10.1148/radiol.2021211244

Table E1

Risk of Bias Assessment for 32 Included Studies Using the QUADAS-2 Tool which Consists of Four Domains

Study	Patient and observation selection	Index CT	Index MRI	Index CEUS	Reference standard	Flow and timing	Overall assessment	Applicability	Possible source of bias
Alhasan A 2019	Low	Low			Low	High	At risk	Low concern	Interval between index test and reference standard
Allen BC 2018	High		Low		Unclear	High	At risk	Low concern	Case-control design, unclear interval between index test and reference standard
An C 2017	High		Low		Low	High	At risk	Concerns	Limited to treated malignancies
Cerny M 2018	Low		Low		Low	High	At risk	Low concern	Interval between index test and reference standard
Chen J 2019	High		Unclear		Low	High	At risk	Concerns	Limited to treated HCC categorized LR-5
Chen LD 2018	Low			Low	Low	High	At risk	Low concern	Case-control design, limited to malignancies
Choi SH 2019	High		Unclear		Unclear	High	At risk	Low concern	Benign observations excluded, many methodology details unclear
Forner A 2019	Unclear		Unclear		Low	High	At risk	Low concern	Limited to biopsied lesions, many methodology details unclear
Fraum TJ 2018	High	Low	Low		Low	Low	At risk	Low concern	Limited to malignancies
Hu J 2020	Low		Low	Low	Low	Low	Low risk	Concerns	Technique deviates from LI-RADS
Jeon SK 2019	High		Low		Low	High	At risk	Low concern	Case-control design, limited to HCC and biphenotypic tumors
Jiang H 2019	Unclear		Low		High	High	At risk	Low concern	Almost exclusively resected observations
Joo I 2017	High	High	High		Low	High	At risk	Low concern	Limited to HCC, readers aware of final diagnosis
Kang HJ 2020	Low	Unclear	Unclear	High	Unclear	High	At risk	Low concern	Limited to large observations without arterial enhancement, suboptimal reference standard
Kang Z 2019	Unclear		High		High	Low	At risk	Concerns	MRI technique and suboptimal reference standard
Kierans AS 2018	Low		Low		Low	Low	Low risk	Low concern	None
Kim DH 2019	High		Low		Low	High	At risk	Concerns	Limited to resected observations that were almost exclusively malignant
Kim YY 2018	Low		Unclear		Low	Low	Low risk	Low concern	None
Kim YY 2019	High		Low		Low	High	At risk	Low concern	Case-control design, limited to malignancies
Lee HS 2019	High		Low		Low	High	At risk	Low concern	Case-control design, limited to HCC and biphenotypic tumors
Lewis S 2019	High		Low		Low	High	At risk	Concerns	Limited to malignancies, LI-RADS features identified after data collection
Lim K 2020	High		Low		Low	High	At risk	Low concern	Limited to LR-M and almost exclusively malignancies
Makoyeva A 2020	Low			Low	Low	Low	Low risk	Concerns	Technique deviates from LI-RADS

Mulazzani L 2019	Low			Unclear	Unclear	High	At risk	Concerns	Many methodology details unclear
Ronot M 2017	Low	Low	Low		Low	Low	Low risk	Low concern	None
Rosiak G 2018	High		Unclear		Low	High	At risk	Low concern	Limited to HCC, regenerative and dysplastic nodules
Seo N 2019	Low	High			Low	High	At risk	Concerns	Limited to explantation, nonperipheral washout identified after data collection
Song JS 2019	High		High		Unclear	High	At risk	Low concern	Limited to HCC
Stocker D 2020	Low		Low		Low	Low	Low risk	Low concern	None
Terzi E 2017	Unclear			Unclear	Unclear	High	At risk	Low concern	Many methodology details unclear
van der Pol CB 2021	Low		Low		Low	Low	Low risk	Low concern	None
Zhang L 2019	High		Low		Low	High	At risk	Low concern	Limited to resected HCC

Table E2

Aggregate Observation Counts for CT, MRI and Contrast-enhanced Ultrasound (CEUS)

	Observations with all five major features reported			Observations with all major features reported except threshold growth	
	CT	MRI	CEUS	CT	MRI
Total	176	711	853	994	2630
HCC					
No	70	335	278	410	689
Yes	106	376	575	584	1941
Size					
<10 mm	46	188	162	23	122
10–19 mm	70	235	307	497	1032
≥20 mm	60	288	384	474	1476
APHE					
No	61	166	189	179	533
Yes (CT/MRI); not rim/peripheral discontinuous globular (CEUS)	115	545	588	815	2097
Rim or peripheral discontinuous globular (CEUS)	/	/	76	/	/
Washout					
No (CT/MRI); no washout of any type (CEUS)	60	386	266	288	919
Yes (CT/MRI); late and mild washout (CEUS)	116	325	424	706	1711
Early (< 60s) washout (CEUS)	/	/	149		/
Marked washout (CEUS)	/	/	14		
Enhancing capsule					
No	160	461	/	741	1533
Yes	16	250	/	253	1097
Threshold growth					
No	141	629	/	/	/
Yes	35	82	/	/	/

Note.—APHE = arterial phase hyperenhancement.

Table E3

CT/MRI Major Features Univariable Analysis

Major feature	Observations with all five major features reported	Observations with all major features reported except threshold growth
	Odds ratio (95% CI)	Odds ratio (95% CI)
Nonrim APHE	6.2 (3.6–10.6)	5.0 (2.6–9.9)
Enhancing “capsule”	8.3 (4.8–14.2)	2.0 (1.1–3.5)
Nonperipheral “washout”	15.3 (9.2–25.2)	5.6 (3.3–9.7)
Size		
Size < 10 mm	0.2 (0.1–0.3)	0.1 (0.0–0.4)
Size ≥ 20 mm	4.6 (2.7–8.0)	2.2 (1.3–3.78)
Continuous	1.02 (0.9–1.1)	1.01 (0.98–1.04)
Binary: > 10 mm	15.4 (3.8–63.0)	14.6 (2.6–57.5)
Binary: > 15 mm	3.0 (1.8–5.2)	1.6 (1.2–7.5)
Binary: > 20 mm	2.5 (1.5–4.2)	3.9 (1.1–8.0)
Threshold growth	2.0 (1.05–4.0)	—

Note.—APHE = arterial phase hyperenhancement.

Table E4

Sensitivity Analysis Including Only Studies at Low Risk of Bias

Major Feature	Observations with or without threshold growth reported (*n* = 4434)	Low risk of bias studies-Observations with or without threshold growth reported (*n* = 1675)
	Odds ratio (95%CI)	Odds ratio (95%CI)
Nonrim APHE	10.3 (6.7–15.6)	15.4 (8.7–27.3)
Enhancing capsule	2.4 (1.7–3.5)	3.5 (2.0–6.0)
Nonperipheral washout	13.2 (9.0–19.2)	8.6 (4.8–15.2)
Size		
Size < 10 mm	0.1 (0.0–0.2)	0.0 (0.0–0.4)
Size ≥ 20 mm	1.6 (0.95–2.7)	1.3 (0.7–2.7)
< 10 mm: MRI[1]	1.2 (0.8–1.9)	3.3 (0.2–42.7)
10–19 mm: MRI	3.6 (1.04–12.4)	0.3 (0.2–0.6)
≥ 20 mm: MRI	3.1 (1.9–5.1)	3.6 (1.8–7.5)

Note.—APHE = arterial phase hyperenhancement.

[1]MRI and CT were compared for all major features and were only found to differ for size. The bottom rows list odds ratios for size cut-offs comparing MRI and CT, with CT as the reference.

Table E5

Contrast-enhanced Ultrasound (CEUS) Major Feature Univariable Analysis

Major feature	Odds ratio (95% CI)
APHE	
Not rim, not peripheral discontinuous globular	11.5 (2.1–62.2)
Rim or peripheral discontinuous globular	0.1 (0.0–0.4)
Nonperipheral “washout”	
Late and mild washout	9.2 (5.4–15.7)
Early (< 60s) washout	0.4 (0.2–0.6)
Marked washout	0.6 (0.2–2.0)
Size	
<10 mm	0.5 (0.3–0.7)
≥20 mm	2.2 (1.5–3.1)

Note.—APHE = arterial phase hyperenhancement.

Appendix E1. Reference Standard

For HCC, histopathology from core needle biopsy, hepatectomy, or explantation was favored. Otherwise, a composite reference standard was used. An observation was considered benign if it was stable on imaging for at least 12 months, or if it demonstrated either an unequivocal spontaneous size reduction of at least 30% diameter or disappearance in absence of treatment, not attributable to resorption of tumoral blood products. An observation was considered positive for HCC if it fulfilled LR-5 criteria on another imaging modality and showed threshold growth (≥ 50% size increase in less than 6 months); or was categorized LR-5 then underwent locoregional treatment and recurred on CT or MRI based on the LI-RADS treatment response criteria. All other malignancies required histopathology for confirmation. LR-3, LR-4 and LR-M observations with recurrence on CT or MRI after local treatment were considered malignant but not specifically HCC.

Appendix E2. Search Strategy

Database: Ovid MEDLINE(R) ALL <1946 to September 12, 2019>

Search Strategy:

#	Search Statement	Results
1	(LI-RADS or LIRADS).tw,kw,kf.	213
2	"liver imaging reporting and data system."tw,kw.	164
3	(LR-1 or LR-2 or LR-3 or LR-4 or LR-5 or LR-5 V or LR-OM or LR-TIV or LR-M or LR1 or LR2 or LR3 or LR4 or LR5 or LR5 V or LRTIV or LRM or LROM).tw.	1381
4	or/1–3	1535
5	Radiology Information Systems/	5601
6	Carcinoma, Hepatocellular/or Cholangiocarcinoma/	87260
7	(hepatocellular carcinoma* or hepatocellular neoplasm* or hepatocellular cancer or hepatic cell carcinoma* or HCC or cholangiocarcinoma* or hepatic nodule* or liver lesion* or adrenocortical carcinoma*).tw,kw,kf.	106476
8	Liver Neoplasms/dg	14552
9	exp Liver Diseases/dg or liver disease*.tw,kw,kf.	125220
10	Liver/dg [Diagnostic Imaging]	14373
11	liver imaging.tw,kw.	948
12	or/6–11	244663
13	5 and 12	63
14	4 or 13	1570
15	Tomography, X-Ray Computed/	366371
16	(computed tomograph* or CT).tw,kw.	465130
17	Magnetic Resonance Imaging/	382106
18	(mri or magnetic resonance or MDCT).tw,kw,kf.	459570
19	Ultrasonography, Doppler, Color/	13621
20	(CEUS or contrast enhanced ultrasound).tw,kw.	4247
21	or/15–20	1131135
22	14 and 21	286
23	limit 22 to yr = "2014-Current"	234

Database: Embase Classic+Embase <1947 to 2019 September 12>

Search Strategy:

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1 (LI-RADS or LIRADS).tw. (296)

2 "Liver Imaging Reporting and Data System".af. (230)

3 (LR-1 or LR-2 or LR-3 or LR-4 or LR-5 or LR-5V or LR-OM or LR-TIV or LR-M or LR1 or LR2 or LR3 or LR4 or LR5 or LR5V or LRTIV or LRM or LROM).tw. (2063)

4 or/1-3 (2277)

5 computer assisted tomography/(703333)

6 (computed tomograph* or ct).tw. (714930)

7 nuclear magnetic resonance imaging/(745564)

8 (MRI or magnetic resonance or mr imaging or MDCT).tw. (679741)

9 contrast-enhanced ultrasound/(3100)

10 (CEUS or contrast enhanced ultrasound).tw. (6818)

11 or/5-10 (1788445)

12 4 and 11 (426)

13 limit 12 to yr="2014 -Current" (352)

Database: EBM Reviews - Cochrane Central Register of Controlled Trials <August 2019>

Search Strategy:

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1 (LI-RADS or LIRADS).tw,kw (5).

2 "liver imaging reporting and data system".tw,kw (4).

3 (LR-1 or LR-2 or LR-3 or LR-4 or LR-5 or LR-5V or LR-OM or LR-TIV or LR-M or LR1 or LR2 or LR3 or LR4 or LR5 or LR5V or LRTIV or LRM or LROM).tw. (392)

4 or/1-3 (396)

5 Radiology Information Systems/ (25)

6 Carcinoma, Hepatocellular/or Cholangiocarcinoma/(1718)

7 (hepatocellular carcinoma* or hepatocellular neoplasm* or hepatocellular cancer or hepatic cell carcinoma* or HCC or cholangiocarcinoma* or hepatic nodule* or liver lesion* or adrenocortical carcinoma*).tw,kw. (5710)

8 Liver Neoplasms/(2229)

9 exp Liver Diseases/or liver disease*.tw,kw. (19094)

10 Liver/(2960)

11 liver imaging.tw,kw (51).

