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# The association of perioperative serum albumin concentrations with outcome after deceased donor liver transplantation

Paul Lichtenegger<sup>1\*</sup>, Alexandra Graf<sup>2</sup>, Judith Schiefer<sup>1</sup>, Aylin Bilir<sup>1</sup>, Dagmar Kollmann<sup>3</sup>, Gabriela A. Berlakovich<sup>3</sup>, Peter Faybik<sup>1</sup>, David M. Baron<sup>1</sup> and Joanna Baron-Stefaniak<sup>1</sup>

## Abstract

**Background** Perioperative hypoalbuminemia has been associated with worse outcome after major surgery. Although hypoalbuminemia is common in patients with chronic liver disease and frequently occurs following liver transplantation (LT), data are sparse regarding perioperative hypoalbuminemia and outcome after LT.

**Methods** In this single-center retrospective study performed at the Medical University of Vienna, we evaluated adult patients undergoing orthotopic liver transplantation (OLT) between 2004 and 2019. The association between perioperative serum albumin concentrations and survival, acute kidney injury (AKI), and postoperative surgical complications was analyzed using cox and logistic regression models.

**Results** In total, 724 patients were analyzed. Serum albumin concentrations decreased from  $32.0 \pm 6.8$  to  $22.8 \pm 4.8$  g/l (nadir within 48 h following OLT). Overall survival was not associated with serum albumin concentrations on day 1, day 2, or at nadir within 48 h after OLT (Day1: HR:0.988, 95%CI:0.966–1.011,  $P=0.306$ ; Day2: HR:1.021, 95%CI:0.991–1.052,  $P=0.167$ ; Nadir: HR:0.998, 95%CI:0.971–1.025,  $P=0.863$ ). Serum albumin concentrations on day 1, day 2, or at nadir within 48 h after OLT were not associated with AKI (Day1: OR:0.975, 95%CI:0.949–1.002,  $P=0.070$ ; Day2: OR:1.011, 95%CI:0.971–1.053,  $P=0.601$ ; Nadir: HR:0.976, 95%CI:0.940–1.013,  $P=0.20$ ) or with postoperative complications (Day1: OR:0.997, 95%CI:0.976–1.059,  $P=0.80$ ; Day2: OR:1.002, 95%CI:0.973–1.032,  $P=0.890$ ; Nadir: HR:0.993, 95%CI:0.966–1.021,  $P=0.610$ ). However, we observed an increased risk for initiation of renal replacement therapy with lower serum albumin concentrations on the day preceding initiation (HR=0.946; 95%CI:0.896–1.000;  $P=0.049$ ).

**Conclusion** Hypoalbuminemia was not associated with reduced survival, the development of AKI, or postoperative surgical complications after OLT. However, postoperative hypoalbuminemia was associated with the timing of initiating renal replacement therapy after OLT.

**Keywords** Hypoalbuminemia, Orthotopic liver transplantation, Survival, Mortality, Morbidity, Acute kidney injury, Renal replacement therapy

\*Correspondence:  
Paul Lichtenegger  
paul.lichtenegger@meduniwien.ac.at

<sup>1</sup>Department of Anaesthesia, Intensive Care Medicine and Pain Medicine,  
Medical University of Vienna, Waehringer Guertel 18-20, Vienna  
1090, Austria

<sup>2</sup>Institute of Medical Statistics, Centre for Medical Data Science, Medical  
University of Vienna, Vienna, Austria

<sup>3</sup>Department of Surgery, Medical University of Vienna, Division of  
Transplantation, Vienna, Austria



## Background

Orthotopic liver transplantation (OLT) is the only curative treatment for patients suffering from acute or chronic liver failure. Several factors such as diabetes mellitus, age, preoperative anemia, transfusion of packed red blood cells, postoperative acute kidney injury (AKI), and peritonitis have been associated with adverse outcome following OLT [1–6]. Despite improvements in perioperative treatment, one-year mortality of patients undergoing OLT remains at around 20% [2, 7]. Hence, in addition to a systematic preoperative assessment [8], the identification of modifiable risk factors is essential to improve postoperative outcomes.

