# **EDITORIAL**

Primary Diagnoses and Relative Risk in Patients With Left Ventricular Assist Devices Visiting an Emergency Department in the United States

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A pproximately 20 years ago, continuous flow left ventricular assist devices (LVADs) were introduced into clinical practice.<sup>1</sup> At that time, it was uncertain whether humans could live long term under conditions of pulseless arterial blood flow. Initially, these devices were intended as a bridge to heart transplantation for up to 180 days.<sup>2</sup> Now, commonly, patients are supported for 10 years or longer, for destination therapy.<sup>3</sup>

## See Article by Edelson et al.

Long-term reliability of these devices and improved quality of life during LVAD support have been well established. The question remains as to why this therapy is not used more frequently. According to estimates, there are about 400 000 patients in Europe and 300 000 in the United States with end-stage heart failure who are eligible for LVAD support.<sup>4</sup> The number of LVAD implants has been rising—but to only 2500 in Europe and 3000 in the United States per annum.<sup>5</sup> Access to LVAD therapy remains poor, and the adverse event profile of LVAD support may also limit widespread use of the device. Even with the most modern LVAD system, within a prospective randomized trial, the rate of rehospitalization was 2.26 per patient year.<sup>6</sup>

In this issue of the *Journal of the American Heart Association (JAHA)*, Edelson and coworkers analyzed 3 years of data, comprising 44 000 emergency department (ED) visits by patients with LVADs.<sup>7</sup> This data set is substantial in size given the small number of LVAD implantations per year. Because the overall number of ED visits was 7.5 million, visits by patients with LVADs represent a small fraction. The authors propose a risk score to help the ED to assess the mortality risk of a given patient. The data presented provide remarkable insights into complications of LVAD therapies. The usefulness of the risk score needs evaluation in the future.

In the Edelson et al study, the primary diagnoses for ED visits were cardiac (21.5%), bleeding (19.4%), infections (12.5%), stroke (5.5%), and device complications (4.2%). Most bleeding complications are caused by gastrointestinal (GI) bleeding. Continuousflow pumps expose the blood to high shear forces that lead to a disruption of the large monomers of the von Willebrand factor.<sup>8</sup> Many patients supported by an LVAD can develop acquired von Willebrand syndrome to varying degrees<sup>9</sup> and are prone to the development of arteriovenous malformations throughout the entire

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LVAD Patients in ED

GI tract. Also, the low pulse pressure associated with continuous-flow LVAD support with preformation of arteriovenous malformations may aggravate the problem. For these reasons, GI bleeding requires blood transfusions in 12% of ED visits and is an important limitation of current continuous-flow devices. Because anticoagulation and platelet inhibition therapy disturb primary hemostasis, the use of such therapy in most patients with LVADs adds to the bleeding risk.

Management of GI bleeding is challenging because most GI bleeding sources are in the small bowel and may not be accessible by endoscopic means.<sup>10</sup> If an experienced gastroenterologist is not available at the admitting hospital, this may require transfer of the patient to a different center. Cardiac as a primary ED diagnosis is surprising because a working LVAD supports the left ventricle. Ventricular arrythmia may play a role in the development of right ventricular failure, the most important predictor of long-term survival. Because a degree of right heart failure is prevalent in all patients with LVADs, volume overload and signs of kidney impairment are hallmarks of this problem. Treatment of right heart failure in patients with LVADs may require a heart failure specialist to titrate medications for unloading of the right ventricle, by reducing the overall volume load and optimizing the left ventricular unloading. These 2 complications (cardiac and bleeding) represent almost half of the ED visits, but they are associated with a lower risk compared with stroke and device malfunction.

All LVADs are associated with an increased risk of hemorrhagic or ischemic stroke. This diagnosis is associated with the highest mortality risk for an ED visit (odds ratio >19). However, it is encouraging that the number of ED visits for stroke is relatively low.

LVAD complications are rare but present another substantial mortality risk (odds ratio >10). The most frequent LVAD complications are ingestion of thrombus or problems with the integrity of the driveline. LVAD complications may require thrombolytic therapy, repair of driveline, or replacement of the device. Finally, infections of the driveline are typical adverse events of LVAD therapy and represent a substantial number of ED visits (12.5%), with a medium mortality risk (odds ratio >5).

The primary diagnosis data of ED visits reflect the adverse event profile of LVAD therapy. It is remarkable that, on average, an ED visit is associated with a 3% mortality risk. This number seems quite robust, owing that the analysis involved data from 44 000 visits. Therefore, all ED visits should be managed with the utmost care and vigilance. Moreover, the leading primary diagnosis often requires the involvement of different specialists. The patient's clinical pathways are quite different, depending on their diagnosis. Stroke requires different care than Gl bleeding, and infections need treatment different than that for right heart failure. An accurate diagnosis that is provided in a short time is the highest priority during an ED visit, because effective treatment of some adverse events is time sensitive. The ED visits by patients with LVADs may be challenging because the presence of an LVAD is associated with elevated risk once adverse events occur. The overall proportion of patients with LVADs in ED visits compared with all ED visits is small. This may pose a problem when ED staff are inexperienced with LVAD-associated adverse events. In these instances, connection to an experienced LVAD center may be especially important.

