correlates with metabolic syndrome risk factors.(14) We used upper normal limits of 40 U/L for males and 35 U/L for females in our assessment based on thresholds used by our laboratory. Given variability among different laboratories and complexity in defining upper normal limits of ALT,(15) we also assessed ALT levels based on conservative upper normal limits of 30 U/L for males and 19 U/L for females.(16)

Image acquisition:

All CT studies were performed on a 64-detector row CT scanner (Revolution EVO, GE Healthcare, Chicago, Illinois, USA) using a specified CT Renal Colic protocol. Patients were scanned in prone position when possible from the diaphragm to pubic symphysis. The scanning parameters were: tube voltage, 120 kVp; collimation, 40 mm; rotation time, 0.5 sec; pitch, 1.375; reconstruction thickness, 3 mm with no reconstruction interval. Automatic exposure was utilised and Adaptive Statistical Iterative Reconstruction (ASIR-V) at a level of 70% was performed as recommended by CT manufacturer. Axial, sagittal and coronal reformats reconstructed in 3 mm thickness. Thin axial slices obtained at 0.625 mm as well as reformats were routinely sent to the Picture Archiving Communication System.

Measurement of hepatic steatosis:

Prior to performing the study reads, a training set for three readers was established to ensure consistency in objective assessment of the images and positioning and placement of region-of-interest (ROI) for measurements of hepatic and splenic attenuation. Images from each CT study were reviewed by one of the three readers (XX, YY, ZZ – *anonymised for review*). Attenuation of the liver and spleen was measured by placing three ROIs on the liver and two ROIs on the spleen using one axial slice that best showed the liver and spleen from the 3-mm axial reconstructed stack. The absolute Hounsfield Units (HU) for each ROI were recorded and a mean HU was calculated for the liver from the three ROIs and for the spleen from the two ROIs (Figures 1 and 2) as described by Speliotes *et al.*(17) Multiple ROIs have been used to assess hepatic attenuation in studies evaluating CT criteria with degree of steatosis on biopsy.(1, 3, 4, 18, 19) ROIs were placed in the liver avoiding large vessels, focal lesions if present, and regions of fatty sparing.

Analysis of hepatic steatosis by using averaged HU measurements for liver and spleen was undertaken using different criteria. These included liver/spleen (L/S) ratio of ≤0.9,(3, 19) L/S ratio of ≤1.0,(4) L/S ratio of ≤1.1,(4) liver-spleen (L-S) difference ≤-10 HU,(3) L-S difference ≤5 HU,(20) absolute liver attenuation ≤45 HU(18) and absolute liver attenuation ≤40 HU.(1, 3, 20) Unenhanced CT has high accuracy for detection of moderate-to-severe steatosis. The criteria we used differ in their sensitivity and specificity for detection and quantification of hepatic steatosis particularly for mild steatosis and we elected to provide prevalence data for the commonly used CT thresholds to allow comparisons to other cohorts.(20) However, we used a L/S ratio ≤1.0 for the final assessment given its relative easier calculation when reading CT studies. Such a ratio also provides a compromise between L/S ratios of 0.9 to 1.1 reported in studies correlating L/S ratios with histopathology.(3, 4)

Statistical analysis:

Study data were collected and managed using REDCap electronic data capture tools hosted at the University of Melbourne.(21) The results are presented using standard summary statistics with frequencies, percentages, means (95% CI) and median (range and interquartile [IQR] range). Prevalence data are also presented sub grouped by gender and presence of urolithiasis given known association of urolithiasis with hepatic steatosis.(22, 23) Proportions of patients with and without documented steatosis in medical charts were compared using Fisher's exact test. Mean ALT levels were compared using two-sample student *t*-test assuming unequal variances. Analysis was performed using Microsoft Excel for Office. A p value <0.05 was considered statistically significant.

Results:

A total of 1290 patients who underwent an unenhanced CT for suspected renal colic met our inclusion criteria. The median age was 52.5 years (range: 16 - 98; IQR 42 - 65) with a male predominance; 835 (64.7%). A total of 754 out of 1290 patients (58.4%) patients had urolithiasis on their CT scans.

Depending on CT criterion used to diagnose hepatic steatosis, its prevalence ranges from 11.9% to 39.1% in our study population: 11.9% (153/1290) using L-S difference of -10 HU, 13.6% (176/1290) using absolute liver attenuation ≤40 HU, 17.3% (223/1290) using L/S ratio ≤0.9, 18.4% (237/1290) using absolute liver attenuation ≤45 HU, 26.0% (336/1290) using L/S ratio ≤1.0, 38.7% (499/1290) using L-S difference of 5 HU, and 39.1% (505/1290) using L/S ratio ≤1.1. Subgroup differences between males and females and between patients with and without urolithiasis are shown (Table 1).

