Case Report

# Perioperative management of liver transplantation with concurrent coronary artery disease: Report of two cases

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## ABSTRACT

Coronary artery disease (CAD), even if asymptomatic, has been known to complicate the perioperative management of patients undergoing liver transplantation. Perioperative outcome for such patients is worse than those without CAD despite improvement in risk stratification and management of CAD. We hereby report the successful perioperative management of two patients with CAD undergoing living-related liver transplantation. Maintaining systemic vascular resistance, goal-directed volume administration and surgical technique avoiding total clamping of IVC was the mainstay of stable intraoperative course. Moreover, a lower model for end stage liver disease (MELD) score at the time of liver transplant may also have been contributory to successful outcome in our patients.

**Key words:** Coronary artery disease, liver transplantation, post reperfusion syndrome

## INTRODUCTION

Coronary artery disease (CAD) has been known to adversely affect the outcome of patients undergoing liver transplantation. High resting cardiac output (CO) and low systemic vascular resistance (SVR) in end-stage liver disease (ESLD) and perioperative haemodynamic alterations during surgery contribute adversely to the outcome.[1-3]

Over the last two decades more stringent pretransplant evaluation and better management of CAD have improved outcomes.[1] Diedrich *et al.*[1] observed an overall mortality and morbidity of 26% and 38%, respectively (in 2008), that were significantly lower than reported in 1996 (50% and 80%, respectively).[2]

The history of CAD significantly increases adverse perioperative outcome in a 30-day period.[3] Many studies have described preoperative cardiac evaluation and optimization. However, there are only few reports regarding perioperative management. We describe successful perioperative management of living-related liver transplantation (LRLT) in two patients with varying spectrum of CAD.

## CASE REPORTS

### Case 1

A 62-year-old man (156 cm, 48 kg), scheduled to undergo LRLT for cryptogenic ESLD (Child-Turcotte-Pugh score 9, MELD 12), was decompensated with hepatic encephalopathy, ascites and hepatorenal syndrome. He also had hypertension and diabetes mellitus. He suffered cardiac arrest lasting approximately 30 seconds during large volume paracentesis 8 months ago. A quicker decompression probably induced asystole. Post-cardiac arrest, there was no neurological deficit. He had effort tolerance of NYHA class II. Preoperative echocardiogram showed ejection fraction (EF) of 55% with no pulmonary hypertension. Dobutamine stress echocardiogram was negative for inducible ischemia. Preoperative angiography revealed 30% block in proximal left-anterior descending

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artery (LAD), 100% block in posterior descending artery with good collateralization. The patient was on metoprolol, terlipressin, aspirin and insulin. Airway examination was normal. Preoperative laboratory values are summarized in Table 1. Aspirin was discontinued 7 days before surgery while metoprolol was continued.

Anaesthesia was induced with fentanyl 200 mcg, propofol 70 mg and intubation was facilitated with rocuronium 50 mg. Anaesthesia was maintained with 1-1.5% isoflurane in air/oxygen and fentanyl at 2 mcg/kg/h. Intraoperative monitoring included a five-lead electrocardiogram (ECG) with ST trends, invasive arterial blood pressure; EV1000® (version-1.2)/ flotrac® (Edward life sciences, USA) for CO, SVR, systolic volume variation (SVV) and central venous pressure (CVP) and pulmonary artery catheter (PAC) for mean pulmonary artery pressure (MPAP) and pulmonary capillary wedge pressure (PCWP). Thromboelastograhy, PT/INR, haemoglobin, platelet count and ABG were monitored at regular intervals.

The intraoperative goals for mean arterial pressure (MAP), heart rate (HR), MPAP, CO, SVR and urine output were 65-75 mmHg, 60-90 beats/min, 15-20 mmHg, 6-10 l/min, 500-800 dyne.s/cm$^5$ and 0.5 ml/kg/h, respectively. They were maintained with intravenous fluids along with noradrenaline and terlipressin infusions.

Inferior vena cava (IVC) was partially clamped during hepatic vein reconstruction. Transient fall in MAP at reperfusion was managed with boluses of noradrenaline and phenylephrine. No intraoperative ST-segment changes were detected.

Intraoperative haemodynamic variables are summarized in Table 2. Total blood loss was approximately 1500 ml. The patient was shifted to liver transplant ICU and extubated 12 hours later. Antiplatelet therapy and metoprolol were restarted 48 hours after the surgery. Twelve-lead ECG 12 hourly and Troponin-I level 24 hourly were monitored for the first 5 days. The patient was shifted from ICU on the 10$^{th}$ day and discharged on the 16$^{th}$ postoperative day.

