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DIAGNOSTIC PERFORMANCE OF TRIPLE-PHASE CT IN DIFFERENTIATING BENIGN AND MALIGNANT FOCAL HEPATIC LESIONS: A SYSTEMATIC REVIEW

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ABSTRACT
Focal hepatic lesions comprise a heterogeneous group of benign and malignant abnormalities with overlapping imaging appearances. Triple-phase computed tomography (TPCT) enables dynamic assessment of lesion vascularity across arterial, portal venous, and delayed phases, potentially improving lesion characterization. The objective of this systematic review was to evaluate the diagnostic performance of triple-phase CT in differentiating benign and malignant focal hepatic lesions. This systematic review was conducted according to PRISMA principles. A total of 366 records were identified, and 11 eligible studies published between 2017 and 2026 were included in the qualitative synthesis. Data were extracted on study design, population, lesion type, CT characteristics, reference standards, and diagnostic performance. Methodological quality was assessed using QUADAS-2. Triple-phase CT demonstrated generally favorable diagnostic performance for focal hepatic lesion characterization. Hepatocellular carcinoma commonly showed arterial hyperenhancement followed by portal venous or delayed washout, whereas hemangiomas typically demonstrated progressive centripetal enhancement. Metastatic lesions were frequently hypovascular or showed peripheral enhancement. Delayed-phase behaviour, lesion morphology, size, and vascular invasion provided additional discriminatory information. However, diagnostic performance varied because of differences in study populations, lesion distributions, imaging protocols, and reference standards. Triple-phase CT provides clinically useful non-invasive differentiation of benign and malignant focal hepatic lesions. Combined interpretation of all contrast phases improves characterization, although standardized prospective multicentre studies are required to strengthen the evidence.

KEYWORDS: Triple-phase CT, Focal hepatic lesions, Hepatocellular carcinoma, Benign liver lesions, Diagnostic accuracy

INTRODUCTION
Focal hepatic lesions (FHLs) include a wide variety of benign processes (simple cysts, hemangiomas, focal nodular hyperplasia and hepatic adenoma), as well as malignant processes (hepatocellular carcinoma, intrahepatic cholangiocarcinoma and hepatic metastases). Accurate characterization of their clinical importance is crucial since the treatment varies markedly between benign and malignant disease; in the benign situation, observation may be sufficient while in the malignant situation, surgical, locoregional, or systemic therapy may be warranted. Patil et al. (2024) noted the importance of advanced imaging for better characterization of FHLs, and Akbar et al. (2024) explained the benefits of triphasic CT in cases that were initially diagnosed on ultrasonography.

The differential diagnosis of benign and malignant hepatic lesions is not always easy because there are multiple lesions with overlapping appearances on conventional imaging. Because of its availability and lack of ionizing radiation, ultrasound is often used as the first modality, but this modality may not be as useful in characterizing lesions if they are operator dependent, patient dependent, located in different areas of the body or have similar echogenic patterns. Comparative studies have thus investigated the value of multiphasic CT, and Hameed et al. (2026) found that triphasic CT enhanced the detection and staging of lesions, in addition to ultrasonography. Abidi et al. (2026) also assessed the complementary value of triphasic CT and sonoelastography in the assessment of focal liver lesions.

Triple-phase CT takes advantage of the different blood supply to the liver and the lesions by acquiring images during the arterial, portal venous and delayed/equilibrium phase. The arterial phase is especially useful to show hypervascularity and tumour neovascularisation, while the portal venous phase will enhance the contrast of many hypovascular abnormalities from the liver. These sequential acquisitions have been described by Tatikonda et al. (2021) to serve as complementary to diagnosis in liver lesions. The delayed phase also helps to characterize by showing the enhancement that remains for a long time, delayed retention or appearance of capsules or delay in washout. Zafar et al., (2018), also demonstrated the advantage of multiphasic acquisition in terms of information gained in focal tumoral liver lesions over more restricted phase acquisition. Therefore, the diagnostic value of triphasic imaging is highly dependent on the time course of contrast enhancement, not its morphology. Hemangiomas are usually hyperenhanced on the periphery and then fill in toward the

center over time, while HCC is hyperenhanced on the arterial phase and then becomes hypoattenuated or “washed out” in subsequent phases. HCC washout has been measured in the triphasic setting and evaluated specifically for diagnosis of HCC as the reference standard by Hameed et al (2018) making washout an important objective imaging characteristic. Similarly, Shalmol et al. (2024) showed that the enhancement differences in the arterial, portal venous, and equilibrium phase have the potential to help differentiate benign from malignant focal liver lesions.