Out of 336 (26.0%) of studies with hepatic steatosis defined by a L/S ratio ≤1.0, 94 patients (27.9%) had radiology reports noting steatosis. In the 94 patients with reports mentioning hepatic steatosis, the measured L/S ratio was ≤1.0 in all patients (100%). Only 49 out of 336 patients (14.6%) had reports noting hepatic steatosis in both body and conclusion sections of radiology reports and the remaining 45 out of 336 patients (13.4%) were mentioned in the body section only. Documentation of hepatic steatosis in medical charts and discharge summaries was noted in 18 out of 94 patients (19.1%) for whom steatosis was mentioned in the radiology reports (Figure 3). Out of 49 patients who had reports noting hepatic steatosis in both body and conclusion sections of radiology reports, 16 (32.7%) were documented in medical charts compared to only two out of 45 patients who had reports noting hepatic steatosis in only the body section of radiology reports (p=0.0005).

Liver enzymes performed within 24 hours of CT were available for 704 (54.6%) patients. There was a significantly higher mean ALT level in patients with hepatic steatosis (42.2 U/L; 95% CI 38.4 – 46.0) compared to patients without (28.8 U/L; 95% CI 25.7 – 31.9) (p<0.0001). In 185 patients with hepatic steatosis and available liver enzymes, 87 (47%) patients had ALT levels above the upper normal limit used by our laboratory (40 U/L for males and 35 U/L for females). When we used the conservative upper normal limits (30 U/L for males and 19 U/L for females), 130 (70.3%) patients with hepatic steatosis had elevated ALT levels (Table 2).

Discussion:

In our cohort of 1290 patients with a CT for suspected renal colic, we demonstrated that 26% of patients had hepatic steatosis identified on CT. The prevalence of hepatic steatosis in our study resonates with a global prevalence of NAFLD(7) and likely correlates with the prevalence of obesity which is estimated to be at more than a quarter of the Australian population.(11) The percentage of our patients with hepatic steatosis noted in radiology reports was low (28%). Wells *et al.* assessed hepatic steatosis using a relatively similar technique in measuring hepatic and splenic attenuation among 450 emergency patients in a Canadian cohort. Less than half of their patients had hepatic steatosis mentioned in radiology reports.(24) Documenting hepatic steatosis in both the body and conclusion sections compared to just the body of the radiology report resulted in more frequent documentation in medical charts and discharge summaries. This was also shown in a study of 127 patients with incidental hepatic steatosis and infrequent documentation in medical charts.(25) Unfortunately, this is expected as clinicians may not necessarily read the body of report and may rely on the conclusion section to answer specific clinical questions in a busy emergency work environment.

Nearly half of our patients (47%) with hepatic steatosis had elevated ALT levels suggesting a possible associated hepatic inflammatory process and higher risk of NASH. The presence of elevated ALT levels in addition to hepatic steatosis warrants further assessment particularly for advanced liver disease.(5) Moreover, patients with hepatic steatosis and normal ALT levels are still at risk of having underlying advanced liver disease and should receive further assessment particularly in the presence of other features of metabolic syndrome.(26) Such patients are also at risk of cardiovascular disease and several factors may affect these normal levels.(27) The upper limits of normal range used in our assessment were based on thresholds used by our laboratory. We also assessed our patients using conservative upper normal limits.(16) However, the conservative upper normal limits increased the proportion of patients without hepatic steatosis who have above normal ALT levels from 15.6% using our laboratory thresholds to 40.3% (Table 2). This prevalence is slightly higher than 32.1% reported in a recent cross-sectional study of 9,447 Australian people using similar conservative levels.(14) This could simply be due to differences between characteristics of our patient population and the general population. We suggest careful interpretation of our ALT findings when comparisons are made to other cohorts given different laboratories use different methods to measure ALT levels and multiple factors can affect ALT levels.(15)

Our cohort of ED patients with suspected renal colic provided us with unenhanced CT studies in which assessment of hepatic steatosis could easily be performed. There is a known association between metabolic syndrome and urolithiasis(28) and several factors that we could not account for may have influenced our prevalence data. Recent studies reported direct association between hepatic steatosis and urolithiasis.(22, 23) This explains the higher prevalence of hepatic steatosis in patients with urolithiasis compared to without (Table 1). While the prevalence of hepatic steatosis among the group of patients without urolithiasis is potentially more generalizable, this may underestimate the true prevalence in the population by excluding more patients with metabolic syndrome. We used different CT criteria for diagnosis of hepatic steatosis and reported prevalence data for these criteria given the general lack of Australian prevalence studies on hepatic steatosis using imaging.(11)

