Ann Surg Oncol (2018) 25:550–557
https://doi.org/10.1245/s10434-017-6265-9

Annals of
SURGICAL ONCOLOGY
OFFICIAL JOURNAL OF THE SOCIETY OF SURGICAL ONCOLOGY

ORIGINAL ARTICLE – HEPATOBILIARY TUMORS

Effectiveness of Hepatic Artery Infusion (HAI) Versus Selective Internal Radiation Therapy (Y90) for Pretreated Isolated Unresectable Colorectal Liver Metastases (IU-CRCLM)

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ABSTRACT

Background. In the era of modern effective systemic chemotherapy, the comparative effectiveness of hepatic artery infusion (HAI) versus selective internal radiation therapy (yttrium-90 [Y90]) for pretreated patients with isolated unresectable colorectal liver metastasis (IU-CRCLM) remains unknown. This study sought to compare the overall survival (OS) after HAI versus Y90 for IU-CRCLM patients treated with modern chemotherapy and to perform a cost analysis of both regional methods.

Methods. This study retrospectively reviewed patients receiving HAI or Y90 in combination with modern chemotherapy as second-line therapy for IU-CRCLM. Overall survival was calculated from the time of IU-CRCLM diagnosis. Uni- and multivariate models were constructed to identify independent predictors of survival.

Results. The inclusion criteria were met by 97 patients (48 HAI patients and 49 Y90 patients). Both groups were similar in terms of age, gender, body mass index (BMI), synchronous disease, carcinoembryonic antigen (CEA), liver tumor burden, and chemotherapy-related characteristics including use of biologics and lines of chemotherapy (all $p > 0.05$). The HAI group had a better OS than the Y90 group (31.2 vs. 16.3 months; $p < 0.001$). A trend toward reduced cost favored the HAI group (median, \$29,479 vs. \$39,092; $p = 0.296$). The multivariate analysis showed that receipt of HAI (hazard ratio 0.465) and number of chemotherapy lines (HR 0.797) were associated with improved OS from the date of IU-CRCLM diagnosis.

Conclusions. This is the first study to evaluate the comparative effectiveness of HAI versus Y90 in the era of modern chemotherapy, and the findings suggests that HAI is associated with better survival than Y90 for patients with pretreated IU-CRCLM.

Colorectal cancer (CRC) is the third most common cancer and the second leading cause of cancer-related mortality in the United States.[1] Liver metastases develops ultimately in approximately 60% of patients, 10–25% of whom have liver-only disease.[2,3] Whereas the response rates to first-line systemic chemotherapy for patients with isolated unresectable CRC liver metastasis (IU-CRCLM) can be up to 60%, the response rates for second-line therapy are generally poor (20–30%), with a median survival period of approximately 1 year.[4–15] Consequently, various regional therapies have been combined with systemic chemotherapy to improve survival in this salvage setting.

Recent studies have reported impressive response rates and survival for hepatic artery infusion (HAI) therapy with floxuridine (FUDR) as the first- or second-line therapy for

Electronic supplementary material The online version of this article (https://doi.org/10.1245/s10434-017-6265-9) contains supplementary material, which is available to authorized users.

First Received: 19 July 2017;
Published Online: 27 November 2017

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IU-CRCLM, particularly when HAI is combined with modern systemic chemotherapy.[16–19] However, HAI therapy requires unique surgical multidisciplinary expertise and is therefore limited to a few centers.[20,21]

A more commonly used regional therapy is selective internal radiation with yttrium-90 (Y90), also known as radioembolization. Studies have investigated Y90 extensively for metastatic CRC, most recently in the phase 3 SIRFLOX trial (Selective internal radiation (Y90) + mFOLFOX6 ± bevacizumab vs. mFOLFOX6 ± bevacizumab).[22,23] In this trial, a significant improvement in liver progression-free survival (PFS) was noted in the Y90 group (20.5 vs. 12.6 months; $p = 0.002$) compared with the chemotherapy-alone group. Notably, however, overall PFS was comparable in the two arms (10.7 vs. 10.2 months).[23]

One limitation of the aforementioned trial and other studies evaluating various regional hepatic therapies for CRCLM was the inclusion of patients with extrahepatic disease (EHD), a subset less likely to benefit from regional therapies and the likely reason for the lack of observed difference in PFS in the SIRFLOX 3 trial.[22,24,25] Due to the lack of available studies comparing HAI with Y90 in IU-CRCLM, we sought to compare the survival of patients with radiologically verifiable IU-CRCLM who underwent HAI or Y90 treatment in conjunction with modern-day chemotherapeutic regimens at our institution during the last decade. Additionally, due to the paucity of data on the cost of these regional therapies, our secondary aim was to perform a cost analysis of HAI versus Y90.

