

Diagnostic Accuracy of Imaging in Assessing Nonviability of Disappearing Colorectal Liver Metastasis

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IMPORTANCE In patients with colorectal liver metastases (CLMs), the optimal treatment of disappearing liver metastases (DLMs) diagnosed on postchemotherapy computed tomography (CT) is controversial.

OBJECTIVE To examine the diagnostic value of magnetic resonance imaging (MRI) (diffusion weighted, T1/T2, and contrast enhanced) and CT for accurate assessment of the nonviability of DLMs.

DESIGN, SETTING, AND PARTICIPANTS This was a prospective international study including patients with initially unresectable CLMs downstaged to liver resection after chemotherapy at 21 centers in France, Austria, Belgium, the US, and Japan. A total of 233 patients were registered and 112 were enrolled between November 2016 and March 2021 with a minimum 2-year follow-up. Clinical cutoff was in September 2023, and data were analyzed from August 2024 to May 2025.

EXPOSURES Postchemotherapy evaluation with both CT and MRI was performed. DLMs were defined as lesions that had disappeared on CT. Confirmed DLMs (cDLMs) were defined as those that had disappeared on both CT and MRI.

MAIN OUTCOMES AND MEASURES The primary end point was the negative predictive value (NPV) of MRI and CT in assessing the nonviability of cDLMs using either pathological complete response (for resected lesions) or the absence of recurrence at the site of cDLMs during the 2-year follow-up (for lesions left behind) to confirm the true lesion status. The planned sample size was 149 evaluable cDLMs, aiming at excluding an NPV of 0.85 or lower with a 1-sided α of 5% and a power of 90%.

RESULTS Among 112 total patients (mean [SD] age, 60.0 [10.4] years; 67 [59.8%] male) a total of 152 cDLMs and 227 DLMs were evaluable. The NPV of all evaluable cDLMs, either resected or left behind, was 62.5% (95/152; 90% CI, 50.8-74.2), which was lower than the prespecified threshold. The NPV of DLMs was 52.9%. The NPVs of resected cDLMs vs those left behind were 56.8% (50/88; 90% CI, 44.2-69.5) and 70.3% (45/64; 90% CI, 48.6-92.0), respectively. For patients without extrahepatic metastases who had RO/1 resection, there was no significant difference in disease-free survival and overall survival between those with all cDLMs removed vs those with at least 1 cDLM left behind.

CONCLUSIONS AND RELEVANCE Although the combination of MRI and CT was more accurate in detection of nonviable DLMs compared to CT alone, cDLMs did not correspond to nonviability in patients with initially unresectable CLM. Survival benefit associated with removal of cDLMs is still unclear in this setting.

TRIAL REGISTRATION ClinicalTrials.gov Identifier: [NCT02781935](https://clinicaltrials.gov/ct2/show/study/NCT02781935)

JAMA Surg. doi:10.1001/jamasurg.2025.3600
Published online September 17, 2025.

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For borderline resectable and initially unresectable colorectal liver metastases (CLMs), systemic chemotherapy with targeted therapy is widely recognized as a strategy to increase the chance of conversion to potentially curative liver resection.¹⁻³ Accurate preoperative staging with computed tomography (CT) or magnetic resonance imaging (MRI) is critical for planning the most effective therapeutic approach. A notable challenge arises when liver metastases become undetectable on imaging after chemotherapy; these metastases are termed disappearing liver metastases (DLMs). According to the literature, approximately 20% of liver lesions may disappear on CT scans after 6 to 12 cycles of chemotherapy.^{4,5} DLMs present a therapeutic dilemma due to difficulty in intraoperative identification and the uncertainty regarding the presence of residual viable tumor cells. The optimal management of DLMs—whether they should be resected or left behind—remains controversial as described in a recent international survey,⁶ and the relevant literature is currently limited.^{7,8} Previous studies have shown that radiological complete response does not consistently correspond with pathological complete response; the proportion of DLMs that revealed nonviable tumor cells by pathology or no recurrence by follow-up imaging varies widely, ranging from 33% to 83%.⁹⁻¹⁷

These findings were primarily obtained from retrospective, single-center studies that predominantly used CT, with limited integration of MRI. Furthermore, acquisition parameters for imaging were inconsistently defined, and the use of targeted therapies was less common than it is today. Thus far no multi-institutional prospective international studies have addressed the optimal treatment of disappearing CLMs. To address these gaps, we initiated an international prospective study to evaluate the diagnostic performance of CT scans and multiparametric MRI in predicting the nature of confirmed DLMs (cDLMs). The aim of this study was also to assess whether cDLMs should be resected or left behind after surgery, providing valuable insights for improving patient outcomes.

