ISCHEMIA-REPERFUSION INJURY AND COMPLICATED IMMEDIATE POST-OPERATIVE COURSE INCREASE HEPATOCELLULAR CARCINOMA RECURRENCE RATE AFTER LIVER TRANSPLANTATION.

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General data

Topic: 4: Transplant

Abstract body

Text: **Introduction**

Liver transplantation (LT) remains the only curative treatment for cirrhosis complicated by hepatocellular carcinoma (HCC). However, HCC recurrence significantly impairs long-term outcomes and is influenced by pre-LT (e.g., tumor morphology and biology) and post-LT factors (e.g., immunosuppressive regimens). Emerging evidence suggests that perioperative factors, including ischemia-reperfusion injury (IRI), may also contribute to HCC recurrence.

Methods

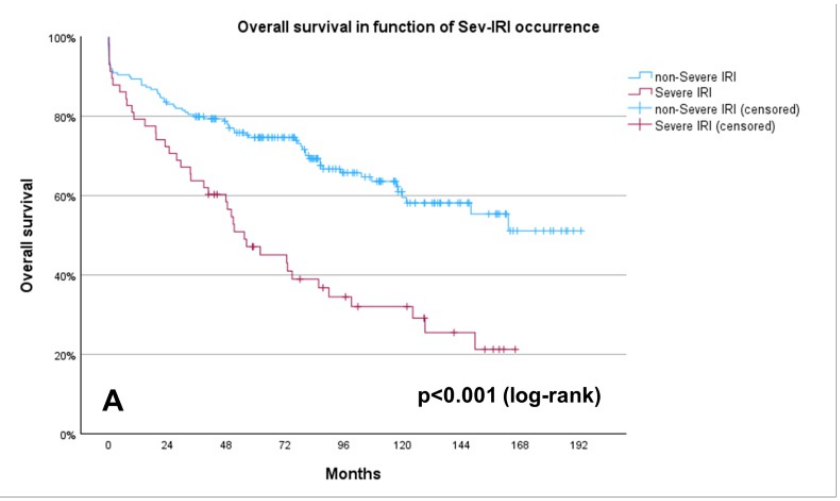
We retrospectively analyzed clinical data from 248 patients who underwent LT for HCC between 2009 and 2021. IRI was considered as severe (Sev-IRI) when combining both occurrence of reperfusion syndrome (RPS) and IRI-related clinical events (primary non-function, early allograft dysfunction, or ischemic-type biliary lesions). Immediate post-operative course at intensive care unit (ICU) was considered as complicated when one of following events was noticed: relaparotomy within 48H after LT, prolonged intubation after LT (> 12H), need for reintubation, continuous veno-venous hemofiltration or molecular adsorbent recirculating system. A double step (univariate then multivariate) regression analysis explored risk factors for decreased disease-free survival (DFS) after LT.

Results

HCC recurrence was observed in 37 patients (14.9%) with a mean interval of 30.0 ± 33.4 months following LT. Patients experiencing Sev-IRI demonstrated a higher HCC recurrence rate: 18/58 (31.0%) vs. 19/190 (10.0%) ($p<0.001$). Pathological analysis revealed similar Milan-out status in both groups: 16/58 (27.6%) vs. 46/190 (24.2%) ($p=0.603$). With a mean follow-up of 75.9 ± 51.3 months, DFS and overall survival were significantly shorter in Sev-IRI subgroup: 55.3 ± 52.3 vs. 77.6 ± 52.4 months ($p<0.001$) and 62.0 ± 50.5 vs. 80.2 ± 50.9 months ($p<0.001$), respectively (Figure 1). Multivariate regression analysis enlightens 5 factors decreasing DFS: pre-operative Charlson comorbidity index, presence of microvascular invasion at pathology, poorly differentiated tumors, severe IRI occurrence and complicated ICU post-operative course ($p<0.05$) (Table 1).

Conclusions

These findings suggest that both severe IRI and complicated immediate post-operative course contribute to HCC recurrence following LT. Further research involving larger patient cohorts is warranted for results validation. If so, strategies to mitigate IRI could play a pivotal role in reducing HCC recurrence rate after LT.



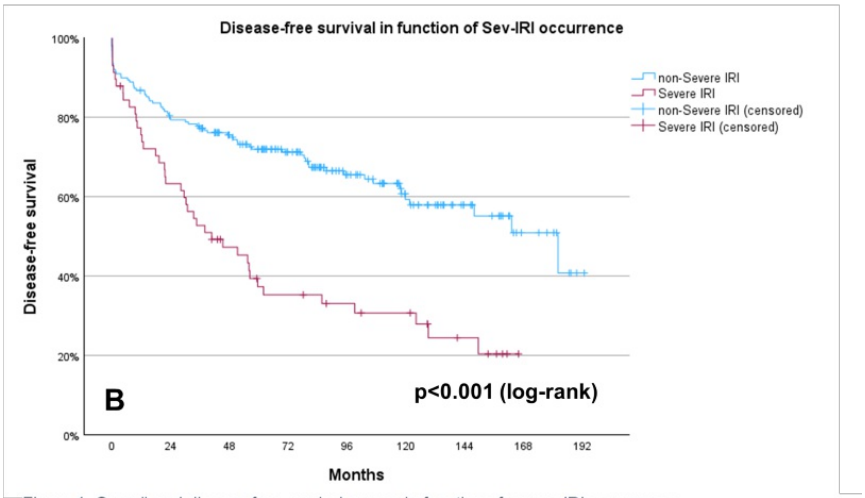


Figure 1. Overall and disease-free survival curves in function of severe IRI occurrence.

TABLE 1. Multivariate regression analysis of factors affecting DFS after LT for HCC *

Factor	HR	HR 95% CI	p-value

Charlson comorbidity index	1.220	1.0401 – 1.4305	0.015
Microvascular invasion	1.522	1.0128 – 2.2862	0.043
Poorly differentiated tumor	2.437	1.3719 – 4.0165	0.002
Severe IRI	1.894	1.0779 – 3.3295	0.026
Complicated ICU evolution	2.211	1.4376 – 3.3995	<0.001
*AFP > 100 ng/mL at LT, AIT > 100 min, CIT, FFP administration, Milan-out status before LT and at pathology, RPS, TIT, and WT > 120 days were factors reaching statistical significance for decreased DFS at univariate analysis (p<0.20) but not in the multivariate model (p<0.05). Similarly, HBV cirrhosis had a protective factor after univariate but not in the multivariate model.			
Legend: AFP: alpha-foetoprotein, AIT: arterial ischemia time, CI: confidence interval, CIT: cold ischemia time, FFP: fresh-frozen plasma, HBV: hepatitis-B virus, HCC: hepatocellular carcinoma, HR: hazard ratio, ICU: intensive care unit, IRI: ischemia-reperfusion injury, LT: liver transplantation, RPS: reperfusion syndrome, TIT: total ischemia time, WT: waiting time.			

Conflict of interest statement

Conflict of interest to declare?: I and/or the Additional Authors have no disclosures to make

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