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CASE REPORT

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Hypertrophic obstructive cardiomyopathy in liver transplant patients

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Abstract

The optimal treatment strategy for patients with symptomatic hypertrophic obstructive cardiomyopathy (HOCM) and end-stage liver disease (ESLD) is not well defined. Although medical management is the accepted first line treatment, patients who are unresponsive to medication require further interventions. Since ESLD patients have a high operative risk for surgical myomectomy, alcohol septal ablation (ASA) emerges as a good alternative in these cases. The timing of ASA in relation to liver transplantation is still unclear. We report here on the first case of an orthotopic liver transplant-recipient undergoing ASA and the second of a cirrhotic patient requiring ASA as a bridge to liver transplantation. Both patients had a good clinical outcome and we argue that ASA in HOCM patients should be driven by symptom onset, and that in the asymptomatic patient it can be safely deferred until after liver transplantation. (Cardiol J 2008; 15: 74–79)

Key words: cardiomyopathy, liver transplantation, liver failure, alcohol, hypertrophy, ablation

Introduction

Hypertrophic obstructive cardiomyopathy (HOCM) is a heterogeneous disorder, affecting patients of all ages. It has a diverse clinical course where some individuals remain asymptomatic throughout life while others develop severe symptoms of heart failure, angina or syncope, and a minority present with sudden cardiac death. The left ventricular outflow gradient is an independent predictor of HOCM-related death, progression to New York Heart Association (NYHA) class III or IV heart failure, and for death from heart failure or stroke when it exceeds 30 mm Hg [1]. The optimal treatment strategy for patients with symptomatic HOCM and end-stage liver disease (ESLD) is not well defined. ESLD patients have a high operative risk for surgical myomectomy [2–5]. Alcohol septal ablation (ASA) emerges as a good alternative to surgical myomectomy in these patients. The presence of symptomatic HOCM is considered a contraindication for liver transplantation in ESLD [6]. We report on two patients with ESLD who underwent ASA, the first secondary to worsening symptoms after liver transplant and the second as a bridge to liver transplantation.

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Case No. 1

A 58-year-old white female with HOCM and ESLD secondary to longstanding autoimmune hepatitis presented for evaluation for liver transplantation due to deteriorating hepatic function. She was relatively asymptomatic from the cardiac standpoint with no angina, heart failure or syncopal symptoms. On physical examination, she was jaundiced but had no jugular venous distention (JVD). The carotid upstrokes were bifid, the first and second heart sounds were normal, and a fourth heart sound was