PATIENTS AND METHODS

Study Design, Definitions, and Patient Selection

This retrospective institutional review board-approved (PRO#17040450) analysis included all IU-CRCLM patients who underwent second-line HAI or Y90 in combination with modern systemic chemotherapy at the University of Pittsburgh Medical Center (UPMC) between 2004 and 2015. All cross-sectional imaging (CT ± MRI ± PET of the chest, abdomen, and pelvis) was reviewed to document absence of EHD and confirm unresectability, defined as a remnant liver volume too small in relation to the extent of a resection ± ablation needed to extirpate all metastasis or deemed unresectable by an experienced Hepatopancreatobiliary (HPB) surgeon. Modern chemotherapy was defined as the use of multidrug regimens containing oxaliplatin and/or irinotecan ± biologics.

Patients referred for regional therapy typically are those who have previously received systemic chemotherapy as first-line therapy for IU-CRCLM. Although UPMC is composed of a large multihospital network, regional therapy typically is administered at one of two flagship sites, one possessing expertise in HAI and Y90 and the other possessing expertise in Y90 only. Thus, in the absence of prior comparative efficacy data for both methods, the multidisciplinary tumor board's decision to purse a particular regional method was driven largely by the availability and institutional expertise of HAI versus Y90 at the two different sites.

HAI Group

The technique for HAI pump placement and FUDR treatment dosages has been described previously.[16,26] Placement of HAI was performed via laparotomy ($n = 40$), robotically ($n = 6$), or laparoscopically ($n = 2$). Primary tumor resection typically was performed (if not previously done) at the time of HAI pump insertion. To evaluate the impact of HAI therapy fully for patients with IU-CRCLM, the study excluded HAI patients if they had an HAI pump placed at the time of (1) concurrent isolated liver perfusion, (2) resection ± ablation of liver metastasis, (3) resection of limited abdominal EHD, or (4) definite or suspected EHD.

Figure 1a details the search strategy for the HAI group. After HAI placement, these patients undergo further systemic chemotherapy concurrently with HAI-FUDR. Although no current guidelines exist for the duration of

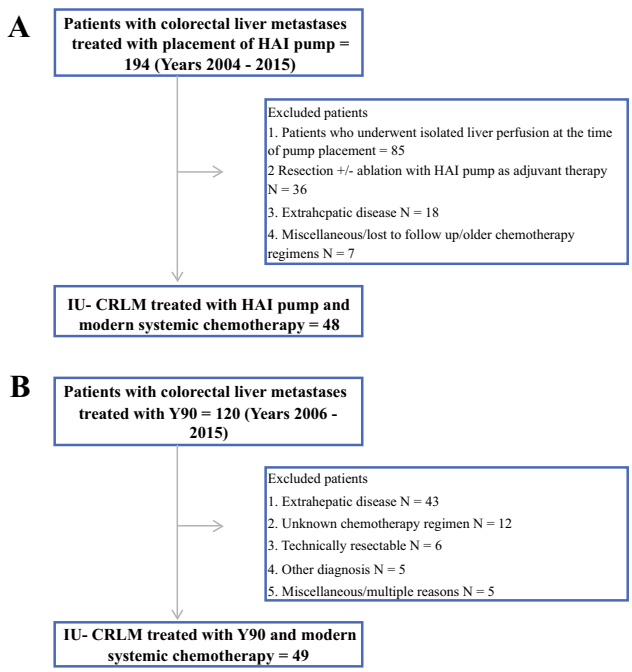

FIG. 1 **a** Flow chart depicting the search strategy for hepatic artery infusion (HAI) plus modern systemic chemotherapy. **b** Flow chart depicting the search strategy for yttrium-90 (Y90) plus modern systemic chemotherapy

HAI therapy, we have favored administering six cycles (6 months) of total therapy if possible or continued therapy until toxicity or disease progression.

