Is Concurrent LR-5 Associated with a Higher Rate of HCC in LR-3 or 4 Observations? An Individual Participant Data Meta-Analysis

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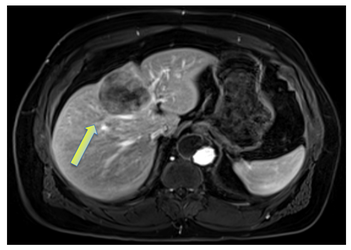
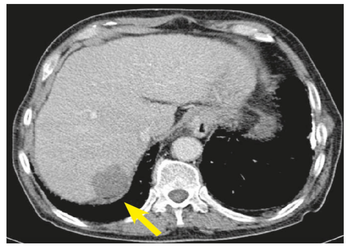
INTRODUCTION

Hepatocellular carcinoma (HCC) is the most prevalent form of primary liver cancer (~90%) and the third leading cause of cancer-related deaths worldwide.



MRI



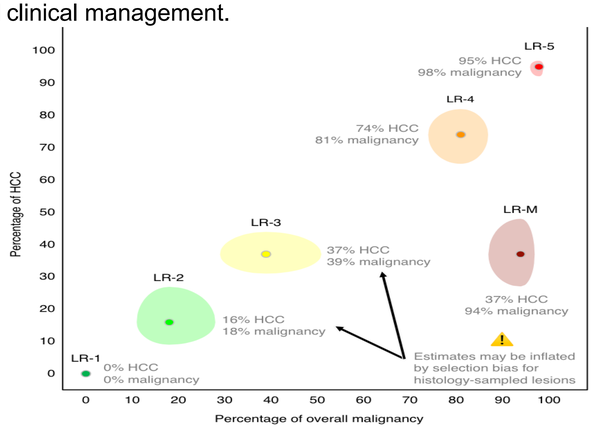
CT

The Liver Imaging Reporting and Data System (LI-RADS) is used to diagnosed HCC and categorizes liver observations from LR-1 (definitely benign) to LR-5 (definitely HCC). LR-3 indicates intermediate probability of HCC with a PPV of 38%, and LR-4 indicates probable HCC with a PPV of 74%.

Treating LR-5 observations can be straightforward, however, the management of intermediate LR-3 and LR-4 category observations is complicated by diagnostic uncertainty.

Currently, LI-RADS does not incorporate factors extrinsic to an individual liver observation, such as the presence of a concurrent LR-5 observation elsewhere in the liver. The ability to improve risk stratification for LR-3 and -4 observations as more or less likely to be HCC could help guide surveillance, diagnostic steps, and clinical management.

Percentage of HCC and malignancy associated with each LI-RADS category.



OBJECTIVES

To evaluate whether the presence of a concurrent LR-5 observation is associated with a difference in the probability that LR-3 or LR-4 observations represent HCC through an individual participant data (IPD) meta-analysis.

METHODS

We conducted a meta-analysis using a previously described individual participant database. The database is composed of observations from over 20 sites globally. Observations were categorized by CT/MRI for HCC using LI-RADS v2014/2017/2018.

We used a generalized linear mixed model to pool and model the IPD across studies simultaneously, to estimate positive predictive value of LR-3 and LR-4 observations without and with concurrent LR-5 for the diagnosis of HCC.

The risk of bias was assessed using a composite reference standard and Quality Assessment of Diagnostic Accuracy Studies 2.

RESULTS

Table 1. Concurrent and non-concurrent LR-3 observations.

	Concurrent LR-5	No concurrent LR-5
Observations	587	1373
Patients	405	604
*Female	74	138
*Male	312	438
Mean Age +/- SD	59.3 +/- 9.9	59.0 +/- 10.9
Number of HCC	196	417
% HCC	33.4%	30.4%

*Number of female and male participants does not add up to total participant counts because one included study did not report participant sex.

Table 2: PPV of LR-3 with and without concurrent LR-5

	Concurrent LR-5	No Concurrent LR-5
PPV (95% CI)	45.4% (22.3% - 70.7%)	37.1% (17.5% - 62.3%)
Tau^2	7.0	6.7
Between group p value: 0.63 (two-sided z-test)		

Table 3. LR-4 Observations with concurrent and non-concurrent LR-5 observations.

	Concurrent LR-5	No concurrent LR-5
Observations	264	367
Patients	191	256
*Female	30	48
*Male	143	190
Mean Age +/- SD	59.3 +/- 10.7	58.2 +/- 10.2
Number of HCC	212	243
% HCC	80.3%	66.2%

*Number of female and male participants does not add up to total participant counts because one included study did not report participant sex.

Table 4: PPV of LR-4 with and without concurrent LR-5

	Concurrent LR-5	No Concurrent LR-5
PPV (95% CI)	88.6% (71.1% - 96.1%)	69.5% (49.1% - 84.4%)
Tau^2	6.6	3.9
Between group p value: 0.08 (two-sided z-test)		

RESULTS

- The final cohort included a total of 2591 observations from 1456 patients (mean age 59 years, 1083 [74%] male), from 29 studies.
- Of the studies included, 3 reported CT data only, 19 reported MRI data only, and 7 reported both CT and MRI data.
- For LR-3 observations, the point estimate was not higher in the presence of a concurrent LR-5 vs without (45.4% vs 37.1%, p=0.63).
- For LR-4 observations, the point estimate for PPV was not higher in the presence of LR-5 vs. without (88.6% vs. 69.5%, p=0.08)

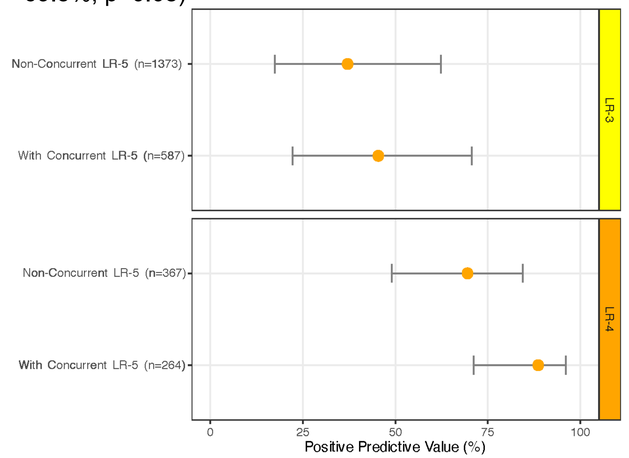


Figure 1. PPV for LR-3 observation (top) for LR-4 observation (bottom)

CONCLUSIONS

-This IPD meta-analysis found that concurrent LR-5 was not associated with differences in PPV for HCC in LR-3 (p=0.63) or LR-4 observations (p=0.08).

-Our results support the current LIRADS paradigm, wherein the presence of concurrent LR-5 should not change the categorization of LR-3 and LR-4 observations.

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