Abdominal Radiology (2019) 44:4028–4036
https://doi.org/10.1007/s00261-019-02237-3

HEPATOBILIARY

Diagnostic imaging of hepatocellular carcinoma at community hospitals and their tertiary referral center in the era of LI-RADS: a quality assessment study

Andrew Chan[1] · Madeleine Sertic[1] · Jennifer Sammon[1,2] · Tae Kyoung Kim[1,2] · Hyun-Jung Jang[1,2] · Luis Guimaraes[1,2] · Martin O'Malley[1,2] · Korosh Khalili[1,2,3]

Published online: 25 September 2019

Abstract

Purpose To assess guideline compliance and quality of hepatocellular carcinoma, (HCC) diagnostic imaging within community hospitals (CH) and their Tertiary referral center (TRC) in a moderately high incidence region.

Methods Initial diagnostic workup CT/MRI scans of 251 patients (122 CH, 112 TRC, 17 Non-TRC academic) with HCC over a 15-month period were assessed for Liver reporting and Data System (LI-RADS) guideline compliance. 269 scans (182 CT, 87 MRI) were qualitatively evaluated by 2 independent blinded radiologists for arterial timing, overall image quality, noise and sharpness, with quantification of interobserver variability. The contrast enhancement ratio (CER) for the largest HCC on each scan was calculated using pre- and post-contrast images.

Results 103/104 (99%) of TRC and 44/78 (56%) of CH CTs adhered to LI–RADS imaging guidelines ($P<0.0001$). Lack of delayed phase accounted for 32/34 (94%) of noncompliant CH CTs. Regarding MRI, 19/19 (100%) of TRC and 60/68 (88%) of CH scans were adherent ($P=0.12$). For both modalities, overall image quality, noise and sharpness were rated significantly higher for TRC than CH. There was moderate interobserver agreement with intraclass correlation coefficient of 0.73, 0.70 and 0.63, respectively. Arterial-phase timing was rated adequate for CT in 75/104 TRC (72%) and 10/68 (14%) CH scans ($P<0.0001$) and for MRI in 8/19 (42%) TRC and 23/68 (33%) CH scans ($P=0.17$). The CER was significantly higher for TRC versus CH (2.9 vs. 1.9, $P<0.001$) and MRI (0.9 vs. 0.7, $P=0.03$).

Conclusions Community hospital HCC diagnostic scans significantly lag in critical quality parameters of tumor enhancement, arterial phase timing, perceived image quality, and LI-RADS CT technique compliance compared to a TRC.

Keywords Hepatocellular carcinoma · Diagnosis · Quality · Liver · CT · MRI · LI-RADS

Abbreviations

HCC	Hepatocellular Carcinoma
AASLD	American Association for the Study of Liver Disease
LI-RADS	Liver imaging reporting and data system
TRC	Tertiary referral center
CH	Community hospitals
DWI	Diffusion-weighted sequence
HAP	Hepatic arterial phase
CER	Contrast enhancement ratio
SI	Signal intensity
ROI	Region of interest
SD	Standard deviation
ICC	Intra-class correlation coefficient

✉ Korosh Khalili
Korosh.khalili@uhn.ca

[1] Department of Medical Imaging, University of Toronto, Toronto, ON, Canada

[2] Joint Department of Medical Imaging, University Health Network, Sinai Health System, Women's College Hospital, Toronto, ON, Canada

[3] Joint Department of Medical Imaging, University Health Network, Princess Margaret Cancer Centre, 610 University Ave, Toronto, ON M5G 2M9, Canada

Introduction

Hepatocellular carcinoma (HCC) poses a significant health burden in North America and throughout the world. Within the United States, Liver and intrahepatic bile duct cancers are the fifth deadliest cancer in men and seventh deadliest in women [1]. HCC is among the few cancers for which the

diagnosis is made in most cases by imaging, without the need for histological confirmation [2]. Therefore, standardization and optimization of imaging techniques, diagnostic criteria and reporting are of utmost importance. Diagnostic imaging criteria for HCC were proposed by various liver disease associations including the American Association for the study of Liver Disease (AASLD) and subsequently validated by a number of prospective studies [3–6]. In 2008, the American College of Radiology sponsored a panel to create guidelines for the optimal imaging and reporting of HCC using CT and MRI [4]. The resultant guidelines, the Liver Imaging Reporting and Data System (LI-RADS), were launched in 2011 and addressed the standardization of imaging techniques and reporting. Significant effort has gone into the revision and validation of these guidelines throughout the last several years [7–9]. However, less effort has gone into the translation of these guidelines into daily practice, particularly at non-academic centers where HCCs are often first encountered.

It is our own anecdotal experience at a tertiary referral center (TRC) that there is a wide heterogeneity regarding HCC image quality and protocol adherence. We believe that the protocol and technique recommendations of LI-RADS are a critically important component of optimized HCC diagnostic imaging.

We hypothesized that CT and MRI studies performed at community hospitals (CH) do not adhere to the LI-RADS imaging technique guidelines and the image quality from community sites is lower than that of the TRC, despite the presence of established guidelines. The purpose of this study was to assess and compare specific measures of LI-RADS imaging technique guideline compliance and imaging quality between CH and TRC.

