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Letters to the editor

Toward standardization and translation of stem cell therapy in liver failure

Dear Editor,

We read with great interest the article by Lin et al. entitled "A comprehensive meta-analysis of stem cell therapy for liver failure: assessing treatment efficacy and modality" [1]. The authors provide a timely synthesis of evidence supporting the potential of mesenchymal stem cell (MSC) therapy in improving survival and reducing Model for End-Stage Liver Disease (MELD) scores. While the work is commendable, several points warrant further clarification and discussion to enhance translational value.

First, although the meta-analysis concludes that allogeneic MSCs outperform autologous sources, the heterogeneity of donor characteristics and cryopreservation protocols across trials is not sufficiently addressed. Recent evidence highlights that cell senescence, donor age, and culture conditions significantly influence MSC potency and immunomodulatory function [2]. Could the authors clarify whether subgroup analyses considered these biological variabilities? Without harmonization of manufacturing practices, reproducibility across centers remains uncertain.

Second, while the paper emphasizes administration routes (deep vessel vs. peripheral), the "pulmonary-first" phenomenon remains a translational bottleneck. Preclinical studies indicate that cell modification strategies, such as CXCR4 overexpression to enhance homing, improve hepatic engraftment [3]. Future clinical designs might benefit from integrating such engineered approaches rather than focusing solely on infusion routes.

Third, the clinical endpoints assessed predominantly center on MELD and survival. Yet, patient-centered outcomes such as quality of life, hospitalization frequency, or transplantation-free survival are underexplored. Incorporating such outcomes would better align stem cell trials with real-world clinical decision-making, as recently advocated in hepatology research frameworks [4].

Finally, while safety was noted as favorable in the included trials, long-term surveillance data remain scarce. MSC tumorigenicity, although rare, is a legitimate concern given the proliferative and immunomodulatory nature. Registries and multicenter collaborative trials with extended follow-up should be prioritized to establish definitive safety profiles [5].

In conclusion, Lin et al. have provided an important contribution to the field, but the path to clinical translation will depend on harmonizing cell preparation protocols, integrating mechanistic insights into trial design, and expanding outcome measures. Clarification on the above points would enrich the impact of this meta-analysis and guide future hepatology research.

Declaration of generative AI

The authors declare that AI-based language assistance was used solely for grammar refinement. All intellectual content, interpretation, and conclusions are the sole responsibility of the authors.

Declaration of competing interest

None.

References

[1] Lin S, Gao H, Ma H, Liao Z, Zhang D, Pan J, et al. A comprehensive meta-analysis of stem cell therapy for liver failure: assessing treatment efficacy and modality. Ann Hepatol 2025;30:101586. https://doi.org/10.1016/j.aohep.2024.101586.
[2] Hoang DM, Pham PT, Bach TQ, Ngo ATL, Nguyen QT, Phan TTK, et al. Stem cell-based therapy for human diseases. Signal Transduct Target Ther 2022;7:272. https://doi.org/10.1038/s41392-022-01134-4.
[3] Xu R, Ni B, Wang L, Shan J, Pan L, He Y, et al. CCR2-overexpressing mesenchymal stem cells targeting damaged liver enhance recovery of acute liver failure. Stem Cell Res Ther 2022;13:55. https://doi.org/10.1186/s13287-022-02729-y.
[4] Liu Y, Dong Y, Wu X, Xu X, Niu J. The assessment of mesenchymal stem cell therapy in acute-on-chronic liver failure and chronic liver disease: a systematic review and meta-analysis of randomized controlled trials. Stem Cell Res Ther 2022;13:59. https://doi.org/10.1186/s13287-022-02882-4.
[5] Wang MF, Li YB, Gao XJ, Zhang HY, Lin S, Zhu YY, et al. Efficacy and safety of autologous stem cell transplantation for decompensated liver cirrhosis: a retrospective cohort study. World J Stem Cells 2018;10(10):138–45. https://doi.org/10.4252/wjsc.v10.i10.138.

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