Circulatory support system as a bridge to decision in patients with refractory acute cardiogenic shock: Is there a space for extracorporeal membrane oxygenation?

To the Editor:

We read with interest the timely report by John and colleagues¹ about the elective use of the Levitronix CentriMag as a bridge to decision in cardiogenic shock. We commend them for their encouraging results in 12 patients assisted with biventricular support.

Although the concept of cardiac assistance as bridge to decision is well addressed by the authors, we believe that extracorporeal membrane oxygenation (ECMO) could play a more valuable role in this context. This is especially so when the expected assistance time is relatively short (eg, an average support length of 9.4 days, as reported in John and colleagues' experience¹).

In our institution, we routinely use both ECMO and the Levitronix device. The latter is mainly used for patients with postcardiotomy syndrome or primary graft failure; we advise the use of ECMO in nonsurgical situations, such as cardiogenic shock after acute myocardial infarction or failed percutaneous coronary interventions.

In this selected group of patients, ECMO offers some advantages. These include avoidance of sternotomy and central cannulation, which may cause catastrophic bleeding after aggressive thrombolysis and antiplatelet treatment, and ease of emergency implantation, even in the intensive care unit or catheter laboratory, with consequent rapid institution of assistance.

Furthermore, newly designed oxygenators and ECMO circuits (Quadrox Jostra, Permanent Life Support PLS; MAQUET GmbH & Co KG, Rastatt, Germany) require a lower priming volume and present a bioinert surface treatment, guaranteeing assistance for an extended 14 days with a reduced risk of device-related complications and a less strict anticoagulation regimen. Moreover, ECMO can be easily switched to cardiopulmonary bypass at the time of transplantation or long-term device implantation.

In our institution, since the beginning of 2006, the PLS ECMO system has been extensively used to treat either lung (6 patients) or cardiac (8 patients) failure (venovenous and venoarterial cannulation,

respectively). No device failures have been recorded, even for assistance extending longer than 60 days.

In our experience, ECMO units are managed by intensive care unit nurses, and dedicated personnel are usually not required. Activated thromboplastin time is kept between 40 and 50 seconds, with a level of antithrombin III activity greater than 80%. In cases of bleeding, we have withheld heparin for more than 30 hours without any thrombotic events.

Leg ischemia, related to common femoral artery cannulation, is the complication we have seen most frequently. In most cases, however, this condition can be resolved by cannulating the superficial femoral artery as well with a small perfusion cannula.

In conclusion, although the many advantages offered by the Levitronix pump are remarkable, patient-tailored assistance can be achieved for selected candidates with new versions of ECMO systems, such as the PLS. Thanks to modern technology, these systems couple ease of implantation and management with device reliability and long-term durability.

Gianluca Santise, MD

Sergio Sciacca, MD

Giuseppe D'Ancona, MD

Michele Pilato, MD

Department of Cardiothoracic Surgery
Mediterranean Institute for Transplantation
and Advanced Specialized Therapies
University of Pittsburgh Medical Center
Palermo, Italy

Reference

1. John R, Liao K, Lietz K, Kamdar F, Colvin-Adams M, Boyle A, et al. Experience with the Levitronix CentriMag circulatory support system as a bridge to decision in patients with refractory acute cardiogenic shock and multisystem organ failure. *J Thorac Cardiovasc Surg.* 2007;134:351-8.
doi:10.1016/j.jtcvs.2007.10.051

Reply to the Editor:

I appreciate the comments of Santise and colleagues regarding the role of extracorporeal membrane oxygenation (ECMO) in the care of patients with refractory cardiogenic shock. Clearly, ECMO has been, and will probably always remain, a useful treatment in the ever-changing armamentarium options for this critically ill group. It is still the primary option for pediatric patients, but the frequency of its use for adults has

been significantly reduced thanks to improved short-term ventricular support devices (eg, CentriMag, Abiomed). Such devices provide more reliable support, with markedly improved durability with respect to the Bio-Medicus systems, the first generation of short-term ventricular assist devices.