Methods

Patient Flow

Diffusion-Weighted Magnetic Resonance Imaging Assessment of Liver Metastasis to Improve Surgical Planning (DREAM) was an international, multicenter prospective intergroup study led by the European Organisation for Research and Treatment of Cancer (EORTC), Japan Clinical Oncology Group (JCOG) and European Society of Surgical Oncology (ESSO). Patients with borderline resectable or unresectable CLMs at initial diagnosis were registered. Registration after initiation of chemotherapy was also allowed, provided that CT scans and multiparametric MRI—including T1 and T2 weighted, diffusion weighted (DW), and contrast enhanced (CE)—were performed during the chemotherapy period. Patients eligible for registration had unresectable or borderline resectable CLM at diagnosis with World Health Organization performance status of 0 or 1, regardless of the presence of resectable extrahepatic metastases. After chemotherapy, patients were considered for surgical resection through

Key Points

Question How accurately can computed tomography (CT) and magnetic resonance imaging (MRI) assess the nonviability of disappearing liver metastases (DLMs) after neoadjuvant chemotherapy in patients with colorectal liver metastases (CLMs)?

Findings In this diagnostic study including 112 patients with initially unresectable CLMs, the negative predictive value of confirmed DLMs (disappeared on both CT and MRI) was below the prespecified threshold. Survival outcomes were not significantly improved with resection of confirmed DLMs.

Meaning The findings suggest that MRI may improve the accuracy in nonviable DLM detection; however, confirmed DLMs did not reliably indicate nonviability, and survival benefit of removal of cDLMs is still unclear in this setting.

discussion among a multidisciplinary team composed of surgeons with hepatobiliary expertise, oncologists, radiologists, and pathologists. Patients who were eligible for enrollment had received at least 2 cycles of chemotherapy, were considered resectable by the multidisciplinary team, and had undergone 2 sets of CT and MRI scans (baseline and prior to surgery). Hepatic resection was scheduled within 8 weeks of the latest imaging. This study was approved by the relevant institutional review board at each center, and conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all patients.

Collection of Lesions and Definition of Disappearing Lesions

Information regarding disappearing lesions was systematically collected and assessed. DLMs were defined as lesions undetectable on CT scans regardless of confirmation of disappearance by multiparametric MRI. Confirmed DLMs (cDLMs) were defined as lesions undetectable on both preoperative CT scan and multiparametric MRI, including DW-MRI, T1- and T2-weighted MRI and CE-MRI (either hepatocyte specific or extracellular contrast agent). Therefore, non-cDLMs were defined as lesions undetected by CT but not confirmed on MRI. In addition, data regarding the 2 largest lesions were collected.

Quality Assurance of Imaging, Surgery, and Pathology

Imaging

Quality assurance of imaging, surgery and pathology were conducted in accordance with established guidelines (eAppendix in Supplement 1). CT and MRI scans were uploaded by the participating centers using the EORTC Imagys platform or provided on CD or DVD. Quality assurance and control check were performed on all scans to ensure image quality and consistency in acquisition protocols.

An imaging guideline, including recommended acquisition parameters of CT, T1- or T2-weighted MRI, DW-MRI, and CE-MRI, was developed through consensus among radiologists from the participating centers (eAppendix in Supplement 1). For DW-MRI, a minimum of 3 *b* values, with the highest being 700 or greater, was recommended. The identification of cDLMs on DW-MRI was based on the apparent diffusion coefficient calculated using 3 different *b* values.

Surgery and Pathology

The definitions of initially unresectable and borderline resectable CLM were as follows. Unresectable CLMs were defined as no possibility of resecting all metastases with tumor-free margins (R0) and preserving at least 30% of the liver volume as the future liver remnant with viable vascular inflow, outflow, and biliary drainage. Borderline resectable CLMs were defined as potentially operable but technically more challenging to achieve R0 resection. The surgical approach to cDLM/DLM, whether resected or left in place, was determined at the discretion of the surgeons at participating centers. All lesions underwent intraoperative ultrasonography in accordance with each institution's standard practice.

Pathological evaluation was conducted in accordance with pathological guidelines, as incorporated in the trial protocol. The location of cDLMs was documented using a specific illustrated template. To identify a cDLM, the area of the cDLM was initially sectioned at 5-mm intervals. A second close inspection was performed by the pathologist near the site of the target lesion if the no lesion was detected during the first cutting, sectioning at 1-mm intervals.

Complete pathologic response was defined as absence of residual cancer cells and large amount of fibrosis (TRG1). Grade of tumor regression was evaluated according to Rubbia-Brandt criteria.¹⁸

End Points

The primary end point was the negative predictive value (NPV) of MRI and CT in declaring cDLMs to predict lesion nonviability using either pathological complete response or the absence of local recurrence at the site of cDLMs at 2-year follow up as the best available reference for true lesion status. For resected cDLMs, lesions classified as TRG1 by local diagnosis were regarded as truly free of viable tumor cells. For cDLMs left in place, no liver recurrence at the cDLM site, as confirmed by diagnostic imaging 2 years postsurgery, was regarded as a true negative. CT and MRI scans at 2 years postsurgery were mandatory to confirm the absence of tumor recurrence.