Hypoalbuminemia has been linked with adverse outcome following major surgery [9–16]. Furthermore, low postoperative serum albumin concentrations have been associated with AKI following living donor liver transplantation [17]. However, it remains unknown whether serum albumin concentrations are associated with adverse outcome following deceased donor liver transplantation.

The primary objective of this study was to evaluate whether serum albumin concentrations were associated with decreased survival following OLT. The secondary aim of this study was to evaluate whether serum albumin concentrations were associated with the development of AKI, the requirement of renal replacement therapy (RRT), or the development of postoperative surgical complications following OLT.

## Methods

This single-center retrospective study was performed at the Medical University of Vienna after local ethics committee approval (EK 2347/2016) in accordance with the ethical standards laid down in the Declaration of Helsinki. Due to the retrospective design of the study, the requirement for patient consent was waived by the local ethics committee. All patients undergoing their first OLT between January 2004 and December 2019 were evaluated for inclusion. All patients received immunosuppressive therapy as described previously [2]. “Statistik Austria” publishes an annual mortality registry for the preceding year. Thus, date of death was assessed using the mortality registry published in 2020. Exclusion criteria were an age below 18 years and combined liver-lung or liver-kidney transplantation. We present our findings according to the STROBE guidelines [18].

## Study endpoints

The primary endpoints were overall survival and survival within 1 year after OLT. We investigated whether serum albumin concentrations at day 1, day 2, or at nadir within 48 h after OLT were associated with overall survival or survival within 1 year. As secondary endpoints,

we investigated whether perioperative serum albumin concentrations were associated with the development of AKI, the requirement of RRT, and occurrence of postoperative surgical complications after OLT.

Furthermore, in a subgroup analysis including 256 patients undergoing OLT after 2013, for which precise daily information on the amount of transfused blood products and administered colloids, as well as the meticulous timing of RRT initiation, was available, we assessed whether serum albumin concentrations or infusion of albumin influenced the timing of RRT initiation.

## Definition of acute kidney injury

Acute kidney injury was classified by assessing changes of serum creatinine concentrations according to the “Kidney Disease: Improving global outcomes” (KDIGO) criteria [19]. Patients who developed AKI stages 1, 2, or 3 within the first week after OLT were compared to patients who did not develop AKI. In addition, the requirement of RRT after OLT was recorded. Patients requiring RRT within 1 week after OLT were compared to those not requiring RRT within 1 week after OLT. While clinicians at our institution are generally following international guidelines [20], the exact timing and indication of RRT were at the discretion of the treating physicians during the observed period.

## Definition of postoperative surgical complications

Postoperative surgical complications were categorized as all complications requiring surgical revision within 28 days after OLT. We categorized early postoperative surgical complications as those requiring surgical revision within 7 days after OLT and late postoperative complications as those requiring surgical revision from days 8 to 28 after OLT.

## Statistical analyses

For initial data analysis, we evaluated descriptive statistics of continuous (mean  $\pm$  standard deviation) and categorical variables (values and percentages).

Statistical analyses for the primary endpoints were performed as follows: We investigated the influence of serum albumin concentrations as a continuous variable on overall survival by performing univariable cox regression models for death as an event for overall survival. In addition, we calculated logistic regression models for death within one year for one-year survival. Potentially influencing factors, described in detail in our previous study, were further investigated using univariable cox or logistic regression models [2]. To avoid overfitting, a stepwise modelling procedure was performed: univariable regression models were followed by a multivariable cox-regression model with stepwise variable selection for overall survival (or multivariable logistic regression

model for one-year survival) including all factors being significant ( $P < 0.05$ ) in the univariable models.

