Right Heart Dysfunction, Pulmonary Embolism, and Paradoxical Embolization during Liver Transplantation

A Transesophageal Two-Dimensional Echocardiographic Study

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ELLIS JE, LICHTOR JL, FEINSTEIN SB, CHUNG MR, POLK SL, BROELSCH C, EMOND J, THISTLETHWAITE JR, ROIZEN MF. Right heart dysfunction, pulmonary embolism, and paradoxical embolization during liver transplantation: a transesophageal two-dimensional echocardiographic study. Anesth Analg 1989;68:777–82.

In 16 adult patients, we performed continuous intraoperative two-dimensional transesophageal echocardiography (2DTEE) to help elucidate the mechanism of myocardial dysfunction that accompanies liver transplantation. In 4 of the 16 patients "paradoxical" motion of the interventricular septum consistent with right ventricular failure was seen. An additional three of the 16 patients showed right atrial enlargement and right-to-left deviation of the interatrial septum. Two patients showed evidence of paradoxical embolization (one of whom had right ventricular and right atrial enlargement), and a third patient (who had right atrial enlargement) embolized a large right atrial thrombus into the pulmonary circulation. Two-dimensional transesophageal echocardiography demonstrated that isolated right ventricular failure might account for some of the hemodynamic instability seen during liver transplantation. Venous, pulmonary, and paradoxical embolization of air and thrombi documented by transesophageal echocardiography likely contribute to right heart failure.

Key Words: LIVER, TRANSPLANTATION. SURGERY, LIVER TRANSPLANTATION. MEASUREMENT TECHNIQUES, ECHOCARDIOGRAPHY. HEART, ECHOCARDIOGRAPHY.

Improvements in surgical technique, the intraoperative use of venous bypass, and cyclosporin immunosuppressive therapy have all contributed to the more frequent use of liver transplantation as a therapeutic option for patients with end-stage liver disease. These operations are of long duration (five to fifteen hours) and are performed on patients who often present with multisystem organ failure. Massive, rapid transfusions of many blood volumes are the rule, further complicating management of these patients.

Unique hemodynamic changes accompany the different stages of orthotopic liver transplantation. The release of tense ascites, temporary occlusion of the inferior vena cava, and reperfusion of the donor liver all cause profound and characteristic alterations in cardiovascular homeostasis. Measurements made with Swan-Ganz catheters have been used to manage and describe these processes (1), but there are limitations to their accuracy in assessing left ventricular preload (2). We have used two-dimensional transesophageal echocardiography to monitor cardiovascular performance during liver transplantation and to obtain insights into the accompanying circulatory pathophysiology.

Materials and Methods

This study was approved by our Clinical Investigations Committee. Sixteen adult patients undergoing

Presented in part at the American Society of Anesthesiologists, October 1987, in Atlanta, Georgia.

Received from the University of Chicago Hospitals and Clinics, Department of Anesthesia and Critical Care, 5841 South Maryland Avenue, Chicago, Illinois. Accepted for publication November 18, 1988.

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liver transplantation were included in the study after consenting to our data collection protocols. Anesthesia, induced with thiamylal and followed by succinylcholine, was maintained with oxygen, air, isoflurane, and fentanyl, with pancuronium for relaxation. Monitoring consisted of measurements obtained from radial and pulmonary artery catheters and from pulse oximeters. Blood products were rapidly administered through two 8 French introducers with the aid of a rapid volume infusion device. 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 (1 mEq/kg), 50% dextrose (1 ml/kg), and calcium chloride (20 mg/kg). This treatment regimen, with the addition of 10 units of regular insulin, was repeated immediately after reperfusion.

After endotracheal intubation, we inserted a gastroscope tipped with a 3.5-MHz echocardiographic probe (Diasonics, Milpitas, CA) into the esophagus and connected it to a Diasonics 6400 Ultrasonograph. The echocardiogram was monitored continuously, and qualitative judgments of cardiac filling volumes and contractility guided patient management. Echocardiographic views were obtained at two levels: 1) the long-axis four-chamber view to evaluate the interaction of left and right ventricles and detect possible venous air embolism, and 2) the short-axis view to evaluate left ventricular size, contractility, and segmental wall motion. Adjustments in transducer position were occasioned by upper abdominal retraction and our intentional variation from long-axis to short-axis views. We attempted to obtain short-axis views as identical as possible during these adjustments, using the mid-papillary muscles as landmarks. We recorded echocardiographic sequences of interest on one-half inch VHS videotape for off-line analysis by a cardiologist who was unaware of clinical conditions.

