Clinical Significance of Spontaneous Echo Contrast on Extracorporeal Membrane Oxygenation

Shinya Unai, MD, My-Le Nguyen, MD, Daizo Tanaka, MD, Nataliya Gorbachuk, BA, Gregary D. Marhefka, MD, Hitoshi Hirose, MD, and Nicholas C. Cavarocchi, MD

Division of Cardiothoracic Surgery, Department of Surgery, and Division of Cardiology, Thomas Jefferson University, Philadelphia, Pennsylvania

Background. **Spontaneous echo contrast (SEC) is known to be a predisposition to thromboembolism and cerebrovascular accident. The aim of this study was to investigate the risk factors and the consequences of SEC in patients who were placed on venoarterial extracorporeal membrane oxygenation (VA-ECMO) because of cardiogenic shock.**

Methods. **Between January 2011 and December 2014, 98 patients underwent the insertion of VA-ECMO because of cardiogenic shock in our institution. Transthoracic and transesophageal echocardiography was performed and interpreted by National Board of Echocardiography certified cardiologists. Patients were divided into 2 groups based on the presence or absence of SEC. Clinical data, echocardiographic measurements, and outcomes were compared between the 2 groups.**

Results. **Of the 98 patients, 22 patients (22%) had SEC on echocardiography. Patients in the SEC group had a lower ejection fraction (8.0% versus 29%; $p < 0.001$), a lower pulsatility index (defined by [systolic blood pressure – diastolic blood pressure]/mean blood pressure) while receiving ECMO (0.13 ± 0.14 versus 0.26 ± 0.22; $p = 0.009$). The SEC group had a higher rate of intracardiac thrombus (46% versus 13%; $p = 0.002$) and stroke (36% versus 7.9%; $p = 0.002$). On univariate analysis, intracardiac thrombus, SEC, and low pulsatility were significant risk factors for the development of stroke. On multivariate analysis, SEC was the only independent risk factor for stroke.**

Conclusions. **SEC on VA-ECMO resulted in an increased risk of intracardiac thrombus and stroke. Maintaining pulsatility while the patient is on ECMO may result in a decreased chance of developing SEC and stroke.**

(Ann Thorac Surg 2016;■:■–■)

Spontaneous echo contrast (SEC) is a smoke-like echo density observed on transthoracic or transesophageal echocardiograms caused by increased red blood cell aggregation during low-flow states and blood stasis. SEC is known to be a predisposition to thromboembolism [1] and can be graded objectively as mild, moderate, or severe, or quantified using a computer software program incorporated into the echocardiographic equipment [2]. SEC is seen in patients who have mitral stenosis [3], cardiomyopathy, ventricular aneurysm [4], or atrial fibrillation [5]. Patients who are receiving venoarterial extracorporeal membrane oxygenation (VA-ECMO) have decreased ventricular function and stasis of blood within the cardiac chambers, which may lead to the formation of SEC.

The aim of this study was to investigate the occurrence of SEC in patients who were placed on VA-ECMO for cardiogenic shock and analyze the outcomes with attention to cerebral thromboembolic complications.

Patients and Methods

This study was approved by our institutional review board (IRB approval No. 10D185). Individual informed consent was waived because of the retrospective nature of the study. Between January 2011 and December 2014, 98 consecutive adult patients (age > 18 years) in our institution underwent VA-ECMO because of cardiogenic shock. VA-ECMO was initiated if the patient had persistent profound cardiogenic shock despite fluid resuscitation, high doses of multiple intravenous inotropes and vasopressors, insertion of an intra-aortic balloon pump (IABP), ventricular tachycardia/fibrillation refractory to anti-arrhythmic medications and cardioversion, or a combination of these treatments.

A bolus of 5,000 to 7,500 units of heparin was given at the time of cannulation, and continuous heparin was initiated 8 to 12 hours after ECMO initiation, with a goal activated partial thromboplastin time of 50 to 60 seconds.

Accepted for publication July 7, 2016.

Presented at the Fifty-second Annual Meeting of The Society of Thoracic Surgeons, Phoenix, AZ, Jan 23–27, 2016.

Address correspondence to Dr Cavarocchi, Division of Cardiothoracic Surgery, Department of Surgery, Thomas Jefferson University, 1025 Walnut St, Ste 607, Philadelphia, PA 19107; email: nicholas.cavarocchi@jefferson.edu.

0003-4975/$36.00
http://dx.doi.org/10.1016/j.athoracsur.2016.07.019

ECMO flow rate was set to achieve a goal of a cardiac index greater than 2.2 L/min/m^2, and mean arterial pressure was maintained at 65 to 85 mm Hg. Inotropic agents (epinephrine, milrinone, dobutamine) were weaned to decrease oxygen consumption and the use of IABP was discontinued after the ECMO was started, because we believe that there are no benefits to using IABP during ECMO [6]. After ECMO was begun, transthoracic or transesophageal echocardiography, or both, was performed within 24 hours, and the results were interpreted by National Board of Echocardiography certified cardiologists. Patients were divided into 2 groups based on the presence or absence of SEC (SEC group and non-SEC group). Clinical data, echocardiographic results, and outcomes were compared between the 2 groups.