12 or/6-11 (24377)

13 5 and 12 (1)

14 4 or 13 (397)

15 Tomography, X-Ray Computed/(4051)

16 (computed tomograph* or CT).tw. (29214)

17 Magnetic Resonance Imaging/(6879)

18 (mri or magnetic resonance or MDCT).tw. (28896)

19 Ultrasonography, Doppler, Color/(440)

20 (CEUS or contrast enhanced ultrasound).tw. (280)

21 or/15-20 (56293)

22 14 and 21 (31)

23 limit 22 to yr="2014 -Current" (24)

SCOPUS

((TITLE-ABS-KEY **(***li-rads* OR *lirads***))** OR **(**TITLE-ABS-KEY **(***"liver imaging reporting and data system"***))** OR **(**TITLE-ABS-KEY **(***lr-1* OR *lr-2* OR *lr-3* OR *lr-4* OR *lr-5* OR *lr-5v* OR *lr-om* OR *lr-tiv* OR *lr-m* OR *lr1* OR *lr2* OR *lr3* OR *lr4* OR *lr5* OR *lr5v* OR *lrtiv* OR *lrm* OR *lrom***)))** AND **((**TITLE-ABS-KEY **(***"computed tomograph**" OR *ct***))** OR **(**TITLE-ABS-KEY **(***mri* OR *magnetic* AND *resonance* OR *mdct***))** OR **(**TITLE-ABS-KEY **(***ceus* OR *contrast* AND *enhanced* AND *ultrasound***)))** AND **(**LIMIT-TO **(**PUBYEAR, *2019***)** OR LIMIT-TO **(**PUBYEAR, *2018***)** OR LIMIT-TO **(**PUBYEAR, *2017***)** OR LIMIT-TO **(**PUBYEAR, *2016***)** OR LIMIT-TO **(**PUBYEAR, *2015***)** OR LIMIT-TO **(**PUBYEAR, *2014***))** = **255**

Appendix E3. Outreach Letter to Corresponding Authors

Dear Dr. *XXXX*,

We need your help as a collaborator on our individual patient data (IPD) meta-analysis of the accuracy of LI-RADS for diagnosing hepatocellular carcinoma. On behalf of the Liver Imaging Reporting and Data System (LI-RADS) Steering Committee and Research Working Group, we would like to invite you as a co-author.

We previously completed a study-level systematic review exploring the diagnostic accuracy of LI-RADS:

• van der Pol CB, Lim CS, Sirlin CB, et al. Accuracy of the Liver Imaging Reporting and Data System in Computed Tomography and Magnetic Resonance Image Analysis of Hepatocellular Carcinoma or Overall Malignancy-A Systematic Review. Gastroenterology. 2019;156(4):976-86.

Several important questions remain that we believe can be addressed using IPD meta-analysis. This study design is seen as the standard for evidence in many fields and tends to be published in high-impact journals. Your study poster titled *XXXXXXX* has been identified for possible inclusion.

We have attached our current study protocol along with a detailed invitation letter for your interest.

We would be happy to contact you at your convenience to discuss this study in more detail if that would be helpful. We hope that you will join us on this important project.

Regards,

Jean-Paul Salameh, MSc

Research Associate,

Ottawa Hospital Research Institute

Email: Jsalameh@toh.ca

Appendix E4. Data Contribution Agreement Letter

Dear Dr. *XXXX*,

Thank you for agreeing to contribute your dataset to the Liver Imaging Reporting and Data System (LI-RADS) individual patient data (IPD) Systematic Review and Meta-Analysis Project. By accruing a large number of original datasets, including yours, and conducting IPD meta-analyses to explore factors that impact the diagnostic accuracy of LI-RADS on CT, MRI, and CEUS, we will be able to move research in this area forward substantially. On behalf of the LI-RADS IPD Systematic Review and Meta-Analysis Project Steering Committee, we want to express our gratitude to you for your contribution to this endeavor. Your contribution of data, as well as manuscript editing and final approval will qualify you for co-authorship on this project.

The transfer of data (anonymized) for use in our IPD meta-analysis has been approved by the Research Ethics Board at the Ottawa Hospital Research Institute (Protocol ID#: 20190664-01H).

We will use the IPD dataset for an initial meta-analysis. It may also be possible to conduct additional meta-analyses with the dataset. Access to data for this purpose will be open to Steering Committee members and to investigators who have contributed data. Permission to use LI-RADS IPD data will be granted for specific IPD meta-analyses, not for use of the dataset generally, and will be granted for a 12-month period. Once permission to conduct a proposed IPD meta-analysis is obtained from the Project Steering Committee, investigators will need to submit proof of registration via Prospero (http://www.crd.york.ac.uk/prospero) or another publicly accessible registry prior to the release of data.

Investigators who contribute data to any IPD meta-analysis will be invited to be authors of the meta-analyses that include their primary study data. Once investigators complete an IPD meta-analysis with LI-RADS IPD data and have prepared a manuscript for submission to a journal for possible publication, the manuscript must be submitted to the LI-RADS IPD Systematic Review and Meta-Analysis Steering Committee to circulate among all potential authors. Potential authors will be required to provide any comments and edits and to confirm authorship within 14 days of initial distribution of the manuscript to be included as authors.

Please sign this letter below, above your name and return a copy of a PDF of the signed letter. By signing, you will be indicating that you are aware of the LI-RADS IPD Systematic Review and Meta-Analysis Project objectives and your rights and responsibilities as a contributing investigator and member of the LI-RADS IPD Systematic Review and Meta-Analysis Project Group. You also confirm that in your original study, all participants provided informed consent or the need to obtain informed consent was waived, and that ethics approval was obtained.

We very much look forward to working with you. Please do not hesitate to contact us at any point, now or in the future, if you have questions or concerns related to the Project.

Sincerely,

Jean-Paul Salameh, MSc

Research Associate,

Ottawa Hospital Research Institute

Email: Jsalameh@toh.ca

Appendix E5. Data Extraction Sheet

Demographic

DATASET_ID:																						
OBSPRI	PATPRI	AGE	GENDER	COUNTRY	LIRADS_CAT	LIRADS_ASSIGN	REF	MAX_DIAM	CIRRHOSIS_HISTORY	CHRONIC_HBV	CUR_PRI_HCC	CHILD-PUGH_CLASS	TUMOR_LOCATION	FINAL_DIAG	HISTOLOGICAL_DIFF	SERUM_AFP	SERUM_AFPL3%	SERUM_DCP	SERUM_CEA	SERUM_CA19–9	UNIT_CA19–9	LIRADS_VERSION	IMAGING_MODALITY

Technical

DATASET_ID:									
OBSPRI	PATPRI	CT_DELAYED_PHASE	CT_UNEHNACED_PHASE	CT_DETECT	CT_CONT	MRI_AGENT	MRI_CONT	MRI_AMOUNT	MRI_DIL	FIELD_STRENGTH

LI-RADS Major Features

DATASET_ID:																	
				MRI LIRADS MAJOR FEATURES						CT LIRADS MAJOR FEATURES				CEUS LIRADS MAJOR FEATURES			
OBSPRI	PATPRI	MRI_SIZE	MRI_APHE	MRI_NONPER_WASHOUT	MRI_ENHAN_CAPSULE	MRITHRESHOLDV14	MRITHRESHOLDV18	CT_SIZE	CT_APHE	CT_NONPER_WASHOUT	CT_ENHAN_CAPSULE	CTTHRESHOLDV14	CTTHRESHOLD18	CEUS_SIZE	CEUS_APHE	CEUS_WASHOUT	

LI-RADS LR-M | LI-RADS TIV Features

				CT/MRI																			
								Targetoid Features (apply even if observation meets LR-5 criteria)				Nontargetoid Features (apply only if observation does not meet LR-5 criteria)				LR-TIV Feature (apply even if observation meets LR-5 criteria or if there is no parenchymal mass)				CEUS LR-M			
OBSPRI	PATPRI	MRI_RAPHE	MRI_PER_WASHOUT	MRI_DELAY_ENHAN	MRI_TAR_REST	MRI_TAR_APP	CT_RAPHE	CT_PER_WASHOUT	CT_DELAY_ENHAN	CT_TAR_REST	CT_TAR_APP	MRI_REST	MRI_NEC	MRI_APP	MRI_OTHER	CT_REST	CT_NEC	CT_APP	CT_OTHER	MRI_TIV	CT_TIV	US_RIM_APHE	US_PER_WASHOUT

Ancillary Features

					CT/MRI								CEUS												
OBSPRI	PATPRI	US_VISIBILITY	SUB_GROWTH	RESTRICT_DIFF	MILDT2_HYPERINT	COR_ENH	FAT_SPAR	IRON_SPAR	TRANS_HYPO	HEPA_HYPO	NON_CAP	NOD_NOD	MOS_ARCH	BLOOD_PROD	FAT_MASS	SIZE_STAB	SIZE_RED	PARA_POOL	UNDIS_VESS	IRON_MASS	MARKEDT2_HYPER	HEPA_ISO	USDEF_GROWTH	USNOD-NOD	USMOS_ARCH	USSIZE_STAB	USSIZE_RED

Appendix E6. Data Dictionary

Please code any data that has not been collected (not available) with "NA" for any of the variables below.

If you have any questions, feel free to contact Jean-Paul Salameh (jsalameh@ohri.ca) at any time.

Demographic

Variable	Definition	Values
DATASET_ID	Dataset identifier assigned to dataset by Registry team to each dataset	00001, 00002, 00003…
OBSVPRI	Primary observation identifier used in primary database	As recorded in primary database
PATPRI	Primary patient identifier used in primary database	As recorded in primary database
AGE	Patient's age, measured continuously	As recorded in primary database
GENDER	Patient's gender	0 = Female 1 = Male
COUNTRY	Country where patient was recruited.	As recorded in primary database
LIRADS_CAT	LI-RADS category	0 = NC 1 = 1 2 = 2 3 = 3 4 = 4 5 = 5 6 = M 7 = TIV
LIRADS_ASSIGN	How was LI-RADS category assigned	0 = Prospective clinical radiology report 1 = Retrospective research read of clinical examination 2 = Other (specify)
REF	What was the reference standard	0 = Biopsy 1 = Resection pathology 2 = Explant pathology 3 = Other (specify)
MAX_DIAM	Maximum diameter of the observation (mm)	As recorded in primary database
CIRRHOSIS_HISTORY	Patient's History of Cirrhosis	0 = No History 1 = History of Cirrhosis
CHRONIC_HBV	Patient's History of chronic hepatitis B	0 = No History 1 = History of HBV
CUR_PRI_HCC	Current or prior HCC	0 = No History of HCC 1 = Prior HCC 2 = Current HCC
CHILD-PUGH_CLASS	Child–Pugh Classification	0 = None 1 = A 2 = B 3 = C 4 = Not known
TUMOR_LOCATION	Segment location of largest observation	1 to 8
FINAL_DIAG	Final diagnosis	0 = None 1 = HCC 2 = Non-HCC malignancy (specify) 3 = Benign 4 = Other (specify)
HISTOLOGICAL_DIFF	Histologic differentiation	0 = Not applicable (not a tumor) 1 = Very well 2 = Well 3 = Moderately 4 = Poorly
SERUM_AFP	Serum AFP levels	As recorded in primary database
SERUM_AFPL3%	Serum AFP L3% levels	As recorded in primary database

SERUM_DCP	Serum DCP levels	As recorded in primary database
SERUM_CEA	Serum CEA levels	As recorded in primary database
SERUM_CA19–9	Serum CA19–9 levels	As recorded in primary database
Unit_CA19–9	Units used for Serum CA19–9 levels	As recorded in primary database
LIRADS_VERSION	Version of LI-RADS used	1 = CT/MR v2018 2 = CT/MR v2017 3 = CT/MR v2014 4 = CT/MR v2013 5 = CEUS v2017 6 = CEUS v2016
IMAGING_MODALITY	Imaging Modality used	1 = CT 2 = MRI 3 = CT + MRI 4 = CEUS

Technical Parameters

Variable	Definition	Values
DATASET_ID	Dataset identifier assigned to dataset by Registry team to each dataset	00001, 00002, 00003…
OBSVPRI	Primary observation identifier used in primary database	As recorded in primary database
PATPRI	Primary patient identifier used in primary database	As recorded in primary database
CT_DELAYED_PHASE	Use of a delayed phase on CT	0 = without 3-minute delayed phase 1 = > 3-minute delayed phase
CT_UNENHANCED_PHASE	Use of unenhanced phase on CT	0 = without unenhanced phase 1 = with unenhanced phase
CT_DETECT	Number of detectors on CT	As recorded in primary database
CT_CONT	CT contrast generic name	As recorded in primary database
MRI_AGENT	Type of agent used	0 = use of extracellular agent 1 = gadobenate without HBP 2 = gadobenate with HBP 3 = gadoxetate disodium
MRI_CONT	MRI contrast generic name	As recorded in primary database
MRI_AMOUNT	Amount administered of contrast agent	As recorded in primary database
MRI_DIL	Dilution of contrast agent	0 = Not diluted 1 = Diluted
FIELD_STRENGTH	MRI field strength	0 = 1.5 T 1 = 3.0 T

LI-RADS Major Features

Variable	Definition	Values
DATASET_ID	Dataset identifier assigned to dataset by Registry team to each dataset	00001, 00002, 00003…
OBSPRI	Primary observation identifier used in primary database	As recorded in primary database
PATPRI	Primary patient identifier used in primary database	As recorded in primary database
MRI_SIZE	MRI Size (mm)	0 = <10 mm 1 = 10–19 mm 2 = ≥20 mm
MRI_APHE	MRI nonrim Arterial phase hyperenhancement (APHE)	0 = No 1 = Yes
MRI_NONPER_WASHOUT	MRI Nonperipheral “washout”	0 = No 1 = Yes
MRI_ENHAN_CAPSULE	MRI Enhancing “capsule”	0 = No 1 = Yes
MRTHRESHOLDV14	MRI Threshold growth LIRADS v2014–2017	0 = No 1 = Yes
MRTHRESHOLDV18	MRI Threshold growth LIRADS v2018	0 = No 1 = Yes
CT_SIZE	CT Size (mm)	0 = <10 mm 1 = 10–19 mm