Incidental findings on unenhanced CT studies performed in ED for suspected renal colic are common. However, hepatic steatosis is not always reported in such studies.(13) For example, a large retrospective study of 5,383 CT studies for suspected renal colic categorised incidental findings according to recommendations by the American College of Radiology (ACR) Incidental Findings Committee white papers' recommendations.(29) However, ACR white papers' recommendations focus on incidental *focal* lesions and do not provide guidance on assessment, reporting or follow-up of the incidental finding of hepatic steatosis.(30, 31) In addition, studies reporting hepatic steatosis as an incidental finding are very likely to underestimate the true prevalence of hepatic steatosis given reliance on radiology reports to identify hepatic steatosis rather than reassessment of obtained images. The findings from Wells *et al.*(24) and our study confirm this observation.

We used different CT criteria to assess hepatic steatosis on unenhanced CT and relied on mean hepatic attenuation from three ROIs and mean splenic attenuation from two ROIs. We used multiple ROIs in our study to reduce attenuation variability in different regions of the liver and to provide a reproducible measurement of hepatic and splenic attenuation.(17) Assessing hepatic steatosis with a single ROI in the liver rather than comparison to splenic attenuation is quicker and potentially more practical. Given preferential accumulation of fat in the right lobe of the liver, a single ROI placed over the right lobe is potentially easier and still valid approach for assessing hepatic attenuation (Figure 2).(32) A cut-off of 40 HU measured using multiple ROIs has been shown to be most specific for moderate-to-severe hepatic steatosis (histopathological fat content ≥ 30%).(1, 3) Interestingly, another study with biopsy correlation showed a threshold of 48 HU using multiple ROIs to have a 100% specificity and 54% sensitivity for moderate-to-severe steatosis.(18) The use of such specific CT criteria can potentially be on the expense of missing mild steatosis (histopathological fat content of 5 to 30%). There is no evidence at this stage that clinical outcomes of NAFLD are associated with the degree of steatosis. Therefore, reporting radiologists may choose one criterion over the other depending on whether they want to diagnose or screen for hepatic steatosis.

Our study has several limitations. First, this was a single centre retrospective study with issues inherent to documentation in ED medical charts and discharge summaries. We did not assess for secondary causes of hepatic steatosis or cardiovascular risk factors as most patients were assessed for a different clinical presentation in an emergency setting (suspected renal colic / abdominal pain) and comprehensive history and clinical assessment was not necessarily documented. In addition, some ED notes were very brief and LFTs were not performed in nearly half of our patients. Secondly, we could not assess whether there was any undocumented history taking or communication with patients nor whether counselling was provided when hepatic steatosis was reported or when ALT levels were elevated. Thirdly, CT studies were reported by various radiologists and radiology trainees at our centre reflecting a broad spectrum of experience and attitudes towards recognising and / or reporting of hepatic steatosis. Fourthly, we did not correlate hepatic steatosis with other potential measurements associated with metabolic syndrome such as visceral and subcutaneous adiposity on CT nor with BMI. We tried to assess findings on CT that could be implemented in routine radiology reporting settings such as attenuation measurements rather than apply research tools requiring additional reading or post-processing time. Lastly, the prevalence of hepatic steatosis in our cohort is not necessarily reflective of the general population but rather a select group of patients as discussed earlier.

In conclusion, our findings highlight multiple gaps in the reporting and evaluation of hepatic steatosis among radiologists and emergency clinicians alike. Emergency physicians and other clinicians need to recognise the importance of hepatic steatosis as an incidental finding and initiate appropriate management steps. Radiologists play an important role in alerting emergency physicians and other clinicians who have access to patients' radiology reports, including primary care physicians, to the presence of hepatic steatosis. For example, a comment can be made in the conclusion section of the report: "Incidental hepatic steatosis warrants further assessment for advanced hepatic and cardiovascular disease." Radiologists should set the wheels in motion first for clinicians to do their part in this complex and evolving public health issue.

Figure legends:

Figure 1. Three ROIs are placed over the liver and two ROIs over the spleen. Axial CT slice showing the liver and spleen in a patient without hepatic steatosis demonstrating mean hepatic attenuation of 56 HU, mean splenic attenuation of 48 HU and L/S ratio > 1.

