

ORIGINAL RESEARCH ARTICLE

Quartile deviation as a novel indicator of response evaluation regularity in liver cancer patients

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Abstract

Regular response evaluation (RE) is essential for whole-process cancer management, yet no standardized quantitative indicator exists to assess its regularity in clinical practice. This study proposed the quartile deviation (QD) of RE intervals as a novel indicator of RE regularity and examined its association with clinical characteristics and survival outcomes in patients with liver tumor lesions. Clinical data from patients treated at Shanghai General Hospital between January 1, 2015, and December 31, 2021, were retrospectively analyzed. A total of 102 eligible patients with at least four upper abdominal computed tomography or magnetic resonance imaging examinations were included, yielding 587 valid RE records; 60.8% completed seven or more REs during treatment. QD values of RE intervals were calculated to assess voluntary RE regularity. Using the mean QD value (6.77) as the cut-off, patients were classified into a regular RE group ($QD \leq 6.77$, $n = 67$) and an irregular RE group ($QD > 6.77$, $n = 35$). Patients with regular RE were younger (61.6 ± 1.218 years), had significantly shorter RE intervals (10.57 ± 0.4566 weeks), and achieved a longer median overall survival (39 versus 30 months) than those with irregular RE. Median progression-free survival did not differ significantly between groups. Patients with metastatic colorectal cancer exhibited lower QD values than those with hepatocellular carcinoma, indicating better RE regularity. In conclusion, QD is a practical indicator of RE regularity. More regular RE is associated with improved survival outcomes, supporting standardized cancer management.

Keywords: Response evaluation; Liver cancer; Regularity; Quartile deviation; Survival outcomes

1. Introduction

The clinical management of cancer patients encompasses more than just diagnosis and treatment; regular response evaluations (REs) are also critical. Therapeutic response is commonly assessed by changes in tumor burden, including tumor shrinkage and disease progression. Globally, cancer remains a major cause of mortality and economic loss. In 2020, there were 19.3 million new cancer cases and nearly 10 million cancer-related

deaths worldwide.¹ Encouragingly, in regions with a high prevalence of chronic hepatitis B virus infection, such as Eastern and Southeastern Asia, including China, the incidence and mortality rates of liver cancer have declined since the late 1970s.² The previously rising mortality rate of liver cancer has stabilized in the past five years.³ This plateau in incidence suggests the potential to manage certain cancers as chronic diseases, underscoring the need for standardized long-term management and regular RE in cancer patients with extended survival.

Treatment efficacy is typically evaluated through biochemical parameters and radiographic assessment of bidimensional tumor size using computed tomography (CT) or magnetic resonance imaging (MRI). According to current guidelines for liver cancer and colorectal liver metastases,^{4–6} a comprehensive response assessment is recommended 6–8 weeks after treatment. Upper abdominal imaging is important for diagnosing and evaluating tumors. Given the measurability of liver lesions, treatment response is often assessed using the RECIST criteria.⁷ In both primary and metastatic liver lesions, changes in liver target lesions reliably reflect therapeutic effects.^{8–11} However, social, familial, and personal factors may prevent some patients from adhering to regular RE schedules. In addition, limited medical resources, regional disparities in healthcare access, and disruptions caused by the COVID-19 pandemic have further complicated timely evaluation and follow-up.¹² Reduced access to care has been associated with a short-term decrease in cancer incidence, increased advanced-stage disease, and higher mortality.³

Although patient-level (biological), system-level (healthcare resource), and policy-level (insurance-related) factors all influence cancer outcomes, the negative consequences of irregular follow-up, such as disease progression or shortened survival times, should not be ignored. Currently, no standard definition of RE regularity exists, and the impact of irregular RE remains insufficiently studied. To address this gap, we propose a novel indicator to quantify RE regularity in cancer patients with liver lesions and evaluate the influence of RE regularity on treatment outcomes.

2. Methods

2.1. Study design and patients

To investigate the regularity of RE among cancer patients, we focused on patients with liver tumor lesions, including hepatocellular carcinoma (HCC) and metastatic liver lesions. We obtained data from the Clinical Research Intelligence System, an independently developed and maintained system at Shanghai General Hospital that

contains all records of inpatient and outpatient visits between January 1, 2015, and December 31, 2021. The platform was used to collect comprehensive data on treatment and examinations. Eligible patients were included based on the following criteria: (i) a previous pathological diagnosis of HCC or metastatic liver lesions, (ii) availability of complete clinical data since diagnosis, and (iii) at least four upper abdominal CT or MRI examinations performed at our hospital after treatment. Patients with missing radiographic assessment (CT/MRI) records or other variables required for analysis were excluded. This study was approved by the Ethics Board of Shanghai General Hospital (approval number: 2015SQ258).