Histopathological examination is still important in cases with indeterminate or atypical imaging findings. In some cases however, characteristic imaging features allow for a confident diagnosis without the need for tissue sampling, which is an invasive procedure. In a systematic review and meta-analysis of triphasic CT for evaluation of diagnostic accuracy, Alturiqy (2025) studied cirrhotic patients and showed the ongoing value of tissue diagnosis for validating imaging-based differentiation. Concurrently, non-invasive characterization capabilities of triphasic CT may minimize the need for unnecessary invasive procedures in lesions with sufficiently specific enhancement patterns. Recent studies have also been ventured beyond traditional visual interpretation. Wang et al. (2025) studied the machine-learning based radiomics derived from triphase-enhanced CT, showing that quantitative evaluation of imaging heterogeneity can help distinguish between malignant and benign focal liver lesions. These methods also confirm the diagnostic information provided by multiphasic enhancement information, and they also provide methodological variety to an already diverse evidence base.

Although a great deal of clinical research has been conducted, the reported diagnostic performance of triphasic CT has been inconsistent due to variations in patient populations and lesion spectrum, acquisition timing, interpretation criteria, reference standards, and diagnostic endpoints. Certain investigations are mainly aimed at HCC, while others examine a combination of benign and malignant lesions. Patil et al (2024) and Akbar et al (2024) agree that triple-phase CT has an important role in characterization of focal liver lesions, but differences in protocol and study design make it difficult to compare easily with other studies. Therefore, a systematic synthesis is required to better understand the complete diagnostic value of this imaging method. Thus, the purpose of the present systematic review was to assess the diagnostic value of the triple-phase CT in differentiating benign and malignant FHLs, focusing on the enhancement pattern of each phase, the diagnostic value of each lesion, and the methodological consistency of the evidence on which this judgment is based.

2. METHODOLOGY

2.1 Study Design

The aim of this systematic review was to assess TPCT for the differentiation of benign and malignant FHLs. The review process was designed in line with the PRISMA guidelines for systematic reviews and meta-analyses in order to ensure the transparent identification, screening, assessment of eligibility and inclusion of relevant studies. Human and canine investigations were reviewed to ensure the diagnostic evidence available for the triphasic CT for FHLs is included.

2.2 Search Strategy

Google Scholar, PubMed and ScienceDirect were used to conduct a systematic literature search, which was then complemented by a manual literature search of the references of relevant articles. In the development of search strategy, the terms related to the imaging modality, target condition, and diagnostic objective were used. The search string used was: "triphasic CT" ("focal liver lesions" OR "hepatic lesions") ("benign" OR "malignant") diagnostic.” Studies for the use of triple-phase, triphasic or equivalent multiphasic contrast-enhanced CT protocols in the assessment of focal liver lesions were assessed. Studies were selected for the searches if they included diagnostic performance, lesion characterization, enhancement behavior, or histopathological correlation.

2.3 Eligibility Criteria

Studies were included if they were original full-text investigations that examined focal hepatic or liver lesions with triple-phase or triphasic computed tomography (CT). Studies on humans and dogs were taken into account when the objective was to differentiate, or characterize, benign from malignant lesions. Only studies that yielded clinically relevant diagnostic information such as sensitivity, specificity, positive predictive value, negative predictive value, diagnostic accuracy, area under the curve or clearly defined imaging features of benign or malignant pathology were included in the eligible studies. Diagnostic verification was accepted using histopathology, cytopathology, surgical and/or an appropriately described composite reference standard. Single- or dual-phase CT were excluded from the studies if a diagnostically useful multiphasic or delayed-phase assessment was not performed. When studies compared a phase-specific component of the CT relevant to the benign–malignant differentiation were available, and the component was extractable and relevant to the review objective, those studies were evaluated. Studies with no useful diagnostic results, inadequate characterization information or obvious overlap in populations were also omitted.

2.4 Study Selection Process

Electronic and additional database search and reference screening identified a total of 366 records at this stage. After eliminating duplicate studies, the remaining studies were further evaluated for their title and abstract in line with the predetermined eligibility criteria. The articles were then subjected to full text assessment for further inclusion or exclusion. Studies were discarded if they did not assess any relevant FHLs, did not have a suitable triple-phase CT protocol, included studies that did not differentiate benign from malignant, did not include sufficient diagnostic data, did not have a suitable reference standard, or were non-original or overlapping publications. The 11 studies that passed the screening and eligibility process have been retained for qualitative synthesis after meeting all the inclusion criteria published from 2017 to 2026.