The NPV of multiparametric MRI and standard CT combined, was derived as $NPV = \frac{\text{left-behind cDLMs (without recurrence within 2 years)} + \text{resected cDLMs (TRG1 pathological response)}}{\text{all evaluable left-behind or resected cDLMs}}$. Key secondary end points were NPV of multiparametric MRI and CT combined for the detection of nonviable lesions in the subgroups of resected cDLMs: $NPV(\text{resected}) = \frac{\text{resected cDLMs (TRG1 pathological response)}}{\text{all evaluable resected cDLMs}}$ and cDLMs left behind: $NPV(\text{left behind}) = \frac{\text{left-behind cDLMs (without recurrence within 2 years)}}{\text{all evaluable left-behind cDLMs}}$. Other end points included the number of disappearing lesions per patient and NPV of each imaging modality. Postoperative complication rate, disease-free survival (DFS) and overall survival (OS) after surgery were also assessed.

Statistical Analysis

This study aimed to confirm whether an NPV was greater than 0.85 using a 1-sided test with a type 1 error of 5%. Since the unit of analysis was the number of cDLMs and a single patient may present with several cDLMs, the variance for the NPV ac-

counting for within-patient correlation¹⁹ was used in generating the normally approximated 2-sided 90% CI. Testing proceeded by checking whether the lower confidence limit of this CI was above 0.85. Targeting a power of 90% under the alternative that the NPV was 0.95 or greater and assuming a within-patient correlation between lesions of 0.2, for an average of 2 cDLMs per patient, it was initially estimated that 92 evaluable cDLMs were needed. Further assuming that 15% of the patients would present with at least 1 cDLM, and that 80% of these cDLMs would be evaluable for their true status, 383 eligible patients were required. The sample size was increased to 400 considering a 4% dropout rate due to being lost to follow-up or ineligibility. Monitoring during the study revealed that some design assumptions did not hold. Consequent recalculation resulted in 149 required evaluable cDLMs to maintain 90% power for the study. Patient accrual and follow-up after the end of accrual lasted for 5 and 2 years, respectively.

DFS was calculated as the time in days elapsed from the day of initial hepatic surgery until the day of first local relapse, extrahepatic progression, or death from any cause, whichever occurred first. Patients alive and progression free at their last visit were censored on that date. Occurrence of second cancers was ignored in this analysis. OS was defined as the time in days from the day of initial hepatic surgery to the day of death. Patients alive at their last follow-up visit were censored on that date. Survival probabilities were estimated using the Kaplan-Meier method, and association with treatment was summarized through hazard ratios (HRs) and 2-sided 95% CIs via Cox regression model. For postoperative complications, overall grading was based on the Clavien-Dindo classification.^{20,21} The study followed the Standards for Reporting of Diagnostic Accuracy (STARD) reporting guideline. Clinical cutoff was in September 2023, and data were analyzed from August 2024 to May 2025.

Results

Patients and Lesions

Between November 2016 and March 2021, 233 CLM patients were registered across 21 participating centers in France, Austria, Belgium, the US, and Japan. After chemotherapy, 112 patients (mean [SD] age, 60.0 [10.4] years; 67 [59.8%] male and 45 [40.2%] female) were deemed suitable for conversion surgery by the multidisciplinary team and enrolled for analysis (Table). Of those, 109 patients underwent liver surgery. Median (IQR) follow-up duration after surgery was 26.1 (24.3-32.6) months.

A total of 296 DLMs were identified on CT scans, 203 (69%) of which were classified as cDLMs. The median (IQR) numbers of DLMs and cDLMs per patient were 3 (2-6) and 3 (1-5), respectively. Among these, 227 DLMs (158 resected and 69 left behind) and 152 cDLMs (88 resected and 64 left behind), respectively, were considered evaluable according to the imaging protocol (Figure 1). Baseline characteristics of enrolled patients are listed in the Table. A median (IQR) of 8 (5-11) chemotherapy cycles was administered preoperatively. The numbers of liver metastases based on the imaging modality are

Table. Patient Characteristics

| Variable | Enrolled patients (N = 112), No. (%) |
|--|--------------------------------------|
| Age at registration, median (IQR), y | 60.5 (53.0-67.0) |
| Sex | |
| Male | 67 (59.8) |
| Female | 45 (40.2) |
| Primary tumor location | |
| Right-sided colon | 25 (22.3) |
| Left-sided colon | 50 (44.6) |
| Rectum | 37 (33.0) |
| Clinical T stage of primary tumor | |
| T1/T2 | 9 (8.0) |
| T3 | 43 (38.4) |
| T4 | 35 (31.3) |
| Missing | 25 (22.3) |
| Clinical N stage of primary tumor | |
| N0 | 22 (19.6) |
| N1 | 31 (27.7) |
| N2 | 29 (25.9) |
| Missing | 30 (26.8) |
| Resection of primary tumor | |
| Yes | 65 (58.0) |
| No | 47 (42.0) |
| Presence of extrahepatic metastases | |
| Yes | 14 (12.5) |
| No | 98 (87.5) |
| Number of liver metastases at initial diagnosis, median (IQR) ^a | 7 (4.0-10.0) |
| WHO performance status | |
| 0 | 84 (75.0) |
| 1 | 28 (25.0) |
| KRAS | |
| Wild | 74 (66.1) |
| Variant | 34 (30.4) |
| Missing | 4 (3.6) |
| BRAF | |
| Wild | 71 (63.4) |
| Variant | 3 (2.7) |
| Missing | 38 (33.9) |
| Microsatellite instability | |
| High instability | 7 (6.3) |
| Stable | 45 (40.2) |
| Missing | 60 (53.6) |
| First chemotherapy regimen | |
| Doublet | 21 (18.8) |
| Doublet + EGFR | 38 (33.9) |
| Doublet + VEGF | 27 (24.1) |
| Triplet | 9 (8.0) |
| Triplet + EGFR | 6 (5.4) |
| Triplet + VEGF | 10 (8.9) |
| IAH | 1 (0.9) |
| Total cycles of chemotherapy, median (IQR) ^b | 8 (5.0-11.0) |
| Type of contrast-enhanced agent | |

