ORIGINAL ARTICLE

DOI: 10.4274/eamr.galenos.2024.02259
Eur Arch Med Res 2024;40(2):110-113

Investigation of 90Yttrium Radioembolisation Absorbed Radiation Dose to ALBI Scores in Liver Malignancies: Is It Safe Over 500 Gy Tumor Absorbed Dose with Voxel Based Dosimetric Approach? Preliminary Results

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Abstract

Objective: This retrospective study aimed to assess the correlation between absorbed doses using 90Yttrium (90Y) radioembolization and liver function test results in patients with primary or metastatic liver malignancies.

Methods: This study involved 35 patients diagnosed with primary or metastatic liver cancer who underwent treatment with 90Y glass microspheres. Absorbed doses of the tumor and perfused tissue were calculated using voxel-based dosimetry. Albumin-bilirubin (ALBI) scores were calculated before treatment and at 2 and 4 weeks post-treatment. Associations between the absorbed dose and ALBI scores were analyzed.

Results: Thirty-five cases were included in the study. The median radiation doses were 618 Gy for tumors, 497 Gy for the total perfused liver, 281 Gy for the perfused normal liver, 8.5 Gy for the normal liver, and 52.5 Gy for the total liver. Before treatment, 28 (80%) patients had grade 1 ALBI scores, whereas the remainder had grade 2 scores. In two patients, ALBI scores increased to grade 2 during the second week of treatment. Treatment response correlated with partial regression. Although their absorbed doses were not significantly higher than those of other cases (618/550 Gy for tumors, 116/97 Gy for perfused normal tissue, 12/8.5 Gy for normal liver), their tumor-to-whole liver ratios were significantly higher than those of other cases (27-35%). In one patient, the score increased to grade 2 in the fourth week of treatment. However, in this case, liver function failure was attributed to progressive disease post-treatment. None of the grade 2 patients' scores increased to grade 3.

Conclusion: The study concluded that, through voxel-based dosimetry and a selective treatment approach, higher tumor doses with low absorbed doses in the whole liver were safe.

Keywords: Radiation segmentectomy, 90Yttrium, dosimetry, radioembolization

INTRODUCTION

Around 75-80% of normal liver perfusion is facilitated by the portal vein. However, malignant lesions, particularly those larger than 2 cm, receive their blood supply from the hepatic artery. This dual blood supply characteristic makes locoregional therapies, such as radiofrequency ablation, transarterial chemoembolization (TACE), and transarterial radioembolization (TARE), appealing options for managing liver malignancies.

90Yttrium (90Y) is a beta-emitting radionuclide (with an Eβ-max =2.28 MeV). 90Y-loaded microspheres have been employed

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Received: 05.12.2023
Accepted: 12.07.2024

Cite this article as: Akgün E, Akkaş BE. Investigation of 90Yttrium Radioembolisation Absorbed Radiation Dose to ALBI Scores in Liver Malignancies: Is It Safe Over 500 Gy Tumor Absorbed Dose with Voxel Based Dosimetric Approach? Preliminary Results. Eur Arch Med Res. 2024;40(2):110-113

Presented in: This study was presented orally at the 2023 International Medicine and Health Sciences Researches Congress (UTSAK).

worldwide for years for the radioembolization of primary and secondary liver cancers (1).

The objective of this study was to assess the impact of absorbed doses on liver function in patients undergoing high-absorbed doses during 90Y radioembolization.

METHODS

The study included 35 patients who underwent TARE using 90Y glass microspheres. Absorbed doses from hepatic artery perfusion scintigraphy images obtained using 99mTechnetium-labeled macroaggregate albumin were calculated using a voxel-based dosimetric approach using Simplicity^{Y90} (Mirada Medical, Oxford) software.

Albumin-bilirubin (ALBI) scores were calculated before, 2, and 4 weeks after treatment. Response to treatment was evaluated at 2 months after treatment according to the modified response evaluation criteria in solid tumours (RECIST 1.1) and positron emission tomography response criteria in solid tumours (PERCIST).

This study was approved by the Clinical Research Ethics Committee of University of Health Sciences Turkey, Başakşehir Çam and Sakura City Hospital (approval number: 2023.06.267, date: 22.06.2023). Informed consent form was obtained from all patients.

Statistical Analysis

Numerical variables are presented as median (range), whereas categorical variables are presented as percentages. Kruskal-Wallis tests were employed to compare ordinal variables among the groups. Additionally, the Mann-Whitney U test was used to assess the significance of pairwise comparisons.

Statistical significance was defined as a p-value of less than 0.05. All statistical analyses were executed using SPSS (version 22.0; IBM Corp, Armonk, New York, USA).

RESULTS

Thirty-five patients (17 females, 18 males) were included in the study. The median age was 64 years (range: 31-82) and the ages of male and female patients were similar. No serious treatment-related side effects were observed in any of the patients.

Twenty-two patients (63%) were diagnosed with hepatocellular carcinoma (HCC), 2 cases were diagnosed with cholongioselular carcinoma, and the others were metastatic cases (colon adenocancer: 7, neuroendocrine tumor: 3, breast ductal carcinoma: 1). Thirty-one (89%) patients were treated selectively and 4 (11%) were treated with the lobar approach.