2.5 Data Extraction

A data extraction framework was used in a systematic manner to extract data from each included study. Variables retrieved were those of author and publication year, country, study design, study population/species, sample size, type of lesions, CT acquisition protocol, reference standard, and principal imaging findings. Where available, diagnostic performance measures such as sensitivity, specificity, positive predictive value, negative predictive value, diagnostic accuracy, and AUC were noted. Phase-specific results in all three phases (arterial, portal venous and delayed or equilibrium) were also obtained for comparison of enhancement characteristics of benign and malignant lesions.

2.6 Quality Assessment

The methodological quality of the studies included was evaluated using the Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2). The risk of bias assessment focused on the four domains of patient selection, index test, reference standard and flow and timing, and applicability concerns were taken into account when applicable. Special focus for patient and/or lesion selection, the interpretation of the CT findings, the independence and reliability of the reference standard, and the completeness of diagnostic verification. The QUADAS-2 judgments at the domain level were then entered into the ROBVIS (Risk-of-Bias Visualization) tool to create traffic-light and summary plots of the methodological quality of the studies for graphical display.

2.7 Data Synthesis

Due to the presence of heterogeneity among studies in terms of population characteristics, species, lesion spectrum, CT acquisition protocol, reference standards, and reported diagnostic outcomes, a narrative qualitative synthesis was conducted. The diagnostic performance estimates were compared among the studies in which they were provided, and the enhancement characteristics were observed during the arterial, portal venous and delayed phases were summarized descriptively. Where appropriate, clinical contexts and biological applicability (human or canine) were interpreted separately. This method enabled evaluation of the overall value of triple-phase CT for diagnosis and retained the methodological differences between the studies included.

3. RESULTS

3.1 Study Selection

A total of 366 records were found through the systematic search, of which 14 were retrieved by reference screening and 352 were retrieved from electronic databases. 320 records were left after 46 records were identified as duplicates. Of this number, 236 records were eliminated for not satisfying the pre-established eligibility requirements. The remaining 84 full text articles were evaluated for eligibility, 73 of which were excluded for various reasons such as non-relevant liver lesions, lack of triple-phase CT, HCC-only detection or staging, insufficient diagnostic information, misdiagnosed target organ, non-original publication type, full text not accessible, overlapping study populations, and inadequate reference standards. Lastly, 11 studies meeting all the inclusion criteria published between 2017 and 2026 were selected for qualitative synthesis. Figure 1 shows the whole process of selection of the studies.

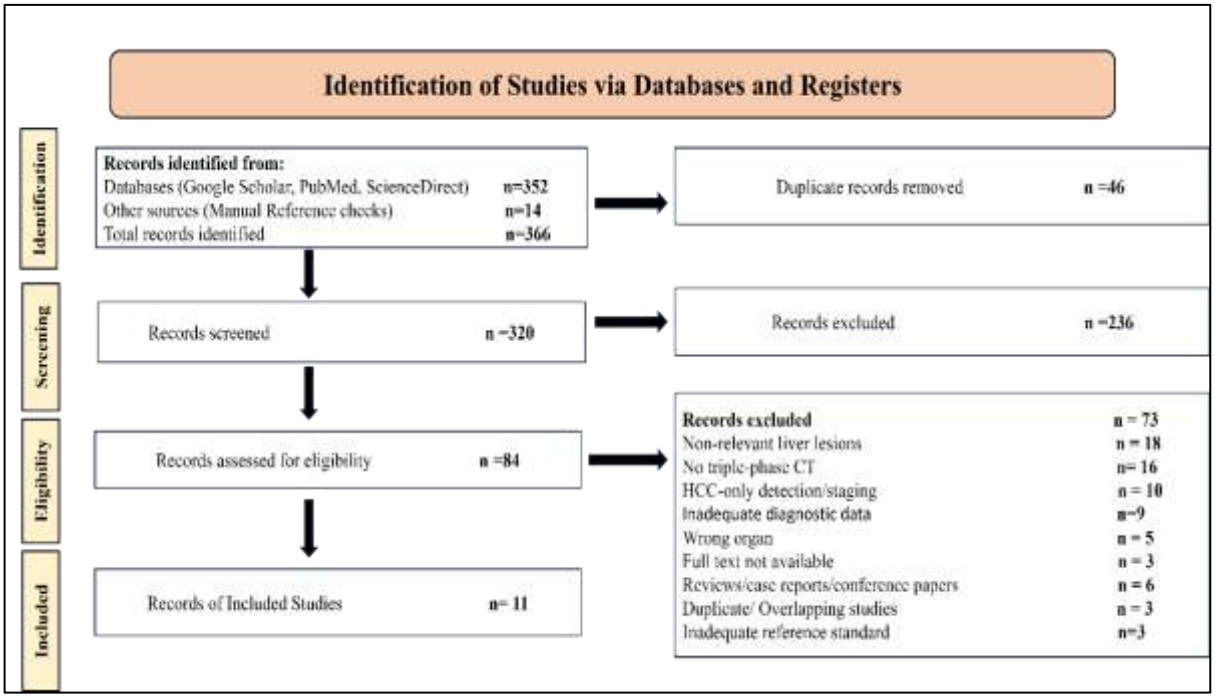

Figure 1. PRISMA flow diagram of study identification, screening, eligibility assessment, and final inclusion

