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## **A New Pathophysiology in Heart Failure Patients**

**Short Title:** LVAD weaning in heart failure

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**Abstract**

In the treatment of patients with severe heart failure, left ventricle assist device (LVAD) plays an important role, especially as a destination therapy. Nevertheless, even in successful cases, patients' progressive weaning is rarely taken into

consideration. The recovery of more physiological circulation conditions is not a main goal. This hypothesis is discussed in this paper.

Keywords: LVAD therapy, pathophysiology, heart failure

The management of severe heart failure has radically changed over the last 20 years, being codified within guidelines<sup>(1)</sup> and constantly updated. Left ventricular assist devices (LVADs) have progressively evolved in their indication, becoming a treatment to support end-stage heart failure (HF) patients in several different clinical scenarios: as a bridge to heart transplantation, as a destination therapy, as a bridge to decision, or even as recovery. Patient profile at the time of implant continues to evolve. In the past, the majority of LVAD implantations was performed in patients hospitalized and dependent on intravenous inotropic support, whereas today the trend is to anticipate implantation with the aim of improving survival and maximizing quality of life. That means that we are progressively lowering patients' INTERMACS profile from 1 to 4<sup>(2)</sup>. The most recent randomized trials have been performed in more acute HF patients (INTERMACS profiles 1–3). As the natural outcomes of LVAD are eventual heart transplantation, lifetime support, or bridge to recovery, research efforts over the last years have focused mainly on improving overall device safety, durability, and performance. Indeed, in successful destination therapy LVAD patients, the main goals are the improvement of life quality and the optimization of LVAD performance<sup>(3-6)</sup>. With a few remarkable exceptions<sup>(6-9)</sup>, left ventricular recovery is nowadays seldom pursued as a clinical goal, so that LVAD explantation is only occasionally achieved.<sup>(10)</sup> On the contrary, quality of life<sup>(11)</sup>, exercise performance, and survival improvement are the most frequently explored results.<sup>(3, 4, 12, 13)</sup> To obtain the latter results, we look for the highest possible cardiac output, which is identified with the highest tolerated flow generated by the original ventricle and the LVAD, to improve organ oxygenation both at rest and during exercise. Accordingly, physical rehabilitation and transitory LVAD pump increase have been suggested to improve patients' fitness.<sup>(14, 15)</sup> Indeed, several factors limit exercise performance in LVAD patients.<sup>(15)</sup> In this regard, the knowledge of left ventricle/LVAD coupling is considered of utmost importance to understand whether we are going the right way if either left ventricular recovery or the highest cardiac output are the major goals in LVAD patients.

The intraventricular dynamics of the flows and the kinetic energy distribution present interesting differences between the native ventricle with reduced ejection fraction and the ventricle with implanted LVAD.<sup>(16)</sup> In the native ventricle, the flow presents a peculiar, well-defined pattern: from the mitral valve, blood flow is posterolaterally directed towards the apical region, along the wall of the ventricle, from where it changes direction towards the aortic valve. In ventricles with LVAD, the presence of the axial vortex and the size of the cannula determine a lower uniformity of kinetic energy distribution, and a significant slowing of flow in the apical site. (Figure)

Therefore, we believe that a different approach should be considered. Specifically, patients with LVAD could be evaluated in light of the peculiar intracardiac hemodynamic pattern due to the effects of continuous flow in the heart as well as in the peripheral vessels. Specifically, LVAD influences the left ventricular mechanics in all its phases.<sup>(16)</sup> However, intraventricular mechanical analysis in LVAD patients is rarely performed, and it is not a part of routine ultrasound evaluation. However, a possible reduction of wall stress could be caused by a modification of ventricular flow, particularly in apical and periapical sites, as proposed by an experimental model.<sup>(17)</sup>

Viola and colleagues<sup>(17)</sup> showed that LVAD modifies intraventricular hemodynamics and pressure. The increase of LVAD flow speed induces a significant reduction of intraventricular pressure at systolic peak, hopefully leading to a recovery of left ventricular volumes and function.