Materials and methods

The institutional review board approved this retrospective cross-sectional study. The need for patient consent was waived.

Study setting

The study was performed in the province of Ontario, Canada, with a population of 14 million, 29.1% of which were foreign born [10, 11]. The provincial age-standardized incidence rate of liver cancer in men and women was 14.2/100,000 and 4.9/100,000 respectively, making Ontario a "moderately high incidence" region on a global scale [12, 13]. The TRC studied is the only designated liver cancer treatment center in the province's largest metropolitan area and treats patients across the province. An estimated 1/5 of Canada's HCC population is seen at the study TRC.

Patient selection

Three hundred and seventy-four consecutive patients referred to the TRC from April 2016 to August 2017 were identified from an institutionally approved HCC registry.

Exclusion criteria were as follows: patients that were previously treated ($n = 103$), HCCs that were incidentally identified on non-dedicated CT or MRI scans ($n = 9$) and patients with alternative diagnoses such as liver metastases or cholangiocarcinoma ($n = 11$).

A total of 251 patients remained and constituted the study population. One hundred and twenty-two patients had available scans performed in CH sites, 112 patients had scans performed at the TRC (either without prior imaging, or with CH prior imaging that was unavailable) and 17 patients were scanned at non-TRC academic sites. Eleven patients in TRC, 24 patients in CH and 2 patients in academic non-TRC had both a CT and MRI for their initial work up available for review (Fig. 1). The study population included 207 males and 44 females. The mean age of patients scanned at these sites were not significantly different, with the age of patients in TRC 66.2 ± 9.5, CH 65.6 ± 9.8 and academic non-TRC 62.02 ± 8.5 years.

LI-RADS phase/sequence adherence

Phases and sequences of respective initial diagnostic workup CT and MRIs were recorded to assess LI-RADS adherence using the 2014–2017 LI-RADS standards [14]. The 2017 version was used because it was the most up-to-date version that overlapped the study accrual period. The 2017 technical standards overlap with 2014 version and are identical to the 2018 update [15]. Adequate CT was defined as inclusion of arterial, venous and delayed (2–5 min post contrast injection) phases. Specifically, delayed phases that were outside of the recommended range (for example, 10–15 min delays) did not satisfy the criteria for adherence. Adequate MRI was defined as inclusion of T2, T1 pre-contrast, arterial, venous and delayed phases. Additionally, the inclusion of pre-contrast images for CT and diffusion weighted imaging (DWI) for MRI were recorded, these images are suggested but not required by LI-RADS guidelines.

CT & MRI technique

Details of CT and MRI technique at TRC are outlined in Appendix 1.

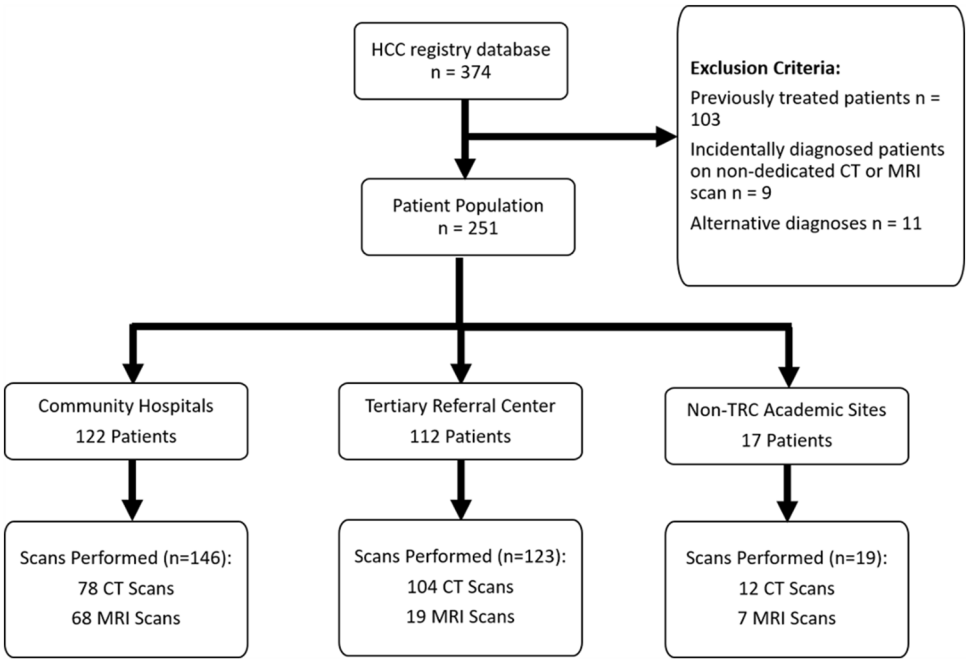

Fig. 1 Flowchart of study population. A total of 288 CT and MRI scans from 251 patients were reviewed

