# Influence of Hydroxyethyl Starch on Renal Function After Orthotopic Liver Transplantation

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ABSTRACT

Background. Postoperative renal impairment (RI) is one of the most common complications in orthotopic liver transplantation (OLT), and it occurs in 17% to 95% of the patients who undergo the surgery.

Methods. We reviewed 394 consecutive patients who underwent OLT. On the basis of the preoperative renal function level (presence of renal failure (RF): SCr >1.5 mg/dL before OLT), the patients were divided into an RF group and a non-RF group. In each group, the patients were subdivided into 4 subgroups according to the type and dosage of the intra-operative use of HES (hydroxyethyl starch). The changing tendency of the SCr (serum creatinine) of each group and the ratio of the change in the SCr within the first postoperative week were compared.

Results. In total, 139 of 394 patients (35%) had RI within the first week after OLT (RI group); 104 patients (75%) in the RI group and 181 patients (71%) in the non-RI group required HES transfusions. The multivariate logistic regression analysis identified old age, a low pre-operative platelet level, and massive red blood cell transfusions as risk factors for the postoperative development of RI. The changing tendency of the SCr and the ratio of change in the SCr among the different HES subgroups showed no significant difference in the RF group or in the non-RF group.

Conclusions. Perioperative use of HES 200/0.5 or HES 130/0.4 has no significant effect on renal function in the first postoperative week in patients undergoing OLT.

POSTOPERATIVE renal impairment (RI) is one of the most common complications in patients undergoing orthotopic liver transplantation (OLT), and it occurs in 17% to 95% of the patients [1]. Renal dysfunction after OLT is multifactorial. Several preoperative, intra-operative, and postoperative patient conditions contribute to the deterioration of renal function after OLT, including pre-operative renal function, hemodynamics, immunosuppressive or nephrotoxic drugs, graft dysfunction, and sepsis [2].

Hydroxyethyl starch (HES) is widely used as an inexpensive and effective volume replacement substitute for albumin. However, the use of HES might exacerbate the development of renal dysfunction and has been reported to be the major reason for avoiding its use [3–5].

The data regarding the safety of HES in patients undergoing OLT are limited. Scholars disagree regarding whether HES damages the renal function of patients. Pillebout et al [6] found that of 26 patients with chronic renal failure after OLT, 16 had renal cortex atrophy associated with the use of HES; whether there are histological changes in impaired renal function is unknown. There is no conclusive evidence of whether HES has a causal relationship with RI in the early phase after OLT.

On the basis of this assumption, this study aimed to assess the influence of HES (6% HES 200/0.5 and 6% HES 130/0.4) on renal function during the immediate postoperative OLT period.

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## METHODS

We reviewed the clinical and biochemical data of the first 432 consecutive patients who underwent liver transplantation from May 2003 to December 2013 at the First Affiliated Hospital of Sun Yet-Sen University. In total, 394 patients met the inclusion criteria. Four patients were below the age of 18, 25 patients died within the first postoperative week, and 9 patients who underwent combined liver and kidney transplantation were excluded.

A comparative analysis was performed between the patients in the group that had development of renal impairment during the first postoperative week (RI group) and the group that did not have development of renal impairment (non-RI group). Postoperative renal impairment was defined as a 1.5-mg/dL increase in the serum creatinine (SCr) in patients previously having a normal renal function or a 50% increase in the SCr in patients with a preexisting renal dysfunction [7]. Several variables in the pre-operative, intra-operative, and early postoperative periods were analyzed. The pre-operative parameters were as follows: sex, age, height, weight; presence of renal failure (RF), hepatitis B virus infection (HBV), diabetes mellitus, and hypertension; the MELD Score (the Model for End-Stage Liver Disease); and the platelet (PLT), hematocrit (HCT), and serum albumin levels. The intra-operative factors were as follows: the surgical time; the duration of the anhepatic phase; the duration of hypotension (a mean arterial pressure below 60 mm Hg); the minimum mean arterial pressure; HES transfusions; the volume of packed red blood cells; fresh-frozen plasma and 5% albumin; blood loss; dopamine dosage; adrenaline dosage, noradrenaline dosage; and the OLT surgical procedure (the use of the veno-venous bypass or the "piggyback" technique) and the vena cava anastomosis type (standard or side-to-side). The postoperative variables included the following: the length of the intensive care unit (ICU) stay and the serum tacrolimus levels.

