Editorial

The need for deepened molecular mechanism exploration in new onset diabetes after transplantation (NODAT)

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New onset diabetes after transplantation (NODAT) has begun to receive attention from transplant surgeons in recent years. NODAT is a common metabolic complication that occurs after liver transplantation (LT), with a reported incidence ranging from 9–63.3% in recipients who are previously nondiabetic (1). The development of NODAT has been associated with an increased risk of cardiovascular disease, infection, chronic renal insufficiency, and graft dysfunction after LT, and leads to increased long-term mortality in liver recipients (2-7). The study by Man Kim *et al.* (8) was the first to investigate the incidence and risk factors of NODAT in Korean LT patients and was completed with the Korean Organ Transplantation Registry (KOTRY) database. Nearly 70% of LTs recorded in the KOTRY are living donor LTs (LDLTs); the incidence and the risk factors of NODAT in the KOTRY are not entirely consistent with those reported in studies based on deceased donor LT (DDLT) (2,9,10).

The study (8) indicated that in addition to increasing recipient age, high recipient BMI, steroid use, and left-sided LT being risk factors for NODAT, small-size liver graft (GRWR ≤0.8) or minimally invasive donor hepatectomy, including laparoscopic donor hepatectomy or robotic donor hepatectomy, was an independent risk factor of NODAT for LDLT. However, the exact mechanism underlying this association is not clear, and the authors believe it may be related to liver inflammation.

Currently, the study on the mechanism of occurrence of NODAT has been receiving increasing attention from researchers, and thus far interleukin 6 (IL-6) has been associated with the occurrence of NODAT (11). High mobility group box 1 protein (HMGB1), as a marker of hepatocellular injury in LT, is considered to have a possible association with insulin resistance after LT (11), and studies on HMGB1-related pathways may provide novel and practicable ideas for the prevention and treatment of NODAT. More research is needed to determine the connection between liver inflammation and ischemia-reperfusion injury after LT and the occurrence and development of NODAT.

As mentioned above, there are limitations to this study. First, the KOTRY database does not include actual laboratory findings and intraoperative data, such as operative time, cold and hot ischemic time, and other relevant information, which may also be closely related to the development of NODAT after LT. In addition, the immunosuppression protocols and the management of NODAT is important. It has been shown that maintenance immunosuppression with tacrolimus and steroids is a risk factor for NODAT (12-15). The study did not provide data on tacrolimus blood levels and steroid use after LT. Second, the study had a relatively short follow-up period, with a median follow-up time of 1 year. However, the majority (90%) of NODAT cases in the study developed NODAT

within 6 months after LT, and those who developed NODAT at a later time might have been influenced by other factors, such as lifestyle habits of diet, smoking, or physical activity, as well as the development of other comorbidities like hyperlipidemia and hypertension. Further studies with longer follow-up periods are still needed to assess the long-term impact of NODAT on the outcomes in LT patients.

In the meantime, we call for more researchers to focus on NODAT after LT. NODAT may be closely associated with long-term recipient survival, and it is crucial to explore its mechanism and relevant variable factors for improving the long-term outcome of LT patients.

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