(continued)

Table. Patient Characteristics (continued)

| Variable | Enrolled patients (N = 112), No. (%) |
|---|--------------------------------------|
| Primovist (Gd-EOB-DTPA) | 69 (61.6) |
| Multihance (Gd-BOPTA) | 14 (12.5) |
| Gadlinium | 19 (17.0) |
| Missing | 10 (8.9) |
| CEA, median (IQR), ng/mL ^c | 7.2 (3.5-68.0) |
| CA19-9, median (IQR), U/mL ^c | 25.5 (7.8-94.2) |

Abbreviations: CA19-9, carbohydrate antigen 19-9; CEA, carcinoembryonic antigen; EGFR, epidermal growth factor receptor; Gd-BOPTA, gadobenate dimeglumine; Gd-EOB-DTPA, gadolinium-ethoxybenzyl-diethylenetriamine penta-acetic acid; IAH, intra-arterial hepatic; VEGF, vascular endothelial growth factor; WHO, World Health Organization.

^a Data were collected from the prospective cohort only (n = 66) who had not completed conversion therapy at enrollment as part of eligibility criteria specific to this cohort.

^b Including initial and subsequent (if applicable) chemotherapies.

^c CEA and CA19-9 were based on 99 and 90 nonmissing values, respectively.

shown in eTable 1 in Supplement 1. Evaluation of all lesions in each imaging modality is shown in eTable 2 in Supplement 1. Among 75 evaluable non-cDLMs, 69 lesions (92%) remained visible on CE-MRI. Of 224 evaluable non-DLMs, 10 (3%) were not detected on CE-MRI and were detected on CT scans.

NPV

Primary and Key Secondary End Points

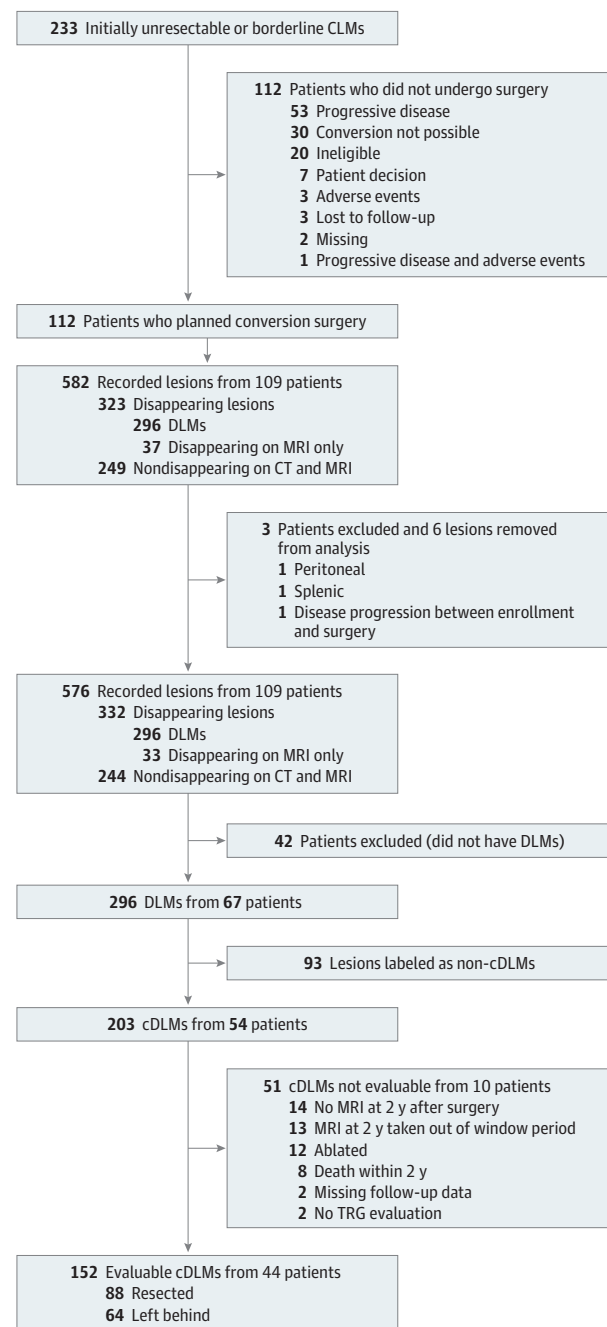
The NPV was calculated as the percentage of nonviable lesions. The NPV of all evaluable cDLMs, either resected or left behind, was 62.5% (95/152; 90% CI, 50.8-74.2), with the lower confidence limit of 50.8%, which was lower than the prespecified threshold of 85% (Figure 2). The NPV of resected cDLMs and those left behind was 56.8% (50/88; 90% CI, 44.2-69.5) and 70.3% (45/64; 90% CI, 48.6-92.0), respectively. Considering the 90% CIs, results were similar between subgroups and consistent with the primary end point. The percentages of nonviable lesions for DLMs, cDLMs and non-cDLMs are shown in Figure 2. The percentage of nonviable lesions was higher for cDLMs (56.8%) than for non-cDLMs (31.4%) in resected DLMs. Only 5 left-behind DLMs were non-cDLMs (7%), thus the percentage of nonviable lesions was not estimated for this subgroup. The percentage of nonviable lesions across different chemotherapy regimens is shown in eFigure 1 in Supplement 1.