Y90 Group

All patients considered for Y90 underwent a planning visceral angiogram to delineate hepatic anatomy and calculate the shunt fraction using a technetium-99m-labeled macroaggregated albumin (99mTc-MAA) study.[27] Our approach was to treat one liver lobe at a time. Usually, the lobe with the greater disease burden was treated first. The other liver lobe was treated after 2–4 weeks. The dose of Y90 was based on the recommendations provided by our nuclear medicine department, which in turn were based on planning studies including pretreatment angiography, single-photon emission computed tomography (SPECT). A modified partition model was used to calculate the Y90 microsphere activity to be administered to the patients. The prescribed activity was calculated to deliver 50 Gy to the targeted liver tissue.

Figure 1b provides a search strategy for the Y90 group patients. Similar to the HAI subgroup, Y90 patients with definite or suspected extrahepatic disease were excluded from this analysis.

Cost Analysis for HAI and Y90

Cost data were abstracted from UPMC's cost informational system, initially implemented in 2012 and updated with modifications until 2013. Thus, the costs obtained in this study were limited to 2013 onward. The costs included in the analysis represented controllable (direct) costs only and included both unit operating costs (e.g., patient and unit supplies, drugs, blood products and services, salaries and benefits, depreciation) and unit supporting costs (physician services, central supplies, administrative fees, utilities and management, clinical engineering, and environmental services) (Fig. 2).

The cost analysis for the HAI group included the cost of the index hospital admission for pump insertion (and any concurrent primary tumor resection) and overall FUDR treatment (including its outpatient administration). Because some HAI procedures involved concurrent primary tumor resection, we calculated the costs for the total HAI cohort in addition to the HAI-only group and the HAI plus primary tumor resection group. For robotically performed procedures, the costs associated with the robot were taken into account. The Y90 costs also included the cost of pre-Y90 planning angiograms and any peri-procedural inpatient admission-related costs.

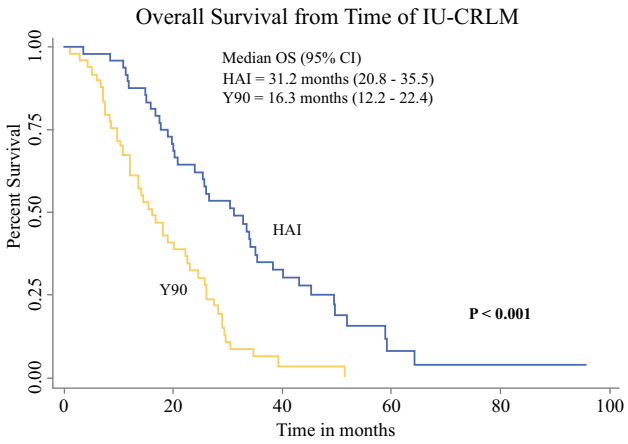

FIG. 2 Kaplan–Meier survival curves for overall survival (OS) after hepatic artery infusion (HAI) versus yttrium-90 (Y90) from the time of diagnosis of isolated unresectable colorectal liver metastasis (IU-CRCLM). The p value was computed using the log-rank test. Compared with Y90, HAI demonstrated a statistically significant association with improved OS (31.2 vs. 16.3 months; $p < 0.001$)

Statistical Analyses

Continuous data were summarized as means ± standard deviations or as medians and interquartile ranges (IQRs). Categorical data were summarized as frequencies and percentages. To examine the baseline differences between the two groups, Fisher's exact test or the Chi square test was used for categorical variables. Continuous variables were analyzed using the independent two-sample t test or the Wilcoxan rank sum test as appropriate.

To avoid lead-in bias, overall survival, the primary end point of this study, was measured as the time from the date that radiologically verified IU-CRCLM was diagnosed to the date of death or last censored follow-up visit. Follow-up evaluation was completed for all the patients.