**Table 1: Preoperative laboratory values**

| | Case 1 | Case 2 |
|---|---|---|
| Blood group | A positive | O positive |
| Hb | 9.2 gm/dl | 8.2 gm/dl |
| Platelet | 152,000 mm$^{-3}$ | 150,000 mm$^{-3}$ |
| PT/INR | 16.8 seconds/1.6 | 19.6 seconds/1.8 |
| Fibrinogen | 352 mg/dl | 212 mg/dl |
| BUN/Cr | 24/1.4 mg/dl | 19/1.3 mg/dl |
| $Na^+/K^+$ | 136/4.2 mEq/l | 134/3.5 mEq/l |
| $HbA_{1c}$ | 6.8% | 7.3% |
| Albumin | 1.8 g/dl | 2.5 g/dl |
| FBS | 132 mg/dl | 110 mg/dl |

## Case 2

A 55-year-old man (167 cm, 93 kg), scheduled to undergo LRLT for hepatitis B associated ESLD (Child-Turcotte-Pugh score 9, MELD 15), was decompensated with ascites and oesophageal variceal bleed. CAD was diagnosed when he had an episode of myocardial infarction 7 months ago. Subsequently, he underwent percutaneous intervention (PCI). Drug eluting stent was placed in LAD and bare metal stents were placed in $D_1$ and $D_2$ artery. He was on aspirin and clopidogrel (75 mg each). He remained asymptomatic subsequently. He also had hypertension and diabetes mellitus. Aspirin was stopped 2 months later in the view of repeated malaena. Preoperative echocardiogram showed EF of 42% with no pulmonary hypertension. During exercise stress echocardiogram, he achieved 90% of target HR but EF reduced from 42% to 35%

**Table 2: Haemodynamic variables during surgery**

| | HR (beats/min) | CO (l/min) | SVR (dyne.s/cm$^5$) | MAP (mmHg) | MPAP (mmHg) | PCWP (mmHg) |
|---|---|---|---|---|---|---|
| Case 1 | | | | | | |
| Baseline | 54 | 5.8 | 1156 | 90 | 18 | 9 |
| During dissection | 84 | 7.3 | 865 | 84 | 16 | 8 |
| Anheptic (partial IVC clamp) | 76 | 6.5 | 1062 | 76 | 13 | 6 |
| Postreperfusion | 60 | 8.5 | 572 | 72 | 18 | 10 |
| Case 2 | | | | | | |
| Baseline | 78 | 9.1 | 706 | 80 | 27 | 14 |
| During dissection | 94 | 12.5 | 371 | 60 | 22 | 12 |
| After terlipressin | 85 | 8.1 | 615 | 74 | 20 | 10 |
| Anheptic (partial IVC clamp) | 92 | 8.7 | 508 | 70 | 18 | 9 |
| Postreperfusion | 108 | 11.8 | 465 | 74 | 20 | 11 |

HR – Heart rate; CO – Cardiac output; SVR – Systemic vascular resistance; MAP – Mean arterial pressure; MPAP – Mean pulmonary arterial pressure; PCWP – Pulmonary capillary wedge pressure

and the mid-anterior septum and distal-inferior wall became akinetic. He became breathless 6 minutes after exercise and his functional capacity was rated good (METs-7, NYHA class II). Preoperative angiography revealed patent stent in LAD, blocked stent in $D_1$ and $D_2$ artery. Left circumflex artery was 10% blocked, while right coronary artery was 40% blocked. No further intervention was deemed necessary by cardiologist. The patient was on bisoprolol, torsemide, atorvastatin, clopidogrel and insulin. Clopidogrel was stopped 1 week prior to surgery and enoxaparin 60 mg OD was started. Airway examination was normal. Preoperative laboratory reports are summarized in Table 1.

Enoxaparin was stopped 12 hours prior to surgery and bisoprolol was continued. Anaesthesia was induced with fentanyl 300 mcg, thiopentone 175 mg and intubation of trachea was facilitated with rocuronium 100 mg. Anaesthesia was maintained with 1-1.5% isoflurane in air/oxygen and fentanyl at 3 mcg/kg/h. Intraoperative monitoring and goals were same as in case 1. In addition, defibrillator pads were applied on chest. A 6 Fr sheath introducer was placed into left femoral artery for emergent establishment of intra-aortic balloon pump; however, the requirement did not arise.

Intraoperative haemodynamic variables are summarized in Table 2. During the later part of the dissection phase, despite high dose of noradrenalin infusion, terlipressin infusion was started to maintain MAP and SVR. IVC was partially clamped during hepatic vein reconstruction. Before reperfusion, portal flush was used to avoid post-reperfusion syndrome (PRPS). A transient fall of MAP was treated with boluses of noradrenaline, phenylephrine and soda-bicarbonate. No intraoperative ST-segment changes were detected. Total blood loss was approximately 1200 ml. The patient was shifted to liver transplant ICU and extubated 6 hours later. Antiplatelet therapy and bisoprolol were restarted 1 day after the surgery. His postoperative recovery was uneventful. Postoperative monitoring was similar to the first patient. The patient was shifted from ICU on the 8$^{th}$ day and discharged on the 16$^{th}$ postoperative day.

