Hepatobiliary & Pancreatic Diseases International 17 (2018) 310–315

Contents lists available at ScienceDirect

Hepatobiliary & Pancreatic Diseases International

journal homepage: www.elsevier.com/locate/hbpd

Original Article/Transplantation

New-onset hyperglycemia immediately after liver transplantation: A national survey from China Liver Transplant Registry

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ARTICLE INFO

Article history:
Received 6 April 2018
Accepted 25 July 2018
Available online 3 August 2018

Keywords:
New-onset hyperglycemia
Liver transplantation
Surveillance
Ischemic injury
Homeostasis

ABSTRACT

Background: New-onset hyperglycemia (NOH) is a common phenomenon after liver transplantation (LT), but its impact on clinical outcomes has not yet been fully assessed. We aimed to evaluate the etiology and prognosis of NOH within 1 month after LT.

Methods: The data of 3339 adult patients who underwent primary LT from donation after citizen death between January 2010 and June 2016 were extracted from China Liver Transplant Registry database and analyzed. NOH was defined as fasting blood glucose ≥7.0 mmol/L confirmed on at least two occasions within the first post-transplant month with or without hypoglycemic agent.

Results: Of 3339 liver recipients, 1416 (42.4%) developed NOH. Recipients with NOH had higher incidence of post-transplant complications such as graft and kidney failure, infection, biliary stricture, cholangitis, and tumor recurrence in a glucose concentration-dependent manner as compared to non-NOH recipients ($P < 0.05$). The independent risk factors of NOH were donor warm ischemic time >10 min, cold ischemic time >10 h, anhepatic time >60 min, recipient model for end-stage liver disease score >30, moderate ascites and corticosteroid usage ($P < 0.05$). Liver enzymes (alanine aminotransferase and gamma-glutamyltranspeptidase) on post-transplant day 7 significantly correlated with NOH ($P < 0.001$).

Conclusions: NOH leads to increased morbidity and mortality in liver recipients. Close surveillance and tight control of blood glucose are desiderated immediately following LT particularly in those with delayed graft function and receiving corticosteroid. Strategic targeting graft ischemic injury may help maintain glucose homeostasis.

Introduction

Hyperglycemia is a common finding after general surgery and is associated with adverse outcomes [1–5]. Glycemic control is recommended in surgical patients and better glycemic control could reduce hospital complications [6]. Compared to general surgery, liver transplantation (LT) has much higher incidence of hyperglycemia, which has been reported to occur in 62%–90% of liver recipients [7,8]. Hyperglycemia (beyond the targeted range) represents a poor post-transplant patient management. However, the etiology and consequence of hyperglycemia after LT have not yet been elucidated. Our previous national registry survey demonstrated that more than one-third of patients with new-onset hyperglycemia (NOH) would develop new-onset diabetes after transplantation, which has a direct impact on post-transplant morbidity and mortality [7]. Another study showed that hyperglycemia increased the risk of acute allograft rejection [9]. In this study, we aimed to evaluate the impact of NOH on the prognosis of post-liver transplant patients, the necessity of tight glycemic control immediately after LT, and to determine the etiology of NOH as well.

Methods

Study population

The data was extracted from China Liver Transplant Registry (CLTR) database (no. 706). There were 5558 adult patients

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https://doi.org/10.1016/j.hbpd.2018.08.005
1499-3872/

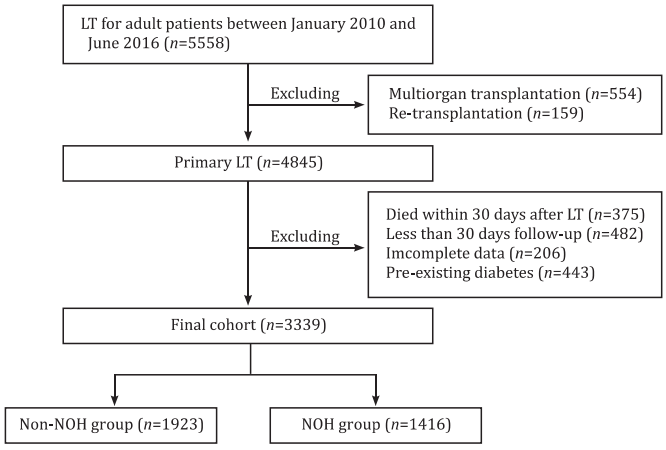

Fig. 1. Flow chart of patient selection procedures. LT: liver transplantation; NOH: new-onset hyperglycemia.

Table 1
The major complications after liver transplantation.[a]

Complications	FBG < 7 mmol/L (n = 1923)	FBG ≥ 7 mmol/L (n = 1416)	FBG ≥ 11.1 mmol/L (n = 703)	P value[b]	P value[c]
Graft failure	34 (1.8%)	50 (3.5%)	27 (3.8%)	**0.001**	**0.002**
Kidney failure	36 (1.9%)	47 (3.3%)	27 (3.8%)	**0.008**	**0.004**
Acute rejection	27 (1.4%)	61 (4.3%)	41 (5.8%)	**<0.001**	**<0.001**
Bacterial infection	217 (11.3%)	356 (25.1%)	272 (38.7%)	**<0.001**	**<0.001**
Biliary complications					
Total	134 (7.0%)	165 (11.7%)	85 (12.1%)	**<0.001**	**<0.001**
Leakage	27 (1.4%)	27 (1.9%)	12 (1.7%)	0.255	0.570
Stricture	31 (1.6%)	45 (3.2%)	28 (4.0%)	**0.003**	**<0.001**
Cholangitis	23 (1.2%)	52 (3.7%)	34 (4.8%)	**<0.001**	**<0.001**
HCC recurrence[d]	96 (11.4%)	88 (14.1%)	54 (19.3%)	0.129	**<0.001**

FBG: fasting blood glucose; HCC: hepatocellular carcinoma.
[a] Complications occurring within the first post-transplant month were excluded.
[b] FBG ≥ 7 mmol/L vs. FBG < 7 mmol/L.
[c] FBG ≥ 11.1 mmol/L vs. FBG < 7 mmol/L.
[d] Only in patients who received liver transplantation for HCC.

