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Title: Anesthetic management of a patient undergoing liver transplantation who had previous coronary artery bypass grafting using an in situ right gastroepiploic artery

Short title: Liver transplantation and RGEA graft

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Key words: liver transplantation, coronary artery, bypass grafting, right gastroepiploic artery
Abstract

We describe successful anesthetic management during living-donor liver transplantation in a 63-year-old man with previous coronary artery bypass grafting that employed an in situ right gastroepiploic artery (RGEA). Anesthesia was maintained with 1.5% isoflurane in air/oxygen and fentanyl. A 5-lead electrocardiogram, transesophageal echocardiogram, and pacing pulmonary artery catheter evaluated cardiac function. A pacing wire was inserted through the catheter to prepare for intraoperative severe bradyarrhythmia. Olprinone and nicorandil were continuously infused to prevent the decrease in coronary arterial blood flow and the collapse of cardiac function. Avoiding disruption of circulation to coronary arteries through injury or spasm of the RGEA graft and preparing for the cardiac insufficiency during liver transplantation of a patient with previous coronary artery bypass grafting using an in situ RGEA is critical.
Introduction

The right gastroepiploic artery (RGEA) recently has become recognized as a safe and effective arterial conduit for coronary artery bypass grafting (CABG) [1,2]. However, abdominal surgery following previous CABG using an in situ RGEA graft can lead to inadvertent injury of the RGEA graft, which could endanger the critical blood supply to the coronary arteries [3,4]. We describe the anesthetic management of a patient during liver transplantation who had previously undergone CABG using an in situ RGEA.
Case Report

A 63-year-old man (162 cm, 53 kg) was scheduled to undergo living-donor liver transplantation because of end-stage liver failure categorized as Child-Pugh grade C secondary to primary sclerosing cholangitis. He had undergone CABG (the RGEA to the right coronary artery, the right internal thoracic artery to the left anterior descending branch and the left internal thoracic artery to the high lateral branch of the circumflex) to relieve unstable angina pectoris 3 years prior to liver transplantation. He had never experienced anginal pain after CABG. No ST-segment change was observed on the preoperative electrocardiogram. Preoperative echocardiogram showed good ventricular function with left ventricular ejection fraction 68% and without pulmonary hypertension. Angiography revealed that the patent RGEA graft was located on the left lobe of the cirrhotic liver and that bilateral internal thoracic arteries maintained sufficient blood flow. Thallium$^{201}$ myocardial stress scintigraphy detected no perfusion defect. Preoperative upper gastrointestinal endoscopy revealed no apparent gastroesophageal varices. Laboratory data before liver transplantation showed hemoglobin, 9.8 g·dl$^{-1}$; hematcrit, 28.9%; prothrombin time (international normalized ratio), 65% (1.26); platelet count, 253,000 mm$^{-3}$.

Anesthesia was induced with propofol 80 mg and fentanyl 200 µg. Intubation of the trachea was facilitated with vecuronium 6 mg. Anesthesia was maintained with 1.5% isoflurane in air/oxygen
and fentanyl. One of the potent cardiotonic and vasodilating phosphodiesterase 3 inhibitors, olprinone, 0.2 \( \mu \text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1} \), and a hybrid drug that combines characteristics of nitrates and K\text{ATP} channel activators, nicorandil, 0.04 mg \( \cdot \text{kg}^{-1} \cdot \text{h}^{-1} \), were continuously infused during anesthesia.

A 5-lead electrocardiogram with continuous ST-segment trends of II, III and V5, cardiac output monitors and transesophageal echocardiogram (TEE) were used in addition to the standard monitors during anesthesia. Cardiac output was measured using a pulmonary artery catheter (Swan-Ganz pacing pulmonary artery catheter; Edwards Lifesciences, Irvine, CA). A pacing wire (Edwards Chandler Transluminal V-pacing probe; Edwards Lifesciences) was inserted through the right ventricular pacing port of the pulmonary artery catheter to prepare for severe bradycardia or complete atrioventricular block induced by RGEA graft insufficiency. Sheath introducers (3-French) were placed into the right femoral artery and vein in preparation for emergent establishment of extracorporeal circulation, with cardiac surgeons on standby.

Laparotomy identified the RGEA graft on the upper surface of the left lobe of the cirrhotic liver. In order to protect the RGEA graft from inadvertent injury, a two-stage explantation of the cirrhotic liver was performed [5], that is, left lateral segmentectomy followed by explantation of the remnant right lobe of the liver. Pulsation of the RGEA graft was continually confirmed during the operation, and blood flow of the RGEA graft was detected using direct Doppler examination after completing
the implantation of a left lobe graft from a living donor.