Qualitative imaging quality assessment

Using standard clinically used proprietary PACS viewers previously developed within the institution, representative images were selected from the hepatic arterial phase by two radiology residents (AC in 2nd year, MS in 3rd year) at three levels: largest HCC, hepatic veins and right portal vein (the left portal vein was alternatively used if the right portal vein was diminutive or thrombosed). All annotations on the images were removed; the images were anonymized and displayed at native field of view in a standardized format. CT images were displayed using soft tissue windows (window 400, level 40) MRI images were shown using the native window/level. Reviewers could not alter the window, level, field of view or display arrangement. Two blinded fellowship-trained abdominal radiologists with 2 and 18 years of staff experience reporting abdominal CT and MRI independently evaluated these 3 representative images. They were tasked to grade overall *image quality*, *image noise* and *image sharpness* each on a 5-point scale. For image quality, a score of 1 was defined as the worst quality and non-diagnostic and a score of 5 was defined as excellent quality. For image noise, a score of 1 was defined as very noisy and non-diagnostic, and a score of 5 was defined as no visible noise. For image sharpness, a score of 1 was defined as presence of significant motion blur and non-diagnostic and a score of 5 was defined as very sharp, allowing visualization of the precise margins of organs. Additionally, the radiologists were asked to score adequate hepatic arterial phase (HAP) timing using enhancement of the portal and hepatic veins as landmarks via a 3-point scale: 1 (too early) portal vein not yet or minimally opacified, 2 (good) portal vein partially opacified and hepatic vein not yet opacified, 3 (too late) hepatic vein opacified [16].

Quantitative image quality assessment

All measurements were performed by 2nd and 3rd year radiology residents (AC, MS). To assess the quality of the arterial phase, quantitative analysis of the degree of HCC enhancement was performed by acquiring a contrast enhancement ratio (CER) for MRI and CT. CER formulas were different for MRI and CT since MRI signal intensity (SI) requires normalization, whereas CT attenuation values are calibrated, and therefore, comparable between machines. The CER for MRI was acquired using the following formula: (Post contrast HCC SI–Pre-contrast HCC SI)/Pre-contrast HCC SI [17]. For CTs, CER was calculated as follows: Post Contrast HCC Hounsfield Units (HU)/Pre-contrast HCC HU [18]. Image 2 demonstrates an example of HCCs with varying CERs. To obtain these measures, a region of interest (ROI) was drawn over the largest HCC in the pre-contrast and hepatic arterial phase; the largest possible cross-sectional area within the margins of the tumor was used. The mean HU and SI were obtained for CTs and MRIs, respectively. Noise for pre-contrast CT scans was measured by recording the standard deviation (SD) from an ROI 2.0 cm^2 large placed over hepatic parenchyma. The ROI was placed in the most homogenous portion of the liver, away from vessels and ducts.

Statistical analysis

To determine the proportion of scans that adhered to LI-RADS guidelines, a single binary outcome variable (adherent and non-adherent) was created by auditing the included phases and sequences of the CTs and MRIs, respectively. A χ^2 test was performed for the comparison of the proportions of CH scans and TRC scans that were adherent.

The overall quality, image noise and image sharpness of the scans from CH sites and the TRC site were each compared separately. This was performed by producing a continuous variable based on averaging the three ratings from the two radiologists for each measure of quality. The intraclass correlation coefficient (ICC) and Cohen's Kappa coefficient were calculated to measure the reliability of the scores between the two radiologists.

To compare the CER from the CT and MRI scans that were performed in CH sites to the ones in TRC sites, the average CER from each of these sites were obtained and an *F*-test was performed for the comparison of the two groups. The average noise between CH and TRC sites were compared by obtaining an average SD from the two respective groups and subsequently performing an F-test.

Results

Demographics

A total of 288 CT and MRI scans from 251 patients originating from 41 different hospital sites across the province were reviewed. An average of 4.7 CT scans and 2.3 MRI scans were performed at each site. Of the CT scans analyzed, 93/194 (48%) were performed at TRC urban sites, 52/194 (27%) were performed at non-TRC urban sites and 49/194 (25%) were performed in suburban and rural sites. Of the 94 MRI scans, 19/94 (20%) were performed at TRC urban sites, 23/94 (25%) were performed at non-TRC urban sites and 52/94 (55%) were performed at suburban and rural sites.

Adherence to LI-RADS phase/sequence guidelines

Regarding CT examinations, 103/104 (99%) of TRC and 44/78 (56%) of CH scans adhered to LI-RADS recommendations (Fig. 2, $P < 0.0001$). The lack of a delayed phase was the most frequent deviation from the LI-RADS recommendations, comprising 32 of the 34 (94%) non-adherent CH CT studies. Two of the 34 (6%) CT studies did not include a portal venous phase. Of the 37 CH sites contributing the 78 CT studies, 14 (38%) were fully adherent, 10 (27%) had some non-adherent scans and 13 (35%) had all non-adherent scans. The suggested pre-contrast imaging was included in 100/104 (96%) of TRC scans and 64/78 (82%) of CH scans ($P = 0.002$).

Regarding MRI examinations, there was no significant difference between adherence to LI-RADS required sequences as 19/19 (100%) of TRC scans and 60/68 (88%) of CH scans were adherent ($P = 0.12$) (Fig. 2). Of the non-adherent CH cases, missing sequences were T2 in 5/8 (63%) cases, pre-contrast T1 in 2/8 (25%) cases, and contrast-enhanced T1 in 1/8 (12%) of cases. The LI-RADS suggested DWI imaging was used in 19/19 (100%) of TRC scans and 51 of 68 (75%) of CH scans ($P = 0.009$).