In nine patients, standard transthoracic echocardiograms were obtained perioperatively for clinical management with the results noted. The presence of cardiac pathology on available postmortem examinations was also noted.

Results

Patient Characteristics

Table 1 summarizes the demographic features of our patient population. Collectively, these patients represent a critically ill group. Two had preoperative respiratory failure requiring mechanical ventilation and 6 presented with renal insufficiency (as documented by a serum creatinine greater than 2.0 mg/dl). Nine of the patients were encephalopathic preoperatively. Nine of the 16 patients underwent routine transthoracic echocardiography in the perioperative period. The findings, summarized in Table 1, included pericardial effusions in four patients, significant tricuspid regurgitation in two patients, and decreased right ventricular systolic function in two others.

Intraoperative Wall Motion Abnormalities

Four patients (1, 5, 9, and 15) had transesophageal echocardiographic evidence of abnormal motion of the interventricular septum. In patient 1, the septal abnormality noted before incision resolved after the release of tense ascites. Paracentesis was accompanied by an increase in left ventricular end-diastolic diameter from 3.3 to 4.2 cm. This septal wall motion abnormality recurred after reperfusion of the donor liver. In three patients (5, 9, and 15), new interventricular septal wall motion abnormalities were identified after graft reperfusion.

In three additional patients (6, 10, and 16), without evidence of abnormal ventricular wall motion, bulging of the interatrial septum from right-to-left was seen, suggesting a positive right-to-left pressure gradient at the atrial level.

Only one patient (7) had evidence of left ventricular decompensation as evidenced by severe global hypokinesis during the procedure; this improved after an infusion of dobutamine was begun.

Air Emboli and Thromboemboli

In all patients, spontaneous echogenic contrast material was seen in the right heart during thermodilution cardiac output determinations, during venous bypass, and at the time of donor liver reperfusion.

In two patients (5 and 12) paradoxical embolization occurred, as spontaneous echogenic contrast material was identified in the left heart at the time of reperfusion of the donor liver (Fig. 1). We believe this echogenic contrast represented air and/or microthrombi.

Transesophageal echocardiography revealed a large thrombus in the right atrium of patient 6 (Fig. 2) during venous bypass. The thrombus later disappeared, presumably embolized into the pulmonary circulation. This patient also demonstrated a very

Table 1. Clinical Information on Patients Undergoing Liver Transplantation with Transesophageal Echocardiographic Monitoring

			Preoperative							
Patient	Age	Diagnosis	Renal insufficiency	Respiratory failure	Prothrombin time	Blood volumes replaced	Transthoracic echocardiography	Paradoxical embolization	Abnormal septal wall motion	Additional tee abnormalities
1	28	Budd-Chiari syndrome	+	+	18.8	1	Dilated, hypokinetic RV	–	+	None
2	56	Chronic active hepatitis B	–	–	15.1	1	Large PA, pericard effusion, MR, TR	–	–	None
3	27	Fulminant hepatitis	+	+	23.4	4	Small pericard effusion; septal WMA	–	–	None
4	36	Cryptogenic cirrhosis	–	–	16.4	16	N/A	–	–	None
5	45	Chronic active hepatitis B	–	–	13.5	12	N/A	+	+	RA>LA, RV>LV, Hypovolemic LV
6	48	Chronic active hepatitis B	+	–	14.6	13	N/A	–	–	RA>LA, RA thrombus, Hypovolemic LV
7	40	Cryptogenic cirrhosis	–	–	16.5	5	RA>LA, paradoxical IVS, poor LV fn, dilated RV	–	–	Global hypokinesis, improved after dobutamine infusion
8	40	Cryptogenic cirrhosis	+	–	14	20	Small pericardial eff, mild MR, small LV	–	–	None
9	21	Fulminant hepatitis	–	–	36.4	5	N/A	–	+	None
10	62	Primary biliary cirrhosis	–	–	14.4	3	Mod AS, gradient=64 mm Hg, mild LVH, MR, TR	–	–	RA>LA, Small pericardial effusion
11	36	Hemangiosarcoma	–	–	11.9	0.5	N/A	–	–	None
12	46	Cryptogenic cirrhosis	+	–	16.9	3	WNL	+	+	None
13	35	Chronic active hepatitis B	–	–	12.1	2	N/A	–	–	None
14	14	Cryptogenic cirrhosis	–	–	13.8	1	Small pericardial effusion	–	–	None
15	46	Primary graft failure	+	–	17.7	2	WML	–	+	None
16	24	Fulminant non-A, non-B hepatitis	–	–	35.9	0.4	N/A	–	–	RA>LA, Hypovolemic LV