3.2 Characteristics of Included Studies

Eleven studies were reviewed, eight human and three canines, from 2017 to 2026, with the majority published in Asia, Africa, Europe and the United States. Most design studies were prospective or cross-sectional, some retrospective diagnostic studies. Human sample sizes ranged from 40 to 190 patients, and the largest lesion-based study was 299 focal liver lesions in 80 patients. The subjects of the included studies ranged from benign to malignant lesions, such as HCC, metastases, cholangiocarcinoma, hemangioma, FNH, adenoma, cysts, abscesses, and nodular hyperplasia. There was a wide range of reference standards from complete histopathological confirmation to selective biopsy and composite clinical/imaging follow-up approaches (Table 1).

Table 1. Characteristics of Included Studies

Study	Design / Population	Sample	Main Lesions Evaluated	Verification Method
Adhikari et al. (2024)	Prospective cross-sectional; human	60 patients	Benign and malignant FLLs; HCC predominant	Histopathology
Burti et al. (2021)	Retrospective; canine	69 dogs	Nodular hyperplasia, HCC, other benign/malignant lesions	Cytopathology and/or histopathology
Khurana et al. (2026)	Cross-sectional observational; human	64 patients	Hemangioma, FNH/adenoma/cyst/abscess, HCC, metastasis/CCA	Final diagnosis; verification method not clearly detailed
Leela-Arporn et al. (2019)	Prospective; canine	57 dogs; 70 lesions	18 benign and 52 malignant lesions	Surgical histopathology
Mansour et al. (2021)	Prospective comparative imaging; human	60 patients; 70 lesions	HCC, metastases, hemangioma, adenoma, regenerative nodules, hydatid cyst	Biopsy for selected lesions; composite standard for others
Mittal & Kumbhar (2026)	Prospective observational; human	80 patients; 299 lesions	154 benign and 145 malignant FLLs	Selective biopsy plus composite reference standard
Musa et al. (2025)	Retrospective; human	190 patients	Hemangioma, cyst, HCC, metastasis, abscess and other hepatic lesions	Biopsy confirmation
Ominde & Mutala (2019)	Prospective multicentre cross-sectional; human	61 patients	HCC, metastases, CCA, FNH, adenoma, abscess	US-guided histology; typical benign lesions not always biopsied
Prashanth et al. (2025)	Prospective correlation study; human	40 patients	Cysts, abscesses, hemangioma, HCC, CCA, metastases	Histopathology/surgery/USG/follow-up
Pang et al. (2018)	Retrospective observational; human	76 patients; 84 lesions	HCC and hemangioma	HCC: biopsy/resection; hemangioma: imaging follow-up and/or biopsy
Griebie et al. (2017)	Diagnostic comparative; canine	44 dogs; 46 masses	Benign and malignant hepatic masses	Histopathological classification

Overall, the included studies demonstrated substantial variation in population, lesion spectrum, study design, and reference standard, supporting a narrative synthesis rather than direct comparison of all studies as methodologically equivalent.

3.3 Triple-Phase CT Characteristics and Diagnostic Findings

In the included studies, differentiation of FHLs was accomplished mainly based on dynamic enhancement patterns in the arterial, portal venous, and delayed phase in triple-phase CT. The arterial phase was the most useful for the detection of hypervascular lesions, whereas the portal venous phase was better for hypovascular lesions and washout. Persistent enhancement, capsule formation, progressive fill-in, and enhancement heterogeneity were additional information received from delayed imaging (Musa et al., 2025; Ominde & Mutala, 2019). Persistent or progressive enhancement was more typical of benign lesions. Peripherally enhancing, centripetal nodular filling was a characteristic feature in the majority of hemangiomas, while the cysts were hypoattenuating and non-enhancing. Malignant lesions, especially HCC, on the other hand, commonly exhibited arterial hyperenhancement with portal venous or delayed washout (Mittal & Kumbhar, 2026; Khurana et al., 2026). The rates of portal venous hypoenhancement and delayed washout were 61.1% and 63.9% in

malignant lesions compared with 21.4% and 7.1% in benign lesions, respectively (Khurana et al. 2026). Other discriminatory criteria evaluated were lesion morphology and quantitative enhancement. The lesion diameter >4.5cm and the presence of a heterogeneous delayed-phase enhancement were independent predictors of malignancy in Leela-Arporn et al. (2019), whereas the perfusion parameters of PVC, AEF, and HAC also aided in the differentiation between HCC and hemangioma in Pang et al. (2018). Many of the results confirm the interpretation of the multiphasic enhancement pattern, but not any one phase of the CT.