Statistical analyses for secondary endpoints: We investigated the influence of serum albumin concentrations as a continuous variable on the occurrence of AKI, requirement of RRT, and the occurrence of postoperative complications by first calculating univariable logistic regression models. Potential influence factors were further investigated in univariable regression models. Following univariable regression, multivariable logistic regression models were calculated using stepwise selection including all factors being significant ( $P < 0.05$ ) in the univariable analyses. To further investigate whether serum albumin concentrations influenced the timing of RRT initiation, univariable cox regression models for RRT as an event accounting for the time-dependent covariate “serum albumin concentration” were calculated for the subgroup of patients with an OLT after 2013. In the corresponding cox-regression models, “serum albumin concentration”, “human albumin infusion”, “units of packed red blood cells”, and “units of fresh frozen plasma” were accounted for as time-dependent covariables. Potential confounding factors, as indicated in our previous study [2], were also investigated in a multivariable

analysis. Furthermore, the time to postoperative surgical complications was investigated using univariable and multivariable Fine and Gray competing risk models for the events “postoperative surgical complications” and “death”.

In addition to the analyses with serum albumin concentrations as a continuous variable, we repeated univariable analyses using a cut-off for serum albumin concentrations. Based on our data and existing literature [17], we used a cut-off value of 30 g/l for preoperative baseline serum albumin concentrations and the primary endpoint of one-year survival. We performed univariable logistic regression analyses with this cut-off value on one-year survival, the occurrence of AKI, and the requirement of RRT. Furthermore, using the same cut-off value, we calculated log-rank tests for overall survival and Fine and Grey models for the time to postoperative surgical complications.

All  $P$ -values smaller than 0.05 were considered as statistically significant. Analyses were performed using R, release 3.6.3, or SAS 9.4 (SAS Institute Inc., Cary, NC, USA).

## Results

During the observation period, 788 patients underwent their first OLT at our center. After excluding 64 patients (34 patients were younger than 18 years at the time of OLT, 6 patients underwent combined liver-lung transplantation, and 24 patients underwent combined liver-kidney transplantation), 724 patients were included in the final analyses. Demographic data, perioperative characteristics, and the perioperative course of serum albumin concentrations of the study population are shown in Table 1. Supplementary Table 1 depicts the etiologies of liver disease in the patient population.

### Serum albumin concentrations and survival after OLT

One-year survival was 80.4%, and median survival was 127 months (95%CI: 107–157). Regression analyses did not show a significant association between perioperative serum albumin concentrations and one-year or overall survival (Table 2A–B and Supplementary Table 2). Also, when using a cut-off value of 30 g/l, we found no significant association between perioperative serum albumin concentrations and one-year or overall survival (Table 2C–D, Supplementary Figs. 1–4).

### Serum albumin concentrations and acute kidney injury after OLT

Among enrolled patients, 491 (68%) developed postoperative AKI within the first postoperative week. Regression analyses revealed that perioperative serum albumin concentrations were not significantly associated with AKI after OLT (Table 3A and Supplementary Table 2).

**Table 1** Demographic data and perioperative characteristics of the study population

| Preoperative characteristics                   |             |
|--|-------------|
| Age, years                                     | 54 ± 10     |
| Male gender, $n$ (%)                           | 532 (74)    |
| Body mass index, $\text{kg m}^{-2}$            | 26.2 ± 4.5  |
| MELD Score                                     | 19 ± 7      |
| Coronary heart disease, $n$ (%)                | 25 (4)      |
| Chronic obstructive pulmonary disease, $n$ (%) | 43 (6)      |
| Diabetes mellitus, $n$ (%)                     | 163 (23)    |
| eGFR   | 80.8 ± 28.3 |
| PreOP hospitalization, $n$ (%)                 | 89 (12)     |
| Serum albumin concentrations (g/l)             |             |
| Preoperative                                   | 32.0 ± 6.8  |
| Day 1  | 24.2 ± 5.7  |
| Day 2  | 24.7 ± 4.4  |
| Nadir within 48 h after OLT                    | 22.8 ± 4.8  |
| Intraoperative characteristics                 |             |
| Cold ischemia time, min                        | 472 ± 140   |
| Warm ischemia time, min                        | 79 ± 19     |
| PRBC transfusions, $n$                         | 4 ± 6       |
| FFP transfusions, $n$                          | 9 ± 8       |
| Platelet transfusions, $n$                     | 1 ± 1       |
| Postoperative characteristics                  |             |
| Surgical complications, $n$ (%)                | 200 (28)    |
| Early allograft dysfunction, $n$ (%)           | 192 (27)    |
| Renal replacement therapy, $n$ (%)             | 162 (22)    |