For academic non-TRC sites, 10/12 (83%) of CT scans adhered to LI-RADS recommendations and all 12 included pre-contrast images. In the 2/12 non-adherent scans, the delayed phase was not included. For MRI, 6/7 (86%) were adherent and all 7 included DWI images.

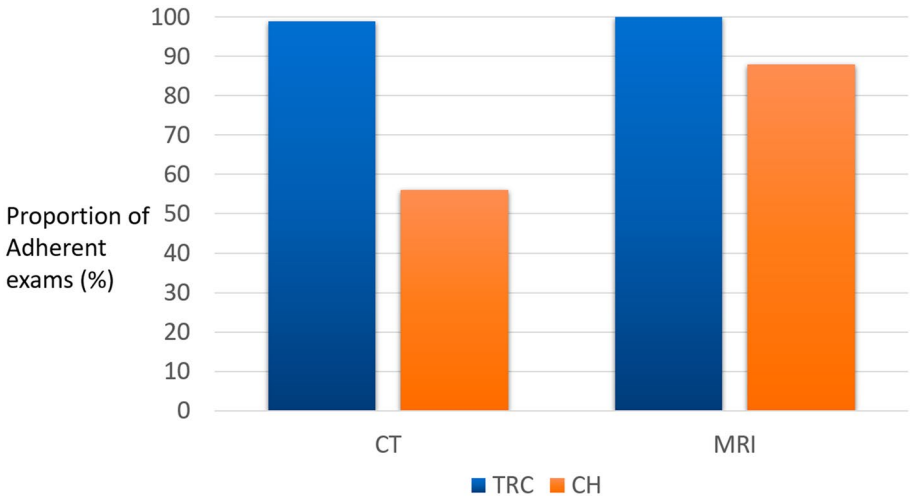

Fig. 2 Proportion of adherent and non-adherent CT scans performed in TRC and CH sites. Regarding CT examinations, 103/104 (99%) of TRC and 44/78 (56%) of CH scans adhered to LI-RADS recommendations. Regarding MRI examinations, there was no significant difference between adherence to LI-RADS required sequences as 19/19 (100%) of TRC scans and 60/68 (88%) of CH scans were adherent ($P = 0.12$)

Qualitative analysis

Analysis of non-TRC academic sites was not performed due to small sample size. The mean rating of overall quality of CT images within TRC was 4.2 compared to 3.3 in CH sites ($P < 0.0001$). The mean rating of TRC image noise was 3.3 compared to 2.8 in CH sites ($P < 0.0001$) and mean TRC image sharpness was 4.7 compared to 4.3 in CH sites ($P < 0.0001$). Figure 3 summarizes the qualitative analysis results.

For MRI, the overall image quality between the two groups was not significantly different: 3.8 at TRC sites versus 3.5 at CH sites ($P = 0.2$). MRI image noise and sharpness ratings also demonstrated similar results: 3.7 and 3.6 for TRC sites versus 3.4 and 3.5 for CH sites, respectively ($P = 0.15$ and 0.69). Figure 4 depicts examples of studies with low and high image quality ratings.

Arterial phase timing of CT scans from TRC was rated as adequate in 75/104 cases (72%) and 10/68 (14%) in CH ($P < 0.0001$) (Fig. 5). Hepatic arterial phase timing was judged to be too early in 27/29 (93%) of the TRC and 58/58 (100%) of CH CTs with inadequate hepatic arterial phase. There was no significant difference between the proportion of properly timed MRI scans between TRC and CH, 8/19 (42%) TRC were adequately timed compared to 23/68 (33%) CH ($P = 0.17$) (Fig. 5). Arterial phase timing was deemed too early in 11/11 (100%) of TRC and 42/45 (93%) of CH MRI scans with inadequate hepatic arterial phase. Table 1 summarizes the qualitative assessment results. Figure 6 depicts examples of early and adequate hepatic arterial phase timing.

The intra-class correlation coefficient (ICC) between the two evaluators measured as follows: overall quality—0.73 (moderate reliability), sharpness—0.70 (Moderate reliability), noise—0.63 (moderate reliability) [19]. A Cohen's Kappa coefficient between the two evaluators for the binary outcome of hepatic arterial timing measured 0.79 (moderate reliability) [20].

Quantitative analysis

The CER amongst CT scans performed was 2.9 in TRC versus 1.9 in CH sites ($P < 0.001$). The CER amongst MRI exam performed in TRC sites was 0.9 versus 0.7 in CH sites ($P = 0.03$). Regarding the measurement of noise, the SD amongst pre-contrast CT scans performed in TRC was 16.0