The Kaplan–Meier method was used to estimate the probability of overall survival, and the log-rank test was used to compare survival functions. Uni- and multivariable analyses were based on Cox proportional hazards regression modeling. Variables were introduced into the multivariable model based on statistical significance. A p value lower than 0.05 was considered statistically significant. All analyses were performed using STATA 14.1 (Statacorp, College Station, TX, USA).

RESULTS

Patient Characteristics

The inclusion criteria were met by 97 patients from 2004 to 2015 (48 HAI patients and 49 Y90 patients). Table 1 displays the demographic, disease, and treatment

TABLE 1 Clinicopathologic, treatment-related, and survival data of the study cohort

	All ($n = 97$)	HAI ($n = 48$)	Y90 ($n = 49$)	p Value
Demographics				
Mean age (years)	59.6 ± 12.5	57.5 ± 11.8	61.6 ± 12.8	0.112
Female gender: *n* (%)	33 (34)	16 (33.3)	17 (34.7)	0.888
ECOG ≥ 1: *n* (%)	40 (41.2)	25 (52.1)	15 (30.6)	0.032
Mean BMI (kg/m^2)	27.7 ± 6.2	28.2 ± 6.5	27.4 ± 6.0	0.521
Synchronous presentation: *n* (%)	83 (85.6)	41 (85.4)	42 (85.7)	0.967
Median CEA at diagnosis of stage 4 (range)	80.6 (15–687)	117 (17–825)	45 (11–322)	0.126
Previous liver resection: *n* (%)	24 (24.7)	6 (12.5)	18 (36.7)	0.006
Liver tumor burden				
Median no. liver lesions (range)	10 (5–28)	12.5 (7–31)	7 (5–19)	0.028
Mean largest lesion (cm)	6.3 ± 3.9	6.9 ± 4.5	5.7 ± 3.1	0.148
Liver replacement by tumor (%)	38.3 ± 24.9	41.7 ± 24.8	34.9 ± 24.8	0.185
Primary tumor-related characteristics*n* (%)				
Left primary tumor location (vs right)	65 (67)	36 (75)	29 (59.2)	0.127
Rectum versus colon	25 (26)	14 (29.2)	11 (22.5)	0.485
Grade well/moderate (vs. poor)	83 (85.6)	40 (83.3)	43 (87.7)	0.360
Primary tumor resected	89 (91.7)	48 (100)	41 (83.7)	0.006
Stage T3/T4 (vs. T1/T2)[a]	67 (75.2)	36 (75)	31 (75.6)	0.216
Positive LN status (vs. negative)[b]	55 (61.8)	34 (70.8)	21 (51.2)	0.187
Perineural invasion[a]	13 (14.6)	13 (27.1)	0 (0)	0.005
Lymphovascular invasion[a]	34 (38.2)	28 (58.3)	6 (14.6)	0.003
Mutated KRAS status ($n = 68$)	19 (27.9)	11 (27.5)	8 (28.6)	0.923
Stable microsatellite status ($n = 41$)	40/41 (97.6)	30/31 (96.7)	10/10 (100)	1.000
Chemotherapy-related data				
Use of biologic therapy: *n* (%)	87 (89.7)	43 (89.6)	44 (89.8)	0.973
Receipt of first-line chemotherapy: *n* (%)	97 (100)	48 (100)	49 (100)	1.000
Median duration of first-line chemotherapy: months (range)	6 (4–6)	6 (4–7)	6 (4–6)	0.356
Receipt of second-line chemotherapy: *n* (%)	85 (92.4)	34 (87)	43 (96)	0.166
Median duration of second-line chemotherapy months (range)	5 (3–6)	5 (3–6)	4 (3–6)	0.245
Median chemotherapy lines received: *n* (%)	3 (2–4)	3 (2–3)	3 (2–4)	0.408
Survival data				
Death: *n* (%)	87 (89.7)	40 (83.3)	47 (95.9)	0.051
Mean follow-up (months)	41.3 ± 26.4	41.5 ± 26.4	41.1 ± 26.7	0.991
Overall survival from stage 4 diagnosis: months (95% CI)	34.2 (29.5–38.4)	34.4 (26.1–43.2)	32 (28.2–38.4)	0.291
Overall survival from IU-CRCLM diagnosis: months (95% CI)	22.6 (18.2–26.2)	31.2 (20.8–35.5)	16.3 (12.2–22.4)	< 0.001