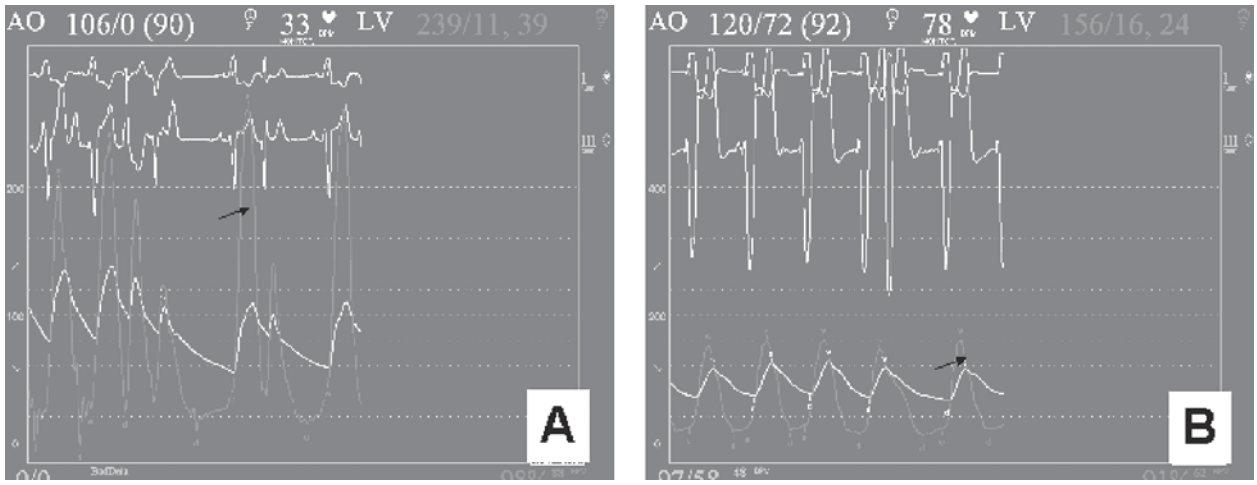

Figure 1. Assessment of left ventricular outflow gradient of patient 1 with hypertrophic cardiomyopathy before **(A)** and after **(B)** alcohol septal ablation using cardiac catheterization. Significant improvement of the gradient is visualized **(B)**. Left ventricular pressure tracing in grey colour and aortic pressure tracing in white. The arrow in A and B denotes post premature ventricular contraction pressure gradients.

present. A 3/6 mid- to late-peaking outflow murmur was heard across the precordium. Lungs were clear, and there was no peripheral oedema. Electrocardiography showed a left bundle branch block and left ventricular hypertrophy. A transthoracic echocardiogram (TTE) showed a left ventricular outflow tract (LVOT) gradient of 91 mm Hg, interventricular septum (IVS) of 15 mm, left ventricular posterior wall (LVPW) of 14 mm and mild systolic anterior motion (SAM). Cardiac catheterization showed a LVOT gradient of 60 mm Hg at rest, a hyperdynamic left ventricle with a left ventricular ejection fraction (LVEF) of 80%, and angiographically normal-appearing coronaries. Since her cardiac symptomatology was stable on beta-blockers, she was considered to be a suitable candidate for orthotopic liver transplantation, which she underwent with no adverse cardiovascular events. Within one year of her liver transplantation, she developed lower extremity oedema and angina despite adequate medical therapy. TTE then showed an LVOT gradient of 99 mm Hg, IVS of 20 mm and LVPW of 16 mm. Surgical myomectomy versus ASA was discussed with the patient, who opted for ASA. This was performed with an infusion of 3 cc of 100% ethanol into the first and second septal arteries under myocardial contrast echocardiography and fluoroscopic guidance. The left ventricle/aorta (LV/Ao) gradient was 100 mm Hg at rest and 200 mm Hg after a premature ventricular contraction (PVC), but decreased to 10 mm Hg and 30 mm Hg at rest and after a PVC, respectively, post-ablation (Fig. 1). She developed complete heart block on the second day after the procedure and required a permanent pacemaker. She became symptom free post ASA and remained without angina or heart failure symptoms one year later. TTE then showed reduction of the IVS and LVPW diameters to 16 and 15 mm, respectively, with a preserved LVEF and no detectable LVOT gradient.

Case No. 2

A 51-year-old white male with ESLD secondary to alcoholism and hepatitis C infection was enrolled on the liver transplantation waiting list after he quit drinking. During his pre-transplant evaluation process, he noted chest tightness, dyspnea on exertion and near syncope. On examination, he was jaundiced and had evidence of JVD. His cardiac exam was relevant for a grade II/VI systolic ejection murmur with a diastolic component and a positive fourth heart sound. The lungs were clear, and he had mild ascites with 1+ pitting oedema of the ankles and feet. Electrocardiography showed nonspecific T wave changes. TTE revealed asymmetric left ventricular hypertrophy (LVH), with IVS of 21 mm, LVPW of 13 mm, a resting LVOT obstruction with a peak gradient of 64 mm Hg at rest and 102 mm Hg with provocation, mild SAM of anterior mitral leaflet (Fig. 2) and moderate mitral incompetence with a normal LVEF, all consistent with HOCM. Cardiac catheterization documented midcavity obliteration with an LV-Ao gradient of 120 mm during sinus rhythm and 220 mm Hg post-PVC, as well as grade II mitral regurgitation (Fig. 3).