		2 = ≥20 mm
CT_APHE	CT nonrim Arterial phase hyperenhancement (APHE)	0 = No 1 = Yes
CT_NONPER_WASHOUT	CT Nonperipheral “washout”	0 = No 1 = Yes
CT_ENHAN_CAPSULE	CT Enhancing “capsule”	0 = No 1 = Yes
CTTHRESHOLDV14	CT Threshold growth LIRADS v2014–2017	0 = No 1 = Yes
CTTHRESHOLDV18	CT Threshold growth LIRADS v2018	0 = No 1 = Yes
US_SIZE	CEUS Size (mm)	0 = <10 mm 1 = 10–19 mm 2 = ≥20 mm
US_APHE	CEUS Arterial phase hyperenhancement (APHE, not rim, not peripheral discontinuous)	0 = No 1 = not rim/not peripheral discontinuous globular 2 = rim or peripheral discontinuous globular
US_WASHOUT	CEUS Nonperipheral “washout”	0 = no washout of any type 1 = late and mild washout 2 = early (< 60s) washout 3 = marked washout

LI-RADS LR-M and LR-TIV Features

Variable	Definition	Values
DATASET_ID	Dataset identifier assigned to dataset by Registry team to each dataset	00001, 00002, 00003…
OBSPRI	Primary observation identifier used in primary database	As recorded in primary database
PATPRI	Primary patient identifier used in primary database	As recorded in primary database
Targetoid Features (apply even if observation meets LR-5 criteria)		
MRI_RAPHE	MRI rim Arterial phase hyperenhancement (APHE)	0 = No 1 = Yes
MRI_PER_WASHOUT	MRI peripheral “washout”	0 = No 1 = Yes
MRI_DELAY_ENHAN	MRI Delayed central enhancement	0 = No 1 = Yes
MRI_TAR_REST	MRI Targetoid restriction	0 = No 1 = Yes
MRI_TAR_APP	MRI Targetoid TP or HBP appearance	0 = No 1 = Yes
CT_RAPHE	CT rim Arterial phase hyperenhancement (APHE)	0 = No 1 = Yes
CT_PER_WASHOUT	CT peripheral “washout”	0 = No 1 = Yes
CT_DELAY_ENHAN	CT Delayed central enhancement	0 = No 1 = Yes
CT_TAR_REST	CT Targetoid restriction	0 = No 1 = Yes
CT_TAR_APP	CT Targetoid TP or HBP appearance	0 = No 1 = Yes
Nontargetoid Features (apply only if observation does not meet LR-5 criteria)		
MRI_REST	MRI Marked restriction	0 = No 1 = Yes
MRI_NEC	MRI Necrosis	0 = No 1 = Yes
MRI_APP	MRI Infiltrative appearance	0 = No 1 = Yes
MRI_OTHER	MRI Other	0 = No 1 = Yes
CT_REST	CT Marked restriction	0 = No 1 = Yes
CT_NEC	CT Necrosis	0 = No 1 = Yes
CT_APP	CT Infiltrative appearance	0 = No 1 = Yes

CT_OTHER	CT Other	0 = No 1 = Yes
LR-TIV Feature (apply even if observation meets LR-5 criteria or if there is no parenchymal mass)		
MRI_TIV	MRI Enhancing tissue in vein	0 = No 1 = Yes
CT_TIV	CT Enhancing tissue in vein	0 = No 1 = Yes
CEUS LI-RADS LR-M Features		
US_RIM_APHE	CEUS rim Arterial phase hyperenhancement (APHE)	0 = No 1 = Yes
US_PER_WASHOUT	CEUS “washout”	0 = no washout of any type 1 = late and mild washout 2 = early (< 60s) washout 3 = marked washout

LI-RADS Ancillary Features

Variable	Definition	Values
DATASET_ID	Dataset identifier assigned to dataset by Registry team to each dataset	00001, 00002, 00003…
OBSVPRI	Primary observation identifier used in primary database	As recorded in primary database
PATPRI	Primary patient identifier used in primary database	As recorded in primary database
US_VISIBILITY	US visibility as discrete nodule	0 = Absent 1 = Present
SUB_GROWTH	Subthreshold growth	0 = Absent 1 = Present
RESTRICT_DIFF	Restricted diffusion	0 = Absent 1 = Present
MILDT2_HYPERINT	Mild-moderate T2 hyperintensity	0 = Absent 1 = Present
COR_ENH	Corona enhancement	0 = Absent 1 = Present
FAT_SPAR	Fat sparing in solid mass	0 = Absent 1 = Present
IRON_SPAR	Iron sparing in solid mass	0 = Absent 1 = Present
TRANS_HYPO	Transitional phase hypointensity	0 = Absent 1 = Present
HEPA_HYPO	Hepatobiliary phase hypointensity	0 = Absent 1 = Present
NON_CAP	Nonenhancing “capsule”	0 = Absent 1 = Present
NOD_NOD	Nodule-in-nodule	0 = Absent 1 = Present
MOS_ARCH	Mosaic architecture	0 = Absent 1 = Present
BLOOD_PROD	Blood products in mass	0 = Absent 1 = Present
FAT_MASS	Fat in mass, more than adjacent liver	0 = Absent 1 = Present
SIZE_STAB	Size stability > 2 years	0 = Absent 1 = Present
SIZE_RED	Size reduction	0 = Absent 1 = Present
PARA_POOL	Parallels blood pool	0 = Absent 1 = Present
UNDIS_VESS	Undistorted vessels	0 = Absent 1 = Present
IRON_MASS	Iron in mass, more than liver	0 = Absent 1 = Present
MARKEDT2_HYPER	Marked T2 hyperintensity	0 = Absent 1 = Present
HEPA_ISO	Hepatobiliary phase iso-intensity	0 = Absent 1 = Present
USDEF_GROWTH	Definite growth	0 = Absent

		1 = Present
USNOD-NOD	Nodule-in-nodule architecture	0 = Absent 1 = Present
USMOS_ARCH	Mosaic architecture	0 = Absent 1 = Present
USSIZE_STAB	CEUS Size stability ≥ 2 years	0 = Absent 1 = Present
USSIZE_RED	CEUS Size reduction	0 = Absent 1 = Present

Appendix E7. Frequently Asked Questions

FAQs Page

(1) Obtaining ethics approval to share data: The transfer of anonymized data for use in our IPD meta-analysis has been approved by the Research Ethics Board at the Ottawa Hospital Research Institute (Protocol ID#: 20190664-01H).

(2) Exporting data: Each contributing author will receive an empty Excel spreadsheet to be filled with the respective individual patient data alongside a list summarizing the variables of interest and a data dictionary detailing the coding of the requested data. If you have data in a different format, you can provide it to us, and we can re-code it if necessary.

(3) Data Management and Access: We understand that data security is important, as is the assurance that data will be used appropriately to a good end. We have described in detail in the LI-RADS data sharing guide that will be followed to ensure both that data is secure and that it is used in a way that will produce useful results that inform patient care.

(4) Authorship: Articles from the LI-RADS IPD Registry will be submitted for publication in peer-reviewed journals. Authorship will be based on current ICMJE guidelines (http://www.icmje.org/recommendations/browse/roles-and-responsibilities/defining-the-role-of-authors-and-contributors.html). Investigators who provide data to the registry will be invited to be authors of the meta-analyses that include their primary study data.

Appendix E8. Customized Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) Tool

Study
Patient and observation selection
Risk of bias
Describe methods of patient and observation selection
Was a consecutive sample of patients, random sample of patients, or all patients over a given time period enrolled?
Was a case-control design avoided?
Did the study avoid inappropriate exclusions? (eg, If a non-pathology-based reference standard was used, might it have inappropriately excluded observations?)
Was it clear when more than one observation arose from the same patient?
Could the selection of patients have introduced bias? (Low = “yes” to all, otherwise refer to phase 2)
Could the selection of observations have introduced bias? (Low = “yes” to all, otherwise refer to phase 2)
Concerns regarding applicability
Describe included patients and included observations (prior testing, presentation, intended use of multiphase CT/MRI and setting):
Is there concern that the included patients do not match the review question?
Is there concern that the included observations do not match the review question?

Index test
CT risk of bias
Describe how multiphase contrast-enhanced CT was conducted and interpreted
Were the multiphase CT results interpreted without knowledge of the results of the reference standard?
Were the multiphase CT results unlikely to be biased by findings on other imaging examinations?
Was a delayed phase consistently used? (delayed between 3–5 mins has increased sensitivity for washout)
Was the index test interpreted by more than one radiologist and were discrepancies resolved in an objective way?
Could the conduct or interpretation of the multiphase CT have introduced bias? (Low = “yes” to all, otherwise refer to phase 2)
CT concerns regarding applicability
Is there concern that the multiphase CT, its conduct, or interpretation differ from the review question?
MRI risk of bias
Describe how multiphase contrast-enhanced MRI was conducted and interpreted
Were the MRI results interpreted without knowledge of the results of the reference standard?
Were the MRI results unlikely to be biased by findings on other imaging examinations?
Was the index test interpreted by more than one radiologist and were discrepancies resolved in an objective way?
Could the conduct or interpretation of the MRI have introduced bias? (Low = “yes” to all, otherwise refer to phase 2)
MRI concerns regarding applicability
Is there concern that the MRI, its conduct, or interpretation differ from the review question?
CEUS risk of bias
Describe how contrast-enhanced US (CEUS) was conducted and interpreted
Were the CEUS results interpreted without knowledge of the results of the reference standard?
Were the CEUS results unlikely to be biased by findings on other imaging examinations?
Did CEUS technical parameters meet the minimum standard in LI-RADS?
Was the index test interpreted by more than one radiologist and were discrepancies resolved in an objective way?
Could the conduct or interpretation of the CEUS have introduced bias? (Low = “yes” to all, otherwise refer to phase 2)
CEUS concerns regarding applicability
Is there concern that the CEUS, its conduct, or interpretation differ from the review question?
Reference standard
Risk of bias
Describe the reference standard and how it was conducted and interpreted
Is the reference standard likely to correctly classify the target condition at the observation level (particularly non-pathology-based reference standards and also explant reference standards–was the method of lesion matching described and likely to be robust)?
Were the reference standard results interpreted without knowledge of the results of the CT, MRI or CEUS?
Could the reference standard, its conduct or interpretation have introduced bias? (Low = “yes” to all, otherwise refer to phase 2)
Concerns regarding applicability
Is there concern that the target condition as defined by the reference standard does not match the review question?
Flow and timing
Risk of bias
Describe any patients who did not receive multiphase CT, MRI, CEUS, and/or reference standard, or who were excluded from the 2 × 2 table (refer to flow diagram)
Describe the time interval and any interventions between multiphase CT, MRI, CEUS and reference standard
Describe any observations within included patients who were excluded from the 2 × 2 table
Was there an appropriate interval between multiphase CT, MRI or CEUS and reference standard?
Did all patients and observations receive a reference standard?
Did patients and observations receive the same reference standard?
Were all patients and observations included in the analysis?
Is there unlikely to be a selection bias from selection of patients only with liver explantation?
Is there unlikely to be verification bias from tissue sampling of only a subset of observations?

Is there unlikely to be incorporation bias for studies including LI-RADS 5 as a reference standard?
Could the patient and observation flow have introduced bias? (Low = “yes” to all, otherwise refer to phase 2)
Overall assessment
Risk of bias
Explanation:
Concerns regarding applicability
Explanation:

Appendix E9. IPD Statistical Analysis Technique

First, each variable was evaluated independently using a univariable approach for CT/MRI and for CEUS, separately (6). Analyses were repeated on different sets of observations, depending on whether the threshold growth variable was reported in the included studies as this major feature was infrequently reported compared to the other major features. The size variable was evaluated as a categorical, as a binary variable at different thresholds (10 mm, 15 mm, 20 mm) and as a continuous variable. Imaging modality (CT vs MRI) was included as a variable and was assessed in the multivariable model as an interaction term with all major features. Using a binomial generalized linear mixed model approach, a bidirectional elimination stepwise regression was performed to optimize the Akaike Information Criterion (AIC) without causing overdispersion. The size variable was considered for inclusion in the multivariable model as a continuous variable and as a categorical variable in separate analyses. The AICs for the different models with the size variables were compared and the final model was selected based on the optimal AIC and most clinically meaningful size variable contribution.

