Title: MECHANISM OF MYOCARDIAL DYSFUNCTION DURING LIVER TRANSPLANTATION: THE ROLE OF ISOLATED RIGHT VENTRICULAR FAILURE

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INTRODUCTION: Liver transplantation procedures are of long duration and are performed on patients who often present with multi-system organ failure. Massive transfusions of many blood volumes are the rule in these patients, further complicating management. Reperfusion of the donor liver causes profound and characteristic alterations in cardiovascular homeostasis. We have used two-dimensional transesophageal echocardiography (TEE) for continuous intraoperative monitoring and to define the mechanism of cardiovascular dysfunction during liver transplantation; we have documented right-sided heart failure occurring at the time of reperfusion (possibly due to the embolization of air or thrombi).

METHODS: Sixteen adult patients undergoing liver transplantation were included in this study, which was approved by our Clinical Investigation Committee. An 11 mm gastroscope tipped with a 3.5 MHz echocardiographic probe (Diasonics) was placed into the esophagus; the long axis four chamber view for evaluation of the interaction of left and right ventricles and for the detection of venous air embolism, and the short-axis view at the mid-papillary muscle level for the evaluation of left ventricular size, contractility, and segmental wall motion were obtained. Non-heparinized veno-venous bypass was used during occlusion of the inferior vena cava to preserve venous return and to facilitate the surgical procedure. Five minutes before perfusion of the donor liver, patients were empirically treated with sodium bicarbonate, 50% dextrose, and calcium chloride.

In six patients, complete hemodynamic profiles and short-axis echocardiograms were recorded before and after reperfusion. End-diastolic diameter (EDD) and end-systolic diameter (ESD) were measured off-line. A "diameter-equivalent" of ejection fraction, % fractional shortening (FS) = {100(EDD - ESD) /EDD}, was used as an index of contractility. Pre- and post-reperfusion values were compared with the paired T-test; $p < 0.05$ was considered significant.

Echocardiograms were analyzed by a cardiologist who was unaware of the hemodynamic indices. The frequency of septal wall motion abnormalities, considered consistent with right ventricular (RV) failure, was noted, as was the frequency of bulging of the intra-atrial septum from right-to-left.

RESULTS: Four of the 16 patients had abnormal septal wall motion. One patient had a septal wall motion abnormality at baseline that improved after paracentesis; the new development of septal wall motion abnormalities was noted after graft reperfusion in three other patients. In an additional three patients, TEE demonstrated deviation of the atrial septum from right-to-left.

In all patients, echogenic contrast was seen in the right heart at the time of donor liver reperfusion. In two patients, spontaneous echogenic contrast was also seen in the left heart at the time of reperfusion of the donor liver, representing paradoxical embolization. TEE also demonstrated a large thrombus in the right atrium of one patient (figure 1), which later disappeared, presumably into the pulmonary circulation.

Table 1 summarizes simultaneous hemodynamic measurements and echocardiographic short-axis dimensions obtained in six patients at the time of donor liver reperfusion. Cardiac output (CO) increased significantly ($p < 0.005$), as did FS; heart rate (HR) and mean arterial pressure (MAP) were unchanged. Statistically significant ($p < 0.05$) increases in pulmonary capillary wedge pressure (PCWP) and central venous pressure (CVP) were seen, but the increases in mean pulmonary artery pressure (PAP) were not quite significant ($0.05 < p < 0.1$). EDD was not significantly different in the post-reperfusion period.

DISCUSSION: Severe hypotension at the time of reperfusion of the donor liver is a well-described phenomenon. Carmichael et al (1), using data from Swan-Ganz catheterization, described a pattern of hypotension associated with elevated PAP and PCWP and associated falls in CO; they attributed this to myocardial depression, purportedly due to the release of vasodepressor substances from the donor liver. In our patients, CO actually increased, in part because we routinely give these patients calcium chloride, bicarbonate, and glucose/insulin at the time of reperfusion.

TEE demonstrated right heart failure, with dilatation of the right-sided chambers to the point where they encroached upon the left heart in 7 of 16 patients. "Paradoxical" motion of the interventricular septum, with the septum behaving as a functional part of the right ventricle, has been reported with RV pressure and volume overload (2). While left ventricular preload, as measured by TEE EDD, was unchanged, PCWP rose significantly. In critically-ill patients, PCWP may not accurately reflect left ventricular filling (3); this may reflect changes in ventricular compliance during the course of the transplantation procedure.

Right heart failure in these patients may result from elevated right ventricular afterload, due to the embolization of air and thrombi and/or the release of humoral factors from ischemic bowel or the donor liver. Similar macro-embolization has been observed with TEE during total hip replacement (4), with associated increases in PAP and PCWP. Resultant pulmonary hypertension may cause reversal of the normal intra-atrial gradient, thereby allowing paradoxical embolization of air or microthrombi across an atrial septal defect or a probe-patent foramen ovale. Paradoxical air embolus during hepatic transplantation has been previously documented (5).

Intraoperative two-dimensional transesophageal echocardiography provided valuable clinical information during liver transplantation and demonstrated the role of isolated right-heart failure in the pathophysiology of the cardiovascular changes occurring with reperfusion of the donor liver.

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TABLE 1: HEMODYNAMIC AND ECHOCARDIOGRAPHIC MEASUREMENTS BEFORE AND AFTER REPERFUSION

	PRE	POST
MAP (mmHg)	90 ± 14	82 ± 7
HR (min^{-1})	98 ± 5	96 ± 5
mean PAP (mmHg)	20 ± 2	30 ± 3
PCWP (mmHg)*	12 ± 2	23 ± 4
CVP (mmHg)*	11 ± 3	19 ± 3
CO (L/min)*	6.6 ± 0.6	11.5 ± 1.0
EDD (cm)	3.5 ± 0.3	3.7 ± 0.2
FS(%)*	45 ± 5	53 ± 7

results = mean ± SEM
* $P<0.05$, PRE to POST

FIGURE 1: RIGHT ATRIAL (RA) THROMBUS; ATRIAL SEPTUM BULGING TOWARD LEFT ATRIUM (LA)