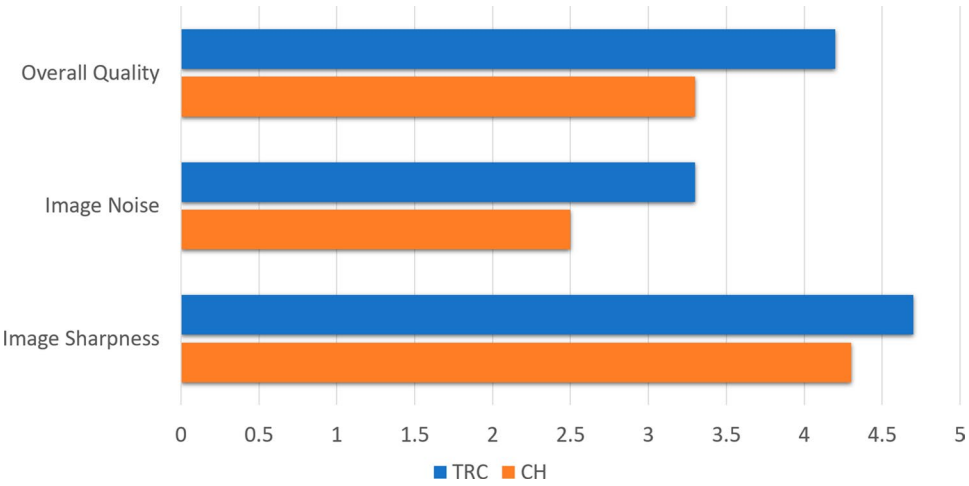

Fig. 3 Comparison of overall image quality, noise and sharpness of ct images from TRC and CH sites. The mean rating of overall quality of CT images within TRC was 4.2 compared to 3.3 in CH sites ($P < 0.0001$). The mean rating of TRC image noise was 3.3 compared to 2.8 in CH sites ($P < 0.0001$) and mean TRC image sharpness was 4.7 compared to 4.3 in CH sites ($P < 0.0001$)

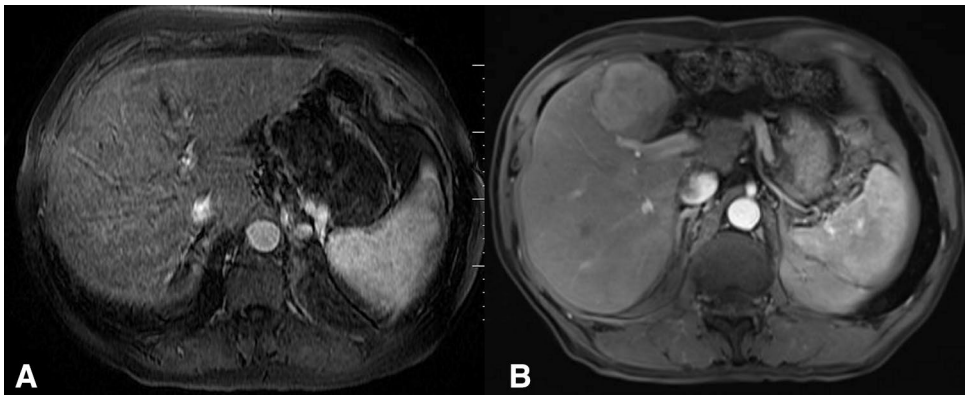

Fig. 4 Examples of low (**a**) and high (**b**) quality diagnostic scans. **a** This scan had a (mean) rating of 1.5/5 for overall quality, 2/5 for image sharpness, and 1.5/5 for image noise. **b** This scan had a (mean) rating of 4.5/5 for all three parameters of overall quality, sharpness, and noise

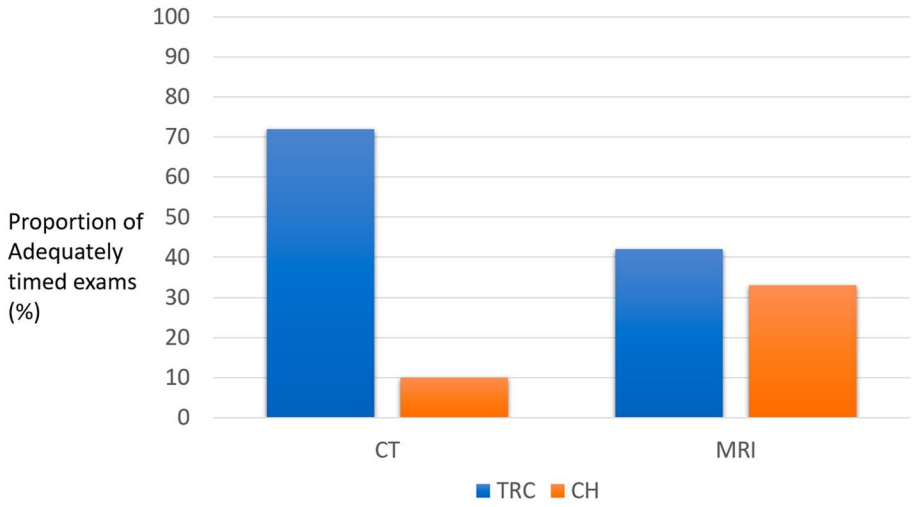

Fig. 5 Proportion of adequately timed CT and MRI scans performed in TRC and CH. Arterial phase timing of CT scans was rated as adequate in 75/104 (72%) of TRC and 10/68 (14%) of CH cases ($P < 0.0001$). There was no significant difference between the proportion of properly timed MRI scans between TRC and CH, 8/19 (42%) TRC scans were adequately timed compared to 23/68 (33%) CH scans ($P = 0.17$)

Table 1 Comparison of parameters of imaging quality for CT and MRIs scans performed at community hospitals and their TRC