Pulsatility index was defined as "(systolic blood pressure–diastolic blood pressure)/mean blood pressure", which was calculated retrospectively using the vital signs obtained from the electronic medical record. The blood pressure to calculate the pulsatility index was averaged for the first 72 hours after ECMO initiation.

Statistical analyses were conducted using R environment (R, version 3.2.2; R Project for Statistical Computing, Vienna, Austria). Continuous variables were expressed as mean ± standard deviation (SD) and compared with a standard t test. Categorical variables were expressed as counts and percentages, and the χ^2 test or Fischer's exact test was used for comparisons. A p Value less than 0.05 was considered significant. The effects of different variables on stroke were analyzed with univariate and multivariate logistic regression analysis. The variables for which the p Value was less than 0.1 in univariate analysis were identified as the potential risk factors for stroke and included in the multivariate logistic regression analysis.

Results

Ninety-eight patients (67 men and 31 women with an average age of 51 ± 15 years) were placed on VA-ECMO during the study period, and 22 (22%) patients had SEC on echocardiography. The patients' baseline characteristics are listed in Table 1. There were no differences between the 2 groups except that the SEC group had significantly more patients with acute myocarditis. SEC was seen in the left ventricle (n = 15), left atrium (n = 6), aortic root (n = 1), and ascending aorta (n = 2) (some patients had SEC in multiple locations). In most cases, SEC was first detected within 3 days after instituting ECMO (average, 3.2 ± 3.8 days). Thrombus was detected on average 3.7 ± 5.3 days after institution of ECMO (Fig 1).

ECMO data averaged for the first 72 hours are listed in Table 2. The average systolic blood pressure and the pulsatility index were lower in the SEC group (0.13 ± 0.14 in SEC group versus 0.26 ± 0.22 in the non-SEC group; $p = 0.009$). Echocardiographic findings of the 2 groups are shown in Table 3. The ejection fraction (EF) was significantly lower in the SEC group (8.0 ± 11 versus 29 ± 27; $p < 0.001$), and the aortic valve opening on every beat was observed less frequently in the SEC group (53% versus 79%; $p = 0.037$).

Complications from ECMO and the outcomes are summarized in Table 4. The SEC group had a higher incidence of intracardiac thrombus (46% versus 13%; $p = 0.002$) and stroke (36% versus 7.9%; $p = 0.002$), compared with the non-SEC group. The 30-day mortality rate of the SEC and non-SEC groups was 77% and 55% ($p = 0.08$), respectively. Univariate analysis demonstrated that intracardiac thrombus ($p = 0.001$), SEC ($p = 0.002$), and low pulsatility ($p = 0.039$) were significant risk factors for the development of stroke (Table 5). Further multivariate logistic regression analysis showed that the presence of SEC was the only independent risk factor for stroke (odds ratio, 6.35; 95% confidence interval, 1.22–33.0) (Table 6).

Comment

The major findings of this study are (1) in patients in whom VA-ECMO was instituted for cardiogenic shock, SEC was seen in 22% of the patients; (2) SEC was an independent risk factor for stroke; (3) the presence of SEC was associated with a worse survival; (4) the majority of the SEC/thrombus was detected within the first 3 days of ECMO; and (5) patients in whom SEC was seen tended to have less pulsatility on ECMO, and fewer patients were observed to have opening of the aortic valve.

Based on the literature, atrial fibrillation, aging, high erythrocyte sedimentation rate, and increased fibrinogen or hematocrit levels increase the risk of SEC developing. Structural abnormalities of the cardiovascular system, such as atrial and ventricular enlargement caused by mitral stenosis or cardiomyopathy, are known to increase the risk of SEC as well [7]. Multiple studies have been published regarding the relationship of SEC, stroke, and thrombus formation in patients who have atrial fibrillation [8]. Bernhardt and colleagues [9] reported that patients who have atrial fibrillation and dense SEC in the left atrium had a 22% likelihood of cerebral embolism or death, or both, during a 12-month follow-up, and 50% of the patients with atrial fibrillation and atrial thrombi had cerebral embolism or died within 3 years, despite oral anticoagulation.

In acute cardiogenic shock, VA-ECMO has multiple benefits, including rapid initiation, restoration of the circulation and oxygenation, and recovery of end-organ function. However, peripheral cannulation will lead to incomplete ventricular unloading and increased afterload resulting from retrograde injection of blood. A failing heart with low contractility will not be able to open the aortic valve against a high afterload. This scenario will result in stasis of blood, possibly leading to SEC formation. SEC on ECMO has not been well studied, and only case reports of massive thrombus formation resulting in stroke and death during ECMO have been published [10–13]. Common findings in these reports are that patients with low left ventricular function with minimal or no aortic valve opening subsequently experienced massive thrombus despite adequate anticoagulation.