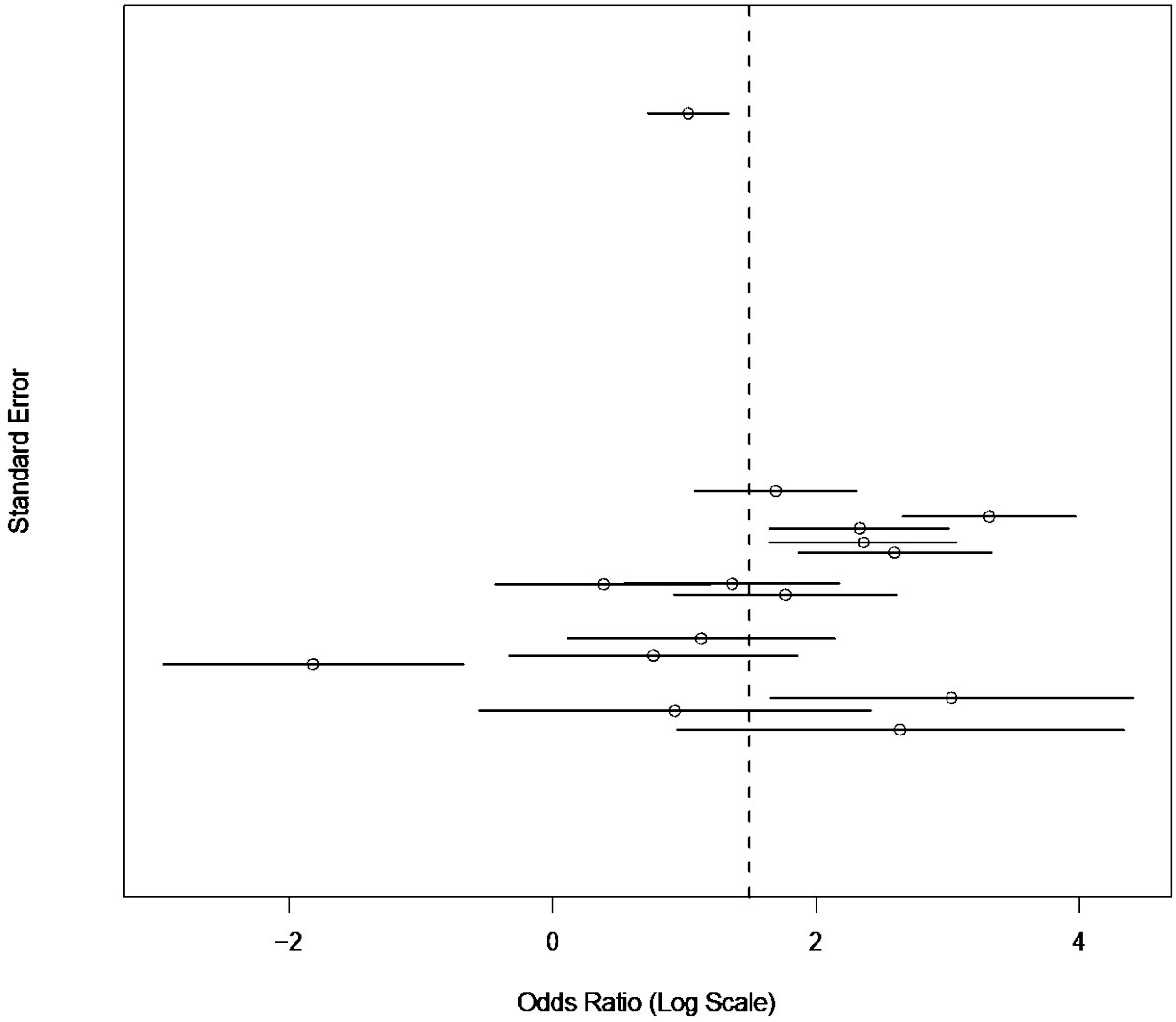
Appendix E10. List of Invited Studies that Did Not Respond

Author	Title
W. Liu, J. Qin, R. Guo, S. Xie, H. Jiang, X. Wang, Z. Kang, J. Wang, H. Shan	Accuracy of the diagnostic evaluation of hepatocellular carcinoma with LI-RADS
D. I. Cha, K. M. Jang, S. H. Kim, T. W. Kang, K. D. Song	Liver Imaging Reporting and Data System on CT and gadoxetic acid-enhanced MRI with diffusion-weighted imaging
S. H. Choi, S. S. Lee, S. Y. Kim, S. H. Park, S. H. Park, K. M. Kim, S. M. Hong, E. Yu, M. G. Lee	Intrahepatic cholangiocarcinoma in patients with cirrhosis: Differentiation from hepatocellular carcinoma by using gadoxetic acid-enhanced MRI and dynamic CT
S. H. Choi, J. H. Byun, S. Y. Kim, S. J. Lee, H. J. Won, Y. M. Shin, P. N. Kim	Liver Imaging Reporting and Data System v2014 with Gadoxetate Disodium-Enhanced Magnetic Resonance Imaging: Validation of LI-RADS Category 4 and 5 Criteria
T. A. Potretzke, B. R. Tan, M. B. Doyle, E. M. Brunt, J. P. Heiken, K. J. Fowler	Imaging features of biphenotypic primary liver carcinoma (hepatocholangiocarcinoma) and the potential to mimic hepatocellular carcinoma: LI-RADS analysis of CT and MRI features in 61 cases
S. M. Lee, J. M. Lee, S. J. Ahn, H. J. Kang, H. K. Yang, J. H. Yoon	LI-RADS version 2017 versus version 2018: Diagnosis of hepatocellular carcinoma on gadoxetate disodium-enhanced MRI
F. Xing, J. Lu, T. Zhang, X. Miao, X. Zhang, J. Jiang	Category modifications and prognosis of cirrhotic nodules depending on MRI imaging report and data system of LR-2, LR-3 and LR-4
S. H. Choi, S. S. Lee, S. H. Park, K. M. Kim, E. Yu, Y. Park, Y. M. Shin, M. G. sLee	LI-RADS Classification and Prognosis of Primary Liver Cancers at Gadoxetic Acid-enhanced MRI
M. Zulfiqar, T. Fraum, R. Tsai, D. R. Ludwig, E. Rohe, J. P. Heiken, K. J. Fowler	LI-RADS v2014 false positives: description of nonhcc lesions misclassified as LR-5 or LR-5 V
S. E. Lee, C. An, S. H. Hwang, J. Y. Choi, K. Han, M. J. Kim	Extracellular contrast agent-enhanced MRI: 15-min delayed phase may improve the diagnostic performance for hepatocellular carcinoma in patients with chronic liver disease

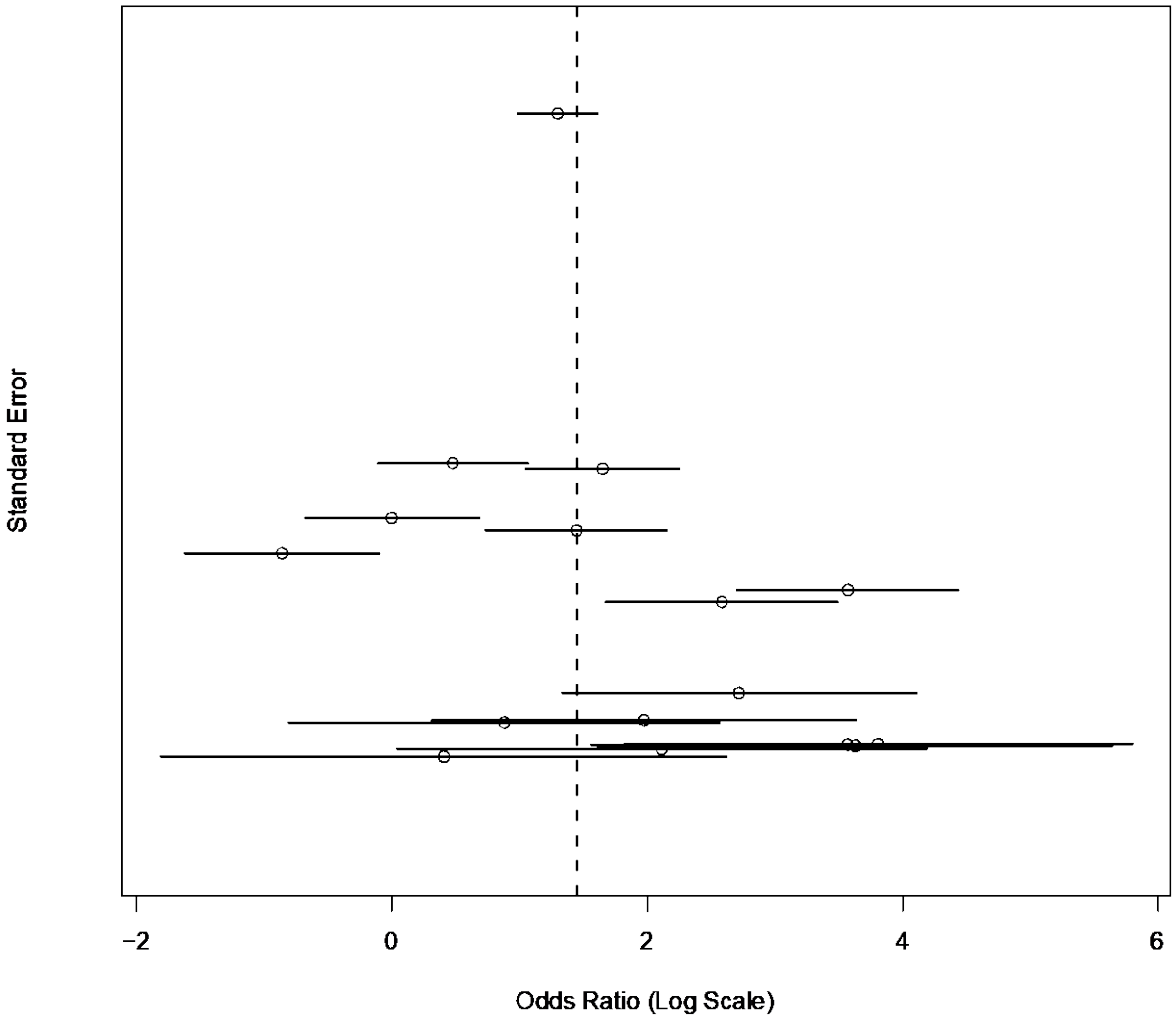
W. Ling, M. Wang, X. Ma, T. Qiu, J. Li, Q. Lu, Y. Luo	The preliminary application of liver imaging reporting and data system (LI-RADS) with contrast-enhanced ultrasound (CEUS) on small hepatic nodules (< = 2 cm)
S. H. Choi, J. H. Byun, Y. S. Lim, S. J. Lee, S. Y. Kim, H. J. Won, Y. M. Shin, P. N. Kim	Liver Imaging Reporting and Data System: Patient outcomes for category 4 and 5 nodules
C. An, H. Rhee, K. Han, J. Y. Choi, Y. N. Park, M. S. Park, M. J. Kim, S. Park	Added value of smooth hypointense rim in the hepatobiliary phase of gadoxetic acid-enhanced MRI in identifying tumor capsule and diagnosing hepatocellular carcinoma
N. Chen, U. Motosugi, H. Morisaka, S. Ichikawa, K. Sano, T. Ichikawa, M. Matsuda, H. Fujii, H. Onishi	Added Value of a Gadoxetic Acid-enhanced Hepatocyte-phase Image to the LI-RADS System for Diagnosing Hepatocellular Carcinoma
W. Zhao, W. Li, X. Yi, Y. Pei, L. Zhang, H. Liu	Diagnostic value of liver imaging reporting and data system MRI on primary hepatocellular carcinoma
J. H. Kang, S. H. Choi, J. H. Byun, D. H. Kim, S. J. Lee, S. Y. Kim, H. J. Won, Y. M. Shin, P. N. Kim	Ancillary features in the Liver Imaging Reporting and Data System: how to improve diagnosis of hepatocellular carcinoma ≤ 3 cm on magnetic resonance imaging
A. M. Stepan, M. Danila, R. Sirli, A. Popescu, T. Moga, C. Ivascu, C. Pienar, I. Sporea	Diagnostic accuracy of contrast-enhanced ultrasound algorithm (ACR CEUS LI-RADSv 2016) for the diagnosis of hepatocellular carcinoma in patients with chronic liver disease
H. Albrecht, R. Gilroy, R. Ash, M. O'Neil	Diagnostic accuracy of the liver imaging reporting and data system (LI-RADS) for hepatic nodules in cirrhotic patients: A 2 year retrospective analysis
S. Ichikawa, U. Motosugi, N. Oishi, T. Shimizu, T. Wakayama, N. Enomoto, M. Matsuda, H. Onishi	Ring-Like Enhancement of Hepatocellular Carcinoma in Gadoxetic Acid-Enhanced Multiphasic Hepatic Arterial Phase Imaging with Differential Subsampling with Cartesian Ordering
S. H. Park, B. Kim, S. Y. Kim, Y. S. Shim, J. H. Kim, J. Huh, H. J. Kim, K. W. Kim, S. S. Lee	Abbreviated MRI with optional multiphasic CT as an alternative to full-sequence MRI: LI-RADS validation in a HCC-screening cohort
A. Ko, H. J. Park, E. S. Lee, S. B. Park, Y. K. Kim, S. Y. Choi, S. Ahn	Comparison of the diagnostic performance of the 2017 and 2018 versions of LI-RADS for hepatocellular carcinoma on gadoxetic acid enhanced MRI
A. M. De Gaetano, M. Catalano, M. Pompili, M. G. Marinp, P. Rodriguez Carnero, C. Gulli, A. Infante, R. Iezzi, F. R. Ponziani, L. Cerrito, G. Marrone, F. Giuliante, F. Ardito, G. L. Rapaccini, F. M. Vecchio, L. Giraldi, R. Manfredi	Critical analysis of major and ancillary features of LI-RADS v2018 in the differentiation of small (< 2 cm) hepatocellular carcinoma from dysplastic nodules with gadobenate dimeglumine-enhanced magnetic resonance imaging
F. Z. Mokrane, L. Lu, A. Vavasseur, P. Otal, J. M. Peron, L. Luk, H. Yang, S. Ammari, Y. Saenger, H. Rousseau, B. Zhao, L. H. Schwartz, L. Dercle	Radiomics machine-learning signature for diagnosis of hepatocellular carcinoma in cirrhotic patients with indeterminate liver nodules
A. H. Ren, J. B. Du, D. W. Yang, P. F. Zhao, Z. C. Wang, Z. H. Yang	The role of ancillary features for diagnosing hepatocellular carcinoma on CT: based on the Liver Imaging Reporting and Data System version 2017 algorithm
H. J. Park, Y. K. Kim, D. I. Cha, S. E. Ko, S. Kim, E. S. Lee, S. Ahn	Targetoid hepatic observations on gadoxetic acid-enhanced MRI using LI-RADS version 2018: emphasis on hepatocellular carcinomas assigned to the LR-M category
Jia-Yan Huang, Jia-Wu Li, Qiang Lu, Yan Luo, Ling Lin, Yu-Jun Shi, Tao Li, Ji-Bin Liu, Andrej Lyshchik	Diagnostic Accuracy of CEUS LI-RADS for the Characterization of Liver Nodules 20 mm or Smaller in Patients at Risk for Hepatocellular Carcinoma
A. H. Ren, P. F. Zhao, D. W. Yang, J. B. Du, Z. C. Wang, Z. H. Yang	Diagnostic performance of MR for hepatocellular carcinoma based on LI-RADS v2018, compared with v2017
JiaWu Li, WenWu Ling, Shuang Chen, Lin Ma, Lulu Yang, Qiang Lu, Yan Luo	The interreader agreement and validation of contrast-enhanced ultrasound liver imaging reporting and data system
S. Sevim, O. Dicle, N. S. Gezer, M. M. Baris, C. Altay, I. B. Akin	How high is the interobserver reproducibility in the LIRADS reporting system?
Ying Ding, Sheng-Xiang Rao, Wen-Tao Wang, Cai-Zhong Chen, Ren-Chen Li, Mengsu Zeng	Comparison of gadoxetic acid versus gadopentetate dimeglumine for the detection of hepatocellular carcinoma at 1.5 T using the liver imaging reporting and data system (LI-RADS v.2017)
Wentao Wang, Chun Yang, Kai Zhu, Li Yang, Ying Ding, Rongkui Luo, Shuo Zhu, Caizhong Chen, Wei Sun, Mengsu Zeng, Sheng-Xiang Rao	Recurrence after Curative Resection of HBV-related Hepatocellular Carcinoma: Diagnostic Algorithms on Gadoxetic Acid-enhanced MRI
S. Nakao, M. Tanabe, M. Okada, M. Furukawa, E. Iida, K. Miyoshi, N. Matsunaga, K. Ito	Liver imaging reporting and data system (LI-RADS) v2018: comparison between computed tomography and gadoxetic acid-enhanced magnetic resonance imaging
Y. D. Zhang, F. P. Zhu, X. Xu, Q. Wang, C. J. Wu, X. S. Liu, H. B. Shi	Classifying CT/MR findings in patients with suspicion of hepatocellular carcinoma: Comparison of liver imaging reporting and data system and criteria-free Likert scale reporting models
M. C. Langenbach, T. J. Vogl, I. von den Driesch, B. Kaltenbach, J. E. Scholtz, R. M. Hammerstingl, T. Gruber-Rouh	Analysis of Lipiodol uptake in angiography and computed tomography for the diagnosis of malignant versus benign hepatocellular nodules in cirrhotic liver

