CORE
Metadata, citation and similar papers at core.ac.uk
Provided by Elsevier - Publisher Connector

treated with doxorubicin and trastuzumab, while at the same time, preventing any detrimental side effects on cardiac health.

Nazanin Fallah-Rad, MD
Jonathan R. Walker, MSc
Anthony Wassef, MD
Matthew Lytwyn, BSc
Sheena Bohonis, BSc
Tielan Fang, MSc
Ganhong Tian, PhD
Iain D. C. Kirkpatrick, MD
Pawan K. Singal, PhD
Marianne Krahn, MD
Debjani Grenier, MD
***Davinder S. Jassal, MD**

*Section of Cardiology
Department of Internal Medicine
Bergen Cardiac Care Centre
Room Y3010
St. Boniface General Hospital
409 Taché Avenue
Winnipeg, Manitoba R2H 2A6
Canada
E-mail: djassal@sbgh.mb.ca

doi:10.1016/j.jacc.2011.09.026

REFERENCES

1. Fallah-Rad N, Walker JR, Wassef A, et al. The utility of cardiac biomarkers, tissue velocity and strain imaging, and cardiac magnetic resonance imaging in predicting early left ventricular dysfunction in patients with human epidermal growth factor receptor II–positive breast cancer treated with adjuvant trastuzumab therapy. J Am Coll Cardiol 2011;57:2263–70.
2. Tocchetti CG,Coppola C, Ragone G, et al. Early identification of left ventricular dysfunction with speckle tracking echocardiography in antineoplastic therapy-induced cardiotoxicity (abstr). Circulation 2010; 122:A18686.
3. Cardinale D, Colombo A, Torrisi R, et al. Trastuzumab-induced cardiotoxicity: clinical and prognostic implications of troponin I evaluation. J Clin Oncol 2010;28:3910–6.
4. Jassal DS, Han SY, Hans C, et al. Utility of tissue Doppler and strain rate imaging in the early detection of trastuzumab and anthracycline mediated cardiomyopathy. J Am Soc Echocardiogr 2009;22:418–24.
5. Di Lisi D, Bonura F, Macaione F, et al. Chemotherapy-induced cardiotoxicity: role of the conventional echocardiography and the tissue Doppler. Minerva Cardioangiol 2011;59:301–8.
6. Ho E, Brown A, Barrett P, et al. Subclinical anthracycline- and trastuzumab-induced cardiotoxicity in the long-term follow-up of asymptomatic breast cancer survivors: a speckle tracking echocardiographic study. Heart 2010;96:701–7.
7. Hare JL, Brown JK, Leano R, Jenkins C, Woodward N, Marwick TH. Use of myocardial deformation imaging to detect preclinical myocardial dysfunction before conventional measures in patients undergoing breast cancer treatment with trastuzumab. Am Heart J 2009;158:294–301.

Cardiovascular Risk Assessment of Liver Transplantation Candidates

We read with great interest the report by Raval et al. (1) on cardiovascular risk assessment of candidates for liver transplantation (LT) and would like to congratulate the investigators on a comprehensive and thorough review.

We disagree, however, with a comment made in the section on heart failure and cardiomyopathy and the evidence provided in the report. The investigators, quite rightly, recommend that all patients undergo pre-operative transthoracic echocardiography, a practice routinely undertaken at LT centers. They then state that patients with left ventricular ejection fractions as low as 10% have successfully undergone LT after aggressive medical management, citing a Canadian case series (2). We believe this deserves further analysis. The publication describes 4 patients with end-stage hypertrophic, dilative, and ischemic cardiomyopathy who underwent combined cardiac transplantation and LT on cardiopulmonary bypass. All patients were highly symptomatic, with New York Heart Association functional class III or IV heart failure, and 3 had congestive cirrhosis due to right ventricular failure. It appears as if the primary indication for transplantation was cardiac, but heart transplantation alone was not possible, because of end-stage liver disease. We believe that the term "aggressive medical management" is misleading in this context and does not appropriately describe the complexity of the procedures performed. We strongly believe that severe and symptomatic heart failure is an absolute contraindication for LT, unless a combined heart and liver transplantation procedure is considered.

In the section on recommendations for assessment, the role of cardiopulmonary exercise testing, in particular the assessment of aerobic capacity, was not commented on. The most sensitive index of aerobic capacity is oxygen consumption at peak exercise (peak Vo_2). Evaluation of peak Vo_2 is increasingly used at LT centers as part of the routine assessment. Dharancy et al. (3) demonstrated that a peak Vo_2 of <60% was associated with reduced 1-year survival in patients listed for LT. The predictive ability of peak Vo_2 was more evident in patients with Model for End-Stage Liver Disease scores >17.

In summary, severe left ventricular failure remains in our view an absolute contraindication for LT despite aggressive medical management. Dynamic cardiopulmonary testing and assessment of aerobic capacity provides important prognostic information and should be considered in all patients undergoing elective LT assessment.

***Deepak Joshi, MB BS**
Chris Willars, MB BS
William Bernal, MD
Julia Wendon, MD
Georg Auzinger, EDIC

*King's College Hospital
Liver Intensive Care Unit
Denmark Hill
London
United Kingdom
E-mail: d.joshi@nhs.net

doi:10.1016/j.jacc.2011.08.058

REFERENCES

1. Raval Z, Harinstein ME, Skaro AI, et al. Cardiovascular risk assessment of the liver transplant candidate. J Am Coll Cardiol 2011;58: 223–31.