Continuous variables are summarized as means and standard deviations, or as medians and interquartile ranges

ECOG Eastern Cooperative Oncology Group, *HAI* hepatic artery infusion, *Y90* yttrium-90, *BMI* body mass index, *CEA* carcinoembryonic antigen, *CI* confidence interval, *IU-CRCLM* isolated unresectable colorectal liver metastasis

[a]Denominator = resected patients only ($n = 89$)

characteristics of the overall cohort. The mean age was 59.6 years, and 34% of the patients were woman.

All the patients were pretreated with systemic chemotherapy for CRCLM a median of 6 months before regional therapy. Only 2 of the 48 patients in the HAI group received Y90 treatment after completing HAI therapy. Given the retrospective nature of the study, these patients were analyzed in the HAI group on an intent-to-treat basis.

The HAI and Y90 patients were comparable in terms of most demographic variables, tumor-related variables, and chemotherapy-related variables (including number of

chemotherapy lines and median duration of first- and second-line chemotherapy regimens) (all $p > 0.05$). The patients in the HAI group were more likely to have an Eastern Cooperative Oncology Group (ECOG) score of 1 or higher (52.1% vs. 30.6%), more liver lesions (median 12.5 vs. 7), and removal of their primary tumor (100% vs. 83.7%; all $p < 0.05$). The Y90 patients were more likely to have had a previous liver resection (36.7% vs. 12.5%; $p = 0.006$).

In the HAI group, 22 patients had concomitant resection of a primary tumor [5 right colon resections, 6 left colon resections, 9 low anterior resections (LARs), 2 abdominoperineal resections (APRs)]. The median hospital stay for the HAI group was 8 days (IQR 7–11 days), and the median number of FUDR cycles was 4 (IQR 2–8). For the patients who underwent Y90 therapy, the median number ofÆ treatments was 2 (IQR 1–2), the median number of planning angiograms was 3 (IQR 3–3), and the mean total dose of Y90 per patient was 1.685 ± 0.9 GBq. All the Y90 patients completed their intended therapy.

Predictors of Overall Survival from the Time of IU-CRCLM Diagnosis

The HAI and Y90 groups did not differ significantly in terms of OS from the time of stage 4 disease diagnosis (34.4 vs. 32 months; $p = 0.291$). However, when OS was determined from the time IU-CRCLM diagnosis, HAI was associated with better OS than Y90 (31.2 vs. 16.3 months; $p < 0.001$). Similarly, the 2-year OS from the time of HAI pump placement and first Y90 treatment was 27.7% for the HAI group versus 4.8% for the Y90 group ($p = 0.007$) (Fig. S1).

The uni- and multivariable analyses of factors associated with OS from the time of IU-CRCLM are displayed in Table 2. Receipt of HAI therapy versus Y90 was associated with a significantly decreased hazard of death in the multivariable analysis [hazard ratio (HR), 0.465; 95% confidence interval (CI), 0.267–0.811; $p = 0.003$]. In addition to HAI therapy, previous liver resection (HR 3.22), largest tumor size (HR 0.933), tumor grade (HR 4.69) and number of chemotherapy lines (HR 0.80) demonstrated a significant association with OS.

Analyses of OS also were conducted from the first diagnosis of stage 4 metastatic liver disease, and HAI therapy (vs. Y90) was associated with a decreased hazard for death in the multivariable model (HR 0.561, 95% CI 0.342–0.919; $p = 0.022$) (Table 2).

Cost Analysis of HAI Versus Y90

Cost data were available for 34 patients (21 HAI patients and 13 Y90 patients) from the years 2013 to 2015 because the cost management system was implemented in 2013 (Table 3). The median cost was $29,479 (IQR $22,448–$35,153) for the HAI patients and $39,092 (IQR $22,028–$45,001) for the Y90 patients ($p = 0.296$). Notably, the median cost for HAI performed in the setting of a concomitant resection of the primary tumor ($n = 14$) was $30,578 (IQR $24,888–$44,253) versus $23,144 (IQR $18,968–$32,426) for the patients who had an HAI pump alone ($n = 7$; $p = 0.086$). When HAI therapy alone was compared with Y90, a median cost reduction of $15,948 was noted in favor of HAI therapy ($p = 0.075$).