Appendix E11. Funnel Plots to Demonstrate Publication Bias

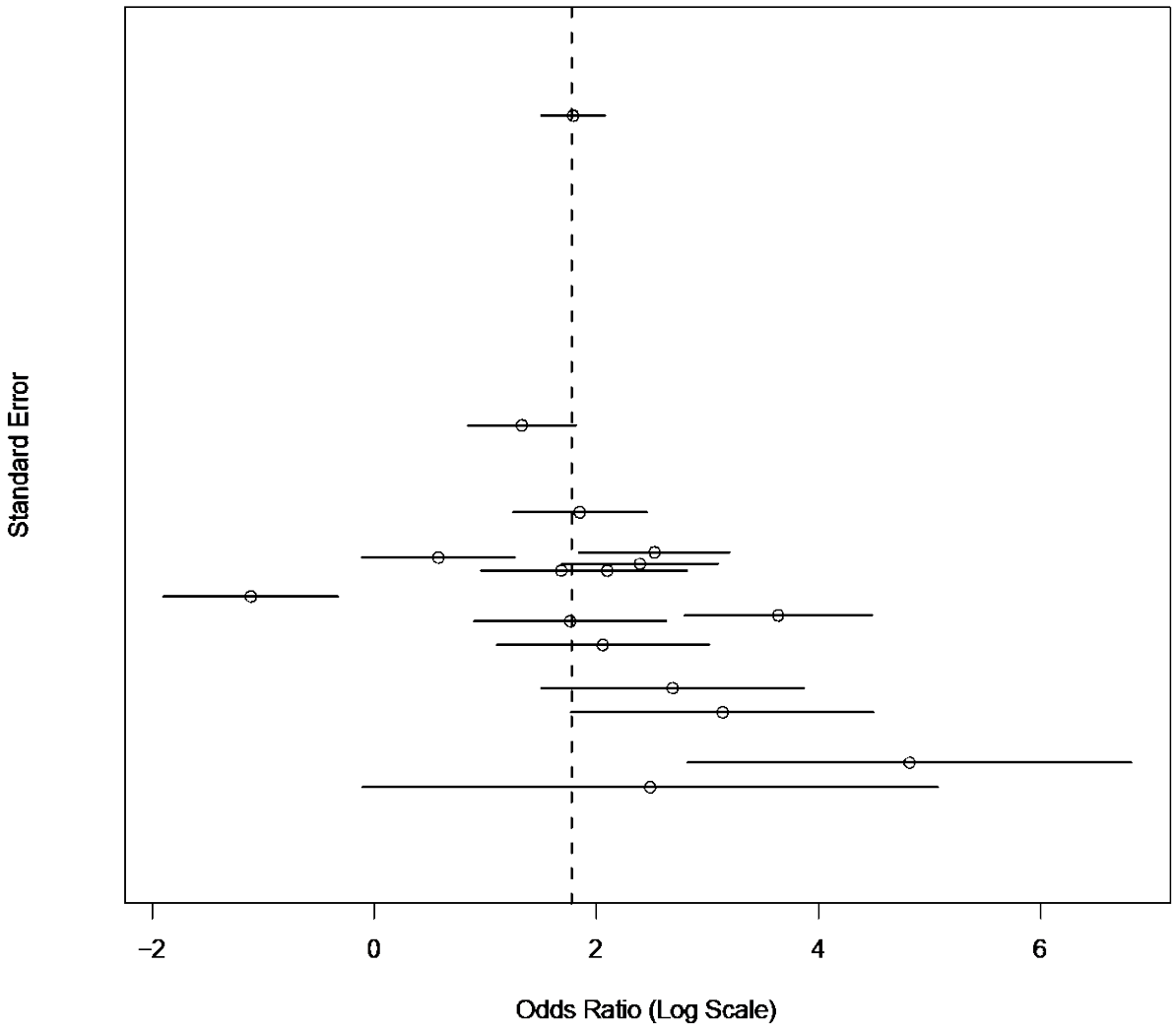
CT/MRI Nonrim Arterial Phase Hyperenhancement (APHE)



