INPLASY PROTOCOL

To cite: Yang et al. Iron overload, Infectious Complications and Survival In Liver Transplant Recipients: A Systematic Review and Meta-Analysis. Inplasy protocol 2022110022. doi: 10.37766/inplasy2022.11.0022

Received: 05 November 2022

Published: 05 November 2022

Corresponding author:
Ming Yang

263805652@qq.com

Author Affiliation:
West China Hospital of Sichuan University.

Support: **81770566, 82000599.**

Review Stage at time of this submission: **Completed but not published.**

Conflicts of interest:
None declared.

Iron overload, Infectious Complications and Survival In Liver Transplant Recipients: A Systematic Review and Meta-Analysis

Yang, M[1]; Wu, YW[2]; Wang, T[3]; Wang, WT[4].

Review question / Objective: **Iron overload conditions is a well-established risk factor for infection of pathogens. The possible association of iron overload with infectious complications and prognosis of patients receiving transplants are not well understood.**
Condition being studied: **Liver transplantation often represents a life-saving treatment for an increasing number of patients with end-stage liver disease. With the improvements in surgical techniques, immunosuppression strategies, and post-LT management of complications, the recipient mortality has steadily declined after LT. The survival rates were 83% at 1 year, 71% at 5 years in western countries. However, the use of immunosuppressants increased risk of infections as an adverse effect resulting in severe morbidity. Globally, infection caused by including bacteria, fungus, viruses remain one of the leading causes of morbidity and mortality among transplant recipients. Knowledge of modifiable risk factors and potentially reversible causes is essential to develop targeted preventive strategies.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 05 November 2022 and was last updated on 05 November 2022 (registration number INPLASY2022110022).

INTRODUCTION

Review question / Objective: **Iron overload conditions is a well-established risk factor for infection of pathogens. The possible association of iron overload with infectious complications and prognosis of patients receiving transplants are not well understood.**

Condition being studied: **Liver transplantation often represents a life-saving treatment for an increasing number of patients with end-stage liver disease. With the improvements in surgical techniques, immunosuppression strategies, and post-LT management of complications, the recipient mortality has steadily declined after LT. The survival rates**

were 83% at 1 year, 71% at 5 years in western countries. However, the use of immunosuppressants increased risk of infections as an adverse effect resulting in severe morbidity. Globally, infection caused by including bacteria, fungus, viruses remain one of the leading causes of morbidity and mortality among transplant recipients. Knowledge of modifiable risk factors and potentially reversible causes is essential to develop targeted preventive strategies.

METHODS

Search strategy: We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statements.

Participant or population: Liver transplant patients.

Intervention: Data reported on the effect of iron overload markers on the prognosis in liver transplant patients.

Comparator: Patients with iron overload and patients with normal iron loadlow iron burden.

Study designs to be included: Retrospective study.

Eligibility criteria: The original trial included patients who underwent liver transplantation.

Information sources: PubMed, Embase, Web of Science and the CochraneLibrary.

Main outcome(s): The iron overload was strongly associated with increased infections after LT (HR 1.66, 95% CI 1.03-2.68). The increase in serum ferritin was associated with an increased risk of infection after LT (HR 1.44, 95% CI 1.09-1.91). Iron overload was a significant predictor of worse OS (HR 1.35, 95% CI 1.11-1.64). In addition, the high levels serum ferritin was statistically significantly associated with an increased risk of death (HR 1.34, 95% CI 1.10-1.64).

Quality assessment / Risk of bias analysis: We tested for publication bias by assessing funnel plots for symmetry. The publication bias funnel indicated that there is no substantial publication bias (Figure 4).

Strategy of data synthesis: The following data were recorded: study characteristics (study design, Study Period, location, sample size, measures of iron-load and outcome measures used), participant characteristics (number, etiology of liver disease and pretransplantation MELD score). Subsequently, we extracted the hazard ratio (HR) with 95% confidence interval (CI) associated with the iron-load and outcome (infection and death). When critical data were missing or unclear in published reports, we attempted to contact the trial authors. We resolved any disagreements in opinion through discussion.

Subgroup analysis: Subgroup analyses showed the increase in serum ferritin was independently associated with an increased risk of infection after LT (HR 1.44, 95% CI 1.09-1.91; p=0.01), with no heterogeneity (I2=0%, P=0.43) (Figure1). To evaluate whether the serum ferritin could be evaluated as a non-invasive prognostic indicator on its own, we performed a subgroup analysis. The pooled results revealed that preoperative or postoperative high levels of serum ferritin was statistically significantly associated with an increased risk of death (HR 1.34, 95% CI 1.10-1.64; p=0.004), with low heterogeneity (I2=46%; P=0.12). Higher preoperative serum ferritin was also associated with poor survival (HR 1.54, 95% CI 1.06-2.25; p=0.003), with moderate heterogeneity (I2=53%; P=0.09).

Sensitivity analysis: We performed various sensitivity analyses and found largely consistent results across the board, supporting the robustness of the main findings.

Language restriction: No.

Country(ies) involved: China (West China Hospital of Sichuan University).

Keywords: Iron; Liver transplantation; Infection; prognosis; meta-analysis.

Contributions of each author:

Author 1 - Ming Yang.
Email: 263805652@qq.com
Author 2 - Youwei Wu.
Email: scdxwyw@163.com
Author 3 - Tao Wang.
Email: wangshoutao1219@163.com
Author 4 - Wentao Wang.
Email: wwtdoctor02@163.com