3.4 Diagnostic Performance of Triple-Phase CT

In conclusion, the included studies showed the utility of triple-phase CT for the characterization and differentiation of FHLs with good diagnostic performance. The diagnostic accuracy of the studies was different depending on the spectrum of lesions, population, imaging protocol, and reference standard. In all studies comparing overall benign-malignancy, multiphasic CT was found to be clinically useful for discrimination; in those studies evaluating the lesion-by-lesion discrimination, multiphasic CT was shown to have particularly good performance for a number of common benign and malignant hepatic lesions. The canine studies also confirmed the usefulness of triple-phase CT, particularly in the role of delayed-phase enhancement, lesion morphology, and lesion size making a significant contribution to classification. Based on the quantitative approaches, it was also suggested that the perfusion heterogeneity and enhancement heterogeneity could benefit diagnostic differentiation in lesions that are difficult to diagnose. In summary, the current evidence suggests that triple-phase CT can be used for reliable lesion characterisation, but with caution when making direct comparisons between studies due to study heterogeneity. Table 2 summarizes the main diagnostic performance measures.

Table 2. Diagnostic Performance of Triple-Phase CT

Study	Diagnostic Target	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy / AUC
Adhikari et al. (2024)	Benign vs malignant FLLs	93.0	50.0	91.0	-	95.5%
Khurana et al. (2026)	Benign vs malignant FLLs	91.7	92.9	-	-	92.2%
Leela-Arporn et al. (2019)	Benign vs malignant canine FLLs	92.3	77.8	92.3	77.8	88.6%; AUC 0.891
Mansour et al. (2021)	Benign vs malignant FLLs	100	81.8	84.0	100	90.7%
Musa et al. (2025)	Lesion-specific diagnosis	80.6–92.0	96.0–99.9	75.0–99.9	90.4–99.4	87.6–95.3%
Ominde & Mutala (2019)	Benign vs malignant FLLs	93.0	50.0	91.0	-	86%
Prashanth et al. (2025)	Lesion-specific diagnosis	84–100	97.5–100	88–100	100	-
Mittal & Kumbhar (2026)	Lesion-specific diagnosis	73.7–100	100	100	98.2–100	98.3–100%

Pang et al. (2018) additionally demonstrated significant differentiation between HCC and hemangioma using quantitative perfusion parameters, while Burti et al. (2021) reported more modest classification performance using delayed-phase CT features. These studies were not directly comparable with conventional diagnostic-accuracy studies and were therefore interpreted separately.

3.5 Diagnostic Performance According to Lesion Type

Diagnostic performance was found to depend on the type of lesion and the characteristic enhancement behaviour played an important role in the diagnosis of these lesions. Typically, HCC was hyperenhanced on the arterial phase and showed portal venous or delayed phase washout. Musa et al. (2025) showed high diagnostic performance for HCC and Prashanth et al. (2025) and Mittal and Kumbhar (2026) also showed high specificity for the diagnosis of HCC, but with varying sensitivity. The most typical and benign pattern was peripheral nodular enhancement with progressive centripetal filling in hemangioma. Musa et al. (2025) reported decreased sensitivity in small or atypical hemangiomas with atypical enhancement, while Mittal and Kumbhar (2026) indicated excellent diagnostic accuracy for this type. Hypovascular or peripheral/rim enhancement was seen in the majority of lesions, and some showed arterial enhancement and subsequent washout of the metastatic lesions. Musa et al. (2025) and Mittal and Kumbhar (2026) reported high specificity and accuracy of the metastatic lesions. Cystic lesions, abscesses, focal nodular hyperplasia and intrahepatic cholangiocarcinoma were also observed with good diagnostic performance. The sensitivity and specificity were found to be 100% for cysts, abscesses, and intrahepatic cholangiocarcinoma by Prashanth et al. (2025) and Mittal and Kumbhar (2026) reported 100% sensitivity and specificity for cysts, abscesses, FNH and intrahepatic cholangiocarcinoma. However, the findings must be interpreted with caution as there were relatively small numbers of cases in some lesion categories. Pang et al. (2018) gave quantitative evidence to distinguish HCC from hemangioma, where the coefficient of the portal vein and the coefficient of the arterial enhancement differed significantly between the two types of lesions and

the coefficient of the hepatic artery differed between the two. These perfusion parameters along with conventional enhancement properties of hemangiomas, including progressive centripetal enhancement and HCC washout.