## DISCUSSION

The incidence of CAD ranges up to 27% in ESLD patients.[3] High morbidity and mortality in CAD patients undergoing orthotopic liver transplantation (OLT) are likely to be multifactorial. Cardiac function of the transplant recipient must be adequate to handle marked perioperative haemodynamic alterations.[4] Additionally, in the immediate postoperative period, SVR is elevated and CO is decreased as normal liver function is reestablished.[5] Another possible cause may be the hypercoagulable state that occurs early after OLT.[6]

Continuation of the antiplatelet agent increases the risk of blood loss. However, post-PCI, withdrawing dual antiplatelet therapy may cause stent thrombosis.[7] OLT is a high-risk surgery with increased possibility of blood loss. Therefore, we discontinued antiplatelet agents 7 days prior to surgery as per recommendations.[7] In case 2, enoxaparin was started as a bridge to reduce the risk of perioperative stent thrombosis.[7] Clopidogrel and aspirin were resumed 24 hours after surgery as per the guidelines.[7] Safadi *et al.*[3] demonstrated that the use of perioperative beta-blockers protects liver transplant patients from adverse cardiac outcomes. Beta-blockers attenuate both the sympathetic and neuroendocrine responses to stress, balance myocardial oxygen supply and demand, reduce inflammatory markers and free radicals, and stabilize atherosclerotic plaques.[3]

Maintaining hyperdynamic circulation is one of the main haemodynamic goals.[4] Using a regimen of maintaining low CVP through a multipronged approach has been shown to be beneficial.[8] In CAD patients, the strategy of lowering filling pressures to reduce bleeding and hepatic congestion should be avoided. It may induce severe reflex tachycardia.[4] Prompt treatment of haemodynamic changes is required to avoid alteration in myocardial oxygen supply and demand ratio.

Cardiovascular instability in liver transplant may occur during liver explantation, during clamping the IVC and at the time of the reperfusion.[4] In the second case, during the dissection phase, hypotension occurred despite a very high dose of noradrenaline infusion. At this point, SVR was very low (371 dyne.s/cm$^5$) but MPAP, PCWP and CO were in the normal range and ABG showed metabolic acidosis (pH-7.18, BE-12.9). The patient responded to 100 ml of 7.5% sodium-bicarbonate and terlipressin infusion (1.5 mcg/kg/h). Terlipressin has greater selectivity for the $V_1$ receptor than vasopressin.[9] Terlipressin administration increases MAP and SVR in patients with portal hypertension. Although its bolus injection may reduce cardiac function, infusion does not have harmful effects.[10] Perioperative fluid

management was aided by PAC, SVV and CVP. Though transoesophageal echocardiography demonstrates close correlation with ventricular volume, it was not used as both patients had gastro-oesophageal varices and were on antiplatelet therapy.

The decrease in venous return caused by cross-clamping of IVC leads to hypotension.[4,11] The change in arterial pressure induced by partial clamping of IVC has been found to be minimal in deceased-donated liver transplants.[11] Hence, during the implantation, surgeons applied partial clamp on IVC.

The venous return from the bowel is occluded when the diseased liver is removed. At the time of reperfusion, hypotension occurs mainly because of fall in SVR mediated by sudden release of accumulated metabolic substances, pooled deoxygenated blood and preservative solution into the circulation.[4] In patients with CAD, acute hypotension may not be tolerated well. Portal flush was employed just before reperfusion to avoid PRPS. This involved venting of approximately 300 ml of blood through portal vein, along with venacaval venting, after establishing all venous connections with suprahepatic cava temporarily occluded. The technique reduces the risk of PRPS by decreasing the load of inflammatory cytokines released into the circulation at the time of reperfusion, thereby decreasing the risk of associated severe haemodynamic changes.[12] Portal flush also leads to quicker decompression of the venous drainage of the bowel.[12]

Further, a lower MELD score (12 and 15) at the time of liver transplant might have contributed to successful outcome in our patients.[1]

## CONCLUSION

The comprehensive strategy of maintaining SVR, PAC- and SVV-guided volume administration, surgical techniques avoiding cross-clamping of IVC and employing portal flush before reperfusion resulted in a stable circulation and outcome during the liver transplantation procedure. The utilization of partial clamping has a physiological basis; however, its merits require further substantiation in LRLT.

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