	Tertiary referral center	Community hospital sites	*P* value
CT			
Overall quality rating (1–5)	4.2	3.3	< 0.0001
Image noise rating (1–5)	3.3	2.8	< 0.0001
Image sharpness rating (1–5)	4.7	4.3	< 0.0001
Proportion of adequately timed exams (%)	72	14	< 0.0001
Contrast enhancement ratio	2.9	1.9	< 0.0001
Noise (standard deviation)	16.0	13.1	< 0.001
MRI			
Overall quality rating (1–5)	3.8	3.5	0.20
Image noise rating (1–5)	3.7	3.4	0.15
Image sharpness rating (1–5)	3.6	3.5	0.69
Proportion of adequately timed exams (%)	42	33	0.17
Contrast enhancement ratio (CER)	0.9	0.7	0.03

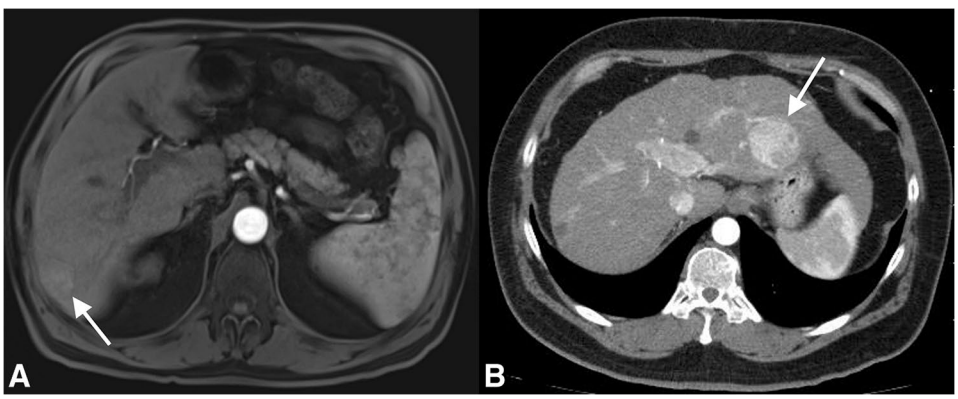

Fig. 6 Hepatic arterial timing. **a** Too Early. The right hepatic artery is enhancing but there is no contrast in the right portal vein. Consequently, the hepatocellular carcinoma (arrow) shows faint enhancement. **b** Appropriate. Not only is contrast seen in the left hepatic artery but there is enhancement within the portal vein. The tumor enhancement (arrow) is easily detectable

in TRC versus 13.1 in CH sights ($P < 0.001$). Table 1 summarizes the quantitative result.

Discussion

Standardized imaging techniques for the diagnosis of HCC are of utmost importance since most HCCs are diagnosed by means of imaging criteria alone. This study has found significant deficiencies in the actual practice of HCC imaging which affect the performance of these criteria. These deficiencies are (a) diminished arterial enhancement of HCC (b) poorly timed hepatic arterial phase, (c) absence of a delayed phase, (d) and overall lower imaging quality. We have previously shown that within the same jurisdiction, patients whose HCC were detected within the TRC were twice as likely to fulfill Milan Criteria for liver transplantation as those who were referred from an external hospital (72% vs. 36%) [21]. This current study points to significantly lower guideline adherence and imaging quality as one cause of up-staging of patients that are referred from CH.

A late hepatic arterial phase is critical to ensuring peak enhancement of the tumor as compared to the background liver, allowing more facile HCC detection and characterization. This study has found that the dominant HCCs noted on TRC CT scans were approximately 1.5 times higher in attenuation than on CH CT scans (CER 2.9 vs. 1.9). Several factors affect the enhancement of HCC including contrast dose, injection rate and arterial phase timing. The wide and significant discrepancy between adequacy rates of hepatic arterial phase timing in TRC and CH CT scans (72% vs 14%) shows that a poorly timed arterial phase is a major contributor to the lower enhancement of CH CT scans. For MRI scans, a less striking, but similar and statistically significant difference was found with regards to quantitative tumor enhancement and qualitative arterial phase timing assessment. For both CT and MRI, an early hepatic arterial phase was nearly always the reason for inadequate arterial phase timing. We speculate that the timing is deficient due to the rapidly improving speed of CT and MRI scanners. As institutions replace and upgrade to faster scanners, timing delays need to be prolonged to allow time for the contrast to get to the liver in sufficient quantity.

This study also shows that there is inadequate translation of the technique requirements noted in HCC guidelines, especially LI-RADS, beyond specialized referral centers. The role of the delayed phase as part of a multiphasic contrast-enhanced evaluation of HCC has been recognized as more important than the venous phase and thus is required by all guidelines [2, 4, 22]. Despite this, 41% of CH CT scans were missing a proper (2–5 min) delayed phase of enhancement. We did not assess the exact timing of the delayed phase or make a determination of which length of delay was optimal. We note that 2014 and 2017 versions of LIRADS do not specify an exact delay but recommend the above range. While the dynamics of optimal HCC enhancement and washout were deciphered in early 2000s, guidelines from radiology organizations outlining technical parameters, such as LI-RADS are a relatively recent phenomenon [23]. Since its inception, much of the efforts in optimizing LI-RADS have been with regards to the reporting lexicon and its alignment with clinical bodies involved in the management of the tumor [3, 24]. Our study suggests that a concerted effort is needed in translating the protocol and technical requirements of optimal HCC imaging to community radiology practice. Another possible contributor to the absence of this phase may be insufficient clinical information provided for the examination not alerting the radiologist to the patient's risk factors for HCC. If the clinical information provided does not specify that the patient is at risk for HCC, the imaging protocol prescribed will likely exclude the delayed phase.