Data are shown in  $n$  (%), mean ± standard deviation. Abbreviations: eGFR, estimated glomerular filtration rate; FFP, fresh frozen plasma; MELD, model for end-stage liver disease; PRBC, packed red blood cell; PreOP, preoperative

**Table 2** Perioperative serum albumin concentrations in univariable analyses for survival to one year and overall survival after OLT

|   | Univariable |             | P-value |
|---|-------------|-------------|---------|
|   | OR/HR       | 95%CI       |         |
| <b>A) Logistic regression analyses for survival within one year after OLT</b> |             |             |         |
| <i>Serum albumin concentrations (continuous variable)</i>                     |             |             |         |
| Preoperative  | 1.022       | 0.993–1.051 | 0.139   |
| Day 1   | 0.990       | 0.956–1.025 | 0.562   |
| Day 2   | 1.042       | 0.995–1.092 | 0.082   |
| Nadir within 48 h after OLT   | 1.003       | 0.961–1.047 | 0.899   |
| <b>B) Cox-regression analyses for overall survival after OLT</b>              |             |             |         |
| <i>Serum albumin concentrations (continuous variable)</i>                     |             |             |         |
| Preoperative  | 1.013       | 0.995–1.032 | 0.166   |
| Day 1   | 0.988       | 0.966–1.011 | 0.306   |
| Day 2   | 1.021       | 0.991–1.052 | 0.167   |
| Nadir within 48 h after OLT   | 0.998       | 0.971–1.025 | 0.863   |
| <b>C) Logistic regression analyses for survival within one year after OLT</b> |             |             |         |
| <i>Serum albumin concentrations (cut-off &gt; 30 g/l)</i>                     |             |             |         |
| Preoperative  | 1.364       | 0.915–2.034 | 0.128   |
| Day 1   | 0.836       | 0.443–1.577 | 0.580   |
| Day 2   | 1.701       | 0.945–3.061 | 0.076   |
| Nadir within 48 h after OLT   | 1.615       | 0.756–3.451 | 0.216   |
| <b>D) Log-rank tests for overall survival after OLT</b>                       |             |             |         |
| <i>Serum albumin concentrations (cut-off &gt; 30 g/l)</i>                     |             |             |         |
| Preoperative  | 1.220       | 0.948–1.570 | 0.122   |
| Day 1   | 0.809       | 0.521–1.255 | 0.344   |
| Day 2   | 1.329       | 0.882–2.004 | 0.174   |
| Nadir within 48 h after OLT   | 1.223       | 0.711–2.106 | 0.467   |

Abbreviations: CI, confidence interval; HR, hazard ratio; OLT, orthotopic liver transplantation; OR, odds ratio. OR/HR larger than 1 indicates a larger risk of death

**Table 3** Perioperative serum albumin concentrations in univariable regression analyses for the indicated outcome

|  | Univariable |             | P-value      |
|--|-------------|-------------|--------------|
|  | OR/HR       | 95%CI       |              |
| <b>A) Logistic regression analyses for postoperative AKI</b>                       |             |             |              |
| <i>Serum albumin concentrations</i>  |             |             |              |
| Preoperative   | 0.960       | 0.937–0.983 | <b>0.001</b> |
| Day 1  | 0.975       | 0.949–1.002 | 0.070        |
| Day 2  | 1.011       | 0.971–1.053 | 0.601        |
| Nadir within 48 h after OLT  | 0.976       | 0.940–1.013 | 0.200        |
| <b>B) Logistic regression analyses for RRT within one week after OLT</b>           |             |             |              |
| <i>Serum albumin concentrations</i>  |             |             |              |
| Preoperative   | 0.981       | 0.956–1.007 | 0.161        |
| Day 1  | 0.973       | 0.943–1.005 | 0.094        |
| Day 2  | 1.039       | 0.995–1.085 | 0.085        |
| Nadir within 48 h after OLT  | 0.990       | 0.951–1.030 | 0.608        |
| <b>C) Cox-regression analyses for time to postoperative surgical complications</b> |             |             |              |
| <i>Serum albumin concentrations</i>  |             |             |              |
| Preoperative   | 1.008       | 0.991–1.024 | 0.360        |
| Day 1  | 0.997       | 0.976–1.059 | 0.800        |
| Day 2  | 1.002       | 0.973–1.032 | 0.890        |
| Nadir within 48 h after OLT  | 0.993       | 0.966–1.021 | 0.610        |

