French Editorial from the ACHBPT

French editorial from the ACHBPT: blood salvage and autotransfusion during liver transplantation for advanced hepatocellular carcinoma

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We read with great interest the recently (*Annals of Surgery*, March, 2021) published article by Kwon and collaborators (1) about the effects of autotransfusion of salvaged blood with single leukoreduction for liver transplant recipients with advanced hepatocellular carcinoma (HCC). This retrospective study assessed the impact of autotransfusion of salvaged blood with post-transplant tumor recurrence.

Liver transplantation (LT) remains a major surgical procedure, in which significant blood loss is often caused by collateral vessels due to portal hypertension, impaired coagulation and vascular procedures on major vascular axes. Consequently, transfusion of homologous blood products is often needed during LTs, and often in very large amounts. The allogeneic red blood cells (RBCs) transfusion has known adverse effects such as metabolic disturbances, transfusion reactions, circulatory overload, microchimerism, post-transplant HCC recurrence, surgical site infection, coagulopathy, acute lung injury and mortality (1,2). Moreover, if allogeneic blood transfusion is used, there is a risk of immunomodulation, alloimmunization and rarely of transfusion-associated graft versus host disease (3). Thus, the need for RBC transfusion may be reduced with the use of intraoperative blood salvage autotransfusion. The principle of this autotransfusion is to collect the blood from the surgical site and re-infuses autologous blood to reduce the use of allogeneic RBCs (4).

The safety of autotransfusion in cancer surgery has been a controversial concern. It could present the theoretical risk of spread neoplastic cells when it is used in cancer surgery (5). This issue remains a concern because the American Medical Council, in its report on autologous blood transfusion in 1986 promulgated a contraindication to the use of cell saver in cancer surgery based on a single case report in 1975, where a 52-year-old patient undergoing pneumonectomy was found to have malignant cells in salvaged blood (3,6). This dogma has become obsolete because since then, many authors have shown that the use of autologous blood in cancer patients can be safely used and does not impact the risk of neoplastic recurrence (1,3,7), event in HCC patients after LT (5,8). Moreover, in advanced HCC patients, who have greater metastatic potential, the uncertainty remains on the need of a single or a double-filtered leukoreduction during the treatment of the collected blood (9-11). This concern has never been assessed while the requirement of double-filtered leukoreduction delays the preparation of autologous blood and possibly increases the use of allogeneic RBCs (1).

In this monocentric retrospective study, 349 patients who underwent living donor LT for advanced HCC were included between May 2002 and December 2017. The primary etiology of HCC in this cohort was hepatitis B virus, which is known as the first cause of HCC in Asia. There were no significant differences between autotransfusion group and nonautotransfusion group regarding tumor biology, pretransplant tumor treatment, patients with HCC beyond the Milan criteria, number and size of nodules, tumor vascular invasion, Edmondson Grading, downstaging and AFP level. In Asiatic cohorts,

there are differences in terms of etiology, epidemiology, tumor biology and HCC mutations compared to Western countries cohorts (12), which could have an impact on the extrapolation of the results of this work to the population of Western countries.

Because of the retrospective nature of this study, the two groups were significantly different regarding platelet count, etiology, graft-to-recipient weight ratio, Model for End-stage Liver Disease (MELD) score, graft ischemia time, recipient age/gender, operative time, neutrophil-to-lymphocyte ratio, amount of allogeneic transfusion and ABO blood-type compatibility ($P<0.05$). A total of 74/129 without autotransfusion were matched with 74/220 with autotransfusion using a propensity score-based matching to get homogeneity between the two groups. The primary outcome was HCC recurrence.

The results of this study showed no significant differences between the two groups in overall recurrence, intrahepatic recurrence, extrahepatic recurrence, overall death, HCC-related death, and HCC-unrelated death. Thus, autotransfusion of salvaged blood with leukoreduction did not increase the risk of post-transplant HCC recurrence even in advanced HCC patients with high metastatic potential. Authors suggested that the loss of viability due to physical traumatisms on neoplastic cells and the morphological changes of these cells during the salvage process prevent crossing the physical barriers which lead to metastasis (13). Other authors have found that tumor cells in shed blood can survive the salvage process and the standard red cell filters, leukocyte depletion filters could completely reduce the risk of reintroduction of tumor cells (14). The authors routinely used a single leukoreduction and emphasize the unnecessariness of double-filtered leukoreduction for the salvaged blood in advanced HCC patients undergoing LT. Nevertheless, other authors have demonstrated the safety of autotransfusion without leukoreduction in HCC patients (15) which was not evaluated in the present study.

Moreover, the risk of HCC recurrence (both in intrahepatic and extrahepatic recurrence) or death showed a trend in favor of autotransfusion, although statistical significance was not reached. Because the amount of transfused allogeneic RBCs was controlled by matching, these results were not thought to be due to sparing of allogeneic RBCs and reduced immunomodulation with autotransfusion but due to the direct effects of autotransfusion (1).

This study was limited to patients with advanced HCC transplanted living donor grafts who would never have had access to deceased donors because of their advanced tumor biology and low expected post-transplant survival. Several authors have shown that intraoperative blood autotransfusion, with leukoreduction, can be safely used without increasing HCC recurrence (5,10,11,14) but none of them studied this subgroup of patients with greater metastatic risk. Although, these results are difficult to extrapolate for LT patients from deceased donors who have more limited disease due to stricter selection criteria, they remain interesting because even in this subgroup of patients with high risk of recurrence autotransfusion can be safely used and does not impact the risk of neoplastic recurrence.

In conclusion, this study shows that the use of autologous blood with leukoreduction in advanced HCC patients can be safely used and does not impact the risk of neoplastic recurrence. The publication of this study in Annals of Surgery was made possible by the interest and novelty of the subject covered, the large size of the cohort and a rigorous methodology, without missing data. It confirms the interest of autotransfusion in LT, even in HCC patients. Furthermore, it shows a trend in favor of autotransfusion compared to allogeneic RBC transfusion although statistical significance was not reached. A multicenter randomized controlled trial would therefore be required to confirm these results.

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Footnote

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