MRI scans are not prone to an absent delayed phase since there is no worry regarding radiation exposure, thus a delayed phase is part of standard abdominal imaging protocols from all major equipment manufacturers and is routinely included for assessment of all hepatic masses. However, obtaining an adequately timed arterial phase is more challenging; the majority of both TRC (58%) and CH (67%) MRI scans evaluated in this study were not timed optimally. This is despite the use of bolus tracking technology in TRC. While DWI is not a required sequence by LI-RADS, its inclusion is suggested due to improved detection and therefore sensitivity [24, 25]. The absence of DWI in 25% of CH MRI scans assessed in this study may further affect the performance of community radiologist in diagnosing HCC.

Sources of bias in this study include a potential familiarity heuristic regarding the evaluators and the qualitative analysis. The evaluators have been working within the TRC institution for 2 and 18 years, respectively. Despite the blinded independent evaluation, there may have been a cognitive bias towards rating TRC images more favorably over CH images regarding overall quality, noise and sharpness. On the other hand, some amongst the TRC group of patients may have been referred from the community for re-imaging due to patient tumor-related factors that would predispose to lower quality scans or atypical tumors, negatively skewing the TRC results. The retrospective nature of the study and the wide referral base also prevents determining exact reasons for deficiencies such as the absence of the delayed phase. The difference in experience of the evaluators (2 verses 18 years) may also account for only the moderate interobserver agreement between the two evaluators. Our CH sample size was also limited; some patients referred to the TRC group with a suspected diagnosis of HCC likely had imaging performed at CH sites, but these

imaging studies were not available when our retrospective review was performed.

In conclusion, this study found that a substantial proportion of CH CT scans did not comply with LI-RADS imaging technique recommendations. We recommend that a major systematic effort be initiated in jurisdictions with moderate and high incidence of HCC to translate LI-RADS' technique-related guidelines into community practice.

Author contributions Study concept and design (AC, MS, JS, TK, HJ, LG, MO, KK), obtaining REB approval (AC, KK), LI-RADS expertise (HJJ, TKK, LG), Jurisdictional quality assurance consultation and translation (MO), acquisition of data (AC, MS, JS, KK), Designing Figures (AC, MS, KK), statistical analysis (AC, MS, HJJ, TKK), analysis and interpretation of data (AC, JS, TK, HJ, LG, MO, KK), drafting of the manuscript (AC, KK), critical revision of the manuscript (AC, MS, JS, TK, HJ, LG, MO, KK), Final approval to be published (AC, MS, JS, TK, HJ, LG, MO, KK), study supervision (AC, KK), Agree to be held responsible for all work (AC, MS, JS, TK, HJ, LG, MO, KK).

Data availability The authors declare that they had full access to all of the data in this study and the authors take complete responsibility for the integrity of the data and the accuracy of the data analysis.

Compliance with ethical standards

Conflict of interest The authors declare no conflict of interest.

Appendix 1: details of CT and MRI techniques at a TRC

At the TRC institution, HCC CT technique involved the use of iodinated contrast material (iodixanol Visipaque 320, GE Healthcare) using a volume of 2 ml/kg with a maximum dose of 180 ml. Injection was through an antecubital vein at a rate of 5 ml/s. A bolus tracking system was used with a trigger of the aorta reaching 100 HU. A four-phase scan was obtained, including unenhanced, hepatic arterial (20 s after trigger), portal venous (60 s after trigger) and delayed (180 s after contrast injection) phases[15]. Images were reconstructed with a slice thickness of 5 mm at every 2.5 mm interval.

MRI scans at the TRC were performed with the use of an extracellular gadolinium contrast agent gadobutrol (Gadovist, Bayer Healthcare) using a volume of 0.1 mmol/kg at 1 ml/s. The MRI acquisition included T2 with TE 90 ms and 180 ms, axial T1 weighted opposed & in phase, axial diffusion-weighted imaging (DWI) sequences and axial T1 weighted pre-contrast and dynamic post-contrast images. Post-contrast imaging included arterial (flouro triggered 5 s after opacification of aorta at level of the liver), two immediate portal venous (approximately 30 – 60 s after trigger), and delayed (5 min post contrast injection) phases.