3.6 Overall Benign–Malignant Differentiation

Across the included studies, the ability of triple-phase CT to distinguish benign from malignant The hepatic lesions were related to the combination of vascularity, temporal enhancement pattern and delayed phase behaviour and lesion morphology. Early enhancement was not specific for malignancy as benign hypervascular lesions could have similar early enhancement (hemangioma, FNH, adenoma). Confidence of the diagnosis was enhanced with the combination of portal veins hypoenhancement, slow washout, capsule formation, progressive fill-in and invasive features. Khurana et al. (2026) showed that peripheral nodular enhancement was significantly correlated with benign lesions, while any of the following features: heterogeneous arterial enhancement, portal venous hypoenhancement, delayed washout, and enhancing capsule, were correlated with malignancy. Vascular invasion and extrahepatic spread were seen in only malignant lesions, further supporting the malignant classification. The delayed phase especially was helpful in the canine evidence. Leela-Arporn et al. (2019) found that there was a heterogeneous delayed phase enhancement, and the maximum diameter of the lesion larger than 4.5 cm were independent predictors of malignancy. These variables provided an excellent discriminating performance. Likewise, delayed phase enhancement was useful in differentiating benign from malignant canine hepatic masses and when combined with venous-phase lesion conspicuity (Griebie et al., 2017). Additionally lesion morphology was complementary to enhancement behaviour. Khurana et al. (2026) reported larger size and multiple lesions in malignant lesions, and Leela-Arporn et al. (2019) showed that lesion size is significantly associated with malignancy in dogs. In general, all evidence provided shows that multiphase enhancement pattern and lesion size and morphology together have more discriminatory value than any single CT feature has.

3.7 Quality and Consistency of Evidence

The QUADAS-2 assessment also revealed methodological quality ranging from the included studies (Figure 2).