2.2. Variables

Patient therapeutic data included structured variables (e.g., examinations and prescribed drugs) and unstructured data (e.g., medical history and clinical course) collected via the Scientific Research Cohort Management Platform from physicians' electronic medical records and related documents. All data were anonymously extracted to protect patient confidentiality.

Clinical characteristics, including age, sex, Eastern Cooperative Oncology Group performance status (ECOG PS), primary tumor location, clinical tumor stage, treatment regimen, and chemotherapy lines, were collected. According to CT/MRI reports and the RE Criteria in Solid Tumors version 1.1 (RECIST 1.1),⁶ RE outcomes included complete response, partial response, progressive disease, and stable disease. Progression-free survival (PFS) was defined as the time from treatment initiation to tumor progression, and overall survival (OS) as the time from treatment initiation to death from any cause or last follow-up. Survival data were obtained from medical records or telephone follow-up.

2.3. Definition of regular response evaluation as an indicator

Radiographic assessment data were extracted from examination records, with the dates of abdominal CT/MRI examinations defined as RE dates. RE frequency was defined as the number of abdominal CT and MRI examinations performed during the treatment period. Evaluation intervals were measured in weeks (seven days). The interval in weeks between consecutive RE dates was calculated as the difference between two examination dates divided by 7. Quartile deviation (QD, $QD = \text{QUARTILE.INC}[\text{array}, 3] - \text{QUARTILE.INC}[\text{array}, 1]$) was then calculated for each patient's evaluation intervals. QD was defined as the difference between the upper and lower quartiles of each patient's RE interval distribution. Lower QD values indicate less variability in interval length and,

therefore, greater regularity of RE.

2.4. Statistical analysis

The data were exported to Microsoft Excel (United States of America [USA]). Statistical analyses were performed via SPSS (version 26.0, SPSS Inc., USA), GraphPad Prism 7.0 (GraphPad Software Inc., USA), and R software (version 3.6.0). Statistical significance was defined as $p < 0.05$ (two-sided).

3. Results

3.1. Study cohort characteristics

After screening, 102 patients were enrolled in the study, and 587 valid RE records were analyzed (Figure 1). All enrolled patients had liver tumor lesions at the time of treatment and required regular upper abdominal CT or MRI examinations. Among patients included in the regularity analysis, the median age was 63 years; a higher

