Efficacy and Safety of Stereotactic Body Radiotherapy in Hepatocellular Carcinoma: A Systematic Review and Meta Analysis

Nayab Shahid[1], **Muhammad Aizaz Ur Rehman[1]**, Haziq Ovais[1], Marrium Sultan Dar[2], Ahmed Nadeem Abbasi[1], Nasir Ali[1], Asim Hafiz[1], Bilal Mazhar Qureshi[1], Maria Tariq[1]

[1]The Aga Khan University Hospital Karachi, [2]Indus Hospital and Health Network

Abstract

Hepatocellular carcinoma (HCC) is a leading cause of cancer-related mortality worldwide. Stereotactic body radiotherapy (SBRT) has emerged as a noninvasive alternative for patients unsuitable for surgery, ablative therapies, or locoregional/systemic treatment, prompting this meta-analysis to compare the efficacy and safety of SBRT with other treatment modalities in HCC.

A systematic literature search was conducted in PubMed, Google Scholar, and the Cochrane Library from inception till February 2026. Studies comparing SBRT with non-SBRT modalities were included.

A total of 24 studies involving 10,382 patients were included in this meta-analysis. Pooled hazard ratio analysis demonstrated improved progression-free survival (HR = 0.62, 95% CI 0.45–0.85, p = 0.003; I^2 = 0%) and local control (HR = 0.26, 95% CI 0.14–0.49, p < 0.0001) in the SBRT group. Separate timepoint analyses using risk ratios showed no significant differences in overall survival at 1 year (RR = 0.99, 95% CI 0.96–1.03, p = 0.70; I^2 = 47%), 3 years (RR = 0.97, 95% CI 0.91–1.05, p = 0.46; I^2 = 74%), or 5 years (RR = 0.89, 95% CI 0.69–1.14, p = 0.35; I^2 = 91%). Grade ≥3 toxicity according to CTCAE showed no significant difference between the SBRT and control groups (RR = 1.18, 95% CI 0.73–1.92, p = 0.49; I^2 = 0%).

This study demonstrates that SBRT is associated with improved progression-free survival and higher local control compared with non-SBRT modalities. SBRT represents a promising and effective treatment option for patients with HCC.

Introduction

Hepatocellular carcinoma (HCC) remains one of the leading causes of cancer-related mortality worldwide, posing significant therapeutic challenges due to high recurrence rates and limited treatment eligibility. Curative options such as surgical resection are often restricted by underlying liver dysfunction and tumor burden, while locoregional therapies like transarterial chemoembolization (TACE) require repeated interventions. Similarly, radiofrequency ablation (RFA) is constrained by tumor size, location, and technical feasibility.

In recent years, stereotactic body radiotherapy (SBRT) has emerged as a noninvasive and highly precise treatment modality, offering the advantage of delivering high-dose radiation with minimal damage to surrounding liver tissue. Despite increasing clinical adoption, the comparative efficacy and safety of SBRT relative to other treatment modalities remain an area of ongoing investigation.

This systematic review and meta-analysis aims to evaluate the effectiveness and safety of SBRT compared with non-SBRT treatments in patients with HCC.

Methods and Materials

A systematic literature search was conducted in PubMed, Google Scholar, and the Cochrane Library from inception till February 2026. Studies comparing the efficacy and safety of SBRT with non-SBRT modalities were included. The primary outcome was overall progression-free survival (PFS), while the secondary outcomes were survival (OS), local control (LC) rates, and Grade ≥3 toxicity according to CTCAE (Common Terminology Criteria for Adverse Effects). A random-effects model was employed to calculate the Risk Ratio (RR) and Hazard Ratio (HR) with 95% Confidence Interval (CI). Meta-analysis was performed using Review Manager version 5.4.1 and openMeta (analyst) software.