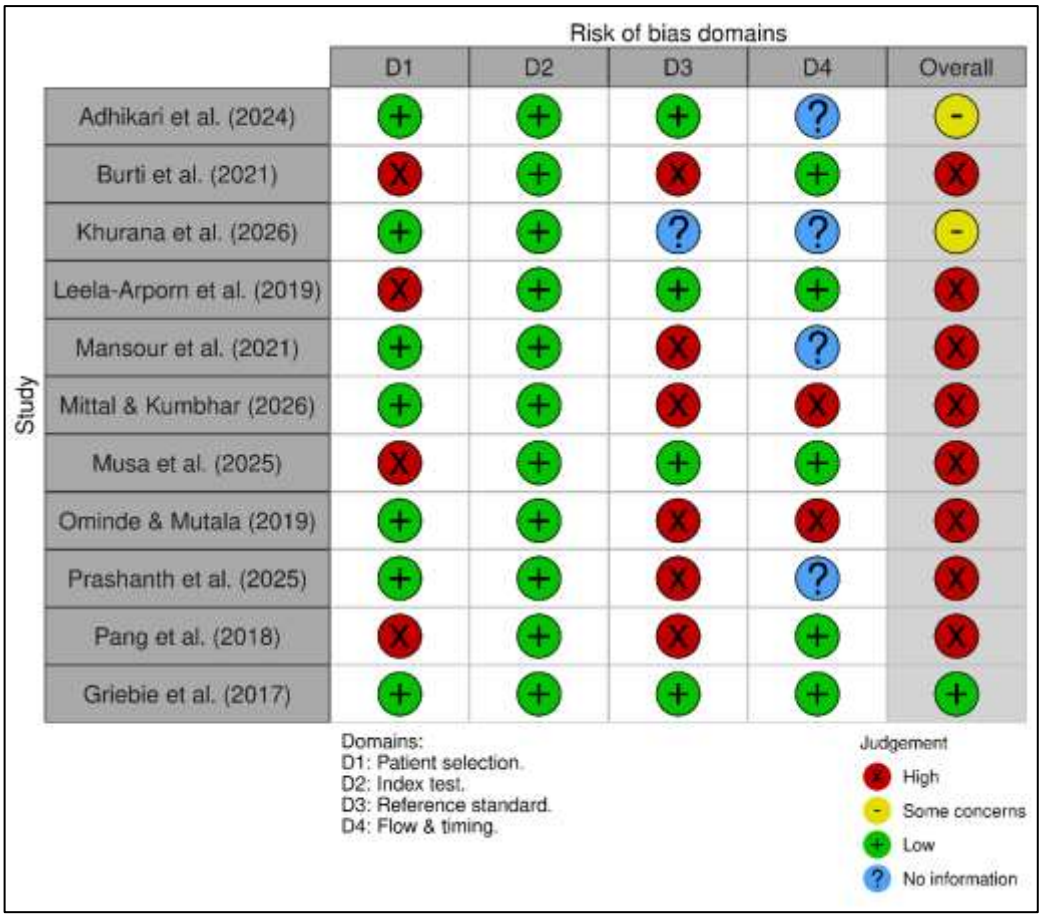

Figure 2. QUADAS-2 traffic-light plot showing risk-of-bias judgments across the included studies

The major concerns related to the index test included patient selection, reference standards, and flow and timing, which tended to be low risk, while greater concerns were seen in areas of patient selection and reference standards, largely due to selective enrolment, lack of histopathological verification, composite reference standards, and variations in diagnostic pathways. Overall, two studies were deemed low risk, two studies were deemed some concerns, and seven studies were deemed high risk of bias (Figure 2). The methodological differences were taken into account, along with the variation in CT procedures and study populations when reading the overall evidence.

4. DISCUSSION

This systematic review of the literature suggests that TPCT is a useful imaging method for distinguishing between benign and malignant FHLs, which combines lesion morphology with temporal enhancement behaviour. In all evidence, the interpretation was enhanced by adding arterial vascularity to the assessment of portal venous attenuation and delayed enhancement or washout. The multiphasic pattern provided a more holistic representation of lesion vascularity and tissue characteristics than was possible with just one morphological feature. Manchikanti et al. (2021) noted that sequential contrast phase is a useful addition to help with characterization of focal hepatic lesions. Triphasic CT has also been shown to be useful in the assessment of a variety of liver abnormalities as has been previously demonstrated by Jabeen et al. (2022) in liver imaging.

In general, the reviewed studies reported good diagnostic accuracy, with differences in accuracy depending on the type of lesions, subjects enrolled, diagnostic criteria and reference standard. Vascular lesions were characteristic and tended to be better discriminated than atypical lesions. Arkesh et al. (2018) also found that triple-phase contrast-enhanced CT is clinically useful for the differential diagnosis of focal liver lesions, as it shows enhancement changes over the course of the phases. In a comparison to ARFI elastography, Goel et al. (2016) demonstrated that multiphasic CT can also make significant contributions to characterization of focal liver lesions. The results all together indicate that TPCT is still beneficial especially in cases where the first ultrasonography is not able to correctly identify the nature of the lesion with complete confidence.

The diagnostic value of TPCT is due to the complementary information gained in the arterial, portal venous and delayed phases. The arterial phase is useful for outlining hypervascular lesions and abnormal tumour-related vascularity, while the portal venous phase is particularly useful to identify lesions that become relatively hypoattenuating in comparison to the enhanced liver parenchyma. Delayed imaging also helps to show contrast retention or progressive enhancement, as well as the appearance or washout of the capsule. Youssef et al. (2021) showed that phase-dependent hepatic attenuation changes can be used to infer hepatic perfusion and hemodynamics, highlighting the need to consider temporal enhancement in interpreting hepatic attenuation changes. Satyampet and Kumar also stressed that the enhancement characteristics of CT is equally important in assessing liver lesions and in conjunction with the morphological and dynamic findings.

For the types of lesions included, there was a high degree of relevance of the findings to the lesion in question, especially for HCC, hemangioma, and hepatic metastases. Typically, HCC showed hyperenhancement of the arteries, followed by relative washout in portal venous or delayed imaging phase due to its mostly arterial tumour vascular supply. These characteristics have been found clinically significant by Zahur et al. (2024) who studied triphasic CT in differentiation of HCC from metastatic disease with reference standard of histopathology. Bevilacqua et al. (2017) also showed that information from the triphasic CT protocol can be used in a computational way to aid the detection and classification of HCC. By contrast, the majority of hemangiomas had a characteristic of benign vascular appearance with progressive filling, while metastatic lesions tended to be hypovascular, were more common to show peripheral enhancement, or were heterogeneous based on tumour type. Ebeed et al. (2024) more specifically illustrated the value of the multislice triphasic CT for the assessment of metastatic hepatic focal lesions in chemotherapy-treated patients with breast cancer.