DISCUSSION

This study compared the effectiveness of second-line HAI with that of Y90 therapy in conjunction with modern systemic chemotherapy for patients with liver-only unresectable colorectal metastasis. In this group of pretreated patients with a heavy liver tumor burden (median of 10 lesions and almost 40% of liver parenchymal replacement by tumor), HAI therapy was associated with significant improvement in OS from the time of IU-CRCLM diagnosis compared with Y90. Additionally, a trend in cost reduction was observed for HAI therapy, particularly in the group that did not undergo concurrent primary tumor resection at the time of HAI pump placement.

Systemic chemotherapy remains the mainstay of treatment for unresectable CRCLM.[28–32] Modern chemotherapy regimens have led to improvements in the survival of this patient subset. However, the prognosis for second-line (salvage) therapy is poor, necessitating the combination of systemic chemotherapy with adjunctive regional therapies such as HAI and Y90.[4–8] In a phase 2 study of HAI in combination with modern chemotherapy, D'Angelica et al.[17] reported a median OS of 32 months for patients with IU-CRCLM treated previously with chemotherapy. In a recent case–control study, we also showed that HAI therapy in combination with modern systemic chemotherapy is associated with better survival than chemotherapy alone (32.8 vs. 15.3 months; $p < 0.0001$).[16] Our HAI survival in the current study (median 31.2 months) is consistent with those reports, indicating that HAI combined with systemic therapy can prolong survival in a pretreated cohort (median of 6 months chemotherapy before regional therapy).

In addition, Y90 has been associated with improved survival for CRCLM patients. Both Van Hazel et al.[33] (randomized phase 2 trial) and Kosmider et al.[25] (cohort study) have reported improved survival for patients receiving Y90 in combination with chemotherapy as first-line treatment for CRCLM. In the latter study, 74% of the patients had IU-CRCLM, and the overall survival was

TABLE 2 Multivariate Cox regression analysis for overall survival

	HR (95% CI)	*p* value
From time of IU-CRCLM		
HAI (vs. Y90)	0.465 (0.267–0.811)	0.003
Age	1.008 (0.989–1.027)	0.377
ECOG (1 vs. 0)	1.201 (0.737–1.956)	0.462
Previous liver resection	3.216 (1.660–6.231)	0.001
Largest tumor size	0.933 (0.873–0.997)	0.042
Grade (poor vs. well/moderate)	4.689 (1.543–14.278)	0.006
No. of chemotherapy lines	0.797 (0.638–0.995)	0.045
From time of first diagnosis of stage 4		
HAI (vs. Y90)	0.561 (0.342–0.919)	0.022
No. of liver lesions	1.031 (1.018–1.043)	< 0.001
Use of biologic agent	3.221 (1.184–8.760)	0.022
First-line chemotherapy regimen duration	0.918 (0.856–0.983)	0.015
Duration of chemotherapy before regional treatment	0.994 (0.964–1.026)	0.724

IU-CRCLM isolated unresectable colorectal liver metastasis, *HR* hazard ratio, *CI* confidence interval, *HAI* hepatic artery infusion, *Y90* yttrium-90, *ECOG* Eastern Cooperative Oncology Group

TABLE 3 Median direct cost of hepatic artery infusion (HAI) versus; Y90, yttrium-90 (Y90)[a]

	n	Median hospital stay (days)	Median cost USD (IQR)
HAI	21	9	29,479 (22,448–35,153)
HAI alone	7	7	23,144 (18,968–32,426)
HAI + primary tumor resection[a]	14	9.5	30,578 (24,888–44,253)
Y90	13	2	39, 092 (22,028–45,001)

p value for HAI versus Y90 = 0.296; *p* value for HAI alone versus Y90 = 0.075; *p* value for HAI + resection versus Y90 = 0.734