AS, aortic stenosis; fn, function; IVS, interventricular septum; LV, left ventricle; LVH, left ventricular hypertrophy; MR, mitral regurgitation; N/A, not available; RA, right atrium; RA>LV, right atrium larger than left atrium and bulging right-to-left; RV, right ventricle; RV>LV, right ventricle larger than left ventricle and bulging right-to-left; PA, pulmonary artery; TR, tricuspid regurgitation; WNL, normal; WMA, wall motion abnormality.

thin intraatrial septum, which bulged into the left atrium. The central venous pressure rose acutely to 38 mm Hg after graft reperfusion, despite systemic hypotension; severe acute hepatic congestion at this time necessitated phlebotomy. Transesophageal echocardiography at that time revealed a small, hyperkinetic left ventricle and a markedly dilated right heart.

Echocardiographic and Pulmonary Capillary Wedge Pressure as Determinants of Preload

We observed an inconsistent relationship between pulmonary capillary wedge pressure (PCWP) and filling volumes. Figure 3, for example, demonstrates end-diastolic frames from patient 9 during venous bypass. The two frames were recorded 30 minutes

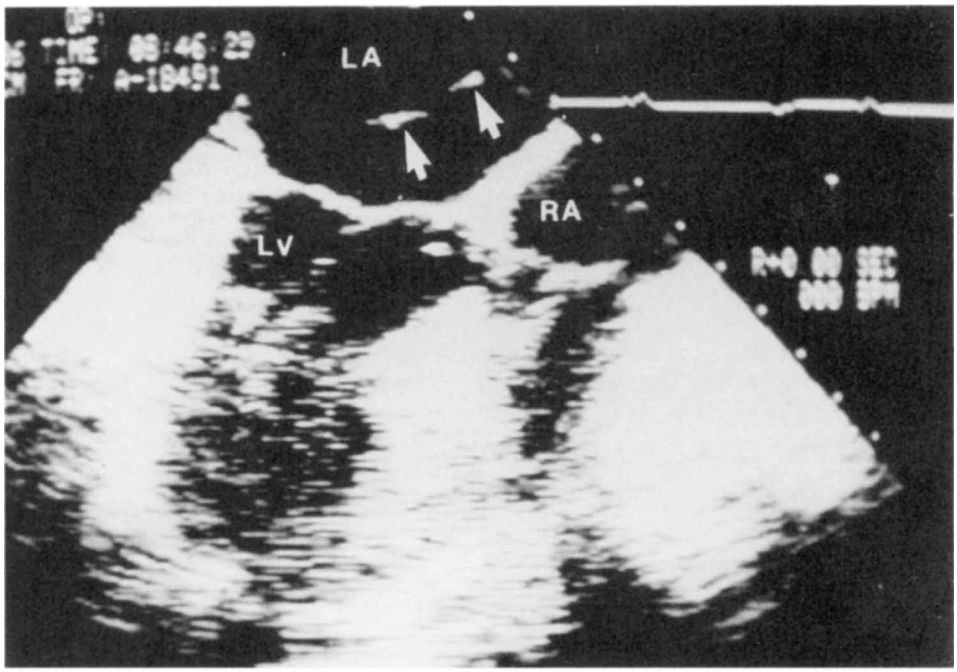

Figure 1. Evidence of paradoxical embolization (arrow) in left atrium (LA) of patient 5. Left ventricle (LV), right atrium (RA).