Results

A total of 24 studies involving 10,382 patients with HCC treated with ≤10 fractions of SBRT were included. Pooled hazard ratio analysis demonstrated improved progression-free survival (HR = 0.62, 95% CI 0.45–0.85, p = 0.003; I^2 = 0%) and local control (HR = 0.26, 95% CI 0.14–0.49, p < 0.0001) in the SBRT group. Separate timepoint analyses using risk ratios showed no significant differences in overall survival at 1 year (RR = 0.99, 95% CI 0.96–1.03, p = 0.70; I^2 = 47%), 3 years (RR = 0.97, 95% CI 0.91–1.05, p = 0.46; I^2 = 74%), or 5 years (RR = 0.89, 95% CI 0.69–1.14, p = 0.35; I^2 = 91%). Grade ≥3 toxicity according to CTCAE showed no significant difference between the SBRT and control groups (RR = 1.18, 95% CI 0.73–1.92, p = 0.49; I^2 = 0%).

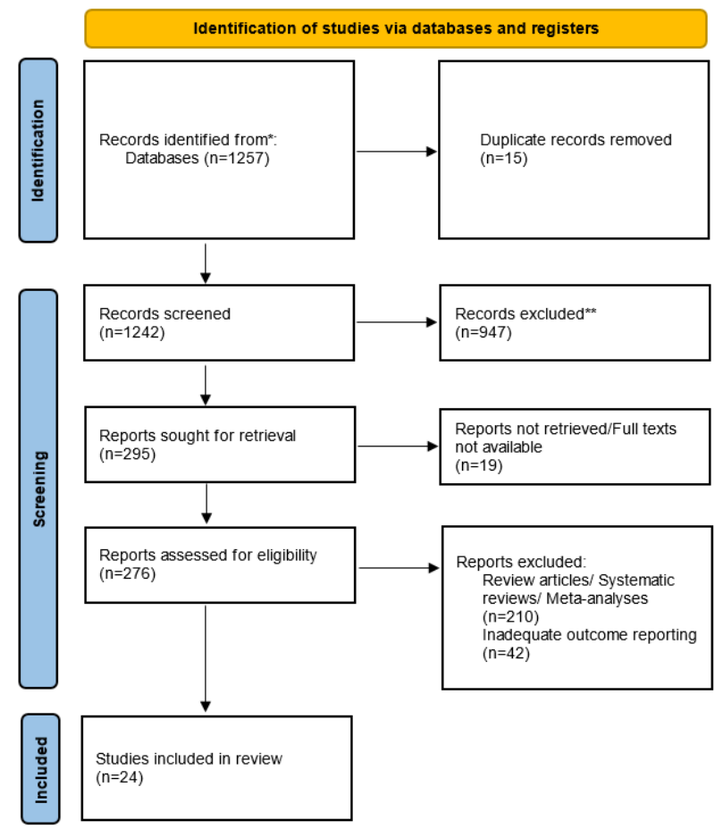


Figure 1: Prisma Chart for the Study

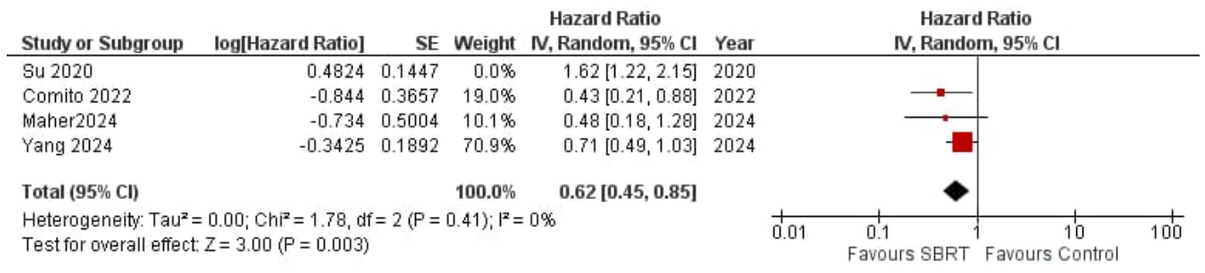


Table 1: Progression Free Survival

Discussion

This meta-analysis demonstrates that SBRT provides significant improvements in progression-free survival (PFS) and local control (LC) compared to non-SBRT treatment modalities. The substantial reduction in hazard ratios for both PFS (HR = 0.62) and LC (HR = 0.26) highlights the strong tumor control achieved with SBRT, likely attributable to its ability to deliver ablative radiation doses with high precision.