Abbreviations: AKI, acute kidney injury; CI, confidence interval; OLT, orthotopic liver transplantation; OR, odds ratio; RRT, renal replacement therapy

**Table 4** Cox-regression model for time to RRT with time-dependent covariables serum albumin concentrations, infused albumin, transfused packed red blood cells, and transfused fresh frozen plasma

|   | Univariable |             |                  | Multivariable |             |              |
|---|-------------|-------------|------------------|---------------|-------------|--------------|
|   | HR          | 95%CI       | P-value          | HR            | 95%CI       | P-value      |
| <i>Serum albumin concentrations</i>   |             |             |                  |               |             |              |
| Day of RRT initiation   | 0.933       | 0.878–0.992 | <b>0.026</b>     |               |             | n.s.         |
| Day before RRT initiation   | 0.940       | 0.893–0.990 | <b>0.018</b>     | 0.946         | 0.896–1.000 | <b>0.049</b> |
| Difference to baseline  | 0.975       | 0.937–1.015 | 0.224            |               |             |              |
| Difference to day before  | 1.019       | 0.963–1.078 | 0.506            |               |             |              |
| <i>Infusion/transfusion on the same day of RRT initiation (before starting RRT)</i> |             |             |                  |               |             |              |
| Albumin   | 1.000       | 0.999–1.002 | 0.464            |               |             |              |
| Packed red blood cells  | 1.098       | 1.038–1.162 | <b>0.001</b>     |               |             | n.s.         |
| Fresh frozen plasma   | 1.109       | 1.054–1.167 | <b>&lt;0.001</b> | 1.162         | 1.038–1.301 | <b>0.009</b> |
| <i>Other covariables</i>  |             |             |                  |               |             |              |
| eGFR  | 0.981       | 0.973–0.989 | <b>&lt;0.001</b> | 0.984         | 0.974–0.994 | <b>0.001</b> |
| MELD score  | 1.064       | 1.029–1.100 | <b>&lt;0.001</b> |               |             | n.s.         |
| Cold ischemia time  | 1.001       | 0.999–1.003 | 0.337            |               |             |              |

Abbreviations: CI, confidence interval; eGFR, estimated glomerular filtration rate; HR, hazard ratio; MELD, model for end-stage liver disease; n.s., non-significant; RRT, renal replacement therapy

In the univariable model, preoperative serum albumin concentrations showed a trend for increasing the risk of AKI with decreasing serum albumin concentrations (OR = 0.960, 95%CI: 0.937–0.983,  $P=0.001$ ). However, this trend did not remain significant in the multivariable model. When using a cut-off value of 30 g/l for serum albumin concentrations, univariable logistic regression analyses showed similar results to the analyses with serum albumin concentrations as a continuous variable (Supplementary Table 3 A).

#### Serum albumin concentrations and renal replacement therapy after OLT

After OLT, 162 (22%) patients required RRT within one week after OLT. Regression analyses revealed that perioperative serum albumin concentrations, whether as a continuous variable or using a cut-off value of 30 g/l, were not significantly associated with the requirement of RRT after OLT (Table 3B and Supplementary Tables 2 and 3B).

In the subgroup analysis including 256 patients undergoing OLT after 2013, for which precise daily information on RRT initiation, administration of colloids, and transfusion of blood products was available, multivariable analysis showed that the risk of RRT initiation increased with lower serum albumin concentrations on the day preceding RRT initiation. Moreover, patients receiving transfusion of fresh frozen plasma had an increased risk of RRT initiation on the day of transfusion (Table 4).