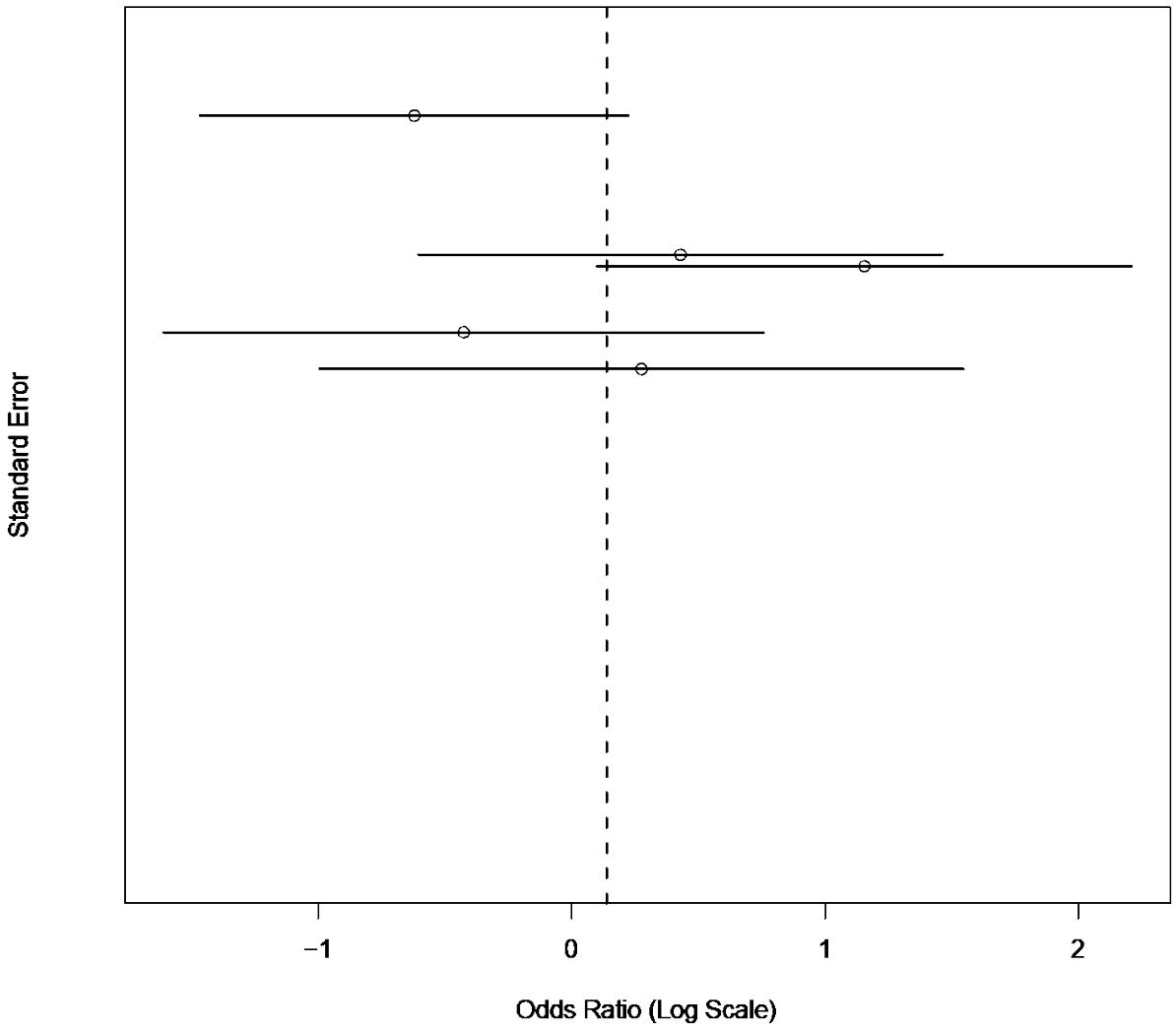
CT/MRI Enhancing Capsule



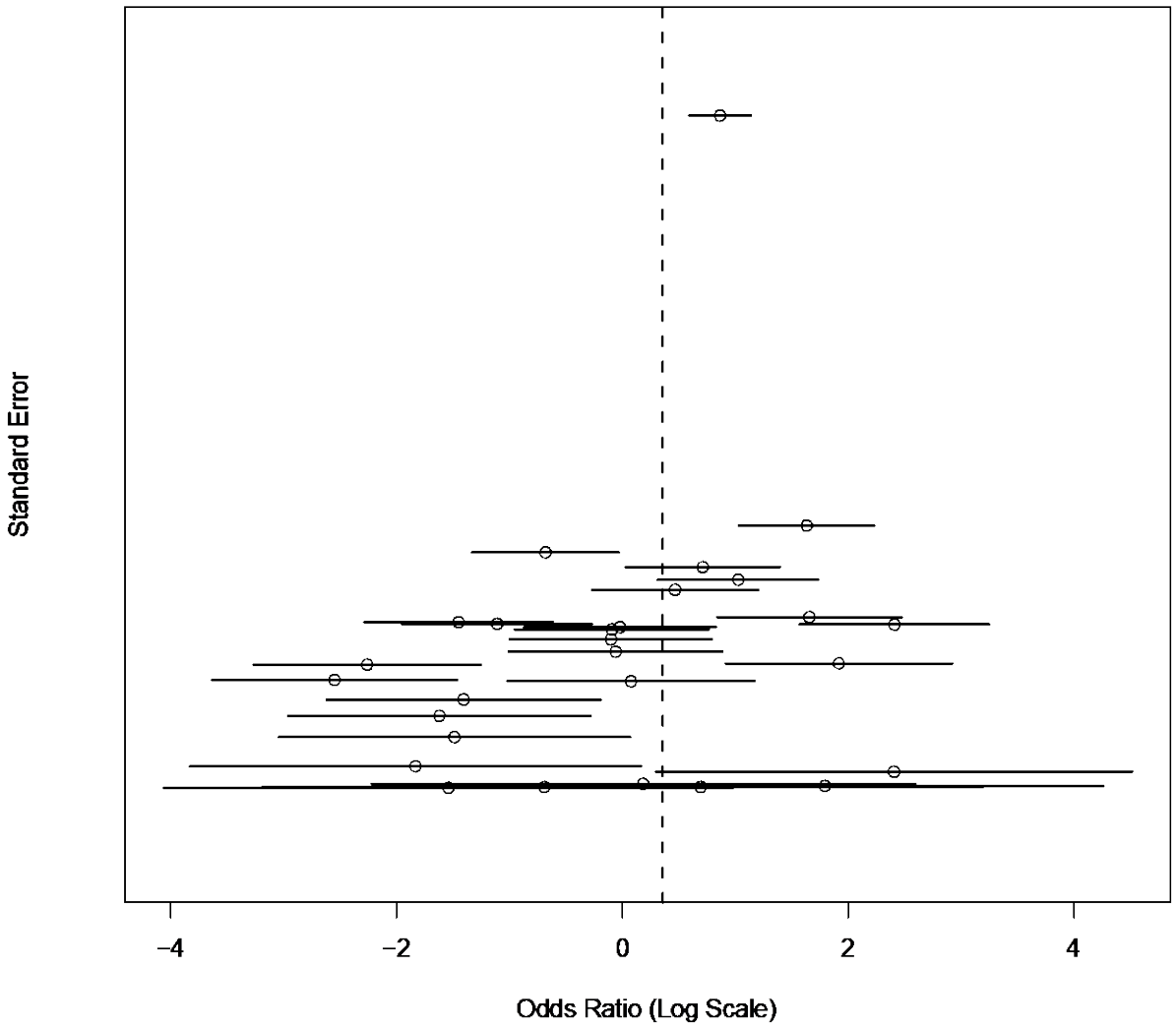
CT/MRI Nonperipheral Washout



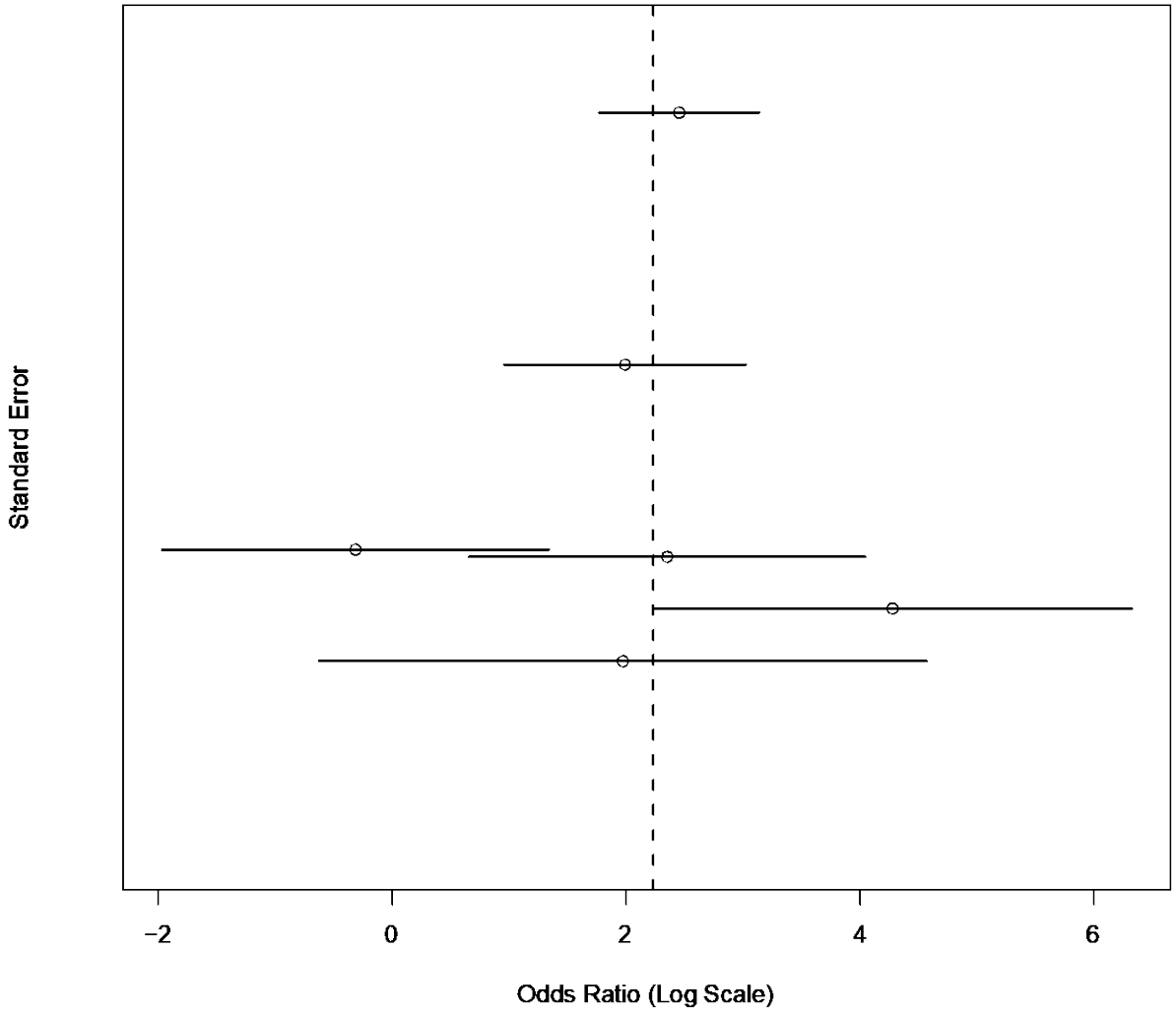
CT/MRI Threshold Growth



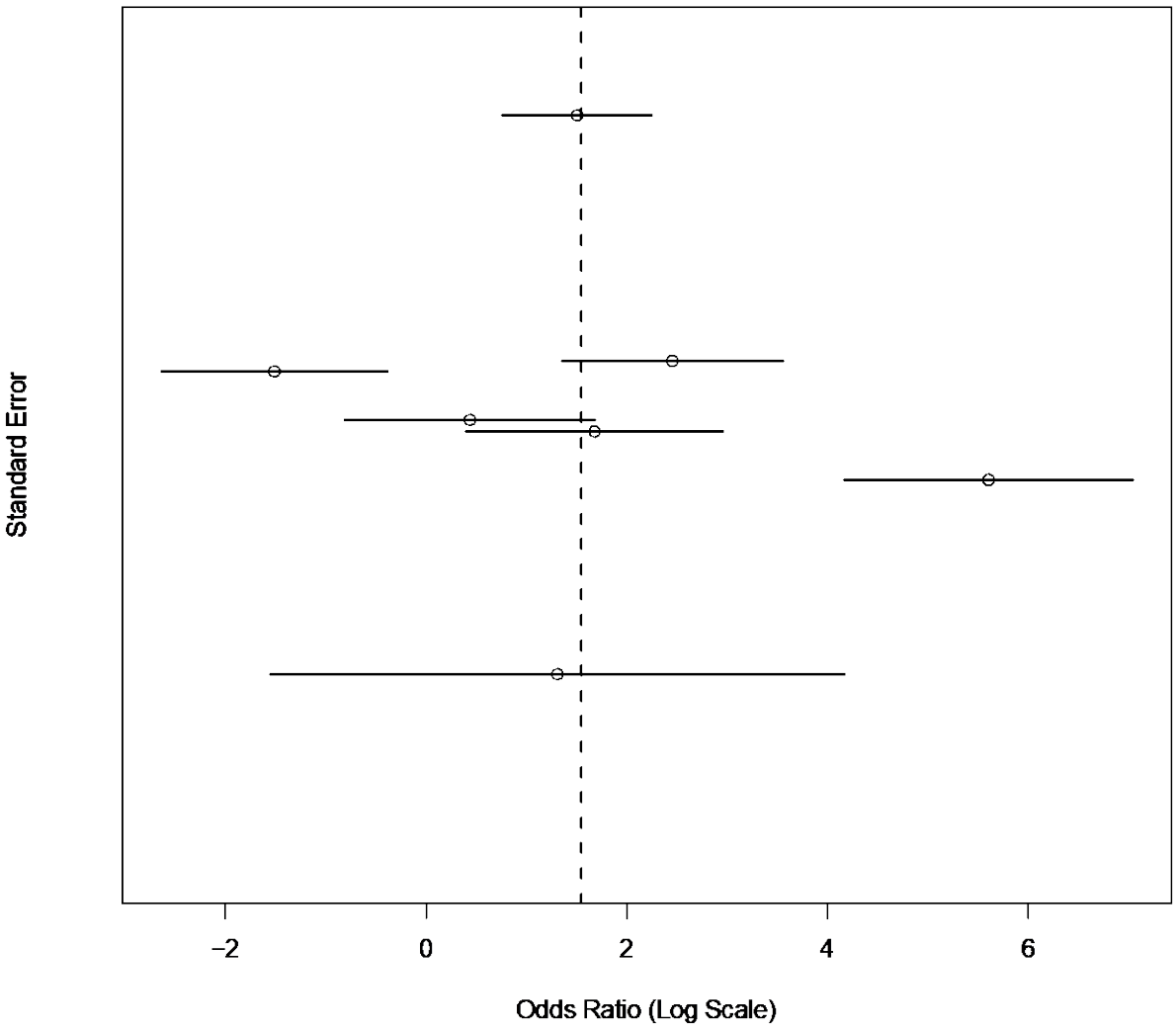
CT/MRI Observation Size



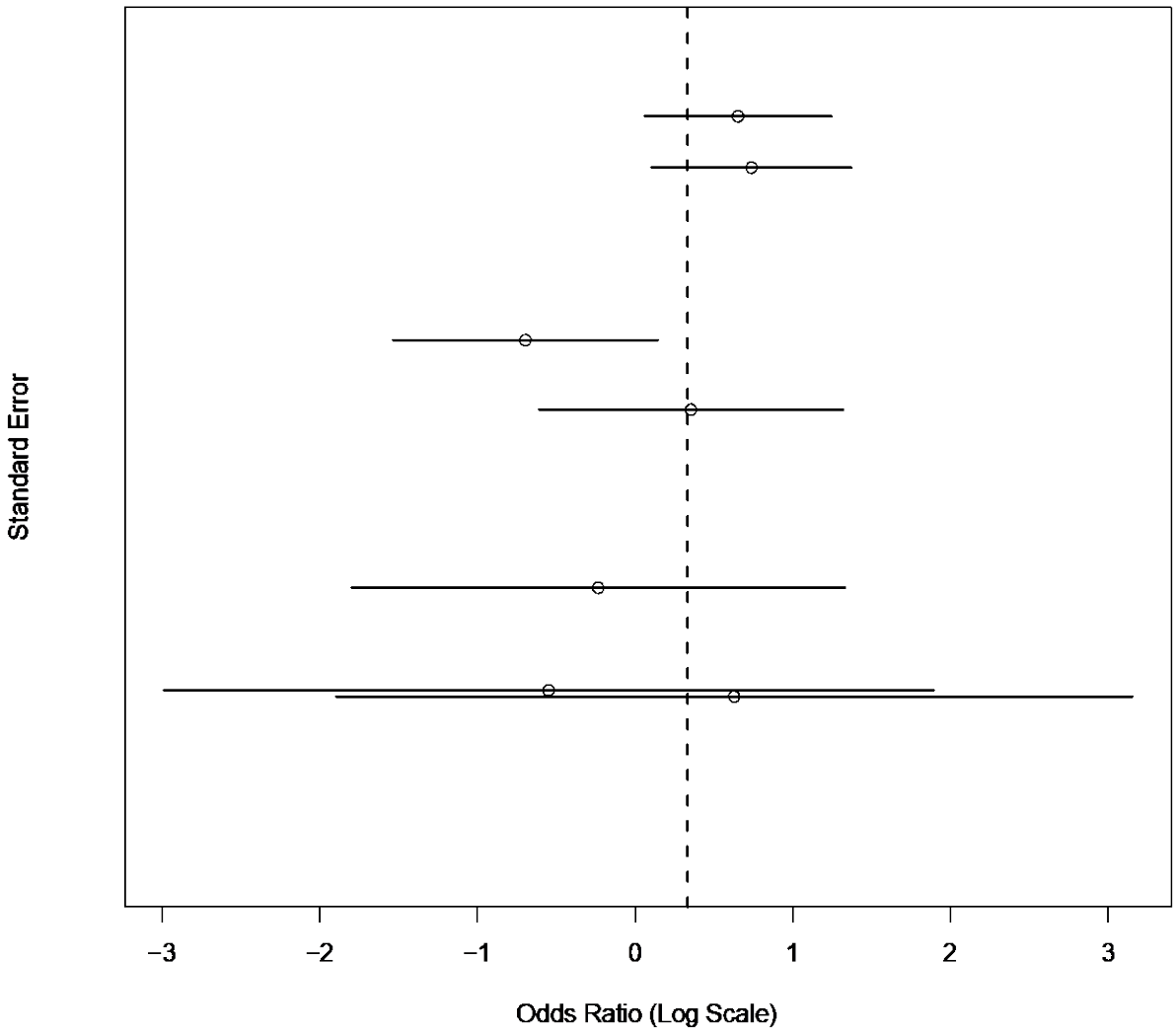
CEUS Arterial Phase Hyperenhancement (APHE)



