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LETTER TO THE EDITOR

Comment on pediatric living donor liver transplantation decade progress in Shanghai: Characteristics and risks factors of mortality

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Abstract

Since the first successful liver transplantation was performed five decades ago, pediatric liver transplantation has become the gold standard treatment choice for pediatric liver disease, including metabolic diseases, liver tumors, and some acute liver failure. With improvements in immunosuppression, surgical techniques, and postoperative medical care, long-term outcomes of patients after liver transplantation have markedly improved, especially in pediatric patients.

Key words: Pediatric end stage liver disease; Living donor pediatric liver transplantation; Survival analysis; Risk factors; Living donor liver transplantation; Outcomes

Core tip: With improvements in immunosuppression, surgical techniques, and postoperative medical care, long-term outcomes of patients after liver transplantation have markedly improved, especially in pediatric patients. We read with great interest the recent article "Pediatric living donor liver transplantation decade progress in Shanghai: Characteristics and risks factors of mortality" published by Pan and colleagues. We would like to share our opinion and criticisms about this valuable work.

TO THE EDITOR

We read with great interest the recent article "Pediatric living donor liver transplantation decade progress in Shanghai: Characteristics and risks factors of mortality" published by Pan *et al*[1]. In this retrospective observational study, the authors stated that they aimed to review the status of pediatric living donor liver transplantation (LDLT) and investigate the factors related to anesthetic management and survival rate in pediatric LDLT. We would like to share our opinion and criticisms about this valuable work.

The authors excluded 15 patients who were older than 12 years. The World Health Organization has stated that any individual younger than 19 years old should be considered in the pediatric age group. Therefore, the authors should have included all patients under the age of 18 years in the pediatric age group.

The authors analyzed four discrete time intervals in terms of survival analysis. The criteria for the choice of time interval are not clear from the author's data. In our opinion, an ROC curve analysis would have determined the optimal time interval (years) in accordance with the survival of the patients[2]. If the time intervals were chosen arbitrarily, a probability of bias during the analysis could exist. Therefore, it is no longer important to calculate clinical cutoff points today because clinical experience is the least important data in evidence-based research[3].

Interquartile range (IQR) is the difference between the third quartile (Q3: 75%) and the first quartile (Q1: 25%) of a given variable, and therefore, IQR is supposed to be a single number. The authors have given the variable range (Q1-Q3) under IQR, which is not the IQR itself[4,5]. This is an important error from a statistical point of view.

The authors have stated that they have performed a multivariate analysis on the parameters that had a *P* value < 0.05 in univariate analysis. In our opinion, this results in the loss of certain parameters that could have been potential risk factors during the process. Other studies have shown that certain factors that were not significant in the univariate analysis could become significant risk factors in a multivariate analysis, which is the most typical example of the interaction between variables. Therefore, we suggest that any parameter with a *P* value between 0.1 and 0.2 should be included in the logistic regression model, which will provide a more valuable result[6-9].

The authors stated that "to identify independent predictive factors of in-hospital survival, the Chi square test with the Yates correction or the Fisher's exact test were used"; this is statistically incorrect. Independent risk factors for any given categoric condition should always be performed using multivariate analysis methods. Any given parameter that is significant in the univariate analysis may not be an independent risk factor in the multivariate analysis.

The authors determined a cutoff value for 14 variables including age, weight, PELD score, hemoglobin level, duration of operation, and anesthesia and evaluated the relationship between these cutoff values and in-hospital mortality. The authors may have caused bias in this analysis. They should have performed an ROC curve analysis to determine optimal cutoff values with the highest sensitivity and specificity, which would result in higher reliability[2].

We believe that there are errors in the results of the statistical analyses stated. When we analyzed the results using SPSS version 25, we found the following results, which we believe should be corrected by the authors using Yates' correction for continuity[9,10]: Anesthesia duration [*P* = 0.046; OR = 0.46 (0.29-0.93)], PELD score [*P* = 0.032; OR = 3.8 (1.15-12.5)], operation time [*P* = 0.006; OR = 0.38 (0.19-0.74)], ICU stay [*P* < 0.001; OR = 0.24 (0.11-0.52)], and intraoperative blood loss (*P* = 0.069).

The authors analyzed the risk factors that had an impact on 1-year and 3-year survival of the patients using univariate analysis methods. Subsequently, they selected the parameters with a *P* value < 0.05 and performed a Cox regression model. They did not perform a multivariate analysis for in-hospital mortality, which means they did not analyze the independent risk factors of mortality in the first postoperative 30-d period. In either case, they did not perform a multivariate analysis to determine the independent risk factors of mortality or factors that have an impact on survival at any time point.

The authors stated that PELD score, anesthesia duration, operation duration, intraoperative blood loss, and ICU length of stay were independent predictive factors of in-hospital patient survival. They also stated that PELD score, operation duration, and ICU length of stay were independent predictive factors of 1-year and 3-year patient survival. However, the authors did not perform any multivariate analysis to determine independent risk factors for in-hospital mortality. In addition, they did not calculate the odds ratio for the univariate analysis to determine the factors that affect in-hospital mortality. The authors stated that the risk factors related to postoperative 1-

year and 3-year mortality were PELD score, operation duration, and ICU length of stay. However, they did not include certain known factors such as biliary complications, infections, type and levels of immunosuppressive drugs, and episodes of acute rejection. We believe there are some major issues regarding this topic. The factors stated by the authors may have an effect on in-hospital mortality, but they do not have an impact on the long-term mortality of the patients.

Although the authors stated that they performed a propensity score analysis and found that ICU-stay predicted the 3-year survival, they did not discuss the rationale behind this finding. In other words, they did not theorize why a perioperative parameter would have an impact on a late outcome such as 3-year survival.

In summary, they provided the 30-d, 90-d, 1-year, and 2-year survival rates. In addition, they analyzed factors that had an impact on 3-year survival. If the factors that had an impact on the survival of the patients three years postoperatively, then the authors should have given the 3-year survival rate of the patients.

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