ECMO certainly offers the advantage of avoiding a median sternotomy, as well as the opportunity for rapid institution of support in the catheterization laboratory and the intensive care unit, as Santise and colleagues report. The use of ECMO is limited, however, by its main drawbacks: limited durability and significant neurologic and peripheral vascular complications. The incidence of such complications may be affected by technologic advances in the design of ECMO circuits and oxygenators or by altered peripheral cannulation techniques. Several published studies, some involving pediatric patients, have looked at the use of ECMO for a wide range of indications (eg, graft failure after lung transplantation, right ventricular failure after heart transplantation, postcardiotomy assistance, resuscitation after cardiac arrest, and bridge to bridge support for cardiogenic shock). All these series reported a mean ECMO duration of about 4 days or less.¹⁻⁵ In one large, experienced single-center series, the complications during ECMO were as follows: infectious, 49%; renal failure requiring dialysis, 40%; neurologic, 33%; and limb complications, 25%.² Of course, not all such complications are related to ECMO itself. Instead, they often are a result of the critical condition of a patient with multiorgan dysfunction. Further, all such complications (with the relative exception of limb complications) can also potentially occur with short-term ventricular assist devices.

In conclusion, I agree with Santise and colleagues that there is definitely a place for ECMO in the treatment of patients with acute cardiogenic shock. In the near future, we do not know what the interplay will be between surgical and percutaneous devices, including ECMO. Until then, it remains imperative that we continue to be innovative, open-minded, and aggressive, continually striving to improve outcomes for this critically ill group of patients.

Ranjit John, MD

Division of Cardiothoracic Surgery
University of Minnesota
Minneapolis, MN 55455

References

1. Pagani FD, Lynch W, Swaniker F, Dyke DB, Bartlett R, Koelling T, et al. Extracorporeal life support to left ventricular assist device bridge to heart transplant: a strategy to optimize survival and resource utilization. *Circulation*. 1999;100(19 Suppl): II206-10.
2. Smedira NG, Moazami N, Golding CM, McCarthy PM, Apperson-Hansen C, Blackstone EH, et al. Clinical experience with 202 adults receiving extracorporeal membrane oxygenation for cardiac failure: survival at 5 years. *J Thorac Cardiovasc Surg*. 2001; 122:92-102.
3. Alsoufi B, Al-Radi OO, Nazer RI, Gruenwald C, Foreman C, Williams WG, et al. Survival outcomes after rescue extracorporeal cardiopulmonary resuscitation in pediatric patients with refractory cardiac arrest. *J Thorac Cardiovasc Surg*. 2007; 134:952-9.
4. Meyers BF, Sundt TM, Henry S, Trulock EP, Guthrie T, Cooper JD, et al. Selective use of extracorporeal membrane oxygenation is warranted after lung transplantation. *J Thorac Cardiovasc Surg*. 2000;120:20-8.
5. Magovern GJ Jr, Simpson KA. Extracorporeal membrane oxygenation for adult cardiac support: the Allegheny experience. *Ann Thorac Surg*. 1999;68:655-61.

doi:10.1016/j.jtcvs.2007.11.009

Mortality associated with pneumonectomy after induction chemoradiation versus chemotherapy alone in stage IIIA-N2 non-small cell lung cancer

To the Editor:

I read with great interest the recent article of the Toronto group on improved results of induction chemoradiation followed by surgery for selected patients with stage IIIA-N2 non-small cell lung cancer.¹ Uy and colleagues¹ are to be congratulated for their detailed analysis and honest data reporting regarding this difficult subset of patients with N2 disease for whom the optimal treatment remains to be defined. As in the Intergroup-0139 trial,² Uy and colleagues¹ adopted an induction therapy of concurrent chemotherapy and radiotherapy, followed by surgical resection if there was no progressive disease on restaging. In 11 cases (27.5%), pneumonectomy was necessary. As previously observed in the INT-0139 trial, mortality in this setting was high: 27% overall, and even 50% for complex pneumonectomies. Causes of death were adult respiratory distress syndrome and postoperative hemorrhage. After induction therapy followed by

pneumonectomy, higher incidences have been reported for empyema, bronchopleural fistula, and adult respiratory distress syndrome than are seen after standard resection without induction therapy.³