CEUS Nonperipheral Washout

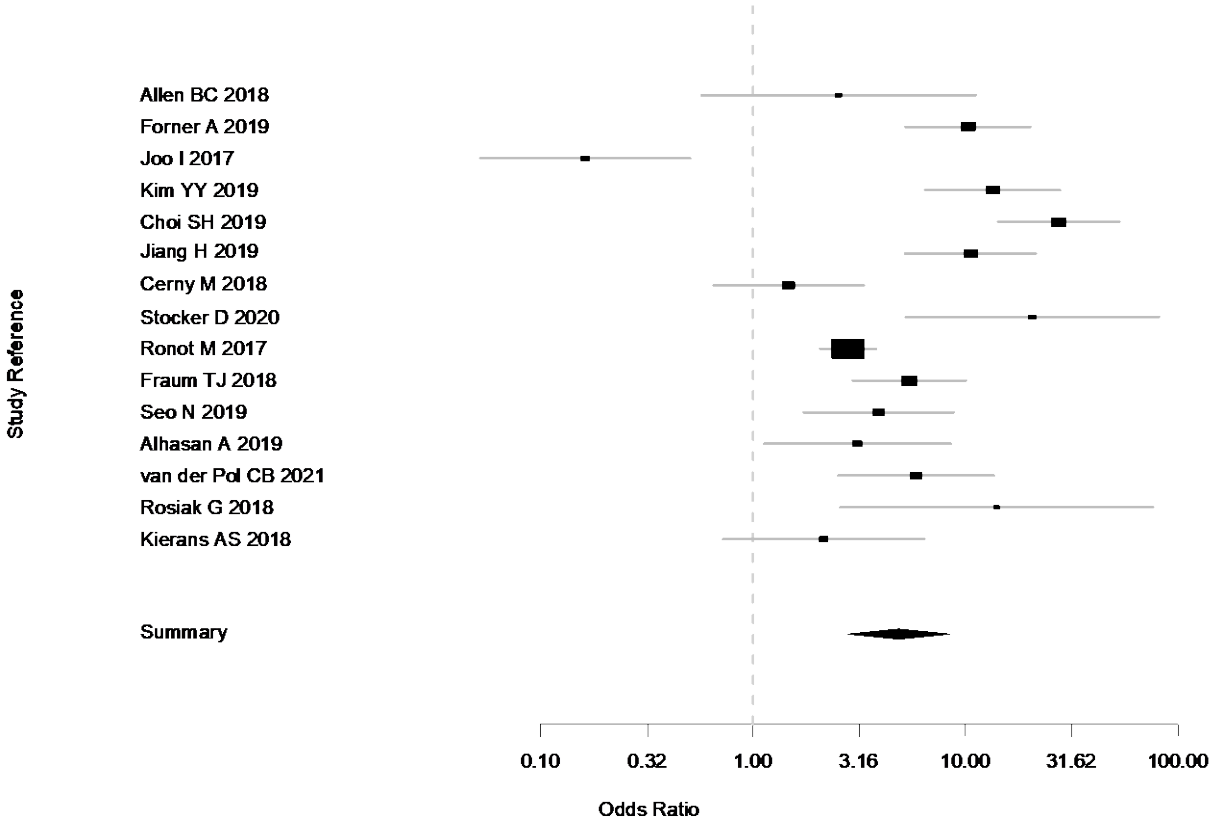


CEUS Observation Size



Appendix E12. Forest Plots of Individual Study Results

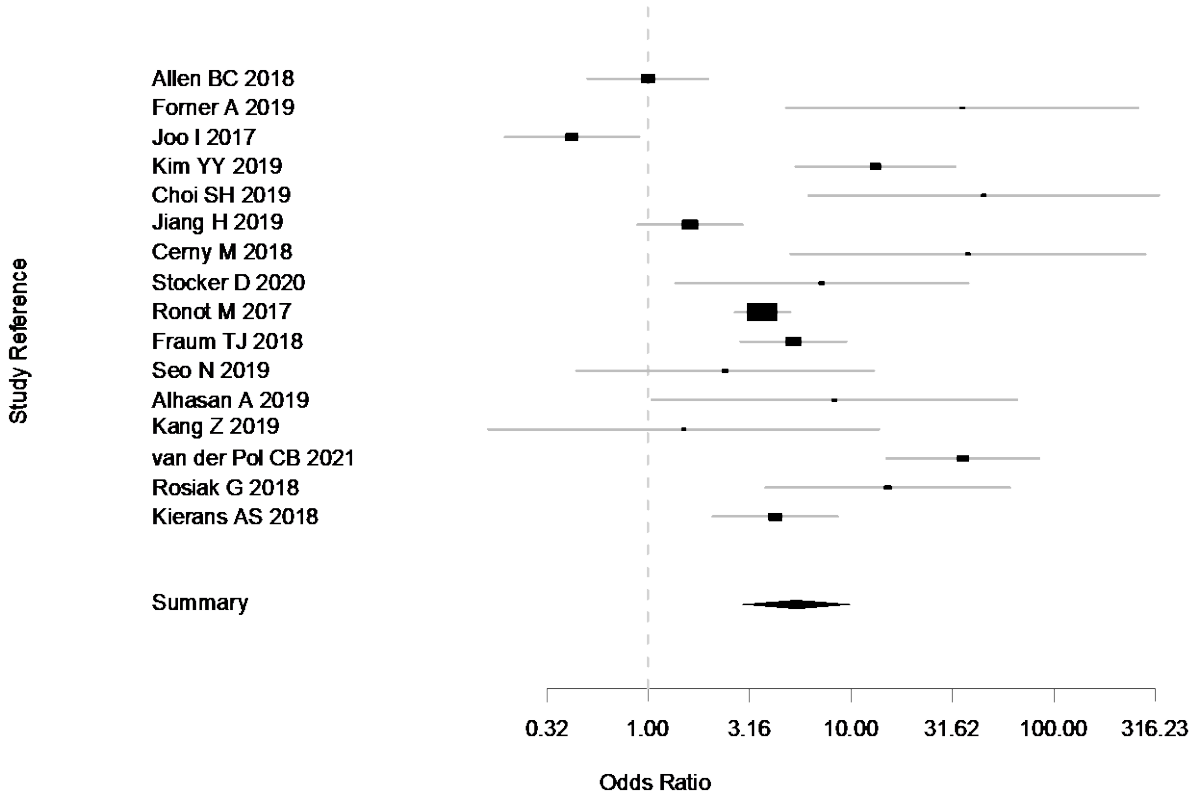
CT/MRI Nonrim Arterial Phase Hyperenhancement (APHE)



Summary OR (95%CI): 4.9 (2.8, 8.5)

Test for heterogeneity: X^2 (14) = 108.37 (p-value 0)

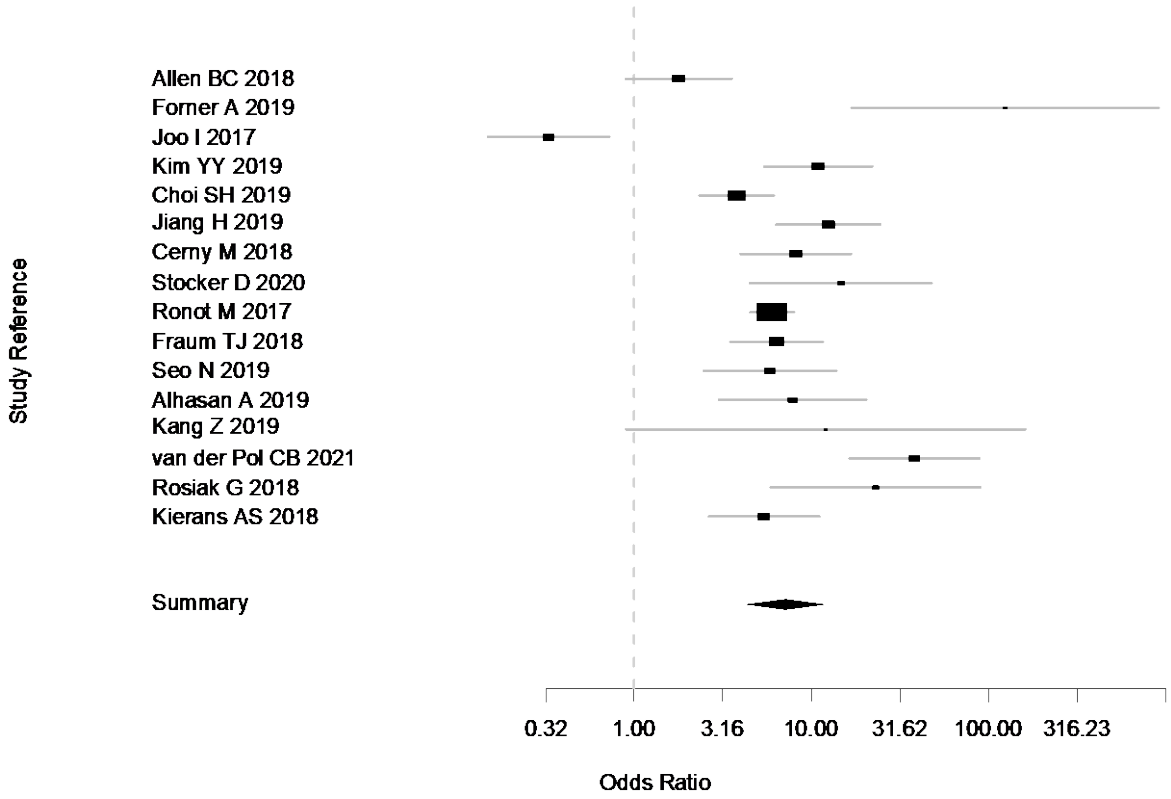
CT/MRI Enhancing Capsule



Summary OR (95%CI): 5.4 (2.9, 10.0)

Test for heterogeneity: X^2(15) = 110.29 (p-value 0)

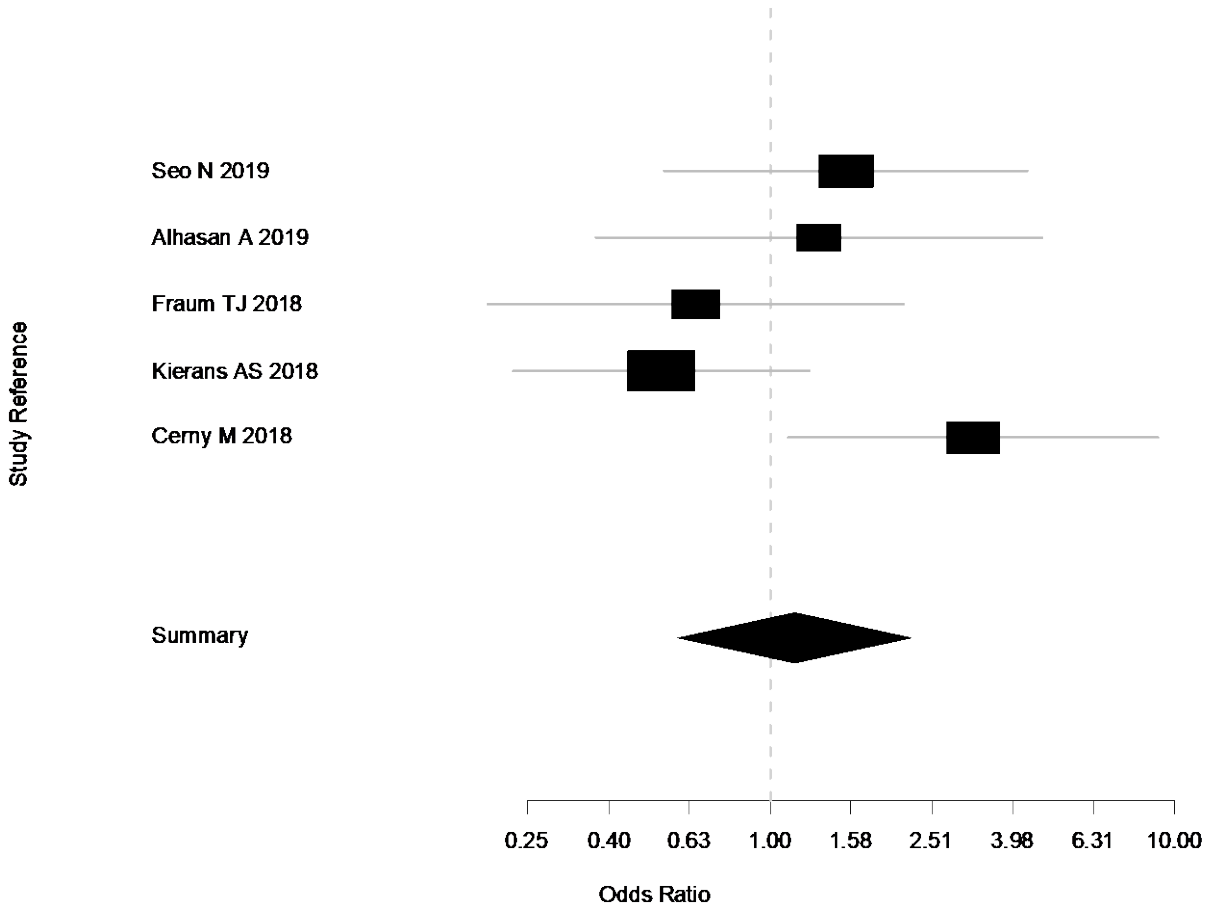
CT/MRI Nonperipheral Washout



Summary OR (95%CI): 7.1 (4.3, 11.7)

Test for heterogeneity: X^2(15) = 109.64 (p-value 0)

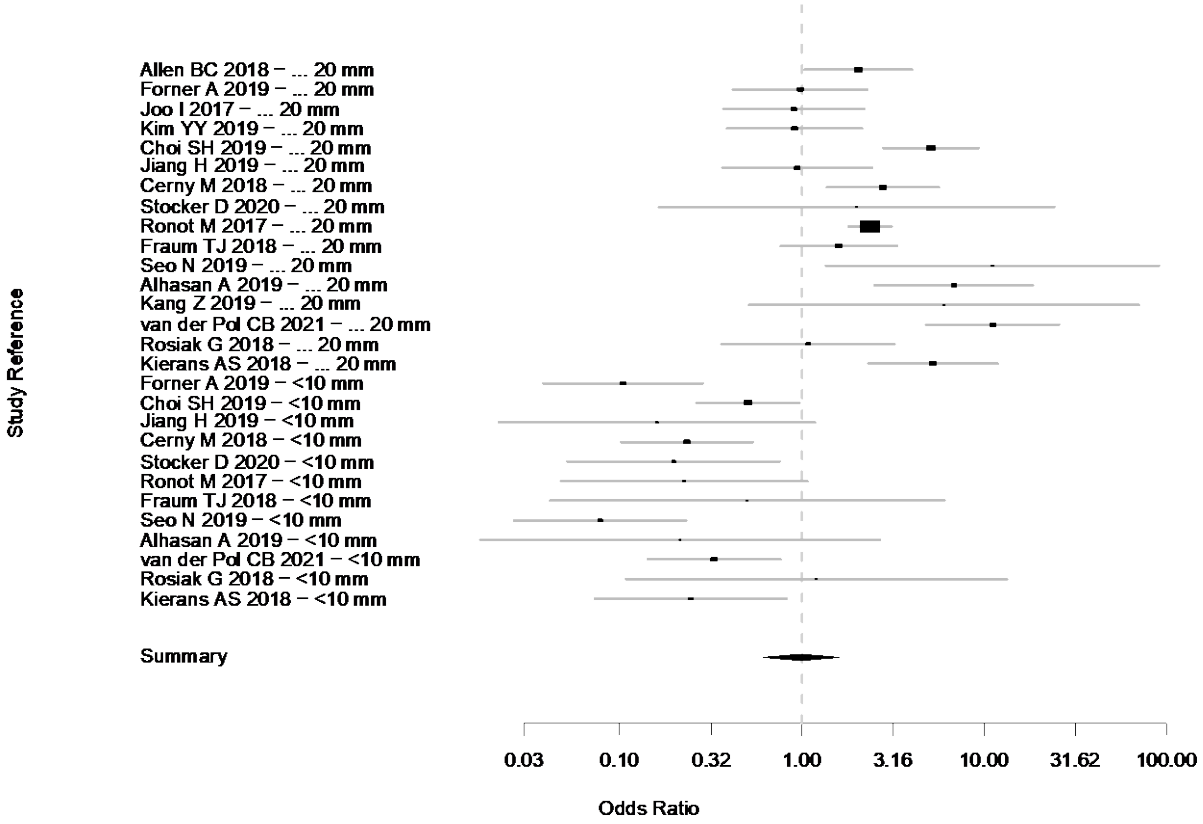
CT/MRI Threshold Growth



Summary OR (95%CI): 1.2 (0.6, 2.2)