#### Serum albumin concentrations and postoperative surgical complications

Postoperative surgical complications requiring surgical revision occurred in 200 patients (28%) within one month after OLT. In 116 patients (16%) the postoperative

complication occurred within 7 days after OLT. In the remaining 84 (12%), the postoperative complication occurred from day 8 to 28 after OLT. Surgical revision was required mainly due to postoperative bleeding, vascular or biliary duct stenosis, biliary duct leak or intraabdominal hematoma, and peritonitis requiring surgical lavage. Multivariable analyses did not show an association between perioperative serum albumin concentrations and time to postoperative surgical complications or their occurrence within 28 days after OLT (Table 3C and Supplementary Table 2). Likewise, repeating the univariable analyses with a cut-off value of 30 g/l revealed no significant associations between serum albumin concentrations and the time to postoperative surgical complications (Supplementary Table 3 C).

#### Discussion

In this study, we investigated the association of perioperative serum albumin concentrations and outcome following OLT. Our results suggest that perioperative serum albumin concentrations are not significantly associated with survival, the development of AKI, or postoperative surgical complications after deceased donor liver transplantation. However, we observed an increased risk for the initiation of RRT with lower serum albumin concentrations on the day preceding initiation.

Albumin plays a role in many physiological processes that are particularly important in critically ill patients. These processes include generation of oncotic pressure, binding and transport of molecules, scavenging of free radicals, immunomodulation, and protection of endothelial integrity [21, 22]. Decreases in serum albumin concentrations during and after OLT occur due to increased losses, decreased synthesis, and increases in volume of distribution [23]. Hypoalbuminemia has been identified

as a risk factor for mortality after major surgery such as radical cystectomy, colon cancer surgery, aortic aneurysm repair, and heart transplantation [11–16]. In liver transplantation, the preoperative albumin-bilirubin (ALBI) score as well as serum albumin concentrations alone have been associated with decreased postoperative survival [24–29]. However, data is sparse with respect to postoperative hypoalbuminemia and survival following liver transplantation. One study categorized 162 propensity-score matched patients into two groups according to the degree of perioperative decrease of serum albumin concentrations. While the SOFA score on postoperative day 5 was statistically significantly higher in the high-decrease compared to the low-decrease group, the authors found no difference in hospital length of stay or 90-day mortality between the groups [30]. In another large retrospective analysis, Sang et al. demonstrated that postoperative hypoalbuminemia was associated with increased mortality following living donor liver transplantation [17]. In contrast, we did not observe an association between perioperative serum albumin concentrations and survival following OLT. It must be noted that while Sang et al. included patients following living donor liver transplantation, we only included patients following deceased donor OLT [17].

In addition to suggesting an impact of postoperative hypoalbuminemia on survival, Sang et al. also reported that low postoperative serum albumin concentrations increased the risk for AKI after living donor liver transplantation [17]. In contrast, we did not observe any significant association between perioperative serum albumin concentrations and AKI following deceased donor OLT in our patient population. Supporting our findings, Kim et al. found that intraoperative albumin therapy during liver transplantation failed to prevent postoperative AKI in a prospective randomized trial including 134 patients [31]. Of note, Sang et al. excluded all patients with pre-existing chronic kidney disease defined by baseline serum creatinine values  $>1.5$  mg/dl, while we included all patients following deceased donor OLT, regardless of their preoperative kidney function, in our final analysis [17].

However, varying inclusion/exclusion criteria between the studies may not entirely explain the discrepancies between our results and the ones described by Sang et al. In their study, Sang et al. used the propensity score analysis and performed a matched population comparison. The propensity score analysis is a method which was originally designed to account for a potential treatment-selection bias due to a missing treatment randomization in retrospective or observational studies [32, 33]. In Sang et al. study, the cohort was therefore divided in two groups according to serum albumin concentrations with a cut-off value of 30 g/l [17]. Keeping in mind that

the serum albumin concentration cut-offs used for the Child-Turcotte-Pugh classification are  $>35$  g/l, 35–28 g/l and  $<28$  g/l, we decided against using a propensity score matching analysis using a serum albumin cut-off of 30 g/l [34]. In order to enable a detailed analysis of our retrospective data, we included serum albumin concentrations as a continuous variable in our models. This approach allows a more nuanced statistical analysis that does not depend on a pre-specified cut-off. To account for potential overfitting due to the large number of possible confounding variables we used a stepwise approach. Univariable models were followed by a multivariable model with stepwise selection including all factors being significant in the univariable models.