References

1. American Cancer Society. Cancer facts and figures 2019. https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2019/cancer-facts-and-figures-2019.pdf. Updated 2019. Accessed 02/24, 2019.
2. Bruix J, Sherman M, American Association for the Study of Liver Diseases. Management of hepatocellular carcinoma: An update. *Hepatology*. 2011;53(3):1020-1022.
3. Bruix J, Sherman M, Practice Guidelines Committee, American Association for the Study of Liver Diseases. Management of hepatocellular carcinoma. *Hepatology*. 2005;42(5):1208-1236.
4. Mitchell DG, Bruix J, Sherman M, Sirlin CB. LI-RADS (liver imaging reporting and data system): Summary, discussion, and consensus of the LI-RADS management working group and future directions. *Hepatology*. 2015;61(3):1056-1065.
5. Khalili K, Kim TK, Jang HJ, et al. Optimization of imaging diagnosis of 1-2 cm hepatocellular carcinoma: An analysis of diagnostic performance and resource utilization. *J Hepatol*. 2011;54(4):723-728.
6. Forner A, Vilana R, Ayuso C, et al. Diagnosis of hepatic nodules 20 mm or smaller in cirrhosis: Prospective validation of the noninvasive diagnostic criteria for hepatocellular carcinoma. *Hepatology*. 2008;47(1):97-104.
7. Ehman EC, Behr SC, Umetsu SE, et al. Rate of observation and inter-observer agreement for LI-RADS major features at CT and MRI in 184 pathology proven hepatocellular carcinomas. *Abdom Radiol (NY)*. 2016;41(5):963-969.
8. Fowler KJ, Tang A, Santillan C, et al. Interreader reliability of LI-RADS version 2014 algorithm and imaging features for diagnosis of hepatocellular carcinoma: A large international multireader study. *Radiology*. 2018;286(1):173-185.
9. Kierans AS, Makkar J, Guniganti P, et al. Validation of liver imaging reporting and data system 2017 (LI-RADS) criteria for imaging diagnosis of hepatocellular carcinoma. *J Magn Reson Imaging*. 2018.
10. Statistics Canada. Canada at a glance 2018. https://www150.statcan.gc.ca/n1/pub/12-581-x/2018000/pop-eng.htm. Updated 2018. Accessed 05/04, 2019.
11. Ontario Ministry of Finance. 2016 census highlights: Factsheet 8. https://www.fin.gov.on.ca/en/economy/demographics/census/cenhi16-8.html. Updated 2017. Accessed 05/04, 2019.
12. Venook AP, Papandreou C, Furuse J, de Guevara LL. The incidence and epidemiology of hepatocellular carcinoma: A global and regional perspective. *Oncologist*. 2010;15 Suppl 4:5-13.
13. Cancer Care Ontario. Ontario cancer statistics 2018. https://www.cancercareontario.ca/sites/ccocancercare/files/assets/OCS2018_rev13122018.pdf. Updated 2018. Accessed 04/13, 2018.
14. American College of Radiology. LI-RADS v2017. https://www.acr.org/-/media/ACR/Files/RADS/LI-RADS/LIRADS_2017_Core.pdf?la=en. Updated 2017. Accessed 09/03, 2019.
15. American College of Radiology. LI-RADS v2018. https://www.acr.org/-/media/ACR/Files/RADS/LI-RADS/LI-RADS-2018-Core.pdf?la=en. Updated 2018. Accessed 09/03, 2019.
16. Shinozaki K, Yoshimitsu K, Irie H, et al. Comparison of test-injection method and fixed-time method for depiction of hepatocellular carcinoma using dynamic steady-state free precession magnetic resonance imaging. *J Comput Assist Tomogr*. 2004;28(5):628-634.
17. Haimerl M, Wachtler M, Zeman F, et al. Quantitative evaluation of enhancement patterns in focal solid liver lesions with gd-EOB-DTPA-enhanced MRI. *PLoS One*. 2014;9(6):e100315.
18. Arai T, Kobayashi A, Fujinaga Y, et al. Contrast-enhancement ratio on multiphase enhanced computed tomography predicts recurrence of pancreatic neuroendocrine tumor after curative resection. *Pancreatology*. 2016;16(3):397-402.

19. Koo TK, Li MY. A guideline of selecting and reporting intraclass correlation coefficients for reliability research. *J Chiropr Med*. 2016;15(2):155-163.
20. McHugh ML. Interrater reliability: The kappa statistic. *Biochem Med (Zagreb)*. 2012;22(3):276-282.
21. Khalili K, Menezes R, Yazdi LK, et al. Hepatocellular carcinoma in a large canadian urban centre: Stage at treatment and its potential determinants. *Can J Gastroenterol Hepatol*. 2014;28(3):150-154.
22. Jang HJ, Kim TK, Khalili K, et al. Characterization of 1-to 2-cm liver nodules detected on hcc surveillance ultrasound according to the criteria of the american association for the study of liver disease: Is quadriphasic CT necessary? *AJR Am J Roentgenol*. 2013;201(2):314-321.
23. Lee KH, Choi BI, Han JK, Jang HJ, Kim TK, Han MC. Nodular hepatocellular carcinoma: Variation of tumor conspicuity on single-level dynamic scan and optimization of fixed delay times for two-phase helical CT. *J Comput Assist Tomogr*. 2000;24(2):212-218.
24. Elsayes KM, Hooker JC, Agrons MM, et al. 2017 version of LI-RADS for CT and MR imaging: An update. *Radiographics*. 2017;37(7):1994-2017.
25. Gluskin JS, Chegai F, Monti S, Squillaci E, Mannelli L. Hepatocellular carcinoma and diffusion-weighted MRI: Detection and evaluation of treatment response. *J Cancer*. 2016;7(11):1565-1570.