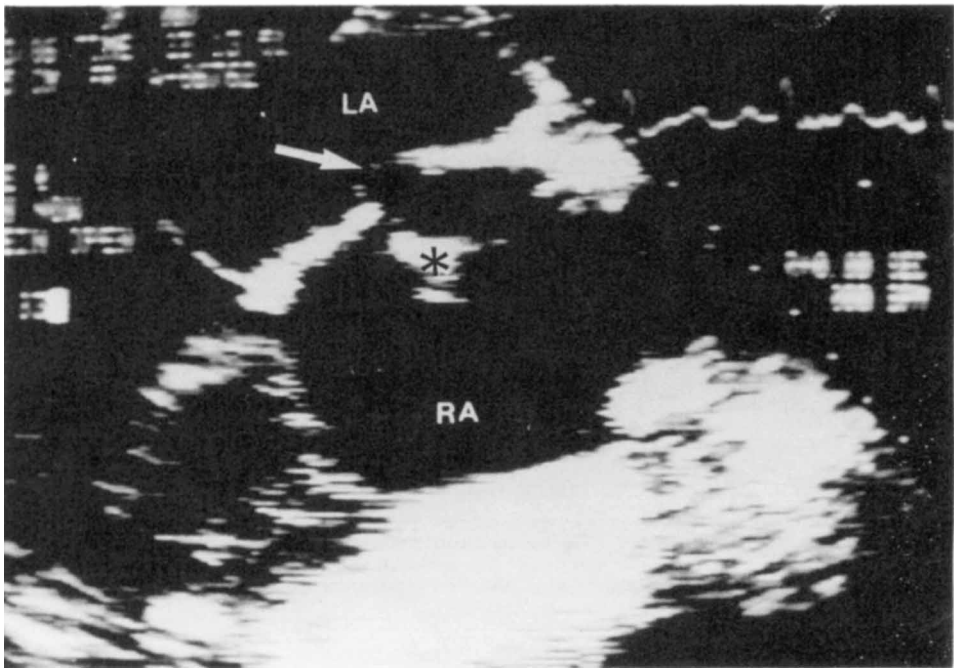

Figure 2. Large thrombus (asterisk) in right atrium (RA) of patient 6, which later embolized into the pulmonary circulation. The intraatrial septum, which is thinned (arrow), bulges in a right-to-left direction. (LA = left atrium).

apart, during which time pulmonary artery pressures increased greatly. While the two frames reveal almost identical end-diastolic dimensions, the PCWP was 20 mm Hg during the first frame, and 40 mm Hg during the second.

Postmortem Examinations

Autopsies were obtained in two patients. Other than the presence of air in the right side of the heart after reperfusion, neither of these patients had any echo-

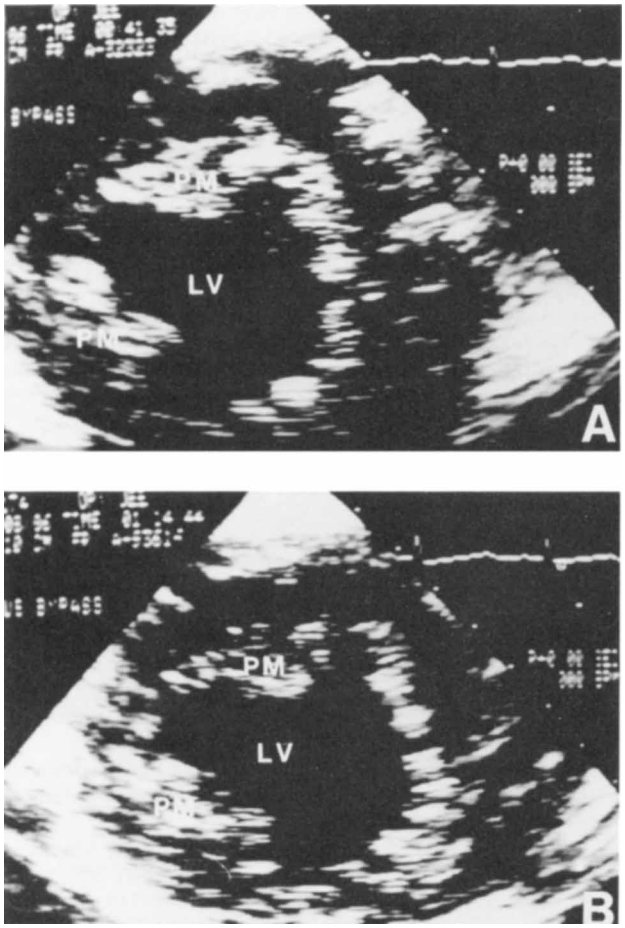

Figure 3. Two end-diastolic frames of short-axis views of the left ventricle (LV), 30 minutes apart, from patient 9 during venous bypass. While end-diastolic areas appear nearly identical, pulmonary capillary wedge pressure doubled from 20 mm Hg (A) to 40 mm Hg (B) during this interval. (PM = papillary muscle).