Figure 2. Axial CT slice in a patient with hepatic steatosis with mean hepatic attenuation of 46 HU, mean splenic attenuation of 56 HU and L/S ratio ≤ 1.0. Focal fatty sparing can be noted in segment IVb/V (arrow).

Figure 3. Proportions of patients with steatosis (HS) and documentation in medical charts and proportions of patients with available and elevated ALT levels.

Table 1. Prevalence of hepatic steatosis using different CT criteria with differences between males and females and with and without urolithiasis.

	With urolithiasis (n=754)			**Without urolithiasis (n=536)**			**Total**
	Total	**Male**	**Female**	**Total**	**Male**	**Female**	

L – S ≤ -10 HU	110 (14.6%)	91	19	43 (8%)	27	16	153 (11.9%)
L ≤ 40 HU	126 (16.7%)	102	24	50 (9.3%)	30	20	176 (13.6%)
L/S ≤ 0.9	160 (21.2%)	128	32	63 (11.8%)	38	25	223 (17.3%)
L ≤ 45 HU	167 (22.1%)	135	32	70 (13.1%)	43	27	237 (18.4%)
L/S ≤ 1	218 (28.9%)	181	37	118 (22%)	75	43	336 (26.0%)
L – S ≤ 5 HU	308 (40.8%)	249	59	191 (35.6%)	114	77	499 (38.7%)
L/S ≤ 1.1	315 (41.8%)	253	62	190 (35.4%)	113	77	505 (39.1%)

Table 2. Differences in ALT levels between patients with and without hepatic steatosis defined by a L/S ratio ≤1.0.

	N=1290					
Hepatic steatosis	**Present (n=336)**			**Absent (n=954)**		
	Overall	Male	Female	Overall	Male	Female
LFTs performed	185	131	54	519	295	224
Mean ALT U/L (95% CI)	42.2 (38.4 – 46)	44.2 (39.7 – 48.8)	37.4 (30.7 – 44.1)	28.8 (25.7 – 31.9)	30.7 (27.6 – 33.7)	26.4 (20.3 – 32.4)
ALT above lab upper normal limit†	87 (47.0%)	62 (47.3%)	25 (46.3%)	81 (15.6%)	56 (19.0%)	25 (11.2%)

ALT above conservative upper normal limit‡	130 (70.3%)	90 (68.7%)	40 (74.1%)	209 (40.3%)	99 (33.6%)	110 (49.1%)

†Upper normal limit used by our laboratory is 40 U/L for males and 35 U/L for females.
‡Conservative upper normal limit for ALT is 30 U/L for males and 19 U/L for females.(16)

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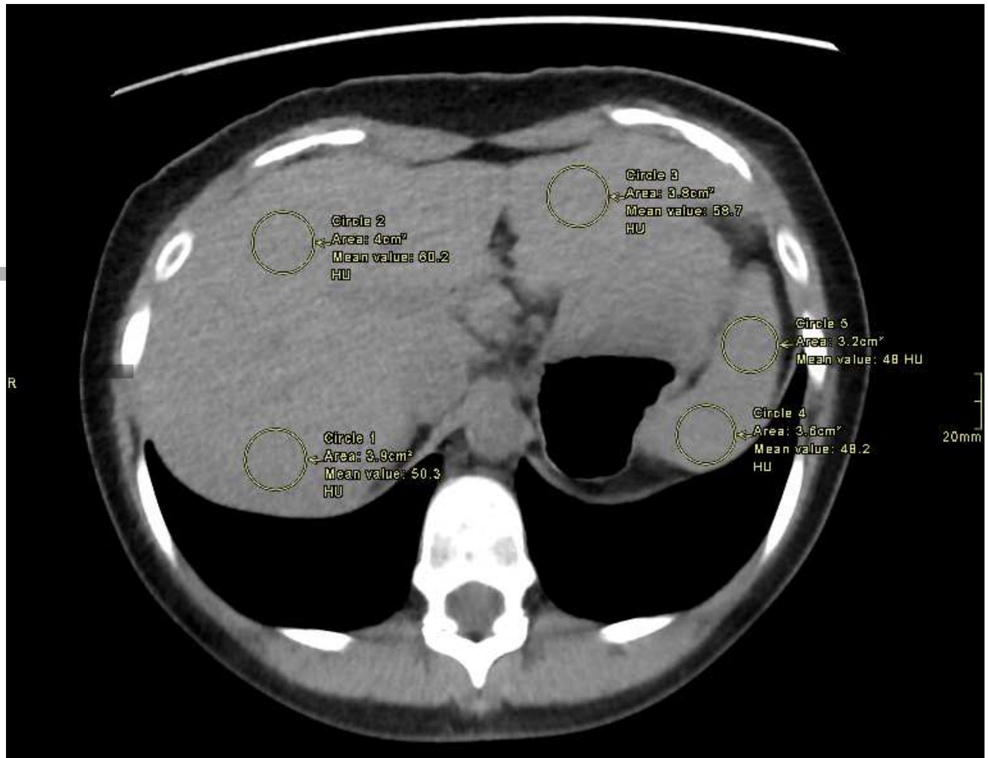