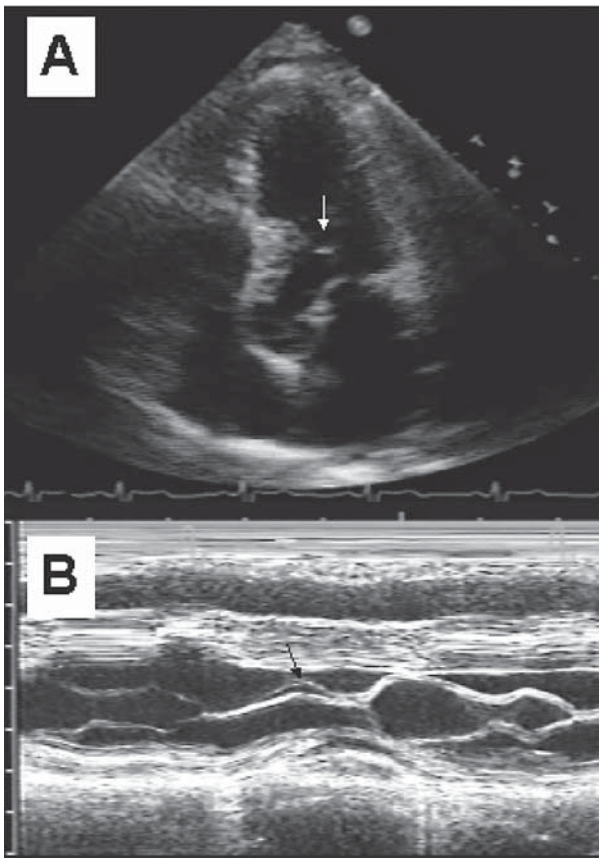

Figure 2. Transthoracic echocardiography of patient 2 with hypertrophic cardiomyopathy before alcohol septal ablation. **A.** 5-chamber view showing hypertrophied interventricular septum and systolic anterior motion (SAM) of the anterior mitral valve leaflet (white arrow); **B.** M-mode across the mitral valve showing SAM of the anterior mitral valve leaflet (black arrow).

He continued to be symptomatic despite treatment with beta-blockers. He was deemed high risk for liver transplantation due to his symptomatic HOCM and high risk for surgical myomectomy due to his ESLD. Under TTE and fluoroscopy guidance, 4 ml of 100% ethanol was injected into the first septal artery. The LV-Ao gradient fell to 3 mm Hg post ablation (Fig. 3). The patient had a good recovery with improvement of his dyspnea and chest pain. Repeat echocardiography six months later showed an improvement of the LVOT resting gradient at 27 mm Hg and amelioration of both IVS and LVPW diameters (15 mm and 13 mm, respectively) with no signs of SAM of the anterior mitral leaflet. The patient underwent orthotopic liver transplantation in November of 2005 without major complications. One year after his transplant the patient continued to report no dyspnea or angina even with exertion.

Discussion

Hypertrophic cardiomyopathy is a complex genetic cardiac disease, diagnosed principally with TTE by demonstrating LVH, wall thickness of at least 15 mm in adults, typically asymmetric, in the absence of another cardiac or systemic disease capable of producing a similar degree of hypertrophy (e.g., hypertension or aortic stenosis) [7]. HOCM refers to the presence of a dynamic LVOT obstruction usually caused by SAM of the anterior mitral valve leaflet and projection of the hypertrophied interventricular septum into the outflow tract in systole. Management is aimed at alleviating symptoms of heart failure, angina and syncope on one hand, and preventing sudden death in high-risk individuals on the other. Medical therapy is the first line of treatment and consists of beta-blockers, calcium channel antagonists and disopyramide, solely or in combination. Surgical septal myomectomy or more recently ASA are recommended for the small subgroup of patients (5%) who have both a large outflow gradient (usually > 50 mm Hg at rest or on provocation) and moderate to severe heart failure or angina symptoms unresponsive to maximal medical therapy [7]. Historically, surgical septal myomectomy has been the "gold standard" treatment for HOCM patients refractory to medical therapy, perhaps due to more than 40 years of experience, a relatively low perioperative mortality rate (1–3%), high success rate with clinical improvement reported in up to 90% of patients, and excellent long-term survival [7, 8]. ASA emerged in 1995 [9] as an alternative procedure to surgery and has since grown quickly in popularity to the point that it is estimated that more ASAs have been performed since its introduction than the total number of surgical myomectomies performed during the last 45 years [8]. Studies have shown that ASA is as effective as surgery in improving symptoms and reducing LVOT gradient in the short- and intermediate-term; however, there is still a lack of data regarding long-term follow up, which is the main argument of its detractors [10]. At present, there is no general agreement between cardiologists and surgeons regarding which procedure should be the first-line intervention for most HOCM patients after medical treatment failure. Patients with advanced age or significant comorbidities and/or relative contraindications to surgery are often considered good candidates for ASA.