On the basis of the pre-operative renal function (the presence of RF was defined as SCr >1.5 mg/dL before OLT), all the patients were divided into RF (n = 35) and non-RF (n = 359) groups. In each group, the patients were subdivided into 4 subgroups according to the type and dosage of the intra-operative HES infusion as follows: the non-HES group; the 6% HES 200/0.5 (HAES-sterile, Fresenius Kabi, Bad Hombourg, Germany) <33 mL/kg group; the 6% HES 200/0.5 ≥33 mL/kg group; and the 6% HES 130/0.4 (Voluven, Fresenius Kabi, Bad Hombourg, Germany) group. The changing tendency of the SCr in each group as well as the ratio of change in the SCr [(postoperative SCr minus pre-operative SCr)/pre-operative SCr] within the first postoperative week were compared.

### Statistical Analysis

All analyses were completed with the use of SPSS 15.0 software, and we considered the size of the test as having statistical significance when its $P$ value was <.05.

The continuous data were submitted to a test of normality. For those meeting the Gaussian distribution, the average level and variability were described as mean ± standard deviation (SD) and were compared by use of a 2–independent-sample Student's $t$-test; for those not meeting the Gaussian distribution and coinciding with the skewness distribution, the average level and variability were described with the median and interquartile range (M[Q]) and compared by means of the rank-sum test. The classification variables were described for a number of patients and compared by use of a $\chi^2$ test. Logistic regression analysis was used to determine the risk factors of RI. The odds ratios (ORs) and 95% confidence interval (CIs) were obtained. Statistical significance was considered with $P$ values <.05.

An analysis of the mixed linear model for the repeated-measure data was used to compare the changing tendency of the SCr and the ratio of change in the SCr in the first postoperative week between the HES groups. In all the comparisons, $P$ values <.05 were considered to be statistically significant.

## RESULTS

One hundred thirty-nine (121 men and 18 women) of 394 patients (35%) developed RI within the first week after OLT (the RI group). Regarding the age and height, a significant difference was found between the two groups. The RI patients presented a higher MELD score and a lower PLT level compared with the non-RI group ($P < .05$). There was no significant difference between the groups regarding the following characteristics: the sex; weight; the percentage of HBV, diabetes mellitus, and hypertension; and the levels of HCT and serum albumin in the pre-operative period. During the intra-operative period, the RI group presented more blood loss and required more packed red blood cell transfusions than the patients without RI ($P = .001$). No significant difference between the two groups was observed regarding the following factors: the surgical time; duration of the anhepatic phase; duration of hypotension; value of the minimum mean arterial pressure; the plasma requirement; 5% albumin transfusions; dopamine dose, adrenaline, and noradrenaline dose; use of the "piggyback" technique; and the side-to-side vena cava anastomosis in the intra-operative period. No significant difference was found regarding the proportion of patients who were administered HES transfusions, and 104 patients (75%) in the RI group and 181 patients (71%) in the non-RI group required HES transfusions. The mean serum level of tacrolimus in the 4th day after OLT was similar in both groups in the post-operative period. However, regarding the time in the ICU, a significant difference was found: the RI group presented a greater mean time in the ICU than did the non-RI group (Table 1).

Regarding the risk factors for the development of RI, the following parameters were identified: old age; a low pre-operative platelet count; and massive intra-operative red blood cell transfusions (Table 2).

In the RF group, 10 patients did not receive HES transfusions, 16 patients received 6% HES 200/0.5 at <33 mL/kg, 5 patients received 6% HES 200/0.5 at >33 mL/kg, and 4 patients received 6% HES 130/0.4 transfusions intra-operatively. In the non-RF group, 99 patients did not receive HES transfusions, 142 patients received 6% HES 200/0.5 at <33 mL/kg, 52 patients received 6% HES 200/0.5 at >33 mL/kg, and 66 patients received 6% HES 130/0.4 transfusions intra-operatively. In the RF group, the percentage of RI development after OLT did not differ among the 4 HES subgroups within the first postoperative week. Similarly, the percentage of RI development after OLT was not significantly different among the 4 HES subgroups in the non-RF group (Table 3).