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Echocardiographic Ramp Test for Continuous-Flow Left Ventricular Assist Devices

Do Loading Conditions Matter?

Sirtaz Adatya, MD,* Christopher T. Holley, MD,* Samit S. Roy, MSPH,* Hirad Yarmohammadi, MD,* Amy Feng, BA,* Peter Eckman, MD,* Monica Colvin-Adams, MD,* Ranjit John, MD,* Carolina Masri, MD†

ABSTRACT

OBJECTIVES This study investigated whether continuous AI and/or elevated mean arterial pressure (MAP) were associated with false positive results for flow obstruction in echocardiographic ramp speed tests in patients with a continuous-flow left ventricular assist device.

BACKGROUND Failure to reduce the left ventricular end-diastolic diameter (LVEDD) with increasing device speeds in a ramp test is predictive of pump obstruction. Aortic insufficiency (AI) or increased MAP can diminish the ability to unload the left ventricle.

METHODS LVEDD was plotted against device speed, and a linear function slope was calculated. A flat LVEDD slope (≥–0.16) was considered abnormal (suggestive of obstruction). Ramp test results were compared in patients with or without either AI or increased MAP at baseline speed, and receiver-operator characteristic (ROC) curves were constructed for predictors of device obstruction. Device thrombosis was confirmed by direct visualization of clot at explantation or on inspection by the manufacturer.

RESULTS Of 78 ramp tests (55 patients), 36 were abnormal (18 true positive, 18 false positive), and 42 were normal (37 true negative, 5 false negative). In patients with AI, LVEDD slope was –0.14 ± 0.17, which was consistent with device obstruction (vs. –0.25 ± 0.11 in patients without AI; $p < 0.001$), despite no difference in mean lactate dehydrogenase concentration between the 2 groups (1,301 ± 1,651 U/l vs. 1,354 ± 1,365 U/l; $p = 0.91$). Area under the ROC curve (AUC) for LVEDD slope was 0.76 and improved to 0.88 after removal of patients with AI from the study. LVEDD slope in patients with MAP ≥85 mm Hg was similar to that for device obstruction (–0.18 ± 0.07) and was abnormal in 6 of the 12 ramp tests performed. Combining LVEDD slope with lactate dehydrogenase concentration increased the AUC to 0.96 as an indicator of device obstruction.

CONCLUSIONS Abnormal loading conditions due to AI or elevated MAP may result in false positive ramp tests.
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Continuous-flow (CF) left ventricular assist devices (LVADs) provide circulatory support and improve survival, functional capacity, and quality of life in patients with advanced heart failure who are refractory to medical therapy (1). Thromboembolic events are feared complications after implantation of CF-LVADs and are associated with a high degree of mortality and morbidity (2,3). Compared with the initial experience, an increase in the incidence of device thrombosis has recently

From the *Department of Medicine, Cardiovascular Division, University of Minnesota, Minneapolis, Minnesota; and the †Department of Medicine, Division of Cardiology, University of Washington, Seattle, Washington. Dr. John has received research grants from Thoratec and HeartWare Inc.; and has been a consultant for Thoratec. Dr. Eckman is a consultant for Thoratec and HeartWare Inc. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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ABBREVIATIONS AND ACRONYMS

AI = aortic insufficiency

AUC = area under the curve

CF = continuous-flow

LDH = lactate dehydrogenase

LVAD = left ventricular assist device

LVEDD = left ventricular end-diastolic diameter

MAP = mean arterial pressure

PI = pulsatility index

ROC = receiver-operator characteristic

been reported in patients who have received the HeartMate II LVAD (Thoratec, Pleasanton, California) (3).