Intraoperative Description of Lesions

Among 203 cDLMs, 48 (23.6%) were still visible by intraoperative ultrasound and 11 (5.4%) were identified as scars during surgery. Among 93 non-cDLMs, 54 (58.1%) and 12 (13.0%) were visible by ultrasound and identified as scars or calcified lesions. Contrast-enhanced ultrasonography (CEUS) was performed on 107 cDLMs and of these, 23 cDLMs (22%) remained visible by CEUS (eTable 3 in Supplement 1). All cDLMs that were visible on ultrasound were resected, and one-third of those that were invisible were.

In the primary analysis population, among 76 cDLMs examined by CEUS, 19 (25%) remained visible on CEUS and all

Figure 1. CONSORT Diagram



CLMs indicates colorectal liver metastases; cDLMs, confirmed disappearing liver metastases; CT, computed tomography; DLMs, disappearing liver metastases; MRI, magnetic resonance imaging; TRG, tumor regression grade.

were resected, while 57 (75%) were not visible on CEUS (13 resected and 44 left behind). The percentage of nonviable lesions was higher among cDLMs that were not visible on CEUS (73.7% [42/57; 90% CI, 55.0-92.3]) compared to cDLMs that were visible on CEUS (63.2% [12/19; 90% CI, 38.7-87.6]).

Surgical Outcome

The rate of R0 and R1 resection was 96.3%. Surgical information is shown in eTable 4 in Supplement 1. Among 109 patients, early (within 30 days) and late (31-90 days) postoperative complication Clavien-Dindo grade IIIa or greater were observed in 12 (11.0%) and 4 (3.7%) patients without postoperative mortality, respectively. Two-stage hepatectomy was performed in 6 patients (5.5%). TRG based on the resected lesions is shown in eTable 5 in Supplement 1. Adjuvant chemotherapy after surgery was performed in 46 patients (42.2%). Oxaliplatin combined regimen was used in 38 patients (34.2%).

Survival Outcome

The prognostic role of cDLMs and DLMs was evaluated in patients without extrahepatic metastases at the time of surgery who had R0 or R1 resection ($n = 92$), by comparing patients with disappearing lesions vs those without disappearing lesions. The median DFS was similar: 9.3 (95% CI, 7.2-12.8) months vs 8.5 (95% CI, 7.1-13.1) months for patients with and without cDLMs, respectively. Although the median OS could not be estimated for either group, a similar trend was observed (Figure 3). OS in all patients who underwent operation based on presence of cDLM were shown in eFigure 2 in Supplement 1. This was also the case when comparing patients with DLMs vs those without DLMs. (eFigure 3 in Supplement 1). For survival analysis in patients with cDLMs who did not have extrahepatic metastases at the time of surgery and had R0 or R1 resection ($n = 45$), a longer median DFS estimate was observed for patients with all cDLMs removed (11.4 [95% CI, 6.4-18.8] months) compared to those with at least 1 cDLM left behind (7.6 [95% CI, 5.7-12.1] months), but no statistically significant difference was shown in terms of HR (0.92 [95% CI, 0.48-1.77]) (Figure 4). For OS, although the HR (0.80 [95% CI, 0.21-3.08]) was numerically in favor of all cDLMs removed vs those with at least 1 cDLM left behind, there was also no statistically significant difference.

Discussion

Over the past 2 decades, advances in chemotherapy have expanded the technical possibilities for treating patients with initially unresectable CLMs. The development of DLMs following chemotherapy could potentially increase the chances of conversion surgery, assuming that MRI and CT findings can accurately predict tumor nonviability. However, in this prospective international study, cDLMs did not sufficiently predict nonviability of tumor cells in initially unresectable or borderline CLMs. Performing CEUS may increase the diagnostic accuracy of disappearing lesions.²² Furthermore, there was no significant difference in terms of DFS or OS between patients who had all cDLMs resected and those who had 1 or more cDLM left behind. To our knowledge, this is the first study to prospectively investigate the true nature of disappearing CLMs using protocol-defined quality assurance of imaging, surgery, and pathology.

