institutional review board of Fudan University Shanghai Cancer Center. Prospective randomized research of neoadjuvant therapy will be performed soon. We are willing to share the results with our colleagues throughout the world and relate our experience for the treatment of esophageal cancer.

Bin Li, MD^{a,b}

Haiquan Chen, MD^{a,b}

^aDepartment of Thoracic Surgery
Fudan University Shanghai
Cancer Center
Shanghai, China

^bDepartment of Oncology
Shanghai Medical College
Fudan University
Shanghai, China

References

1. Li B, Chen H, Xiang J, Zhang Y, Li C, Hu H, et al. Pattern of lymphatic spread in thoracic esophageal squamous cell carcinoma: a single-institution experience. *J Thorac Cardiovasc Surg.* 2012;144:778-86.
2. van Hagen P, Hulshof MC, van Lanschot JJ, Steyerberg EW, van Berge Henegouwen MI, Wijnhoven BP, et al. Preoperative chemoradiotherapy for esophageal or junctional cancer. *N Engl J Med.* 2012;366:2074-84.
3. Li B, Guo Q, Yang H, Guan J, Liu Z, Li S, et al. Left thoracoabdominal approach in surgical treatment of adenocarcinoma of the esophagogastric junction in the Northern Henan Province of China. *Dig Surg.* 2011;28:2-8.

<http://dx.doi.org/10.1016/j.jtcvs.2012.12.050>

METHYLENE BLUE, SEROTONERGIC SYNDROME, AND HEART TRANSPLANT To the Editor:

Grubb and colleagues¹ report a case of a 60-year-old man with history of nonischemic cardiomyopathy and end-stage heart failure who underwent placement of a left ventricular assist device (LVAD) and replacement of a mechanical aortic valve with a porcine prosthesis complicated by multiple driveline infections. The heart transplant was the last option. During the operation, the authors reported “episodes of hypotension during the extensive lysis of adhesions for

[LVAD] removal. Intermittent boluses of phenylephrine were administered to maintain a sufficient mean arterial pressure.” Subsequently, a methylene blue (MB) 1 mg/kg bolus followed by continuous infusion of 0.5 mg/kg/hour was administered. Postoperatively, the patient presented signals of serotonin syndrome, presumably a consequence of an interaction between MB and antidepressant medications.

This report has two crucial points: the possibility of serotonin syndrome triggered by the association MB and antidepressants, and the routine use of MB to handle vasoplegia in the milieu of heart transplant. Kofidis and colleagues² reported the first experience of vasoplegia treatment with MB after heart transplant and pointed out that this drug deserves attention because of its catecholamine-saving effect, thus preventing possible malperfusion. Kofidis and colleagues’ report is unique in the literature regarding using MB to treat vasoplegia associated with heart transplant.

In 2009, my colleagues and I published an article³ discussing 15 years of questions, answers, doubts, and certainties regarding MB for vasoplegic syndrome treatment in heart surgery. In summary, our report shared that heparin and angiotensin-converting enzyme inhibitors are risk factors; in the recommended doses it is safe (the lethal dose is 40 mg/kg); the use of MB does not induce endothelial dysfunction; the MB effect appears in cases of nitric oxide up-regulation; MB is not a vasoconstrictor—by blocking the cyclic guanosine 3, 5-monophosphate (cGMP) pathway it releases the cyclic adenosine monophosphate (cAMP) pathway, facilitating the norepinephrine vasoconstrictor effect; the most used dosage is 2 mg/kg administered intravenously as a bolus followed by the same continuous infusion because plasmatic concentrations strongly decays in the first 40 minutes; and there is a possible window of opportunity for MB’s effectiveness.³

To circumvent the morbidity and mortality associated with vasoplegic syndrome Grubb and colleagues¹ implemented an intraoperative protocol that includes administration of MB for vasoplegic syndrome resistant to vasopressor drugs. Because serotonin syndrome only occurs in a small percentage of patients and is treatable with benzodiazepines and supportive care, and the possibility of serotonin syndrome is less than the risk of untreated vasoplegia and potential end-organ injury and graft loss, we have continued to include MB in the management of severe vasoplegic syndrome.

I congratulate Grubb and colleagues for reporting the association between MB and antidepressants that may cause serotonin syndrome. Although, to be honest, as a proponent of the use of MB^{4,5} the purpose of my letter is to suggest Grubb and colleagues publish their MB experience in heart transplant. It would be a valuable contribution to the cardiac surgery literature.

Paulo Roberto B. Evora, MD, PhD
Department of Surgery and Anatomy
Ribeirão Preto Faculty of Medicine
University of São Paulo
Ribeirão Preto, São Paulo, Brazil

References

1. Grubb KJ, Kennedy JL, Bergin JD, Groves DS, Kern JA. The role of methylene blue in serotonin syndrome following cardiac transplantation: a case report and review of the literature. *J Thorac Cardiovasc Surg.* 2012;144:e113-6.
2. Kofidis T, Strüber M, Wilhelmi M, Anssar M, Simon A, Harringer W, et al. Reversal of severe vasoplegia with single-dose methylene blue after heart transplantation. *J Thorac Cardiovasc Surg.* 2001;122:823-4.
3. Evora PR, Ribeiro PJ, Vicente WV, Reis CL, Rodrigues AJ, Menardi AC, et al. Methylene blue for vasoplegic syndrome treatment in heart surgery: fifteen years of questions, answers, doubts and certainties. *Rev Bras Cir Cardiovasc.* 2009;24:279-88.
4. Andrade J, Batista M, Evora PR, Tavares JR, Buffolo E, Ribeiro EE, et al. Methylene blue administration in the treatment of the vasoplegic syndrome after cardiac surgery. *Rev Bras Cir Cardiovasc.* 1996;11:207-14.
5. Evora PR, Ribeiro PJ, de Andrade JC. Methylene blue administration in SIRS after cardiac operations. *Ann Thorac Surg.* 1997;63:1212-3.

<http://dx.doi.org/10.1016/j.jtcvs.2012.11.090>