ESLD patients undergoing general anesthesia and non-hepatic surgery are at increased risk for perioperative complications, with an overall 30-day

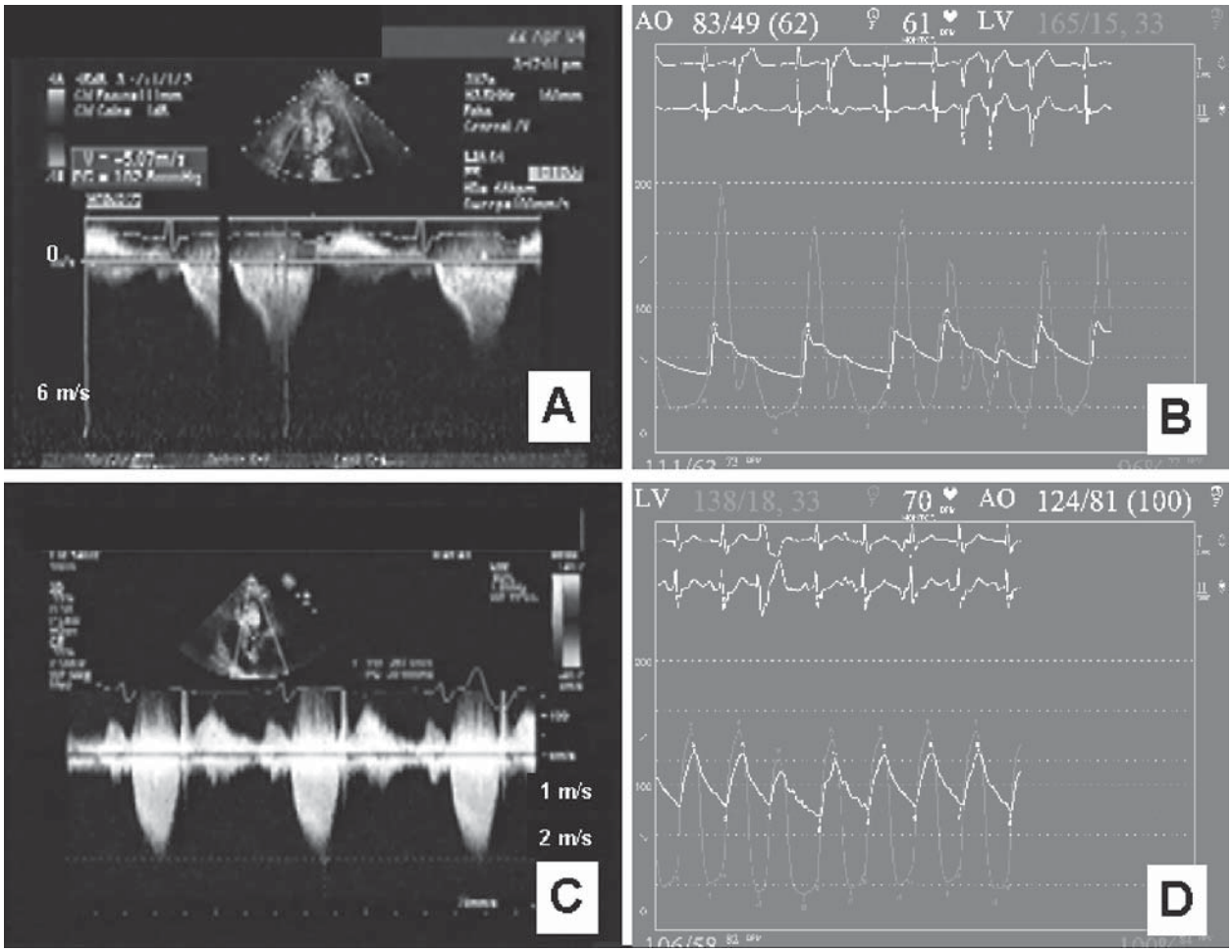

Figure 3. Assessment of left ventricular outflow gradient of patient 2 with hypertrophic cardiomyopathy before **(A, B)** and after **(C, D)** alcohol septal ablation using Doppler echocardiography **(A, C)** and cardiac catheterization **(B, D)**. Significant improvement of the gradient is noted. Left ventricular pressure tracing in grey colour and aortic pressure tracing in white.

