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Editorial

Hemodynamic optimization in patients with a long-term ventricular assist device. A diagnostic and therapeutic challenge

Optimización hemodinámica de los pacientes portadores de un dispositivo de asistencia ventricular de larga duración. Un reto diagnóstico y terapéutico

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Progress in the design of left ventricular assist devices (LVADs) has increased the survival of patients who receive them for the treatment of advanced heart failure (HF).[1] These developments have led to an exponential growth in the number of implantations performed annually worldwide.[2,3] However, such patients still experience a significant number of complications that worsen quality of life, shorten life expectancy, and are associated with a high readmission rate.[4] Although the main function of LVADs is to assist dysfunctional left ventricles (LV) by controlling the signs and symptoms of HF, other studies have reported that a main cause of readmission is still decompensated HF.[5] From the pathophysiological point of view, LVADs increase cardiac output and decrease left chamber filling pressures and, as a consequence, reduce pulmonary pressures, right afterload, and central venous pressure, which are fundamental hemodynamic variables in the treatment of HF. However, excessive LV unloading can make the interventricular septum shift excessively to the left, thus changing the morphology of the right ventricle (RV) and losing the contribution of the septum itself to RV systole. This septal deviation also directly pulls on the tricuspid septal leaflet and increases the degree of prior valvular regurgitation. Both mechanisms directly increase the risk of patients showing evidence of right HF. In contrast, if LV unloading is suboptimal and there is persistent poor LVAD optimization, left filling pressures may remain elevated, patients may show evidence of pulmonary congestion, and impaired RV function may be maintained or worsen.

In this regard, one of the main issues that must be addressed by clinicians during follow-up is the hemodynamic optimization of these patients. Thus, a detailed understanding of heart-pump-cardiovascular system interaction is essential. Despite improvements in recent years, optimization remains insufficient, which is clearly reflected in the results of previous studies showing that only 40% to 60% of outpatients with LVADs have a "normal" hemodynamic profile when assessed by right catheterization.[6,7]

Several strategies are available to achieve the maximum optimization of this therapy. First, it is essential to continue the neurohormonal therapy used in the treatment of HF after LVAD implantation. Neurohormonal drugs not only control blood pressure, but also promote ventricular reverse remodeling and control potential congestion.[8] Secondly, pump flow should be optimized, which is reflected in the normalization of hemodynamic pressures. We emphasize that these strategies are not just a matter of "numbers", because correct hemodynamic optimization is associated with fewer complications and readmissions. Imamura et al.[6] showed that only 50% of patients with LVADs had a normal hemodynamic profile as assessed by right catheterization. After pump optimization, this percentage increased to 61%. After 1 year of follow-up, they found that the annual readmission rates of patients with normal profiles were much lower than those of patients without optimization (1.15 vs 2.86 events/y), and almost half of this reduction was achieved by avoiding HF decompensation. In the same line, these authors found an association between correct optimization and a reduction in pump hemocompatibility-related adverse events (nonsurgical bleeding, thromboembolic events) of close to 30% per year.[9] There are several reasons for this result: on the one hand, as previously noted, an association has been found between inappropriate LV unloading and higher HF rates, which is clearly related to a higher rate of thromboembolic and hemorrhagic events due to increased liver congestion; on the other hand, the loss of laminar flow through the pump rotor favors thrombus formation and increases destruction of the von Willebrand chain. Maximal optimization is also supported by the finding of an association between correct LV unloading and an increased probability of reverse remodeling and ventricular recovery and higher LVAD explantation rates.[8]

Although all these results emphasize the need to match pump speeds to the characteristics of each individual, many questions remain concerning the best way to achieve this. The ramp test is still the most widespread technique; however, there is marked variability between the current protocols and the monitoring technique that guides them. From the pathophysiological point of view, the best approach is probably the invasive monitoring of hemodynamic pressures, although this procedure still carries the risk of potential complications. Therefore, most professionals prefer to monitor the test using transthoracic echocardiography. Despite their widespread use, these protocols are subject to relevant limitations. On the one hand, many studies are affected by the echocardiographic window. On the other hand, it is difficult to accept that hemodynamic optimization in these patients can only be achieved by serial measurements of ventricular diameters in combination with the degree of aortic valve opening under resting conditions. The RAMP-IT-UP study[10] was designed to address this issue. The study included 41 patients with an HVAD pump (Medtronic, United States) who were randomized to optimization

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using the ramp test with echocardiography or catheterization. An association was found between the invasive procedure and fewer events during follow-up (mainly HF and thromboembolic events); however, due to the low sample size, statistical significance could not be reached.[10] What is clear is that joint protocols combining invasive pressure monitoring with echocardiographic assessment could achieve improvements in the hemodynamic profile that, in the best case, could reach 80%[7]; however, most published studies report improvements of around 60%.[9–11]