USD United States dollars, *IQR* interquartile range

[a]Resection cost included

nearly 37.4 months for the patients without EHD versus 13.4 months for the patients with EHD ($p = 0.03$). Similarly, Hickey et al.[34] in a retrospective multicenter analysis of 531 patients reported a median OS of 37.7 months from stage 4 disease. However, more than 50% of the patients had a metachronous presentation (vs. only 15% in the current study), which is a favorable prognostic factor. The final OS results from the SIRFLOX trial are still awaited and will be reported in conjunction with the results from other randomized trials of Y90 (including FOXFIRE: phase 3 trial of chemo-radioembolization as first-line treatment of liver metastases in patients with colorectal cancer and FOXFIRE-Global). Despite initial data suggesting an improved liver PFS, overall PFS was not different, likely due to the inclusion of patients with EHD. Our study had the benefit of excluding patients with radiologically verifiable EHD, and thus reflects a more homogeneous population.

In this study, the OS survival of both the HAI and Y90 groups was similar from the time of stage 4 diagnosis. However, when the subgroup of patients with IU-CRCLM was examined, survival in the Y90 cohort was worse than in the HAI group (16.3 vs. 31.2 months).

Although it is difficult to draw conclusive evidence in the absence of prospective data, our multivariable analysis suggests (within the confines of this retrospective data set) that HAI may be superior to Y90 in the specific subset of isolated unresectable liver-only metastasis. The lack of overall survival benefit from the time of stage 4 diagnosis may be related to the significant heterogeneity between the two groups. For example, more patients in the Y90 group presented with resectable stage 4 disease and underwent previous liver resection. A favorable prognostic factor for overall stage 4 survival but not for survival from the time isolated unresectable CRCLM was diagnosed. It is reasonable to assume that more factors are at play when the

overall survival of patients with stage 4 CRC is assessed compared with the specific subgroup with IU-CRCLM. When these findings are placed in the context of clinical practice, they suggest that for patients presenting with IU-CRCLM, an initial trial of systemic chemotherapy followed by HAI therapy in conjunction with second-line systemic chemotherapy may be a reasonable approach. The role of Y90 in IU-CRCLM may be restricted to those for whom HAI therapy is contraindicated due to poor surgical candidacy or liver dysfunction. Ultimately, randomized trials combining modern systemic chemotherapy with HAI or Y90 in the first- and second-line treatment of IU-CRCLM are needed to confirm these findings.

In addition to comparing survival between HAI and Y90 therapy, this analysis attempted to outline the cost associated with these regional treatment methods. Despite its restriction to a subset of the total cohort, our cost analysis was novel because it took into account actual costs rather than hospital charges or reimbursement, which may vary widely and are influenced by region and third-party payers. Although it did not reach statistical significance, HAI therapy was associated with a trend toward decreased cost, a finding that may require a larger sample for verification. This trend was more pronounced for the subgroup that underwent HAI in the absence of primary tumor resection ($p = 0.075$) despite the fact that HAI insertion entails an operative procedure with a median hospital stay of 7 days.

The limitations of this study included its retrospective design and inherent selection bias that led to differences in the demographic, tumor, and treatment-related characteristics between the two cohorts. The Y90 cohort had better ECOG scores, fewer liver lesions, and greater likelihood of a prior liver resection, whereas the HAI patients were more likely to have their primary tumor resected. Additionally, given the radiographic exclusion of patients with EHD, the sample size was limited in both arms of the study. This however was necessary for assessment of the true impact these regional therapies had on a specific subset of patients with disease confined to the liver. We also acknowledge that radiographically occult disease may have been missed in the Y90 cohort. Our group and others are not currently pursuing diagnostic laparoscopy to rule out occult peritoneal disease in these patients. These would be important points to consider when a randomized controlled trial of regional therapies is contemplated. Finally, our cost data did not capture readmissions. Despite these inherent limitations, this is the first comparative analysis between HAI and Y90 in the era of modern chemotherapy and can form the basis of future comparative studies.

In conclusion, both HAI and Y90 are viable treatment options for patients with IU-CRCLM. Within the confines of a retrospective analysis, this study suggests that HAI may be associated with better overall survival than Y90 for pretreated patients with IU-CRCLM. Further studies are needed to outline the indications and role of these regional methods in the treatment of colorectal liver metastasis.

Compliance with Ethical Standards

Conflict of interest There are no conflicts of interest.

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