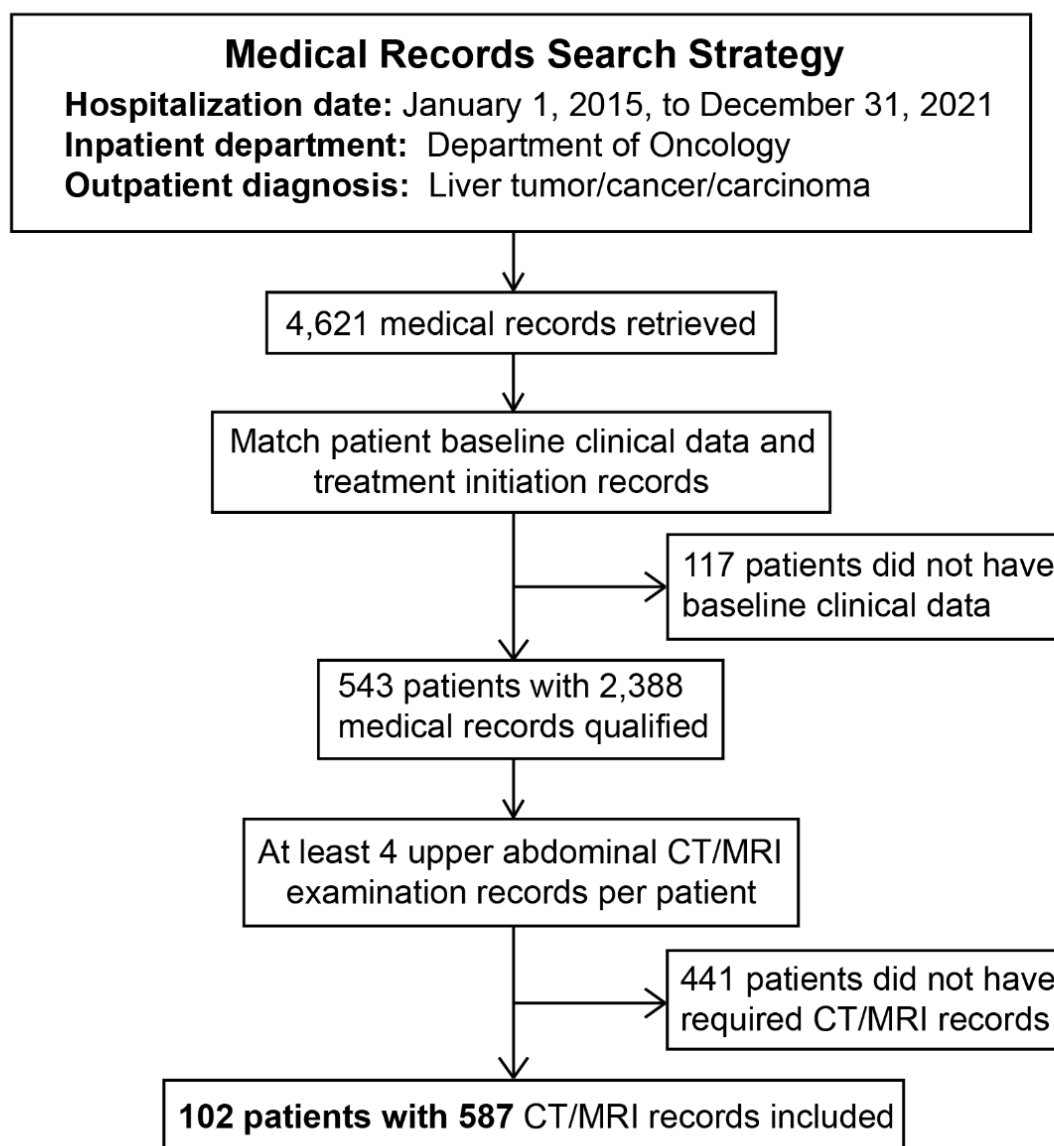


Figure 1. Flow chart of enrolled patients and records screening
Abbreviations: CT: Computed tomography; MRI: Magnetic resonance imaging.

proportion were aged > 63 years (53.92%), male (66.67%), and had an ECOG PS score of 0 (87.26%). Most patients were diagnosed with metastatic liver lesions (71.57%), and among these patients, tumors originating from the colon and rectum (48.04%) accounted for the highest proportion of primary sites. Most patients had metastatic disease at diagnosis, and those with advanced cancer (stage IV) constituted the majority of patients ineligible for surgery, with 70.59% requiring systemic treatment alone (64.71%). Moreover, only one-third of the study population received first-line therapy alone (32.35%); consequently, two-thirds of patients (60.78%) underwent more than seven REs during the treatment period (Table A1).

3.2. Overview of regular response evaluation in the study population

We calculated the patients' RE variables, including frequency, interval duration, and QD value, and visualized them in a heatmap sorted by QD value (increasing from left to right). As shown in the heatmap (Figure 2), most patients had RE intervals within 15 weeks (blue blocks), whereas patients on the right side of the heatmap had intervals exceeding 30 weeks (yellow and red blocks). Patients no. 99–102 underwent more than 15 REs after diagnosis; only no. 99 showed uneven color blocks, indicating irregular RE. In contrast, patients no. 42 and no. 86, both with QD = 0 at the left end of the heatmap, had identical blue blocks, demonstrating that regular RE at fixed intervals is feasible. We then summarized the three RE variables statistically (Table A2). Since diagnosis, most patients had 4 REs, with a maximum of 23 assessments over 5 years. Between each RE, 8.48% of patients were assessed every 9 weeks, while some waited up to 61 weeks, or nearly 16 months, for the next evaluation. The mean RE interval across all patients was 12.86 weeks. As the key indicator of regularity in this study, QD values varied widely. Some patients had

perfectly consistent intervals (QD = 0), while others had a maximum QD of 33.25. The average QD across all patients was 6.77, which was subsequently used as the cut-off to determine whether a patient's RE was regular.

3.3. Younger age and shorter evaluation intervals in the regular response evaluation group

Using QD = 6.77 as the cut-off for RE regularity, the study population was divided into a regular RE group ($n = 67$, $QD \leq 6.77$) and an irregular RE group ($n = 35$, $QD > 6.77$). Analysis of clinical characteristics and RE variables (Table 1) showed that, compared with the irregular RE group, patients in the regular RE group were younger (61.6 ± 1.22 versus 65.8 ± 8.19 years, $p = 0.0333$; Figure 3A). Regarding RE variables, while RE frequency did not differ significantly between groups, the interval duration was significantly shorter in the regular RE group (10.57 ± 0.46 versus 17.31 ± 0.95 weeks, $p < 0.0001$; Figure 3B).