Nevertheless, it has to be noted that several studies have identified preoperative hypoalbuminemia as a significant risk factor for AKI following major surgery including liver transplantation [35–46]. In a retrospective study, Park et al. demonstrated that a preoperative serum albumin concentration below 35 g/l was a significant risk factor for the development of AKI following living donor liver transplantation [44]. Furthermore, Chen et al. found an association between preoperative serum albumin concentrations below 35 g/l and the development of AKI after OLT [45]. Cabezuelo et al. showed that preoperative serum albumin concentrations below 32 g/l were associated with AKI after OLT [46]. In our study, preoperative serum albumin concentrations were associated with AKI in the univariable analysis with serum albumin concentrations as a continuous variable as well as when using a cut-off value of 30 g/l. However, this finding did not remain significant in the multivariable analysis, possibly due to strong influencing factors such as the complexity of the operation, intraoperative blood loss, or ischemia time. In addition, the cut-off values reported in the beforementioned studies were at or above the baseline albumin concentrations of our study population ( $32.0 \pm 6.8$  g/l, Table 1).

It is worth mentioning that our statistical analyses also included cox-regression models with time-dependent covariates to assess whether serum albumin concentrations influenced the timing of RRT initiation. Although we did not observe an association between serum albumin concentrations and AKI, our results suggest an increased risk for RRT initiation with lower serum albumin concentrations on the day preceding initiation. Although a lower serum albumin concentration does not seem to be a significant risk factor for the development of AKI after OLT, it might contribute to an earlier requirement of RRT. Given that the indication for RRT at our institution is based on the clinical situation and remains at the discretion of the treating physicians as well as the retrospective design of our study, our data does not allow us to illuminate the underlying mechanisms behind this

finding. Nevertheless, we hypothesize that lower albumin concentrations might reflect a dilution effect in advanced kidney failure due to impaired urine output. Consequently, we speculate that fluid overload may have been the main reason for the initiation of RRT.

Finally, we assessed whether serum albumin concentrations were associated with postoperative surgical complications. We found no association of perioperative serum albumin concentrations with early or late postoperative surgical complications. In concordance with our results, Hiroi et al. observed no association between perioperative hypoalbuminemia and postoperative complications in a study including 60 patients undergoing OLT [47]. Mor et al. assessed serum albumin concentrations on postoperative days 2, 10, and 30, and reported that only serum albumin concentrations on day 30 were associated with septic complications after liver transplantation [48]. Since we focused on the immediate perioperative period, we examined serum albumin concentrations preoperatively and within three postoperative days. Thus, our results are in agreement with the findings of Mor et al. in that early postoperative hypoalbuminemia was not associated with postoperative surgical complications [48].

Taken together, although our results only partially support previous findings regarding serum albumin concentrations and outcome after liver transplantation, our study has a major strength: it is the first study investigating postoperative serum albumin concentrations in deceased donor OLT. However, the retrospective and monocentric design of our study bears clear limitations. First, the generalizability of the results is limited. Secondly, the indication for and timing of albumin supplementation and the initiation of RRT remain at the discretion of the clinician in charge at the time. Moreover, due to the implementation of a new patient data management system at the end of 2013, covariables such as the meticulous timing of RRT initiation, the precise daily amount of postoperative human albumin administration and the postoperatively transfused units of blood products were only available for patients transplanted after 2013. Hence, we performed the time-dependent analyses on the association of serum albumin concentrations with the timing of RRT initiation on the subgroup of patients transplanted after 2013. Nevertheless, the primary and key secondary endpoints, i.e., survival and AKI, were analyzed including the entire patient cohort. In addition, we were able to include over 200 patients in our subgroup analysis, which still represents more than one fourth of the entire patient cohort. Unfortunately, we could not assess drainage of ascites or pleural effusion due to the retrospective design and lack of data. Another notable limitation is the observation period of 15 years—while providing a large set of data, surgical techniques

and perioperative medical treatment have changed considerably.

