

Reviewer #1:

**Scientific Quality:** Grade B (Very good)

**Language Quality:** Grade C (Good)

**Conclusion:** Minor revision

**Specific Comments to Authors:**

This is timely, given the growing recognition of primary tumor location as a prognostic factor in CRC. The findings align with emerging evidence that right-sided colon cancer (RSCC) is biologically distinct, with worse outcomes due to molecular features (e.g., microsatellite instability, BRAF mutations). The study reinforces the need for site-specific management. The inclusion of 178 patients over a 10-year period provides adequate statistical power for subgroup analyses. The cross-sectional design with clear inclusion/exclusion criteria minimizes selection bias. The authors evaluated a wide range of variables, including demographic, pathological (e.g., differentiation, nodal status), biochemical (D-dimer, albumin), and treatment-related factors (neoadjuvant therapy, surgical margins). This holistic approach strengthens the validity of the conclusions. The use of multivariate logistic regression to identify independent predictors of recurrence (e.g., RSCC, lymph node metastasis, D-dimer  $\geq 180 \mu\text{g/L}$ ) is methodologically rigorous. The forest plot (Figure 1) effectively visualizes effect sizes and confidence intervals. The study convincingly demonstrates that RSCC is associated with higher recurrence rates at 3, 6, and 12 months (55.68% vs. 26.14% for left-sided and 18.18% for rectal primaries). This supports the hypothesis that RSCC is more aggressive, possibly due to its embryological origin and molecular profile. The inclusion of D-dimer and albumin as prognostic markers is innovative. Elevated D-dimer (reflecting hypercoagulability) and hypoalbuminemia (indicating malnutrition/systemic inflammation) are understudied in CRC liver metastases but may guide adjuvant therapy decisions. The finding that ineffective/no neoadjuvant chemotherapy increases recurrence risk (OR=3.52) underscores the importance of optimizing preoperative treatment, particularly for RSCC. The tables and figures are well-designed and supplement the text effectively. Appropriate statistical tests (chi-square, t-tests, logistic regression) were used, and results are reported with P-values and confidence intervals, enhancing transparency. The discussion contextualizes the findings within existing literature, citing embryological (midgut vs. hindgut), anatomical (portal vs. systemic drainage), and molecular differences (e.g., microsatellite instability in RSCC). This strengthens the biological plausibility of the results. The authors correctly note that RSCC's poorer prognosis may stem from delayed diagnosis (due to nonspecific symptoms) and distinct molecular features (e.g., BRAF mutations, CIMP phenotype). This study makes a valuable contribution to the literature by demonstrating that primary CRC location significantly impacts liver metastasis resection outcomes.

Answer: We sincerely thank the reviewer for the comprehensive and constructive evaluation of our manuscript. We are pleased that the reviewer recognizes the timeliness and clinical relevance of our study in demonstrating the prognostic significance of primary tumor location in colorectal cancer liver metastases. We appreciate the positive feedback regarding our methodological rigor, including the adequate sample size, comprehensive variable assessment, and appropriate statistical analyses. The reviewer's acknowledgment of the innovative inclusion of D-dimer and albumin as prognostic biomarkers, as well as the emphasis on optimizing neoadjuvant therapy particularly for right-sided colon cancer, aligns with our clinical observations. We are grateful for the recognition of our study's contribution to the literature and the biological plausibility of our findings through embryological and molecular perspectives. We will carefully address the minor revision suggestions to further enhance the manuscript quality and ensure our findings provide meaningful guidance for site-specific management strategies in clinical practice.