DLMs were observed in 67 of 233 patients (28.8%), which is consistent with previous reports. cDLMs, which were un-

Figure 2. Percentage of Nonviable Lesions for Disappearing Liver Metastases (DLMs), Confirmed DLMs (cDLMs), and Non-cDLMs

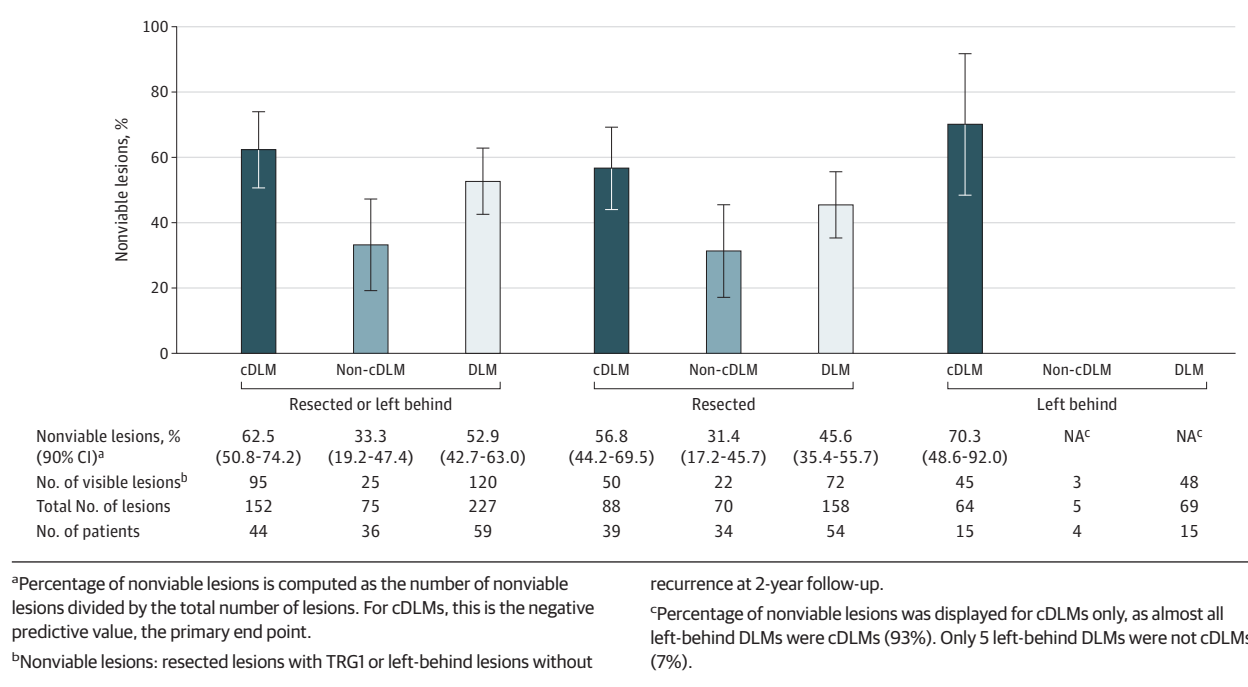
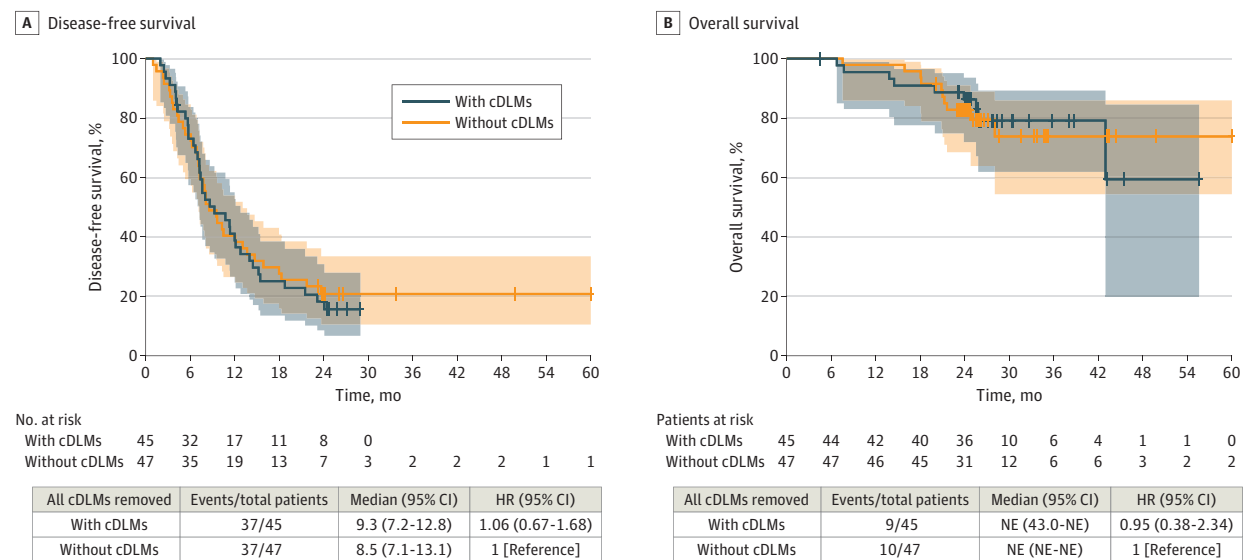