The values for mean arterial pressure, heart rate and cardiac index were 60-75 mmHg, 60-80 beats·min⁻¹ and 3.8 to 7.5 l·min⁻¹·m⁻², respectively, which was maintained with dopamine and fluid supplementation with plasma protein fraction as required. No drastic hemodynamic change was observed during reperfusion of the transplanted liver. Homologous blood was transfused as needed to maintain an adequate hematocrit (approximately 25%). Good bilateral ventricular contractions were observed on TEE throughout the anesthesia. No intraoperative ST-segment change on the electrocardiogram was detected and temporary pacing was not required. The duration of anesthesia and operation were 1154 min and 1015 min, respectively, with total blood loss of 1900 ml. The postoperative course of the patient was uneventful. He has been doing well for about 2 years since the liver transplantation.
Discussion

We have successfully completed the anesthetic management of a patient with previous CABG using an in situ RGEA who underwent living-donor liver transplantation. Because RGEA graft insufficiency can result in severe sequelae, we took extreme care to avoid inadvertent injury or spasm of the RGEA graft. Furthermore, we prepared for intraoperative acute cardiac insufficiency because sudden hemodynamic instability can occur during graft reperfusion or inadvertent massive bleeding during liver transplantation.

RGEA is an excellent conduit for coronary revascularization and has good long-term patency [1,2]. Significant luminal narrowing caused by arteriosclerosis is rare in RGEA [6]. However, in patients who have undergone CABG with an in situ RGEA there is a risk of injury to the pedicle during subsequent abdominal surgery [3]. Even if an RGEA graft is not directly injured, traction or stretching of an RGEA graft may disturb its blood flow and cause myocardial ischemia [4]. RGEA is also more vulnerable to mechanical stimulation-induced spasm compared with the internal thoracic artery [7]. Although Kotoh did not mention the employment of any precautionary measures during surgery and they performed routine surgical procedures without trouble [3], we employed precautionary measures extensively with two preventive vasodilating drugs because liver transplantation is a hemodynamically unstable procedure.
To reduce the risk of spasm of the RGEA and internal thoracic artery pedicles, we continuously infused one of the vasodilating phosphodiesterase 3 inhibitors, olprinone, 0.2 µg·kg⁻¹·min⁻¹. The clinical dose of olprinone is between 0.1 and 0.3 µg·kg⁻¹·min⁻¹. Olprinone induces relaxation of RGEA and internal thoracic artery [8] and decreases the rhythmical contraction of the RGEA as effectively as diltiazem [9]. Olprinone also enhances hepatosplanchnic blood flow and increases hepatic oxygen delivery [10,11], which might be advantageous during liver transplantation.

Nicorandil is a hybrid drug that combines characteristics of nitrates and K<sub>ATP</sub> channel activators, which possesses cardioprotective effect [12,13]. Nicorandil has been reported to reduce the frequency of perioperative cardiac events in patients undergoing non-cardiac surgery with little effect on heart rate and arterial pressure [12]. It could be advantageous during liver transplantation that nicorandil has little effect on heart rate or blood pressure.

Isoflurane is often used during anesthesia for liver transplantation because of its low incidence of liver injury [14]. Isoflurane also has anesthetic-induced preconditioning effect, which protects myocardium from infarction after ischemia [15-17]. Concurrent treatment of nicorandil and isoflurane is reported to enhance post-ischemic recovery of cardiac function [18]. Therefore, use of isoflurane might be beneficial during liver transplantation in a patient who had CABG.

Acute reduction in right coronary artery blood flow, which can be caused by events such as...
coronary spasm [19] or occlusion [20], can induce sinus bradycardia or complete atrioventricular block. The pathogenesis of sinus bradycardia during right coronary artery occlusion is still unclear, but ischemia or infarction of the sinus atrial node or enhancement of parasympathetic activity known as the Bezold-Jarisch reflex is postulated. In the present patient, the blood flow of RGEA was confirmed by angiography before liver transplantation. Then, insufficiency of the RGEA graft which had been anastomosed to the right coronary artery could result in reduction of the right coronary blood flow followed by bradyarrhythmia or right ventricular dysfunction. We applied a ventricular pacing pulmonary artery catheter to prepare for intraoperative severe bradycardia or complete atrioventricular block. Although the appropriateness of the use of a pulmonary artery catheter is controversial [21], the use of a pacing pulmonary artery catheter is beneficial to cope with intraoperative cardiac collapse and severe bradyarrhythmia caused by the loss of right coronary artery blood flow.

Although intraoperative TEE has proved invaluable and accepted for cardiovascular function monitoring, the presence of gastroesophageal varices has been considered an absolute as well as a relative contraindication to TEE, depending on the center and/or operator, because of the blind instrumentation that occurs within the esophagus and the perceived risk for bleeding [22]. Patient with end-stage liver disease presenting for liver transplantation commonly have coagulation disorder
and gastroesophageal varices [23]. However, recent studies have shown that TEE can be performed safely in patients undergoing liver transplantation [24] or with known gastroesophageal varices [25].

In the report by Suriani [24], 25% of the patient examined had gastroesophageal varices. TEE was used in 11.3% of transplant centers in the United States [26]. Because the present patient had no apparent gastroesophageal varices and did not have severe coagulation disorder, the use of TEE during liver transplantation is considered practically acceptable.

In conclusion, we successfully completed the anesthetic management for liver transplantation in a patient who had CABG with an in situ RGEA. Avoiding disruption of circulation to coronary arteries through injury or spasm of the RGEA graft and preparing for the cardiac insufficiency during liver transplantation is critical.
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