When assessing the reasons for these results, it is important to emphasize that the interaction between the dynamic properties of the cardiovascular system and the absolute dependence of the pump on LV preload and afterload makes it very difficult for protocols performed in controlled situations and at rest to provide a true picture of what happens to the pump-cardiovascular system relationship when patients exert effort. Likewise, questions remain regarding whether these changes in hemodynamic profile during exercise can affect pump optimization when the patient is at rest and, more importantly, medium- to long-term prognosis. Current LVAD technology is limited to a fixed pump speed incapable of increasing flow in the event of increased patient demand. This limits the ability of many patients to cope with overexertion, especially those without contractile reserve. A recent study of invasive hemodynamics in patients with LVADs showed that increases in cardiac output during exercise mainly depend on the increase in flow provided by the native heart; in addition, there is also a significant increase in left and right filling pressures in these patients, which indicates a limited RV contractile reserve.[12]

All of these aspects prompt us to reflect on how to detect ambulatory patients with poor unloading. In a recent article published in *Revista Española de Cardiología*, Ruiz-Cano et al.[13] attempted to answer this question. The authors conducted a single-center retrospective study of a cohort of 104 patients from a high-volume center who had undergone LVAD implantation as a bridge to heart transplant and right heart catheterization during follow-up. They divided the patients into 2 groups according to whether they were optimized or not, using a pulmonary capillary wedge pressure of 15 mmHg as the cutoff point. The first noteworthy finding of this study is that up to 72% of the patients had normal values in the invasive test; this is a very high figure compared with those of previous registries.[6,7] This finding undoubtedly goes hand in hand with the low HF readmission rate in their cohort: only 12 patients required admission during a mean follow-up of 23 months (7 in the nonoptimized group). One of the most original aspects of their study is the strong association found between brain natriuretic peptide (BNP) concentrations < 300 pg/mL, and the ability to predict the absence of pulmonary capillary pressure > 15 mmHg (predictive value, 86%; specificity, 75%; sensitivity, 75%) under right catheterization. Previous studies had already found an association between a decrease in BNP and a decrease in cardiomyocyte diameter and collagen deposition and an improvement in LV ejection fraction.[14] However, increases in BNP concentration imply a higher incidence of readmission and death.[15] While awaiting specifically targeted studies, the work of Ruiz-Cano et al. provides results in support of the use of natriuretic peptides to identify patients who may be underoptimized and could benefit from a modification in medical therapy or adjustment of pump speed according to a ramp test.

Another very attractive strategy to achieve maximum optimization is hemodynamic monitoring using wireless implantable devices able to remotely transmit continuous information on pulmonary pressures. This system has proven useful in the chronic HF patients included in the CHAMPION study, which achieved a significant reduction in the number of hospital readmissions.[16] Several theoretical benefits could derive from the application of this technology during the follow-up of LVAD patients. First, the continuous monitoring of the patients' hemodynamic status can better optimize pump speed, not only to avoid HF decompensation but also to detect the possible causes of low-flow alarms. It can also remotely adjust pharmacological treatment without the need for patients to visit the LVAD specialist hospital, thus improving quality of life. However, to date, there are few results on the efficacy of such a strategy in support of the widespread use of these implantable wireless devices for the hemodynamic monitoring of patients with LVADs. Results have been provided by the CHAMPION study, in which 27 patients required LVAD implantation during follow-up (15 in the device implantation group and 12 in the control group). Although firm conclusions cannot be drawn due to the characteristics of the sample, an association was found between better-adjusted medication therapy and greater and earlier decreases in pulmonary pressures in the intervention group. Even though these results did not reach statistical significance, their application could be useful in patients receiving a LVAD as part of a bridging strategy for transplant candidacy for patients with pulmonary hypertension.[17] In the same line, a small pilot study compared historical controls (n = 20) and 10 patients who had already received a CardioMEMS system (Abbott Cardiovascular, United States) and subsequently received a HeartMate 3 LVAD (Abbott Cardiovascular). The combined 1-year primary endpoint of all-cause mortality, acute kidney failure, need for renal replacement therapy, and RV failure occurred in 50% of the CardioMEMS group vs 60% of the historical controls.[18]

Clearly, one of the hindrances to the limited use of this type of therapy in many countries is the price of LVADs. Despite improving the vital prognosis of patients, if we are unable to reduce the readmission rate, many health systems will not be able to assume this additional cost. In the not-too-distant future, smart LVADs will probably incorporate real-time hemodynamic monitoring that, linked to specific algorithms, will be able to assess patient activity and adjust pump speed to achieve optimized cardiac output and normal intracavitary pressures. Until then, clinicians will continue to search for the best strategies to identify patients candidate for optimization and thus improve their quality of life and life expectancy.

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None declared.

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