Figure 3. Disease-Free Survival and Overall Survival Based on the Development of Confirmed Disappearing Liver Metastases (cDLMs)



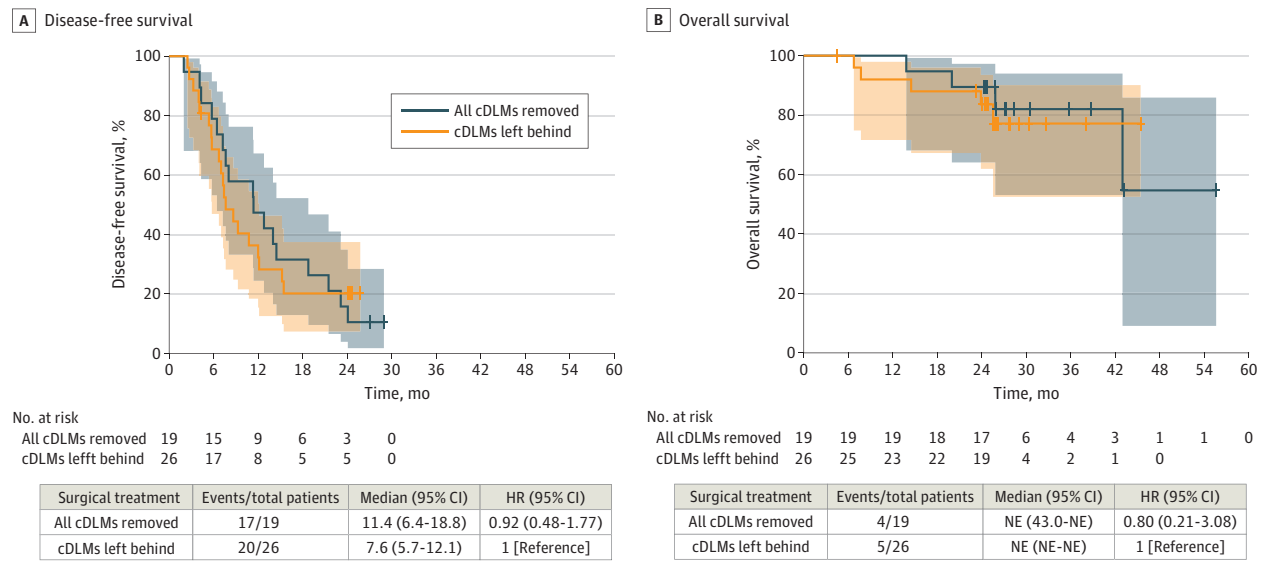
HR indicates hazard ratio; NE, not estimated.

detectable even on multiparametric MRIs, were observed in 54 patients (23%). The percentage of nonviable lesions in cDLMs was higher than in non-cDLMs (lesions undetectable on CT scans but still visible on MRIs), demonstrating the additional benefit of MRI confirmation. The diagnostic performance of CT may be impaired after chemotherapy due to parenchymal changes such as hepatic steatosis and development of sinusoidal obstructive syndrome.²³ In the CAMINO trial,²⁴ liver CE-MRI changed the treatment plan in approximately one-

third of patients with CLMs, supporting the essential role of MRI in the comprehensive diagnosis of liver lesions. Despite using the latest protocol-defined multiparametric MRI technologies, including Primovists, imaging diagnosis in the CAMINO trial did not accurately predict the nonviability of cDLMs.

Our results were comparable with those of previous reports. While the addition of CEUS may improve accuracy, even with CEUS, disappearing lesions on imaging do not suffi-

Figure 4. Disease-Free Survival and Overall Survival in Patients With All Confirmed Disappearing Liver Metastases (cDLMs) Removed and Those With Any cDLMs Left Behind (n = 45)



HR indicates hazard ratio; NE, not estimated.

ciently predict tumor nonviability. The NPV for cDLMs with CEUS confirmation should be interpreted with caution as these data were based on a smaller subgroup of lesions (n = 57). Although NPV may improve in resectable CLMs with a presumably lower tumor burden, a significant breakthrough is unlikely without the development of new, more effective chemotherapy regimens. Integrating tumor biology—such as changes in circulating tumor DNA tumor fraction before and after chemotherapy²⁵—into radiomics is essential to improve the diagnostic performance of cDLMs.