3.4. Correlations between clinical characteristics, response evaluation variables, and overall survival

Correlations were determined for seven variables, including age, ECOG PS, stage, treatment lines, number of REs, QD, and OS (Table A3). Higher ECOG PS scores were associated with fewer REs and shorter OS ($r = -0.20$, $p = 0.04$; $r = -0.22$, $p = 0.04$, respectively). RE and OS times were positively correlated ($r = 0.49$, $p < 0.0001$; Figure 4A). Consistent with the regular RE group analysis, QD values were positively correlated with age ($r = 0.28$, $p = 0.004$; Figure 4B). Although not statistically significant, the QD value showed a negative trend with OS (Figure 4C). In addition, differences in QD values were compared across primary tumor types (Figure 4D). Patients with metastatic colorectal cancer (mCRC) exhibited lower QD values than those with hepatocellular carcinoma (5.96 ± 0.65 versus 8.85 ± 1.48 , $p = 0.045$), indicating that mCRC patients tended to undergo RE more regularly.

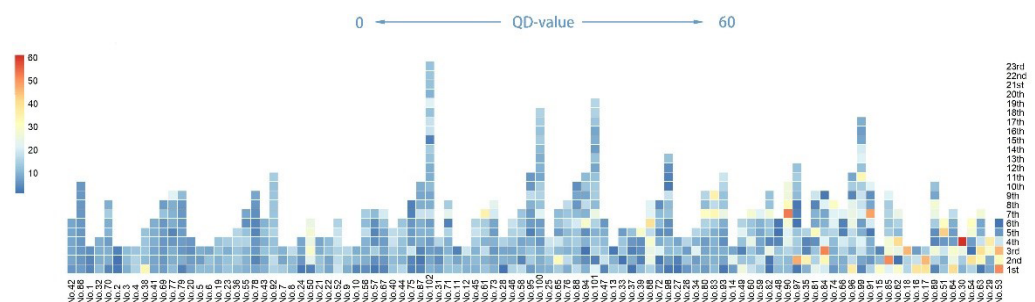


Figure 2. Heatmap overview of response evaluation (RE) regularity. Each column represents a patient's number of REs and interval durations during the treatment period. Patients are ordered along the bottom axis by increasing QD value, from left to right. The color block scale on the left indicates interval duration: blue represents shorter intervals (≤ 15 weeks), while red represents longer intervals (up to 60 weeks). The rightmost scale of each color block corresponds to the number of patient assessments.

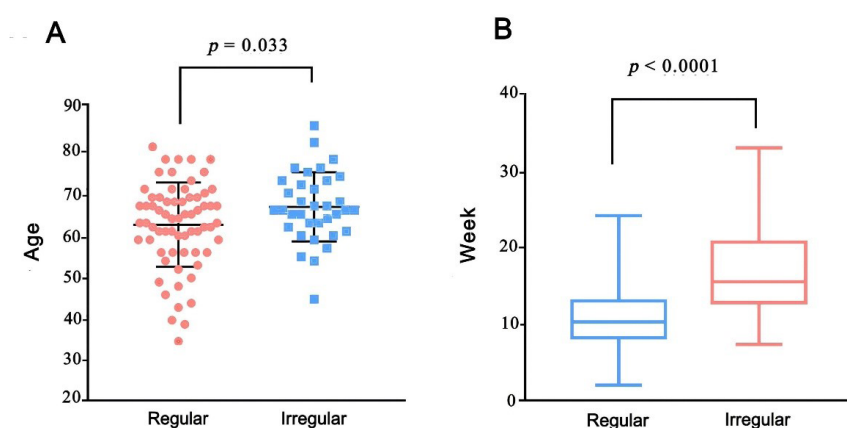


Figure 3. Comparison of age and response evaluation (RE) interval duration between the regular and irregular RE groups. (A) Patients in the regular RE group were younger than those in the irregular RE group ($p = 0.03$). (B) RE interval duration was shorter in the regular RE group than in the irregular RE group ($p < 0.0001$). p -values were calculated using Student's t -test.