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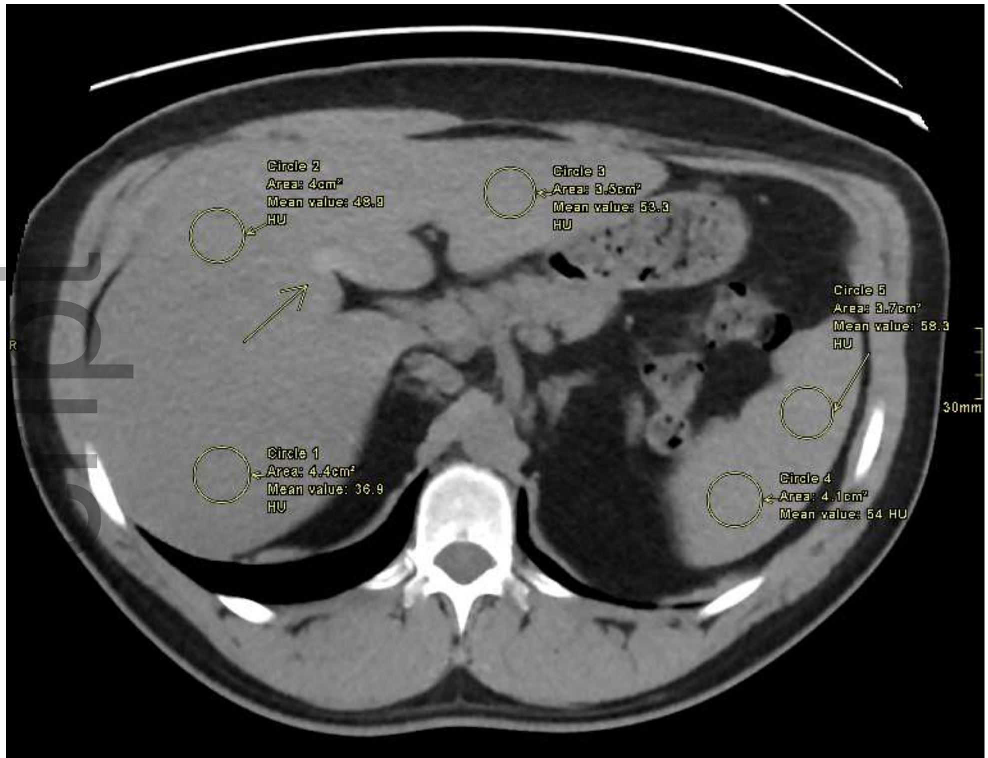

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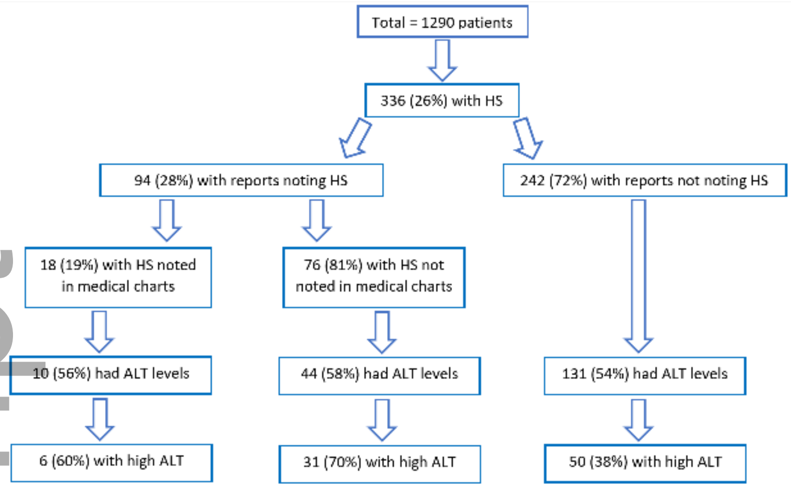

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