mortality rate ranging between 11% and 17% [11–13]. The surgical prognosis correlates with the severity of cirrhosis. In one study, patients with Child class A, B and C had 1-month mortality rates of 3.6%, 31.7% and 54.5%, respectively [11]. The clinical outcomes are even poorer after cardiac surgery in patients with ESLD, with mortality rates of 50% to 80% in class B patients [2, 4, 5, 11] and 100% in class C patients [2, 5]. The difference in mortality between cardiac and non-cardiac surgery in patients with ESLD stems from the use of cardiopulmonary bypass, a known trigger for the production and release of several vasoactive substances and cytotoxic chemicals that are responsible for much of the morbidity associated with open heart surgery [14, 15]. These findings have been verified by the very recent report by Filsoufi et al. [16] in which operative and 1-year mortality as well as postoperative complications were directly related to the Child class in cirrhotic patients who underwent cardiac surgery, and, significantly, no operative mortality occurred in patients who had cardiac surgery without the use of cardiopulmonary bypass.

When this prognostic data is considered, it becomes apparent that patients with cirrhosis, whose diseases are advanced enough for them to be considered as liver transplant candidates, are absolute non-candidates for surgical septal myomectomy. ASA has evolved as a very attractive treatment modality in this high-risk surgical group. However, it still remains uncertain whether patients with HOCM should undergo ASA prior to or after liver transplantation.

On the other hand, little is known about the risk of general anesthesia and major non-cardiac surgery in patients with HOCM. In this regard, the incidence of adverse cardiovascular events such as heart failure,

ischemia and arrhythmias, varied from 16% to 44% in the studies reviewed [17–20], with a strikingly low rate of postoperative death and myocardial infarction (near 0%) in HOCM patients undergoing non-cardiac surgery [18–20]. Perioperative cardiovascular compromise is the main concern when performing a major surgery, such as liver transplantation, on patients with HOCM. However, most of these complications are transitory and treatable, and studies failed to report increased postsurgical mortality rates in these individuals. Moreover, three case reports demonstrated no perioperative cardiovascular events in HOCM patients receiving orthotopic liver transplantation, analogous to our first case [21, 22]. The other option is to perform ASA prior to surgery in order to avoid these reported potential perioperative complications [17–20], with the possible downside of delaying surgery. It is still uncertain whether improvement of the LVOT by ASA will translate into reduction of the aforementioned perioperative adverse cardiovascular events.

We report here on the first case, to the best of our knowledge, of an orthotopic liver transplant recipient undergoing ASA and the second [23] of a cirrhotic patient requiring ASA prior to liver transplantation. Our first patient with cirrhosis and asymptomatic HOCM had an uneventful liver transplantation but required ASA 1.5 years post-transplant due to worsening symptoms. The second patient had ASA performed 15 months before liver transplantation, which facilitated his enlistment on the transplant list. In both scenarios, the clinical outcome was favourable and the decision to perform ASA was mainly driven by symptomatic HOCM. Currently, there is no strong evidence to support either approach.

In conclusion, ASA in ESLD patients with HOCM is safe and effective. ASA can be performed as a bridge to liver transplantation in symptomatic patients. Patients with asymptomatic HOCM can safely undergo liver transplantation and deferring ASA until symptom development.