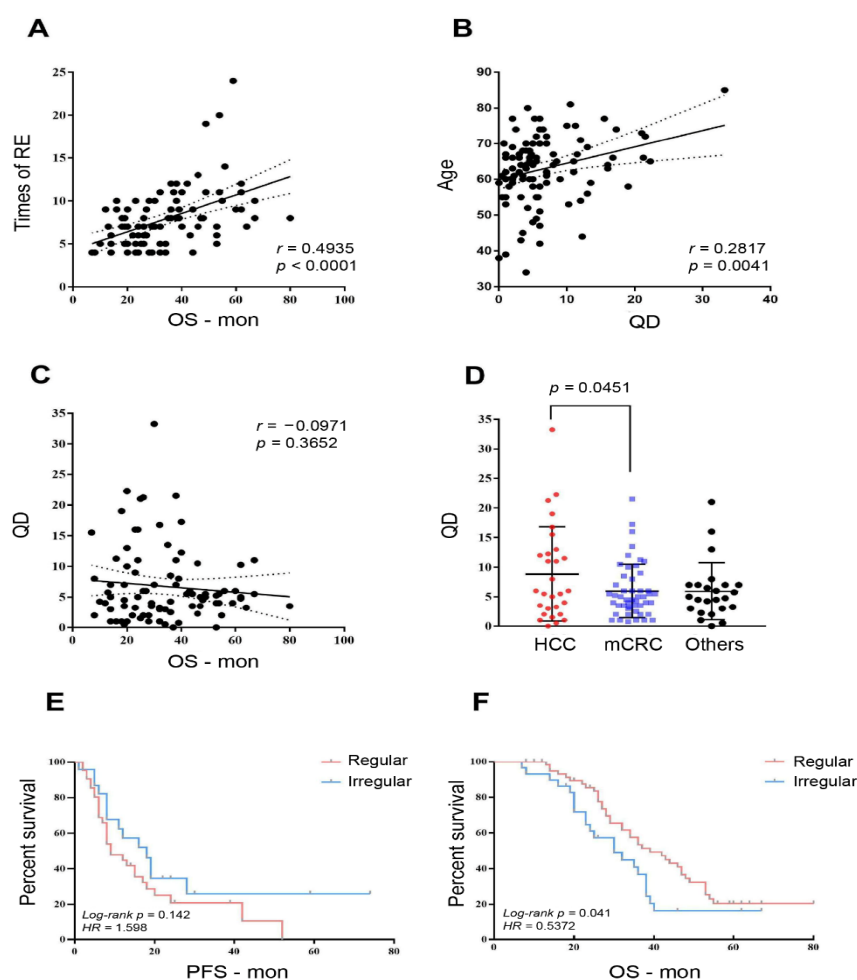


Figure 4. Correlations between clinical characteristics, response evaluation (RE) variables, and overall survival (OS). (A) The number of REs is positively correlated with OS. (B) Age is positively correlated with quartile deviation (QD). (C) QD is negatively correlated with OS. (D) QD values in the metastatic colorectal cancer (mCRC) group were lower than those in the hepatocellular carcinoma (HCC) group. (E and F) Kaplan-Meier curves illustrating differences in progression-free survival (PFS) and OS between the regular and the irregular RE groups.

Table 1. Comparison of general characteristics between the regular and irregular RE groups

Variables	Regular (<i>n</i> = 67)	Irregular (<i>n</i> = 35)	<i>p</i> -value ^a
Age	61.6 ± 1.22	65.8 ± 8.19	0.03
Sex	–	–	0.83
Male	44	24	
Female	23	11	
ECOG PS	–	–	0.79
0	58	31	–
1	8	3	–
2	1	1	–
Liver cancer type	–	–	0.35
Hepatocellular carcinoma	16	12	–
Metastatic liver lesions	51	23	–
Primary tumor location	–	–	0.44
Colon-rectum	35	14	–
Liver	16	12	–
Others ^b	16	9	–
Stage at diagnosis	–	–	0.46
II	7	5	–
III	10	8	–
IV	50	22	–
Type of treatment	–	–	0.61
Locoregional treatment ^c	7	6	–
Systemic treatment	45	21	–
Locoregional and systemic treatment	15	8	–
Prior chemotherapy lines	–	–	0.83
First-line	23	10	–
Second-line	29	16	–
Third-line and above	15	9	–
RE outcomes	–	–	0.23
PR	1	0	–
SD	11	2	–
PD	55	33	–
RE frequency	–	–	–
Times of REs	7.61 ± 0.47	8.2 ± 0.53	0.44
Interval duration (week)	10.57 ± 0.46	17.31 ± 0.95	<0.0001

Notes: Values are expressed as *n* or mean ± SD, as appropriate. ^aA statistical test was performed: chi-square test of independence and *t*-test. ^bOther primary tumor sites include the pancreas, esophagus, stomach, breast, ovary, lung, nasopharynx, peritoneum, and ureter. ^cLocoregional treatment refers to liver-directed locoregional therapies, including transarterial chemoembolization, radiofrequency ablation, microwave ablation, stereotactic body radiation therapy, and hepatic arterial infusion chemotherapy.

Abbreviations: ECOG PS: Eastern Cooperative Oncology Group performance status; PD: Progressive disease; PR: Partial response; RE: Response evaluation; SD: Stable disease.

3.5. Association of regular response evaluation with improved overall survival but not progression-free survival

We obtained PFS results for 66 patients and OS results for 89 patients by follow-up. Univariate analysis (Table 2) revealed that regular RE was a protective factor for longer OS (HR = 0.58, $p = 0.046$), whereas colorectal cancer (CRC) and other cancer types were associated with poorer OS (HR = 2.48, $p = 0.012$ and HR = 2.71, $p = 0.024$, respectively). Multivariate analysis (Table 2) revealed that CRC and irregular RE were associated with poorer OS (HR = 3.05, $p = 0.009$, and HR = 1.86, $p = 0.039$, respectively).