Accordingly, if the recovery from LVAD is the best perspective in LVAD patients, monitoring intraventricular regional hemodynamics during LVAD flow reduction is mandatory to assess the restoration of a normal pattern, although this approach is never applied. In fact, it is known that adaptation to flows in the presence or absence of the cannula determines favorable conditions to the thrombi's formation, even after the explant has taken place.<sup>(18)</sup> Furthermore, many other factors such as cannula material and surface characteristics, as well as the patients' coagulation status may be of some clinical significance, explaining the differences observed in the flow field.

<sup>(19)</sup>

We believe that, once the stabilization and well-being of patients have been achieved, major efforts should be made to progressively and slowly reduce LVAD pump flow, allowing the restoration of left ventricular performance. In our opinion, this approach is the only one that could in principle drive to left ventricular function recovery. It is acknowledged that how to reach this goal, i.e. how to evaluate whether a patient is a potentially recovered case in whom LVAD can be explanted, in terms of LVAD speed reduction and its time frame (how frequently and how much), should be personalized according to patient's conditions, local expertise, and type of LVAD. At present, there is no approved protocol for this, and, in the few reported cases where LVAD was explanted, this was done without a common and definite approach<sup>(6, 10, 15)</sup>. Accordingly, the present "Thoughts & Progress" is a working hypothesis whose clinical efficacy and applicability are unknown.

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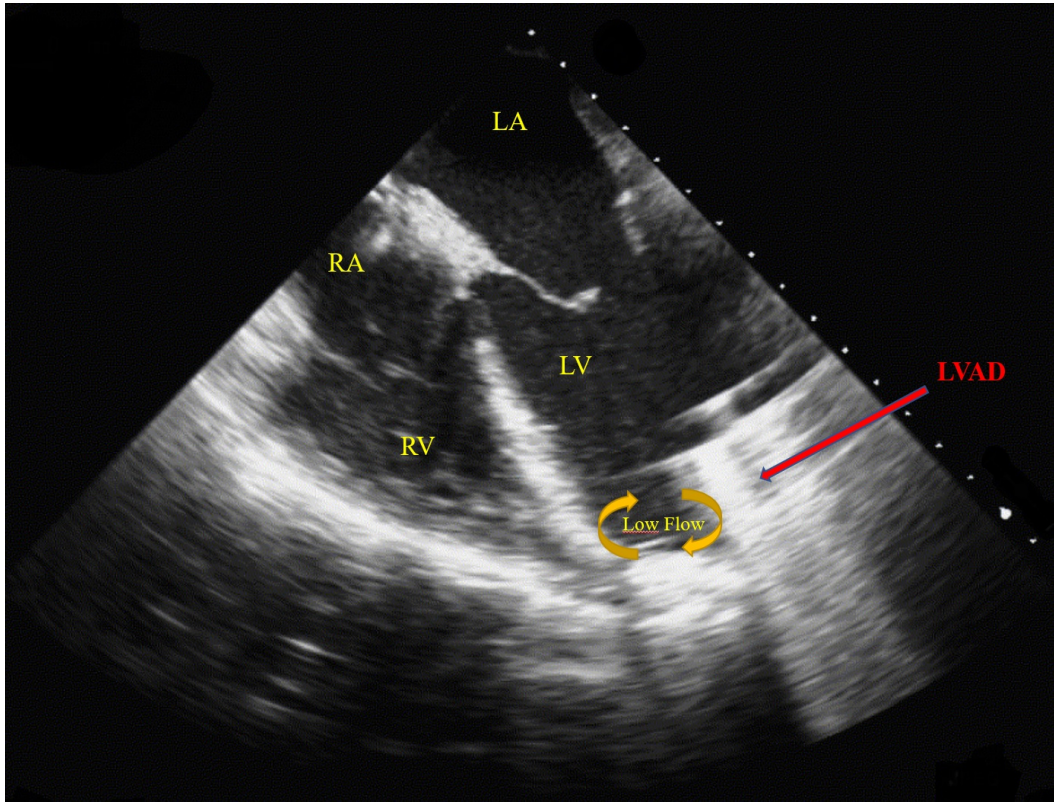
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#### **Figure Caption**

Transesophageal echocardiographic 4-chamber view. Localization of the slowing of flow during LVAD activation. (LV: left ventricle, LA: left atrium, RV: right ventricle, RA: right atrium).





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