Interestingly, despite improved disease control, no statistically significant benefit in overall survival (OS) was observed at 1-, 3-, or 5-year time points. This discrepancy may be explained by the multifactorial nature of survival in HCC patients, including underlying liver function, comorbidities, and high rates of intrahepatic recurrence beyond the treated lesion.

Importantly, SBRT demonstrated a comparable safety profile, with no significant increase in Grade ≥3 toxicities. This supports its role as a well-tolerated option, particularly in patients who are not candidates for surgery or other locoregional therapies.

Heterogeneity observed in long-term OS outcomes may reflect differences in patient selection, tumor characteristics, prior treatments, and variations in SBRT dose-fractionation schedules across studies. Additionally, most included studies were observational, which may introduce selection bias.

Overall, these findings reinforce the growing role of SBRT as an effective locoregional therapy in HCC management, particularly for patients with limited treatment options.

Conclusions

SBRT is associated with significantly improved progression-free survival and superior local control compared to non-SBRT treatment modalities in patients with hepatocellular carcinoma, without an increase in severe toxicity.

While no overall survival advantage was observed, SBRT remains a promising, safe, and effective noninvasive treatment option, particularly for patients unsuitable for surgery or ablative therapies. Further high-quality randomized controlled trials are warranted to better define its role in treatment algorithms and optimize patient selection.

References

1. Fu Y, Yang Z, Liu S, Guan R, Wang X, Chen J, Wang J, Pan Y, Liu M, Chen M, Xi M, Zhang Y. Comparison of resection, ablation, and stereotactic body radiation therapy in treating solitary hepatocellular carcinoma ≤5 cm: a retrospective, multicenter, cohort study. Int J Surg. 2025 Jan 1;111(1):1535-1540. doi: 10.1097/JS9.0000000000001977. PMID: 39093867; PMCID: PMC11745737.
2. Ma ZH, Lin XL, Liu FH, Zhang JL, Yan ML, Song XC, Guo L, Xue J, Lu CD, Shi J, Meng Y, Cheng SQ, Guo WX. Radiofrequency ablation versus stereotactic body radiotherapy for recurrent hepatocellular carcinoma: a multicenter, propensity score matching analysis. BMC Cancer. 2025 Mar 8;25(1):424. doi: 10.1186/s12885-025-13800-1. PMID: 40057688; PMCID: PMC11889815.
3. Romero AM, van der Holt B, Willemssen FE, de Man RA, Heijmen BJ, Habraken S, Westerveld H, van Delden OM, Klümpen HJ, Tjwa ET, Braam PM. Transarterial chemoembolization with drug-eluting beads versus stereotactic body radiation therapy for hepatocellular carcinoma: outcomes from a multicenter, randomized, phase 2 trial (the TRENDY trial). International Journal of Radiation Oncology* biology* physics. 2023 Sep 1;117(1):45-52
4. Zhou B, Ma Z, Cheng X, Yan M, Duan Y, Ye J, Guo L, Xue J, Meng Y, Cheng S, Guo W. Stereotactic body radiotherapy versus laparoscopic liver resection for single hepatocellular carcinoma ≤ 5 cm: a retrospective, multicenter, cohort study. Sci Rep. 2025 Nov 18;15(1):40610. doi: 10.1038/s41598-025-24386-w. PMID: 41254049; PMCID: PMC12627700.