As shown in Figure 4E, the median PFS was 9 months in the regular RE group ($n = 42$) and 18 months in the irregular RE group ($n = 24$), with no significant difference between the groups. However, the median OS was significantly longer in the regular RE group (39 months, $n = 60$) compared with the irregular RE group (30 months, $n = 29$; Figure 4F).

4. Discussion

Recent studies have highlighted that some cancer patients face challenges in attending timely treatment and RE for various reasons, prompting us to investigate whether

Table 2. Hazard ratios for the clinical characteristics and response evaluation regularity in overall survival

Variables	Univariate analysis ^b		Multivariate analysis ^b	
	HR (95% CI)	<i>p</i> -value	HR (95% CI)	<i>p</i> -value
Age ^a	–	0.41	–	0.28
≤63	0.81 (0.49–1.34)	–	1	–
>63	1	–	1.36 (0.78–2.37)	–
Sex	–	0.35	v	–
Female	1.31 (0.75–2.29)	–	–	–
Male	1	–	–	–
ECOG	–	0.11	–	0.17
0	0.16 (0.02–1.22)	–	0.15 (0.02–1.38)	–
1	0.30 (0.03–2.80)	–	0.32 (0.03–3.20)	–
2	Reference	–	Reference	–
Primary tumor site	–	0.03	–	0.03
HCC	Reference	–	Reference	–
CRC	2.48 (1.23–5.01)	0.01	3.05 (1.33–7.03)	0.01
Others	2.71 (1.14–6.42)	0.02	2.29 (0.79–6.66)	0.13
Stage at diagnosis	–	0.55	–	0.23
II	Reference	–	Reference	–
III	1.58 (0.59–4.23)	–	2.13 (0.76–5.94)	–
IV	1.61 (0.68–3.80)	–	1.16 (0.46–2.88)	–
Prior therapy lines	–	0.25	–	0.41
First-line	Reference	–	Reference	–
Second-line	1.17 (0.64–2.15)	–	0.80 (0.39–1.64)	–
Third-line and above	1.71 (0.89–3.30)	–	1.27(0.60–2.70)	–
Regularity	–	0.046	–	0.039
Yes	0.58 (0.34–0.99)	–	1	–
No	1	–	1.86 (1.02–3.35)	–

Notes: ^aThe cut-off value was the median value. ^b Statistical test performed: Cox regression.

Abbreviations: CI: Confidence interval; CRC: Colorectal cancer; ECOG: Eastern Cooperative Oncology Group; HCC: Hepatocellular carcinoma; HR: Hazard ratio.

delayed or irregular RE affects survival outcomes. In this study, we introduced the concept of regular RE for the first time and analyzed differences in clinical variables and survival outcomes between patients with regular and irregular RE.

Our results indicated that among patients with liver tumor lesions requiring regular upper abdominal CT/MRI, those with liver metastases from colorectal cancer accounted for the majority. Although distant metastases were often present at diagnosis, most patients were stage IV, with normal performance status and mobility, allowing multiple regular assessments. Notably, one-quarter of the patients underwent more than 10 REs within 5 years after diagnosis. To quantify regularity, we calculated intervals between examinations, excluding assessments unrelated to RE, such as emergency treatment or treatment at another hospital, and used QD (reflecting dispersion between the 25th and 75th percentiles) as an indicator. Heatmaps visually illustrated RE regularity: uniform blue blocks indicated timely evaluations. By mapping time visually, healthcare providers can review whether patients are overdue for RE or miss it, facilitating clinicians and nurses in alerting patients in a timely manner and accounting for the lag time in the therapy efficacy analysis.

The QD is a novel, practical indicator for RE regularity. In the current clinical study, the sample mean and standard deviation were two commonly used statistics. Some trials used the median, minimum, and maximum values, or sometimes the first and third quartiles, to describe and report the results of the data analysis.¹³ Among all the statistical indicators that reflect the degree of data dispersion, only the QD can prevent the interference of extreme values at both ends of the data, and the difference between the middle two quartiles can visually reflect the dispersion of this group of data; that is, the smaller the QD is, the smaller the change in the data, and the more concentrated the data distribution. In addition, the QD value can be calculated directly using the Excel function, facilitating clinical data collection and statistical analysis. In our cohort, QD values ranged from 0 to 33.25, indicating substantial variability in regularity. Older patients with liver cancer had more difficulty completing RE on time and had a longer lag, consistent with prior findings that age affects cancer diagnosis, follow-up, and treatment planning.¹⁴ The incidence of cancer is higher in elderly individuals, and their care is complicated by multiple age-related conditions.^{15,16} Geriatric evaluation¹⁷ could modify the treatment regimen in 39% of older patients, mostly to a less aggressive therapeutic strategy, which leads to better quality of life.¹⁸ Our results suggest that both treatment planning and RE scheduling should take patient age into

account. However, due to sample size limitations, our study only compared clinical characteristics after simple grouping, and we hope that the application of QD can be broadly generalized. More precise correlation and logistic regression analyses could be performed once the sample size is expanded.