In this study, a significant impact of treatment on survival outcomes was not shown in the subgroup of patients without extrahepatic disease and achieving R0 or R1 resection. For patients who responded to systemic chemotherapy and proceeded to conversion surgery, development of cDLMs and removal of all cDLMs (vs leaving behind ≥ 1 cDLM) were not shown as significant favorable prognostic factors. It should be emphasized, however, that statistical power was limited due to the small sample size and a significant prognostic benefit could be potentially demonstrated with a larger sample size. To expand the indication of conversion surgery, various surgical procedures have been developed, such as 2-stage hepatectomies with or without augmentation of the future liver remnant, or 1-stage mainly parenchymal sparing-resections combined with intraoperative ablations.²⁶ Our present findings indicate that surgically treating cDLMs may not provide clear advantage with unresectable CLM patients. Systemic treatment may be a more appropriate therapeutic strategy for eradicating microcellular proliferation. Indeed, according to other subspecialties in

surgical oncology (eg, breast or ovarian cancer), resection of small metastatic deposits, such as axillary lymph node involvement is currently regarded as futile.^{27,28} Liver transplants may represent a potentially promising treatment strategy for some of the enrolled patients in our study.²⁹

Limitations

This study had several limitations. First, a central review of imaging has not been performed thus far. Second, the study was not powered to formally test survival benefit by design. Correction for potential prognostic factors was not carried out due to the small sample size and low number of recorded events especially for OS. Hence, further investigation would be warranted, which is a task that seems difficult to be achieved after experiences and endeavors of our multi-institutional international trial.

Conclusions

In conclusion, diagnosis of cDLMs based on both CT and MRI did not accurately predict the presence or absence of tumor viability in this study. Survival benefit associated with surgical resection for cDLMs remains unclear due to small sample size and insufficient power for this research question. Although these survival findings should be interpreted with caution, the DREAM study highlights potential concerns regarding the inclusion of DLMs as targets for surgery following conversion chemotherapy.

ARTICLE INFORMATION

Accepted for Publication: July 24, 2025.

Published Online: September 17, 2025.
doi:10.1001/jamasurg.2025.3600

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Obtained funding: Kataoka, Nakamura, Evrard.

Administrative, technical, or material support: Kataoka, Kang, Rivoire, Nakamura, Bonhomme, Caballero, Kanemitsu, Evrard.

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Conflict of Interest Disclosures: Dr Kataoka reported personal fees from Guardant Health, Eli Lilly, Takeda Pharmaceutical, and Merck Biopharma and grants from Sysmex and Nakatani Foundation outside the submitted work. Dr Ducreux reported personal fees from Roche, Servier, Beigene, AstraZeneca, Daichii Sankyo, Pierre Fabre, Takeda, Merck Serono, Bayer, and Agenus outside the submitted work and other (wife was the head of the Oncology Business Unit of Sandoz France Until January 4, 2025). Dr Nakamura reported personal fees from Chugai, AstraZeneca, Takeda, Taiho, and Eli Lilly outside the submitted work. Dr Caballero reported serving as a member of the European Society of Surgical Oncology Board of Directors. Dr Lordick reported personal fees from Amgen, Astellas, Art Temp, Boehringer Ingelheim, Eli Lilly, Elsevier, Incyte, MedUpdate, Merck Serono, Merck Sharp & Dohme, PAGE, Roche, Servier, Springer Nature, StreamedUp!, and Servier; personal fees and scientific grants from Astra Zeneca, Bristol Myers Squibb, and Daiichi Sankyo; and personal fees and grants from Beigene and Gilead lomedico outside the submitted work. No other disclosures were reported.

Funding/Support: This work was funded by Krebsforschung Schweiz, Ligue nationale contre le cancer, Anticancer Fund, Kom Op Tegen Kanker and the Japan Agency for Medical Research, Practical Research for Innovative Cancer Control from the Japan Agency for Medical Research and Development, the Japan Agency for Medical Research (16ck0106211h0001 and 19ck0106495h0001), and the European Organisation for Research and Treatment of Cancer Gastrointestinal Tract Cancer Group. Dr Kataoka's fellowship at the European Organisation For Research And Treatment of Cancer was funded by Fond Cancer Association Sans But Lucratif.

Role of the Funder/Sponsor: The funders had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; or decision to submit the manuscript for publication. European Organisation for Research and Treatment of Cancer and Japan Clinical Oncology Group, as sponsors of the study, were involved in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, and approval of the manuscript; and decision to submit the manuscript for publication.

Data Sharing Statement: See Supplement 2.

Additional Contributions: We thank Laurence Collette, PhD, formerly of European Organisation For Research And Treatment Of Cancer Headquarters, for designing and supervising the study. We thank all of the patients and their families for their participation as well as all study investigators and study teams for their contributions, and European Organisation For Research And Treatment Of Cancer Headquarters staff involved, including Sara Meloen, MSc, for pharmacovigilance management; Cathy Van de

Wiele, MSc, and Hafida Lmalem, MSc, for imaging; Herve Azobou, MSc, for statistical programming; Peter De Burghgraeve, MSc, Yuliya Vostrikova, MSc, Stefanova Tsvetelina, MSc, and Shani De Coster, MSc, for data management; Sofie Verschueren, PhD, for operations; and Corinne Daumer, AA, for project management. No compensation outside of regular wages or salary was provided for these contributions.

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