Device thrombosis is clinically suspected in the presence of hemolysis, elevated lactate dehydrogenase (LDH), worsening heart failure, and/or device malfunction (power spike, low-flow alarms). However, diagnosis can be challenging. Echocardiography plays an important role in the evaluation of such patients. Ramp studies, in which left ventricular end-diastolic diameter (LVEDD) is recorded using echocardiography at increasing LVAD speeds, can be used not only to optimize device speed, but also to evaluate potential device obstruction (4,5). Under optimal loading conditions and with no obstruction to flow, an inverse relationship between LVAD speed and LVEDD should be observed. Uriel et al. (4) recently described a standardized protocol for ramp studies in which results were plotted against speed, and linear function slopes were calculated for each parameter. In a prospective cohort of 17 patients in whom device thrombosis was clinically suspected, failure to reduce LVEDD with increased LVAD speed (LVEDD slope ≥−0.16) was strongly associated with significant obstruction to flow (4).

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Currently, ramp tests are used clinically to rule out device obstruction when the LVEDD slope is <−0.16. However, ramp tests are not perfectly predictive of device thrombosis, and we sought to investigate the conditions under which the test may not perform well. One complication of CF-LVADs that can affect ramp test outcome is the development of de novo continuous aortic insufficiency (AI), which imposes an increase in both pre-load and afterload throughout the cardiac cycle (6). As described in previous case reports, this potentially leads to an inability to decompress the left ventricle, with ensuing recurrent heart failure or hemolysis, which results in a scenario mimicking device thrombosis (7,8). Furthermore, because the flow generated by CF-LVADs varies with the pressure differential across the pump, output depends on both pre-load and afterload; thus, blood pressure control is essential (9,10).

Abnormal loading conditions due to either AI or increased mean arterial pressure (MAP) can result in diminished ability to unload the left ventricle. Therefore, the presence of such conditions during a ramp study in patients with a LVAD could result in an abnormal LVEDD slope (≥−0.16) that might be falsely interpreted as suggesting device obstruction (8). Conversely, a clot may be present, but depending on the degree of obstruction and location, the LVEDD slope may be <−0.16, which could be falsely interpreted as a negative result and suggests no obstruction to flow.

In the present study, we sought to address this question in a larger cohort of patients. We hypothesized that the presence of continuous AI or increased MAP (≥85 mm Hg) at baseline speed without clinical evidence of device obstruction was associated with an abnormal LVEDD slope despite the absence of flow obstruction. In addition, we explored the sensitivity and specificity of various cutoff points for LVEDD slope in the evaluation of ramp test results and the usefulness of including LDH and plasma free hemoglobin in the evaluation of potential device thrombosis.

METHODS

PATIENTS. Data from all patients undergoing ramp tests at the University of Minnesota are collected in a prospectively designed database. We reviewed results of ramp tests performed in patients with an implanted CF-LVAD from June 1, 2012 through February 28, 2014, and the last follow-up took place in May 2014. The study was approved by the University of Minnesota Institutional Review Board, and the requirement for individual consent was waived.

PROCEDURES. All patients underwent implantation of the HeartMate II LVAD device. A ramp study with a standardized protocol, as described by Uriel et al. (4), was performed as a routine study in new implants once medical therapy was optimized. Ramp studies were also performed for evaluation of patients who had clinically suspected device thrombosis or recurrent heart failure. Device thrombosis was suspected clinically, and a ramp test was performed when patients presented with: 1) asymptomatic sustained power elevation 14 days after device implantation, which was defined as power ≥10 W or power >2 W above baseline for >24 h; 2) elevated LDH concentration ≥2 times the upper limit of normal for our laboratory (cutoff = 2 × 750 U/l = 1,500 U/l); 3) clinical signs of hemolysis; or 4) symptoms of heart failure in the absence of other causes (5). Device thrombosis was confirmed by direct visualization of the clot at the time of explantation or by manufacturer analysis of the explanted device.

RAMP TEST PROTOCOL. Transthoracic echocardiography was performed using an IE33 ultrasound system (Philips Medical Systems, Andover, Massachusetts). We performed the ramp test as described by Uriel et al. (4). Patients were first assessed for adequate anticoagulation, which was defined as an international