Importantly, regular RE was associated with significantly better overall survival. The biopsychosocial model suggests that the occurrence, development, outcome, prevention, and treatment of many diseases are influenced by psychosocial factors; at the same time, changes in the patient's disease or physical function defects can also trigger individual psychological and behavioral changes. Cancer is gradually being recognized as shifting from an incurable disease to a chronic disease, such as hypertension and diabetes; therefore, cancer diagnosis and treatment are gradually being replaced by the entire process of cancer management.¹⁹ The core of cancer management involves multidisciplinary standardized treatment, comprehensive monitoring before, during, and after treatment, and concurrent rehabilitation guidance and RE. In our study, we observed a marked difference in the regularity of cancer patients undergoing RE; however, the reasons behind irregular assessment are difficult to explain through univariate or multivariate analysis. For patients who cannot return to the hospital on time, the internal causes are usually related to individual circumstances, including negative psychological status due to the epidemic, changes in attitudes toward life and death, rapid disease progression, or financial factors. Additionally, many external factors may contribute, including traffic obstacles associated with cross-provincial medical treatment, the complexity of inpatient procedures, and epidemic-related closure management policies. Previous studies have shown that in the United States, patients with public or no health insurance, particularly adolescents and young adults, may experience longer delays in cancer diagnosis and poorer survival than their privately insured counterparts.^{20,21} Some patients can achieve prolonged survival while living with a stable tumor burden after appropriate treatment and standardized management. After appropriate treatment and standardized management, it is often possible to control the tumor in a stable state and achieve a survival time exceeding 5–10 years. However, the exact timing of REs appears to be overlooked, and the importance of timely feedback in the clinical decision-making process is undervalued.

This study has certain limitations. Only through a combined analysis incorporating additional biomarkers can QD achieve greater predictive value.^{22,23} Owing to the retrospective single-center design, standardized data

on lifestyle factors such as alcohol consumption—an important etiological factor for hepatocellular carcinoma—were not systematically collected in the Clinical Research Intelligence System. This limitation precludes exploration of the potential impact of alcohol intake (even at relatively small levels) on the regularity of RE and patient survival outcomes, and prevents a full assessment of the proportion of alcohol-related HCC among excluded or lost-to-follow-up patients. Looking ahead, we plan to address this gap by collaborating with other centers specializing in alcohol intake and alcohol-related liver disease, and by adopting multi-center prospective designs in which validated assessment tools will be used to systematically collect alcohol consumption data.

An important observation that warrants clarification is the differential association of RE regularity with OS and PFS: regular RE was linked to significantly better OS (median 39 versus 30 months) but shorter PFS (9 versus 18 months) compared to irregular RE. This pattern arises from the distinct characteristics of these two endpoints and their sensitivity to progression detection. PFS, defined as time from treatment initiation to tumor progression, is susceptible to detection bias: regular and consistent imaging evaluations in the regular RE group enabled timely identification of subtle tumor changes that might have been masked or delayed in the irregular group, leading to earlier documented progression and thus shorter measured PFS. In contrast, OS (time from treatment initiation to death from any cause or last follow-up) is a more robust endpoint, less affected by detection bias. The improved OS in the regular RE group reflects the clinical value of timely detection of progression, which facilitates prompt clinical intervention before disease deterioration. Given the current retrospective design, further validation is needed to strengthen this causal link. Future studies will expand sample sizes and conduct multi-center analyses to explore the timing of treatment adjustments and underlying mechanisms, aiming to better elucidate the relationship between RE regularity, progression detection, and survival outcomes.

In conclusion, to improve the efficiency of medical treatment and achieve individualized early diagnosis and treatment, our findings suggest that oncology clinicians should establish appropriate RE schedules while considering all aspects of the patient's condition when formulating treatment plans. In addition, patients should be encouraged to return to the same hospital on time for treatment and follow-up.

5. Conclusion

This study introduced a novel indicator for monitoring the regularity of RE in patients with primary or metastatic liver tumors. In clinical practice, physicians can calculate the QD value of patient response evaluation intervals using date differences and quartile calculations in Excel and remind patients to undergo follow-up assessments in a timely manner. We also demonstrated that regular assessment can prolong OS to some extent.