2. Hennessey T, Backman SB, Cecere R, et al. Combined heart and liver transplantation on cardiopulmonary bypass: report of four cases. Can J Anaesth 2010;57:355–60.
3. Dharancy S, Lemyze M, Boleslawski E, et al. Impact of impaired aerobic capacity on liver transplant candidates. Transplantation 2008;86:1077–83.

Reply

We appreciate the comments of Dr. Joshi and colleagues regarding our report on the cardiovascular risk assessment of candidates for liver transplantation (1).

We agree that liver transplantation in patients with severe left ventricular systolic dysfunction carries a higher risk for cardiovascular complications and mortality. These patients should be thoroughly evaluated, as we have described, and would benefit from referral to higher volume transplantation centers with experience in caring for such patients. As noted in our report, and by Joshi et al., there have been case reports of successful transplantation in such patients, often requiring combined liver and heart transplantation (2). Several potential etiologies of systolic dysfunction in patients with end-stage liver disease have been described, and some may be reversible (3,4). Therefore, we do not consider severe systolic dysfunction to be an absolute contraindication to liver transplantation. However, liver transplantation in this patient type should be undertaken only at centers with advanced heart failure programs.

With regard to the utility of the measurement of oxygen consumption at peak exercise to assess aerobic capacity, this is certainly another piece of information that can be added to the cardiologist's armamentarium when performing a cardiovascular risk assessment of a liver transplantation candidate. In a multivariate analysis, it was associated with 1-year survival and was also associated with post-operative complications in sicker patients (5). Although we do not believe that this should be a sole reason for exclusion for liver transplantation candidacy, we agree that it may aid in assessing cardiovascular risk.

Matthew E. Harinstein, MD
Zankhana Raval, MD
Mihai Gheorghiade, MD
***James D. Flaherty, MD**

*Department of Medicine, Division of Cardiology
Northwestern University Feinberg School of Medicine
251 E. Huron Street, Galter 8-130
Chicago, Illinois 60611
E-mail: j-flaherty2@md.northwestern.edu

doi:10.1016/j.jacc.2011.09.029

REFERENCES

1. Raval Z, Harinstein ME, Skaro AI, et al. Cardiovascular risk assessment of the liver transplant candidate. J Am Coll Cardiol 2011;58:223–31.
2. Hennessey T, Backman SB, Cecere R, et al. Combined heart and liver transplantation on cardiopulmonary bypass: report of four cases. Can J Anaesth 2010;57:355–60.
3. Zardi EM, Abbate A, Zardi DM, et al. Cirrhotic cardiomyopathy. J Am Coll Cardiol 2010;56:539–49.
4. Donovan CL, Marcovitz PA, Punch JD, et al. Two-dimensional and dobutamine stress echocardiography in the preoperative assessment of patients with end-stage liver disease prior to orthotopic liver transplantation. Transplantation 1996;61:1180–8.
5. Dharancy S, Lemyze M, Boleslawski E, et al. Impact of impaired aerobic capacity on liver transplant candidates. Transplantation 2008;86:1077–83.

The Role of Platelet Function Testing and Genotyping in the Stented Patient Treated With Clopidogrel

We read with interest the study of Campo et al. (1). Their observation that $P2Y_{12}$ reaction units (PRU) decreased at 1 month compared to baseline in patients receiving clopidogrel undergoing percutaneous coronary intervention (PCI) is similar to our report in 2003 (2), where ~30% of patients were resistant at 1 and 5 days post-PCI, and 15% were resistant at 30 days. Similar observation of lower prevalence of 30-day high platelet reactivity compared to 12 to 24 h post-stenting was also reported recently (3). We further presented similar PRU levels at 24 h after 600 mg loading and just before the last maintenance dose at 6 weeks (4). Mean PRUs at 8 h after last maintenance dose decreased by ~25. These findings indicate the "booster" effect of the last maintenance dose by new active metabolite generation. Therefore, clopidogrel response is significantly influenced by measured time after clopidogrel administration even during the maintenance phase. In the study by Campo et al. (1), a decrease in PRU levels at 1 month may be partially related to measured time (~25 PRU in stable patients). However, Campo et al. (1) did not mention the timing of measurements with respect to the last dose administration.

Another important issue is that the post-PCI event occurrence reported by Campo et al. (1) is relatively discordant with most PCI-related studies demonstrating more frequent events within 30 to 60 days post-PCI. Interestingly, the first ischemic event in Campo et al. (1) occurred at ~50 days post-PCI (estimated from Fig. 3 of Campo et al. [1]).

In multivariate analysis, *CYP2C19*17* variant and 30-day PRU together were independent determinants of bleeding, implicating that *CYP2C19*17* effect on bleeding may be independent of clopidogrel response, which requires further explanation. Although platelet function testing and genotyping may play complementary roles in tailoring antiplatelet therapy, numerous clinical factors including drug-drug interaction may influence the magnitude of platelet reactivity and clinical outcomes. In the future, a comprehensive algorithm including clinical as well as laboratory findings may optimize outcomes in the era of potent $P2Y_{12}$ inhibitors.

Young-Hoon Jeong, MD, PhD
Kevin P. Bliden, MBA
Udaya S. Tantry, PhD
***Paul A. Gurbel, MD**

*Sinai Center for Thrombosis Research
Cardiac Catheterization Laboratory
2401 West Belvedere Avenue
Baltimore, Maryland 21215
E-mail: pgurbel@lifebridgehealth.org