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References

1. Maron MS, Olivotto I, Betocchi S et al. Effect of left ventricular outflow tract obstruction on clinical outcome in hypertrophic cardiomyopathy. New Engl J Med, 2003; 348: 295–303.
2. Hayashida N, Shoujima T, Teshima H et al. Clinical outcome after cardiac operations in patients with cirrhosis. Ann Thor Surg, 2004; 77: 500–505.
3. Kaplan M, Cimen S, Kut MS, Demirtas MM. Cardiac operations for patients with chronic liver disease. Heart Surg Forum, 2002; 5: 60–65.
4. Klemperer JD, Ko W, Krieger KH et al. Cardiac operations in patients with cirrhosis. Ann Thor Surg, 1998; 65: 85–87.
5. Suman A, Barnes DS, Zein NN, Levinthal GN, Connor JT, Carey WD. Predicting outcome after cardiac surgery in patients with cirrhosis: A comparison of Child-Pugh and meld scores. Clin Gastroenterol Hepatol, 2004; 2: 719–723.
6. Lopez PM, Martin P. Update on liver transplantation: Indications, organ allocation, and long-term care. Mount Sinai J Med New York, 2006; 73: 1056––1066.
7. Maron BJ, McKenna WJ, Danielson GK et al. American College of Cardiology/European Society of Cardiology clinical expert consensus document on hypertrophic cardiomyopathy. A report of the American College of Cardiology foundation task force on clinical expert consensus documents and the European Society of Cardiology committee for practice guidelines. J Am Coll Cardiol, 2003; 42: 1687–1713.
8. Maron BJ, Dearani JA, Ommen SR et al. The case for surgery in obstructive hypertrophic cardiomyopathy. J Am Coll Cardiol, 2004; 44: 2044–2053.
9. Sigwart U. Non-surgical myocardial reduction for hypertrophic obstructive cardiomyopathy. Lancet, 1995; 346: 211–214.
10. Alam M, Dokainish H, Lakkis N. Alcohol septal ablation for hypertrophic obstructive cardiomyopathy: A systematic review of published studies. J Intervent Cardiol, 2006; 19: 319–327.
11. del Olmo JA, Flor-Lorente B, Flor-Civera B et al. Risk factors for nonhepatic surgery in patients with cirrhosis. World J Surg, 2003; 27: 647–652.
12. Ziser A, Plevak DJ, Wiesner RH, Rakela J, Offord KP, Brown DL. Morbidity and mortality in cirrhotic patients undergoing anesthesia and surgery. Anesthesiology, 1999; 90: 42–53.
13. Farnsworth N, Fagan SP, Berger DH, Awad SS. Child-turcotte-pugh versus meld score as a predictor of outcome after elective and emergent surgery in cirrhotic patients. Am J Surg, 2004; 188: 580–583.
14. Downing SW, Edmunds LH Jr. Release of vasoactive substances during cardiopulmonary bypass. Ann Thor Surg, 1992; 54: 1236–1243.
15. Edmunds LH Jr. Inflammatory response to cardiopulmonary bypass. Ann Thor Surg, 1998; 66: S12–S16 (discussion S25–S18).

16. Filsoufi F, Salzberg SP, Adams DH. Current management of ischemic mitral regurgitation. Mount Sinai J Med New York, 2005; 72: 105–115.
17. Chang KH, Sano E, Saitoh Y, Hanaoka K. Anesthetic management of patients with hypertrophic obstructive cardiomyopathy undergoing non-cardiac surgery. Masui, 2004; 53: 934–942.
18. Haering JM, Comunale ME, Parker RA et al. Cardiac risk of noncardiac surgery in patients with asymmetric septal hypertrophy. Anesthesiology, 1996; 85: 254–259.
19. Kuroiwa M, Arai M, Ueno T, Takenaka T, Okamoto H, Hoka S. Perioperative cardiovascular complications in patients with hypertrophic cardiomyopathy. Masui, 2003; 52: 733–739.
20. Thompson RC, Liberthson RR, Lowenstein E. Perioperative anesthetic risk of noncardiac surgery in hypertrophic obstructive cardiomyopathy. JAMA, 1985; 254: 2419–2421.
21. Cywinski JB, Argalious M, Marks TN, Parker BM. Dynamic left ventricular outflow tract obstruction in an orthotopic liver transplant recipient. Liver Transpl, 2005; 11: 692–695.
22. Harley ID, Jones EF, Liu G, McCall PR, McNicol PL. Orthotopic liver transplantation in two patients with hypertrophic obstructive cardiomyopathy. Br J Anaesthesia, 1996; 77: 675–677.
23. Paramesh AS, Fairchild RB, Quinn TM, Leya F, George M, Van Thiel DH. Amelioration of hypertrophic cardiomyopathy using nonsurgical septal ablation in a cirrhotic patient prior to liver transplantation. Liver Transpl, 2005; 11: 236–238.