- (i) The QD of patient evaluation intervals could reveal the regularity of the RE in cancer patients.
- (ii) Regular response evaluation in cancer patients is associated with significantly improved survival.
- (iii) Oncology clinicians should arrange and encourage patients to undergo regular REs to improve treatment efficiency and prolong survival.

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Conflict of interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Author contributions

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Writing-review & editing: Xuefeng Zhou, Qi Li

All authors have read and approved the final version of the manuscript.

Ethics approval and consent to participate

This study was conducted in accordance with the principles of the Declaration of Helsinki and was approved

by the Medical Ethics Committee of Shanghai General Hospital (approval number: 2015SQ258). As this was a purely retrospective study based on anonymized hospital records, the requirement for written informed consent was waived by the institutional Ethics Committee. All personal information was anonymized to protect participant privacy.

Consent for publication

The requirement for written informed consent for publication was waived by the institutional Ethics Committee and all personal information was anonymized to protect participant privacy.

Availability of data

The data supporting the findings of this study are available from the corresponding author upon reasonable request. We follow academic norms to ensure the transparency and traceability of our research, with full respect for the principles of knowledge sharing and the outcomes of academic exchange. This information has been noted in the text for readers' reference.

Further disclosure

An earlier version of this study was presented as a poster abstract at the 12th Asia-Pacific Primary Liver Cancer Expert Meeting (APPLE 2022), held in Shanghai, China, from August 12 to 14, 2022.

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Appendix

Table A1. Characteristics of the study population

Characteristics	No. of patients (<i>n</i> , %)
Age, years	
≤63	47 (46.08)
>63	55 (53.92)
Sex	
Male	68 (66.67)
Female	34 (33.33)
ECOG PS	
0	89 (87.26)
1	11 (10.78)
2	2 (1.96)
Liver cancer type	
Hepatocellular carcinoma	29 (28.43)
Metastatic liver lesion	73 (71.57)
Primary tumor location	
Colon-rectum	49 (48.04)
Liver	29 (28.43)
Others	24 (23.53)
Stage at diagnosis	
II	12 (11.77)
III	18 (17.65)
IV	72 (70.59)
Type of treatment	
Locoregional treatment ^a	13 (12.75)
Systemic treatment	66 (64.71)
Locoregional and systemic treatment	23 (22.55)
Prior chemotherapy lines	
First-line	33 (32.35)
Second-line	45 (44.12)
Third-line and above	24 (23.53)
Times of response evaluation	
4	18 (17.65)
5~6	22 (21.57)
7~9	36 (35.29)
10~24	26 (25.49)

Abbreviation: ECOG PS: Eastern Cooperative Oncology Group performance status.

Table A2. Response evaluation (RE) related variables in patients ($n = 102$) with liver cancer

Variables	Min	Max	Mode (%)	Average
Times of REs since diagnosis	3	23	4 (17.65)	7.78
Interval between each RE (week)	1	61	9 (8.48)	12.86
QD of RE Interval (week)	0	33.25	1 (7.84)	6.77

Note: QD denotes the quartile deviation, calculated as $QD = QU - QL$, where QU and QL represent the upper and lower quartiles, respectively.

Table A3. Correlation analysis of clinical characteristics, response evaluation variables, and OS

r (p -value)	Age	ECOG PS	Stage	Treatment lines	Times of RE	QD	OS
Age	–	0.14 (0.16)	–0.07 (0.49)	0.16 (0.11)	–0.02 (0.82)	0.28 (0.004)	0.03 (0.76)
ECOG PS	0.14 (0.164)	–	0.22 (0.03)	0.03 (0.79)	–0.20 (0.04)	–0.03 (0.79)	–0.22 (0.04)
Stage	–0.07 (0.49)	0.22 (0.03)	–	0.15 (0.13)	–0.11 (0.29)	–0.12 (0.25)	–0.11 (0.33)
Treatment lines	0.16 (0.107)	0.03 (0.79)	0.15 (0.13)	–	0.03 (0.79)	–0.14 (0.17)	–0.10 (0.35)
Times of RE	–0.02 (0.82)	–0.20 (0.04)	–0.11 (0.29)	0.03 (0.79)	–	0.04 (0.70)	0.49 (<0.001)
QD	0.28 (0.004)	–0.03 (0.79)	–0.12 (0.25)	–0.14 (0.17)	0.04 (0.70)	–	–0.10(0.37)
OS	0.03 (0.76)	–0.23 (0.04)	–0.11 (0.33)	–0.10 (0.35)	0.49 (<0.001)	–0.10 (0.37)	–

Note: Data are presented as Pearson correlation coefficients (r) with corresponding p values.

Abbreviations: ECOG PS: Eastern Cooperative Oncology Group performance status; OS: Overall survival; QD: Quartile deviation.