Test for heterogeneity: X^2(4) = 7.87 (p-value 0.0966)

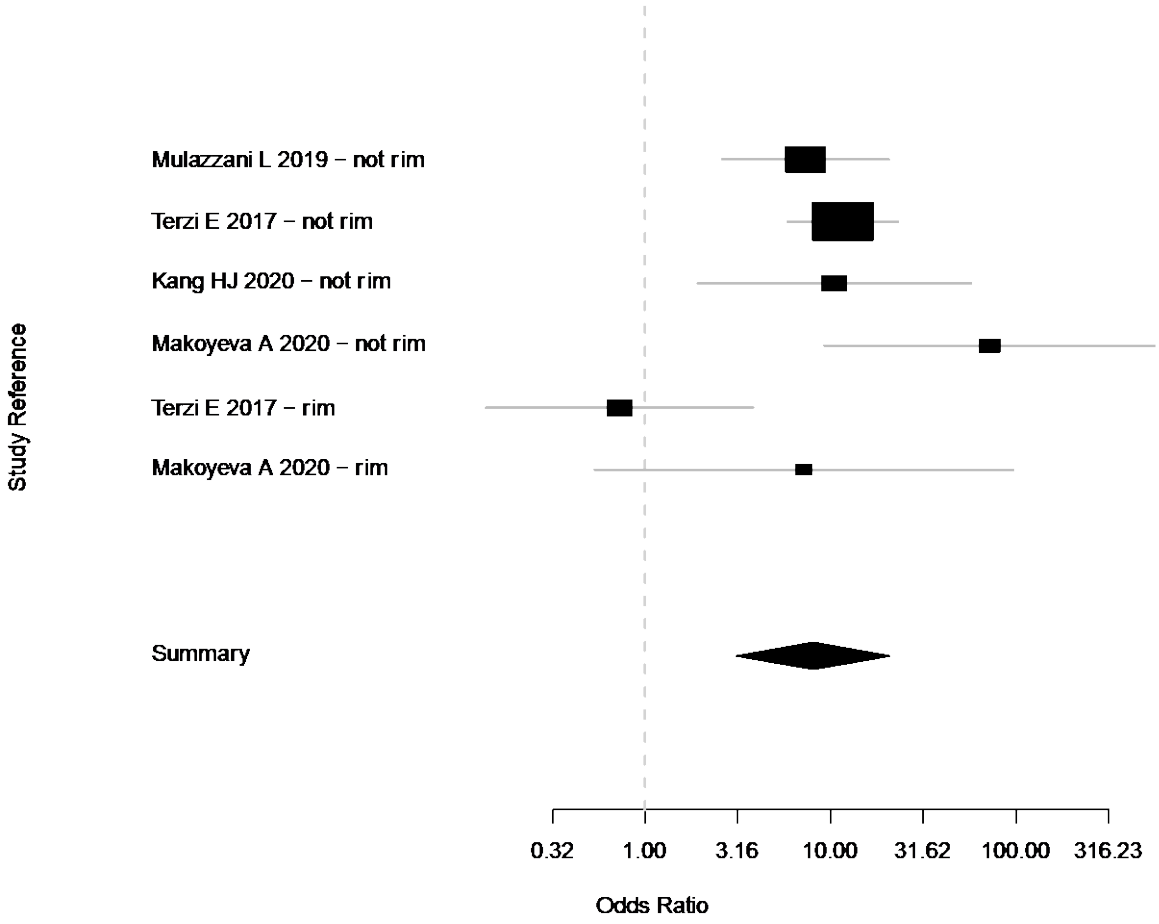
CT/MRI Observation Size



Summary OR (95%CI): 0.99 (0.6, 1.6)

Test for heterogeneity: X^2(27) = 208.29 (p-value 0)

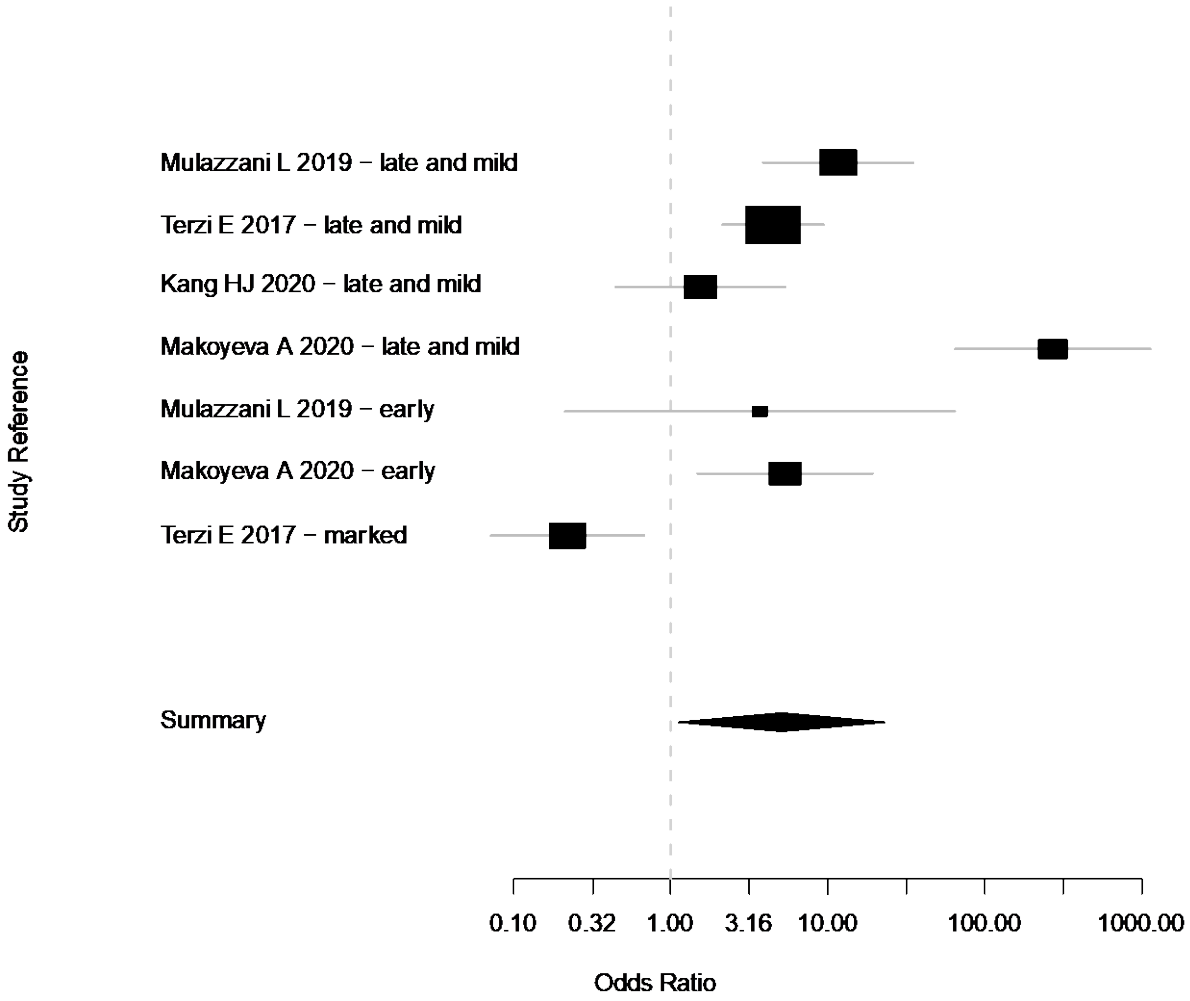
CEUS Arterial Phase Hyperenhancement (APHE)



Summary OR (95%CI): 8.1 (3.1, 20.9)

Test for heterogeneity: X^2(5) = 13.56 (p-value 0.0186)

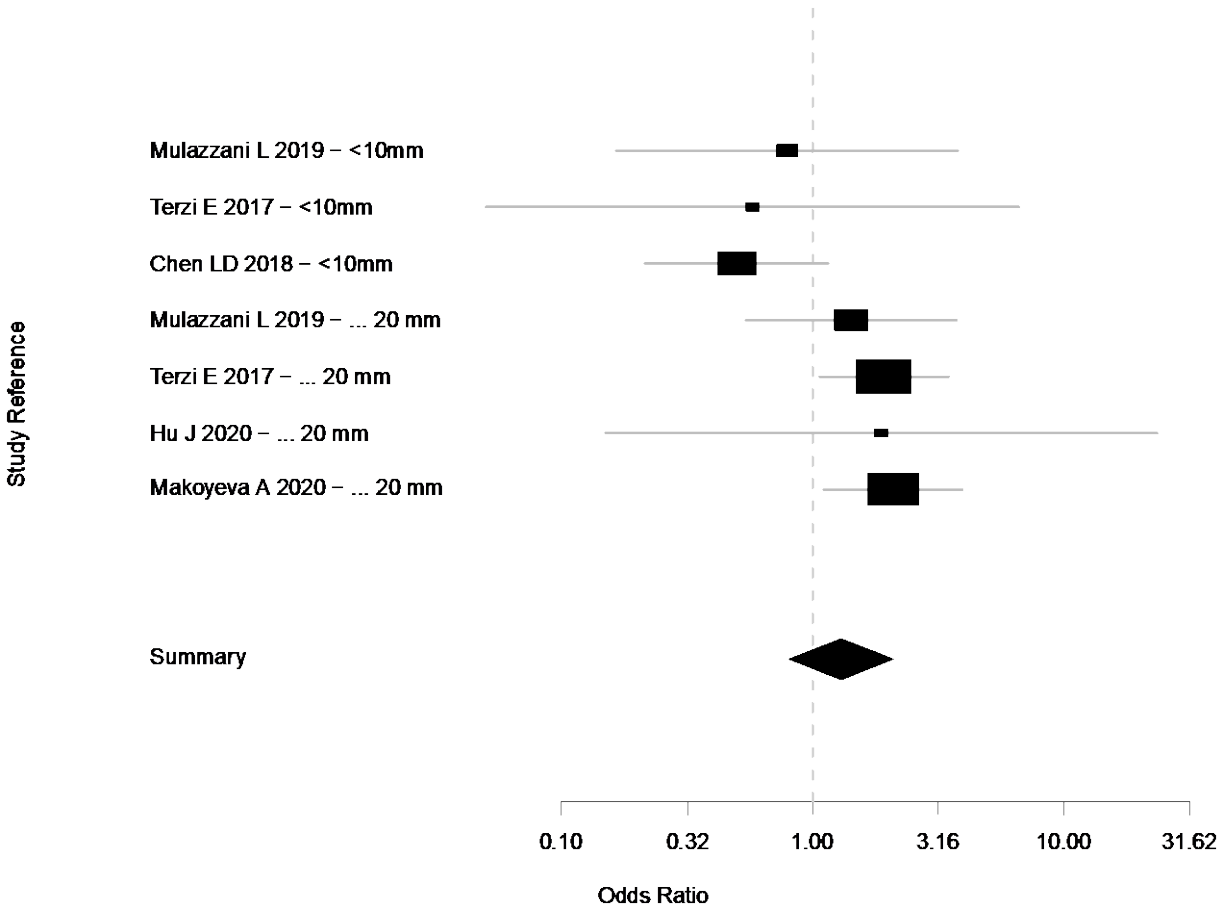
CEUS Nonperipheral Washout



Summary OR (95%CI): 5.1 (1.1, 23.0)

Test for heterogeneity: X^2(6) = 64.71 (p-value 0)

CEUS Observation Size



Summary OR (95%CI): 1.3 (0.8, 2.1)

Test for heterogeneity: X^2(6) = 9.53 (p-value 0.1458)

Appendix E13. τ^2 Values as a Measure of Heterogeneity

CT/MRI major features multivariable analysis (Table 3)

Observations with all five major features reported (n = 887): 0.9212

Observations with all major features reported except threshold growth (n = 3547): 0.9342

Observations with or without threshold growth reported (n = 4434): 0.9416

CEUS model (Table 4): 0.9724

Sensitivity analysis including only studies at low risk of bias (Table E4)

Observations with or without threshold growth reported (n=4434): 0.8214

Low risk of bias studies- Observations with or without threshold growth reported (n=1675): 0.7319