中文題目：胰島素反轉患有肝硬化及糖尿病實驗鼠中因門靜脈高壓造成之血流動力學惡性變化

英文題目：Insulin reverses the major portal hypertension-related derangements in rats with liver cirrhosis and diabetes

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Background: Liver cirrhosis is accompanied by increased intrahepatic resistance and angiogenesis-related portosystemic collaterals formation. Diabetic patients suffer from abnormal vasoresponsiveness and angiogenesis that can be ameliorated by glucose control, but the relevant presentation is not clear in those with cirrhosis and diabetes, in which insulin is the treatment of choice.

Methods: Liver cirrhosis was induced in Sprague-Dawley rats with common bile duct ligation (BDL), sham rats were controls. Streptozotocin 60 mg/kg (STZ, i.p., to induce diabetes) or vehicle was injected. Rats undergoing BDL and STZ injection were injected with insulin. On the 29th day after operations, three series of parallel groups were applied to survey (1) Systemic and portal hemodynamics; (2) Mesenteric vascular density; (3) Severity of portosystemic collaterals; (4) Hepatic resistance using the in situ liver perfusion; (5) Histology survey of mesentery and liver; (6) Mesentery angiogenesis- and liver fibrogenesis-related protein expressions.

Results: Compared with cirrhotic rats, cirrhotic diabetic rats had lower body weight, cardiac output, superior mesenteric arterial (SMA) resistance and portal venous (PV) resistance, higher SMA and PV flow, which were mostly reversed by insulin. Cirrhotic diabetic rats also had increased mesenteric vascular density, enhanced pERK, pAkt, VEGF, VEGFR2 protein expressions that were reversed by insulin. Insulin decreased shunting degree in diabetic cirrhotic rats. The hepatic perfusion pressure and severity of liver fibrosis were not significantly influenced by diabetes and insulin treatment in cirrhotic rats.

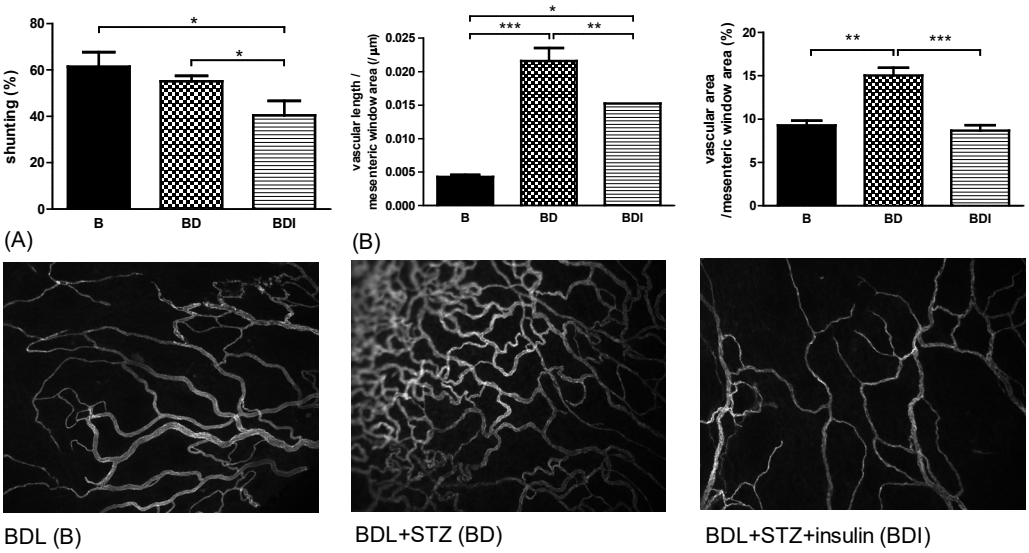

Figure. Mesenteric vascular density and portosystemic shunting degree in BDL groups. Figure (A) shows that insulin significantly reduced shunting degree in cirrhotic diabetic rats as compared with those of cirrhotic and cirrhotic diabetic rats. Figure (B) reveals that in BDL-cirrhotic groups, diabetes significantly increased the mesenteric vascular length and area, which were reduced by insulin (* $P<0.05$, ** $P<0.005$, *** $P<0.001$). The representative CD31 immuonofluorescence images of mesenteric windows are shown below.

Conclusions: Diabetes aggravates hemodynamic derangements, mesenteric angiogenesis and collaterals in cirrhotic rats, which were mostly ameliorated by insulin. Further clinical investigation is anticipated.