cardiographic abnormalities. Postmortem examination of the heart revealed right ventricular hypertrophy and cardiomegaly with a thickened pulmonary outflow tract in patient 8. Patient 4 had pulmonary vascular changes consistent with ARDS (adult respiratory distress syndrome) and pericarditis, but no intrinsic myocardial pathology.

Both patients (5 and 12) who experienced paradoxical air embolus died, but postmortem examinations were not available; the presence of a probe-patent foramen ovale could not be determined.

Discussion

Cardiovascular Response to Donor Liver Reperfusion

Severe hypotension at the time of reperfusion of the donor liver is a well-described phenomenon. It has been variously attributed to hypovolemia or myocardial depression (3). Carmichael et al. (1) using data from Swan-Ganz catheterization, described a pattern of hypotension associated with elevated (pulmonary artery pressure) PAP and PCWP and concomitant decreases in (cardiac output) CO. They interpreted these results as being consistent with acute left heart failure at the time of reperfusion, purportedly due to the release of vasodepressor substances from the donor liver.

In our series, care was taken to flush the donor liver of ischemic metabolites by infusing an albumin solution into the donor liver and discarding the effluent immediately before reperfusion. Also, in an attempt to prevent life-threatening hypotension and hyperkalemia, we routinely administered calcium chloride, bicarbonate, and glucose/insulin at the time of reperfusion of the donor liver. We did so empirically, theorizing that we might also be treating citrate intoxication. Citrate intoxication is a documented cause of decreased left ventricular contractility in patients undergoing liver transplantation (4). We did not believe it safe to examine the circulatory responses to reperfusion in the absence of this empiric treatment. While aggressive therapy may have obscured left ventricular dysfunction due to metabolic causes, our data suggest that right heart failure, due to pulmonary embolism of air and thrombi, plays a role in the hypotension seen after reperfusion of the donor liver.

Embolic Events

Echocardiography enabled us to see microembolization and macroembolization. Similar macroembolization has been observed using transesophageal echocardiography during total hip replacement with associated increases in pulmonary artery and wedge pressures and decreases a PaO_2 and mean arterial pressure (5).

The finding of a dilated right heart on echocardiography and passive congestion of the liver on visual inspection implies acute right heart failure, as does the presence of abnormal interventricular septal wall motion (6). This may limit left ventricle filling by diminishing pulmonary venous return. In several patients, transthoracic Doppler echocardiography performed preoperatively revealed tricuspid regurgitation. "Functional" tricuspid regurgitation, secondary to annular dilatation, may contribute further to dangerous congestion of the new liver and a decreased right ventricular ejection fraction. Tricuspid regurgitation also makes the determination of cardiac output by thermodilution inaccurate.

Humoral factors may be involved in the pathogenesis of pulmonary hypertension, further increasing right heart work; short periods of partial veno-venous bypass increase pulmonary elaboration of thromboxane (7) and cause pulmonary hypertension in sheep. The use of non-heparinized venous bypass may contribute to the formation of thrombi, such as the one we observed (Fig. 2). Others have used heparinized bypass to avoid such thrombotic complications, but this was accompanied by massive hemorrhage and an unacceptably high mortality rate (8). Still, the formation of thrombi in the venous bypass machine may be reduced by keeping flows greater than one liter/minute; in the future, the use of heparin-bonded bypass tubing may reduce the risk of thromboembolism (8). Despite these problems, the use of venous bypass during hepatectomy offers substantial advantages that probably outweigh the risks of thrombosis. Its use during liver transplantation has been shown to preserve venous return and cardiac preload and output, decrease transfusion requirements, and lower the incidence of renal failure and mortality in the first month after liver transplantation (8).