In the scenario where the ED staff lacks experience with LVAD-associate adverse events, it is questionable whether a general risk score may be helpful to the ED staff. The mortality risk assessment is dependent on the main diagnosis. Upon diagnosis, the seriousness of the adverse event is self-evident in most cases and the subsequent treatment pathway can involve other specialties associated with the primary diagnosis.

The adverse events described by Edelson et al are similar to events seen in early readmissions after LVAD placement.<sup>11</sup> It would be interesting, if possible, to combine the data of ED visits and hospital readmissions to acquire even more detailed information about real-life adverse event profiles of patients with LVADs. These findings elucidate the dilemma and limitation of contemporary LVAD therapy and provide future guidance for improvement of next-generation devices. The avoidance of shear stress in the blood pathway and the creation of pulse may have a positive impact on patient support and avoid complications of acquired von Willebrand syndrome. New algorithms for pump speed control may allow for higher efficacy of left ventricular unloading and thereby protect right heart function. A fully implantable system without a driveline may avoid most infections.

In conclusion, the publication by Edelson et al provides a comprehensive overview of the prevalence and relative risk of major adverse events in patients with LVADs who visit the ED. Application by ED staff in the future may be needed to assess the usefulness of the proposed risk score.

## **ARTICLE INFORMATION**

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#### **Disclosures**

Dr Streuber is a consultant to Medtronic, Abbott, and CorWave.

### REFERENCES

1. Frazier OH, Delgado RM III, Kar B, Patel V, Gregoric ID, Myers TJ. First clinical use of the redesigned HeartMate II left ventricular assist system in the United States: a case report. *Tex Heart Inst J.* 2004;31:157–159. Erratum in: *Tex Heart Inst J.* 2004;31:333.

- Strüber M, Sander K, Lahpor J, Ahn H, Litzler PY, Drakos SG, Musumeci F, Schlensak C, Friedrich I, Gustafsson R, et al. HeartMate II left ventricular assist device; early European experience. *Eur J Cardiothorac Surg.* 2008;34:289–294. doi: 10.1016/j.ejcts.2008.05.011
- Schmitto JD, Hanke JS, Rojas S, Avsar M, Malehsa D, Bara C, Strueber M, Haverich A. Circulatory support exceeding five years with a continuous-flow left ventricular assist device for advanced heart failure patients. *J Cardiothorac Surg.* 2015;10:107. doi: 10.1186/s1301 9-015-0306-x
- Miller LW. Left ventricular assist devices are underutilized. *Circulation*. 2011;123:1552–1558; discussion 1558. doi: 10.1161/CIRCULATIONAHA. 110.958991
- Molina EJ, Shah P, Kiernan MS, Cornwell WK III, Copeland H, Takeda K, Fernandez FG, Badhwar V, Habib RH, Jacobs JP, et al. The Society of Thoracic Surgeons Intermacs 2020 annual report. *Ann Thorac Surg.* 2021;111:778–792. doi: 10.1016/j.athoracsur.2020.12.038
- Mehra MR, Uriel N, Naka Y, Cleveland JC Jr, Yuzefpolskaya M, Salerno CT, Walsh MN, Milano CA, Patel CB, Hutchins SW, et al. A fully magnetically levitated left ventricular assist device—final report. *N Engl J Med.* 2019;380:1618–1627. doi: 10.1056/NEJMoa1900486

- Edelson J, Edwards J, Katcoff H, Mondal A, Chen F, Reza N, Hanff T, Griffith H, Mazurek J, Wald J, et al. A novel risk model to predict emergency department-associated mortality for patients supported with a ventricular assist device: the ED-VAD Risk Score. J Am Heart Assoc. 2021;11:e020942. doi: 10.1161/JAHA.121.020942
- Proudfoot AG, Davidson SJ, Strueber M. von Willebrand factor disruption and continuous-flow circulatory devices. *J Heart Lung Transplant*. 2017;36:1155–1163. doi: 10.1016/j.healun.2017.06.004
- Meyer AL, Malehsa D, Bara C, Budde U, Slaughter MS, Haverich A, Strueber M. Acquired von Willebrand syndrome in patients with an axial flow left ventricular assist device. *Circ Heart Fail*. 2010;3:675–681. doi: 10.1161/CIRCHEARTFAILURE.109.877597
- Malik S, Malik SA, Ulmer LL, Jha LK, Strupp MS, Raichlin E, Lyden ER, Hewlett AT. Gastrointestinal bleeding with left ventricular assist devices (LVADs): locating the leak and identifying outcomes. *J Clin Gastroenterol.* 2019;53:e202–e207. doi: 10.1097/MCG.000000000 001041
- Lemor A, Michaels A, Al-Darzi W, Hernandez GA, Nasr Y, Villablanca P, Blumer V, Tita C, Williams CT, Selektor Y, et al. National landscape of hospitalizations in patients with left ventricular assist device. Insights from the National Readmission Database 2010-2015. ASAIO J. 2020;66:1087–1094. doi: 10.1097/MAT.000000000001138