The RECIST 1.1 and PERCIST treatment response evaluation results were similar. Treatment responses were as follows: 7 cases (21%) complete response (neuroendocrine tumor: 1, HCC: 6), 19 cases (53%) partial response (cholongioselular carcinoma: 1, breast ductal carcinoma: 1, neuroendocrine tumor: 2, colon adenocancer: 4, HCC: 11), 3 cases (8%) stable disease (colon adenocancer: 1, HCC: 2), 6 cases (18%) progressive disease (cholongioselular carcinoma: 1, colon adenocancer: 2, HCC: 3).

The median absorbed radiation doses were 618 Gy (range: 500-1000) for the tumor, 497 Gy (range: 270-843) for the total perfused liver, 281 Gy (range: 97-764) for perfused normal liver, 8.5 Gy (range: 1-49) for normal liver, and 52.5 Gy (range: 11-204) for the total liver. There were no significant differences between the absorbed doses according to gender and primary/secondary malignancy groups ($p>0.05$).

Before treatment, 28 out of 35 patients (80%) had grade 1 ALBI scores, whereas the remaining patients had grade 2 scores. In 2 HCC patients, ALBI scores improved to grade 2 in the second week of treatment. The treatment responses of these patients were consistent with partial response. Tumor, normal perfused and normal liver absorbed doses were 618/550 Gy, 116/97 Gy, and 12/8.5 Gy, respectively. The ratio of perfused normal liver volume to whole liver volume was only 0.2/0.7%. It was concluded that the absorbed doses were not significantly higher in these cases compared to all cases. However, tumor/whole liver volume ratios were significantly higher than those in other cases (27-35%).

In 1 metastatic patient, the score improved to grade 2 at week 4 of treatment. However, liver function failure was considered to be associated with progressive disease after treatment in this patient. None of the grade 2 patients experienced an increase in their scores to grade 3.

DISCUSSION

TACE has been a longstanding treatment for inoperable liver malignancies, and recent evidence indicates improved treatment responses and reduced side effects with TARE (2). TARE has emerged as a significant locoregional treatment option for both primary malignant liver neoplasms and liver metastases in cases unsuitable for surgery (3-5).

The ALBI score has superseded the Child-Pugh classification due to its ability to identify liver function decline at an earlier stage (6). Y90 is recommended for use in patients undergoing planned treatment and for monitoring post-treatment hepatotoxicity.

The advent of volumetric dosimetric methodology has signified a shift in our understanding of dosing strategies and subsequent treatment responses in radionuclide therapies. This approach by considering heterogeneity in the activity distribution within the perfused area, enables a more precise estimation of absorbed doses in both perfused tumor and normal tissue. Consequently, it facilitates the safe administration of higher tumor doses.

Initially, discussions regarding the tumor-absorbed dose ranged from 150-200 Gy in the early stages of treatment. However, recent publications have revealed the possibility of safe treatment escalation to up to 1000 Gy (7). Notably, a tumor response rate of only 22.5% was observed in cases of HCC with low tumor absorbed doses (8), a rate even lower than our recorded progression rate. Lam et al. (9) identified an independent correlation between predicted absorbed dose and survival. Our study's high tumor control rates further support the validity of this conclusion.

Kennedy et al. (10) reported transient mild-to-moderate liver-related toxicity in 94% of patients following TARE. They also highlighted that the delivered activity plays a role in toxicity. However, in their multicenter study, there was heterogeneity in activity calculation methods, and they lacked information on absorbed doses in tumor/non-tumor liver segments. In our study, no patient exhibited an increase in ALBI score grade due to high tumor-absorbed doses.

Given that a significant number of these patients had prior multiple chemotherapy treatments or cirrhosis, it is crucial to discern whether the ALBI grade escalation is attributed to TARE, concurrent diseases, or other therapeutic interventions. Typically, the anatomic response occurs later than the metabolic response (11). Surprisingly, in our case, both metabolic and treatment responses manifested similarly. This finding could potentially be linked to the administration of higher tumor-absorbed doses.

Study Limitations

Our primary limitation is the small cohort size. We intend to reevaluate our findings in a larger cohort to strengthen the robustness of our results.

Tailoring the optimal non-toxic dose for each patient through personalized treatment is a pivotal step in enhancing the success of TARE.

CONCLUSION

To conclude, employing voxel-based dosimetry and a tumor-selective approach to achieve high absorbed doses in the tumor while maintaining low doses in the normal liver is an effective and safe strategy for radioembolization treatment for suitable patient management.

Ethics

Ethics Committee Approval: This study was approved by the Clinical Research Ethics Committee of University of Health Sciences Turkey, Başakşehir Çam and Sakura City Hospital (approval number: 2023.06.267, date: 22.06.2023).

Informed Consent: Informed consent form was obtained from all patients.

Authorship Contributions

Surgical and Medical Practices: E.A., Concept: E.A., B.E.A., Design: E.A., B.E.A., Data Collection or Processing: E.A., Analysis or Interpretation: E.A., B.E.A., Literature Search: E.A., Writing: E.A.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declare that they received no financial support for this study.

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