Uy and colleagues¹ referred to European Organization for Research and Treatment of Cancer trial 08941, results of which were recently reported.^{3,4} In this multicenter trial, patients with histologically proven stage IIIA-N2 non-small cell lung cancer were treated with induction chemotherapy—without radiotherapy—and in case of response were subsequently randomly assigned to undergo either surgery or radiotherapy. Pneumonectomy was performed in 46.8% of patients; the 30-day mortality in this subgroup was 6.9%, which was much lower than those reported by Uy and colleagues¹ and in the INT-0139 trial.² Similar results as in the EORTC 08941 study were recently published by a group from Strasbourg; they reported a 30-day mortality of 6.7% in a series of 60 patients undergoing pneumonectomy after induction chemotherapy.⁵

Although Uy and colleagues¹ did not specifically comment on this issue, the type of induction therapy—chemotherapy versus combined chemoradiotherapy—may be important in explaining this mortality difference. Unfortunately, there are no randomized studies directly comparing induction chemotherapy with chemoradiotherapy with respect to outcome after surgical resection for locally advanced non-small cell lung cancer.

Although a pneumonectomy can be safely performed after induction chemotherapy, it remains a high-risk procedure after induction chemoradiotherapy, especially when a complex procedure has to be performed on the right side. Coverage of the bronchial stump with viable tissue is essential to prevent the dreadful complication of bronchial stump dehiscence.

Paul E. Van Schil, MD, PhD

Department of Thoracic and Vascular Surgery
University Hospital of Antwerp
Antwerp, Belgium

Dr Van Schil reports lecture fees from Pierre Fabre Oncology (Laboratoires Pierre Fabre, Castres, France).

References

1. Uy KL, Darling G, Xu W, Yi QL, De Perrot M, Pierre AF, et al. Improved results of induction

chemoradiation before surgical intervention for selected patients with stage IIIA-N2 non-small cell lung cancer. *J Thorac Cardiovasc Surg*. 2007;134:188-93.

2. Albain KS, Swann RS, Rusch VR, Turrisi AT, Shepherd FA, Smith CJ, et al. Phase III study of concurrent chemotherapy and radiotherapy (CT/RT) versus CT/RT followed by surgical resection for stage IIIA-N2 non-small cell lung cancer: outcomes update of North American Intergroup 0139 (RTOG 9309) [abstract 7014]. *J Clin Oncol*. 2005; 23(16 suppl):624s.
3. Van Schil P, Van Meerbeeck JP, Kramer G, Splinter T, Legrand C, Giaccone G, et al. Morbidity and mortality in the surgery arm of EORTC 08941 trial. *Eur Respir J*. 2005;26: 192-7.
4. Van Meerbeeck J, Kramer G, Van Schil P, Legrand C, Smit E, Schramel F, et al. Randomized controlled trial of resection versus radiotherapy after induction chemotherapy in stage IIIA-N2 non-small-cell lung cancer. *J Natl Cancer Inst*. 2007;99:442-50.
5. Mansour Z, Kochetkova EA, Ducrocq X, Vasilescu MD, Maxant G, Buggenhout A, et al. Induction chemotherapy does not increase the operative risk of pneumonectomy. *Eur J Cardiothorac Surg*. 2007;31:181-5.

doi:10.1016/j.jtcvs.2007.10.052

Reply to the Editor:

Dr Van Schil's letter clearly enunciates the concern of many surgeons that the combination of chemotherapy and radiation for induction increases the risk of subsequent surgical intervention, whereas the use of induction chemotherapy alone does not. Although the report from Martin and colleagues,¹ as well as the data from the Intergroup 0139 trial,² support this concern, we believe this not to be the case. In our experience, as outlined in our report, the mortalities all occurred early in our experience with this protocol. There were no mortalities in the last 34 patients, including those undergoing pneumonectomy. In doing the chart audit, we noted that the mortalities in the patients undergoing pneumonectomy occurred in patients with large, bulky central tumors, in whom the hilar dissection could be anticipated to be difficult. In retrospect, we would now not consider such patients for resection. Based on our own experience, we do not think that induction chemoradiation results in excessive risk for resection if patients are selected appropriately. Furthermore, this is supported by the work of Sonett and colleagues,³ who used even higher doses of radiation without any operative mortality.

In selecting patients for trimodality therapy, we believe that both the primary and