## Conclusion

In conclusion, hypoalbuminemia was not associated with reduced survival, the development of AKI, or postoperative surgical complications after deceased donor OLT. However, the perioperative presence of hypoalbuminemia might influence the timing of RRT initiation after OLT.

## Abbreviations

|            |   |
|------------|---|
| AKI        | Acute kidney injury                       |
| ALBI score | Albumin-bilirubin score                   |
| CI         | Confidence interval                       |
| eGFR       | Estimated glomerular filtration rate      |
| FFP        | Fresh frozen plasma                       |
| HR         | Hazard ratio                              |
| ICU        | Intensive care unit                       |
| KDIGO      | Kidney Disease: Improving global outcomes |
| LT         | Liver transplantation                     |
| MELD       | Model for end-stage liver disease         |
| OLT        | Orthotopic liver transplantation          |
| OR         | Odds ratio                                |
| PRBC       | Packed red blood cell                     |
| PreOP      | Preoperative                              |
| RRT        | Renal replacement therapy                 |
| SD         | Standard deviation                        |

## Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12871-025-03016-y>.

Supplementary Figure 1: Kaplan-Meier plot on serum albumin concentrations at baseline and survival after orthotopic liver transplantation (blue: patients with serum albumin concentrations > 30 g/l, yellow: patients with serum albumin concentrations ≤ 30 g/l)

Supplementary Figure 2: Kaplan-Meier plot on serum albumin concentrations at postoperative day 1 and survival after orthotopic liver transplantation (blue: patients with serum albumin concentrations > 30 g/l, yellow: patients with serum albumin concentrations ≤ 30 g/l)

Supplementary Figure 3: Kaplan-Meier plot on serum albumin concentrations at postoperative day 2 and survival after orthotopic liver transplantation (blue: patients with serum albumin concentrations > 30 g/l, yellow: patients with serum albumin concentrations ≤ 30 g/l)

Supplementary Figure 4: Kaplan-Meier plot on serum albumin concentrations at nadir within 48 hours and survival after orthotopic liver transplantation (blue: patients with serum albumin concentrations > 30 g/l, yellow: patients with serum albumin concentrations ≤ 30 g/l)

Supplementary Table 1: Aetiology of liver disease. Supplementary Table 2: Serum albumin concentrations according to indicated outcome. Supplementary Table 3. Perioperative serum albumin concentrations using a cut-off > 30 g/l in univariable regression analyses for the indicated outcome

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Not applicable.

## Author contributions

PL designed and conducted the study, collected and analyzed data, and drafted the first version of the manuscript. AG helped to design the study, analyzed data, and actively contributed to the content of the manuscript. JS, AB, and DK helped to conduct the study, collected data, and actively contributed to the content of the manuscript. GB helped to design the study

and edited the final version of the manuscript. PF helped to design the study and edited the final version of the manuscript. DMB designed and conducted the study, collected and analyzed data, and actively contributed to the content of the manuscript. JBS designed and conducted the study, collected and analyzed data, and drafted the final version of the manuscript. All authors approved the final version of the manuscript.

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#### Data availability

The datasets generated and analyzed during the current study are not publicly available due to data protection regulations but are available from the corresponding author on reasonable request.

#### Declarations

##### Ethics approval and consent to participate

This single-center retrospective study was performed at the Medical University of Vienna after local ethics committee approval (EK 2347/2016) in accordance with the ethical standards laid down in the Declaration of Helsinki. Due to the retrospective design of the study, the requirement for patient consent was waived by the local ethics committee.

##### Consent for publication

Not applicable.

##### Competing interests

The authors declare no competing interests.

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