Paradoxical Air Embolus

Two of our patients (5 and 12) showed transesophageal echocardiographic evidence of paradoxical embolization, possibly due to intracardiac shunting. The acute elevation in right ventricular afterload imposed by pulmonary emboli may cause elevated right heart pressures, allowing the reversal of the normal intraatrial gradient and facilitating paradoxical embolization of air or microthrombi across an atrial septal defect or a probe-patent foramen ovale (9). In four of our patients (5, 6, 10, and 16), intraoperative echocardiography demonstrated bulging of the interatrial septum in a manner consistent with elevated right atrial pressures (Fig. 3), and another patient (7) demonstrated this pattern on preoperative echocardiography.

Others have documented evidence suggesting paradoxical air embolus during hepatic transplantation. Starzl et al. (10) reported that nine of 48 patients in their early experience had neurologic complications consistent with cerebral air embolus. The potential for right-to-left shunts may exist in these patients, even in the absence of intracardiac shunts. Cirrhotics are prone to develop intrapulmonary shunts (11), and echocardiographic contrast studies have been used to document their presence (12).

In summary, these cases and observations confirm the common phenomenon of pulmonary embolism during liver transplantation and demonstrate its sequelae: right ventricular and right atrial encroachment on left heart filling, and paradoxical emboli. Pericardial effusions and tricuspid regurgitation are frequently seen, and may also compromise cardiovascular function. We have also shown that left ventricular pumping function is not generally impaired in this small series of patients when generous doses of calcium chloride are given.

The authors thank Delores Cave for secretarial assistance, and John Erickson, MD, and Casaundra Williams for editorial assistance.

References

1. Carmichael FL, Lindop MJ, Farman JV. Anesthesia for hepatic transplantation: cardiovascular and metabolic alterations and their management. Anesth Analg 1985;64:108–16.
2. Hansen RM, Viquerat CE, Matthay MA, Wiener-Kronish JP, DeMarco T, Bahtia S, Marks JD, Botvinick EH, Chatterjee K. Poor correlation between pulmonary arterial wedge pressure and left ventricular end-diastolic volume after coronary artery bypass graft surgery. Anesthesiology 1986;64:764–70.
3. Joseph WL, Fonkalsrud EW, Longmire WP Jr. Vasodepressive effects of the venous effluent following canine liver allotransplantation. J Surg Res 1968;8:367–72.
4. Marquez J, Martin D, Virji MA, Kang YG, Warty VS, Shaw B Jr, Sassano JJ, Waterman P, Winter PM, Pinsky MR. Cardiovascular depression secondary to ionic hypocalcemia during hepatic transplantation in humans. Anesthesiology 1986;65:457–61.
5. Roewer N, Beck H, Kochs E, Kremer P, Schroder E, Schulte AM, Esch J. Detection of venous embolism during intraoperative monitoring by two-dimensional transesophageal echocardiography. Anesthesiology 1986;63:A169.
6. Kaul S. The interventricular septum in health and disease. Am Heart J 1986;112:568–81.
7. Peterson MB, Huttemeier PC, Zapol WM, Martin EG, Watkins WE. Thromboxane mediates acute pulmonary hypertension in sheep extracorporeal perfusion. Am J Physiol 1982;243:H471–H479.
8. Shaw BW, Martin DJ, Marquez JM, Kang YG, Bugbee AC Jr, Iwatsnki S, Griffith BP, Hardesty RL, Bahnson HT, Starzl TE. Venous bypass in clinical liver transplantation. Ann Surg 1984;200:524–34.
9. Marshall WK, Bedford RF, Miller ED. Hemodynamics during anesthesia in the seated position. Anesth Analg 1982;61:201.
10. Starzl TE, Schneck SA, Mazzoni G, Aldrete JA, Porter KA, Schroter GPJ, Koep LJ, Putnam CW. Acute neurologic complications after liver transplantation with particular reference to intraoperative cerebral air embolus. Ann Surg 1978;187:236–40.
11. Krowka MJ, Cortese DA. Pulmonary aspects of chronic liver disease and liver transplantation. Mayo Clin Proc 1985;60:407–18.
12. Shub C, Tajik AJ, Seward JB, Dines DE. Detecting intrapulmonary right-to-left shunt with contrast echocardiography: observations in a patient with diffuse pulmonary arteriovenous fistulas. Mayo Clin Proc 1976;51:81–4.