While there was evidence of general consensus in favor of TPCT, the included studies showed that there was some meaningful heterogeneity. Variation in reported performance may have been due to differences in scanner technology, timing of contrast phases, lesion prevalence, patient characteristics, and diagnostic thresholds. Some studies had a wide spectrum of lesions, while others focused on HCC or metastatic disease. Background liver changes can also affect the appearance and interpretation of lesions, as demonstrated by Sattar et al. (2021) in their study of triphasic CT in the detection of morphological abnormalities related to the diffuse hepatic disease. In parallel, cirrhosis, changes of hepatic perfusion, and treatment-related changes may affect the expected enhancement pattern and could lead to a decrease in diagnostic confidence. Hence, findings of apparently contradictory diagnoses, as were observed in various studies, should not be seen as evidence of contradiction but as a reflection of the clinical and methodological variability existing between each of the studies.

On a clinical level, TPCT provides helpful non-invasive information for refining the diagnosis of liver focal lesions, further investigation and therapeutic planning. A benign diagnosis with clear characteristics will not require invasive sampling, while recognition of the malignant enhancement characteristics will help expedite biopsy, staging, surgical assessment, or local/regional treatment. Ahmed and Zenat (2021) showed that multiphasic CT still plays a role in assessment of HCC despite the recent introduction of advanced functional imaging modalities. The usefulness of this technique in the routine radiological practice is obvious in terms of accessibility, speed of acquisition and the possibility to evaluate lesion morphology, vascular involvement and extrahepatic abnormalities simultaneously.

The human and animal studies presented to the researcher made it possible to have more evidence to draw from, but it also leads to a factor of generalizability. The value of canine investigations lies in their applicability to human studies in relation to lesion vascularity, delayed enhancement, tumour size and morphological markers of malignancy; however, there are differences in tumour biology in both species, the prevalence of hepatic tumours, indications for imaging in both species, and clinical pathways in both species. Therefore, canine evidence should be treated as secondary to human diagnostic evidence. The uniformity of some of the enhancement principles on the different species still indicates that temporal contrast behaviour stems from common underlying vascular and tissue characteristics, which may be of biological importance for other species.

Some of the evidence available is limited in scope and should be considered. The populations studied were often small and there were only a few cases of some lesion types. Histopathology was not always used as the gold standard, as some used selective biopsy, imaging follow-up, clinical criteria or combined diagnostic methods. This introduces the possibility

of verification and classification bias. There are also some differences in the acquisition protocols and timing of the contrasts, which further diminishes direct comparability. Furthermore, there were several investigations that were single centre or retrospective, which may be subject to patient-selection bias. Another source of complexity is treatment-related changes: chemotherapy may cause changes in the appearance of the metastatic lesions in the liver, and therefore affect enhancement-based assessment as demonstrated by Ebeed et al. (2024).

Future studies should focus on large, prospective, multicentre, studies with standardised acquisition protocols for the arteries, portal vein and delayed imaging, and well-defined diagnostic criteria. Histopathological verification should be performed when clinically appropriate; when this is not possible, a clear report of the alternative standard should be provided. The conventional visual interpretation should be compared with the quantitative enhancement measurements for further improvement in diagnostic reproducibility. Automated analysis, as shown in Bevilacqua et al. (2017), might also be used to complement radiologist interpretation, but these approaches will need to be thoroughly validated with external data before they can be used routinely. Future studies should also compare the performance of TPCT in patients with and without background liver disease, as well as the effects of tumour treatment, lesion size, and atypical enhancement patterns on TPCT. A more uniform approach in these areas would provide more evidence and would make the role of triple-phase CT more clear to current diagnostic pathways for FHLs.

5. CONCLUSION

TPCT is a useful non-invasive imaging modality for the differentiation and characterization of benign and malignant FHLs. The evidence suggests that the interpretation of the diagnosis is enhanced when arterial, portal venous and delayed phase findings are used as a "triad" instead of using the finding alone. Arterial hyperenhancement, portal vein or delayed washout, progressive centripetal filling, persistent enhancement, and delayed phase heterogeneity are important findings to aid in the differentiation of common lesions, including HCC, hemangioma, metastases, cysts, and abscess. Diagnostic performance was generally good, although the reported estimates depended upon the type of lesion, the study population, the CT protocol and the reference standard. Other evidence demonstrated that the morphology, size, vascular invasion and enhancement behaviour of the lesion may further increase the confidence of diagnosis. However, methodological differences and selective histopathological verification, small sample sizes, retrospective study designs, and variations in acquisition protocols hinder direct comparisons across studies. Supportive information from canine studies was not taken into account when interpreting human evidence due to differences in disease biology and clinical pathways. In conclusion, triple-phase CT is important for the diagnosis of FHLs, but further prospective multicentre studies with uniform imaging protocols and reference standards are needed to provide more robust and generalizable diagnostic estimates.

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