(>18 years) undergoing LT from donation after citizen death between January 2010 and June 2016. We excluded those who underwent multiorgan transplantation ($n = 554$) or re-transplantation ($n = 159$), or died within 30 days after transplantation ($n = 375$), or with less than 30 days follow-up ($n = 482$). Among 3988 patients, 443 with pre-existing diabetes were also excluded. Another 206 patients were not accounted because of incomplete laboratory and clinical data. The data from the remaining 3339 patients were used for analysis (Fig. 1). There were 2760 males and 579 females with age of 48.6 ± 10.0 years at transplantation. All patients were routinely followed up at the outpatient clinics, and the last recorded date was December 27, 2016. This study was approved by the CLTR (http://www.cltr.org/), which started the research after obtaining the approval of the Ethics Committee from each participating center according to the Regulations on Human Organ Transplant and National Legal Requirements. This study complied with the guidelines of China Ethical Committee and the *Declaration of Helsinki*. Informed consent was obtained from all donors and recipients before transplantation. No organs were acquired from those executed.

Data from both donor and recipient were collected. The information included age, gender, height, weight, blood type, donor type, ischemic time, cause of death, recipient primary disease, comorbidities, immunosuppressive protocol, post-transplant complications, and mortality. NOH was defined as fasting blood glucose (FBG) ≥7.0 mmol/L confirmed on at least 2 occasions (≥24 hours

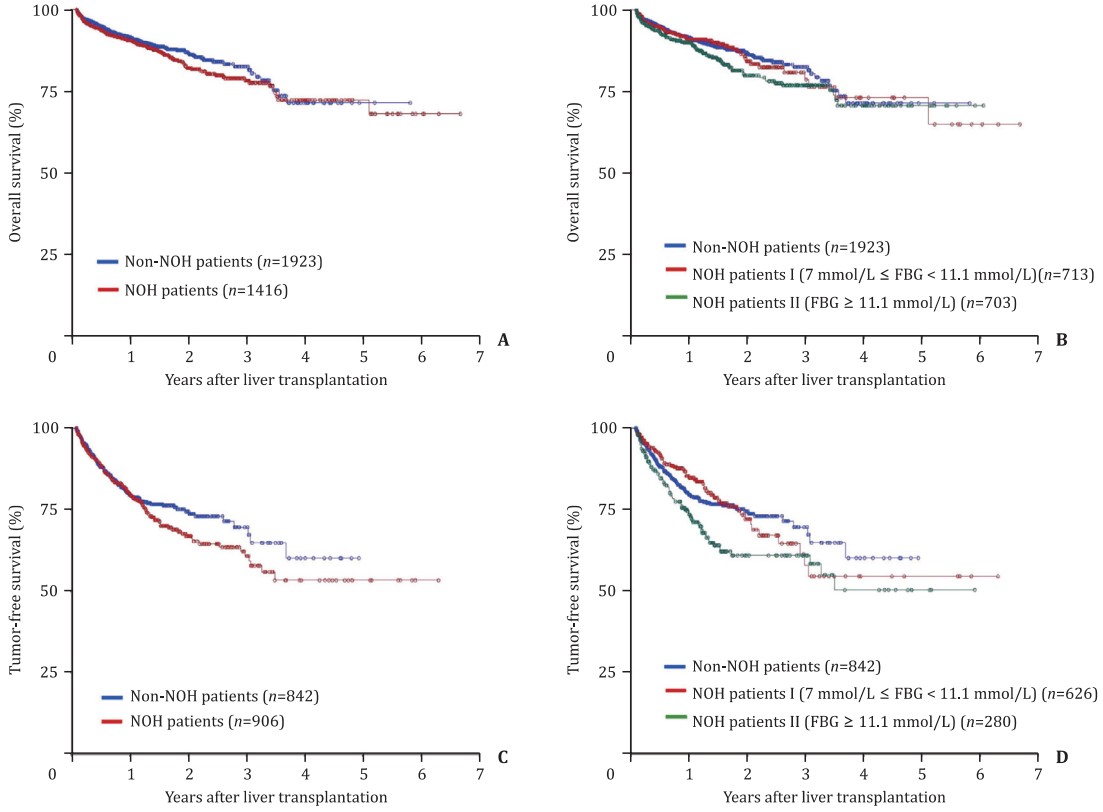

Fig. 2. The overall and tumor-free survival after liver transplantation. (**A**) The overall survival between NOH and non-NOH patients were comparable ($P = 0.137$). (**B**) Those with FBG >11.1 mmol/L had significantly lower overall survival as compared with non-NOH patients ($P = 0.028$). (**C**) The tumor-free survival between NOH and non-NOH patients were comparable ($P = 0.181$). (**D**) These with FBG >11.1 mmol/L had significantly lower tumor-free survival than both non-NOH patients ($P = 0.004$) and NOH patients with 7 mmol/L ≤ FBG < 11.1 mmol/L ($P = 0.005$). FBG: fasting blood glucose; NOH: new-onset hyperglycemia.