≤40% and a dual chamber implantable cardioverter defibrillator (ICD) or cardiac resynchronization device (AATAC trial).[3] The ablation strategy went beyond PVI alone and included ablation of extensive areas of the left atrium plus isolation of the superior vena cava in certain cases and redo procedures if necessary. The results showed that catheter ablation was superior to amiodarone in achieving freedom from AF during long-term follow-up. More stunning was that catheter ablation reduced unplanned hospitalizations and overall mortality, which needs to be confirmed in other trials.

Another complex substrate with recent advances leading to clinical implications is ventricular tachycardia (VT) ablation in patients with underlying coronary artery disease and recurrent VT. The prospective, nonrandomized and multicenter Post-Approval THERMOCOOL VT trial has shown that VT ablation significantly reduced sustained monomorphic VT recurrences by 62% at the 6-month follow-up. Moreover, 41% of patients were free from VT after a 3-year follow-up.[4] This outcome translated into a statistically significant decrease in hospitalizations, ICD shocks, and amiodarone use. The ablation approach to identify target sites was left to the investigators' criteria, while recommending activation and entrainment mapping during VT to guide the ablation sites. Substrate characterization by voltage mapping, identification of split or late potentials and/or pace maps with long stimulus to QRS intervals, in which the QRS mimics the target VT, were recommended when VT was intolerable.

Another step forward in VT ablation came from the VANISH trial,[5] which was a multicenter, randomized study aiming to compare catheter ablation with continuation of baseline antiarrhythmic medications or escalated antiarrhythmic drug therapy in patients with prior myocardial infarction, ICD, and recurrent VT. Patients within the antiarrhythmic drug group were treated with amiodarone or amiodarone plus mexiletine. The primary outcome was a composite of death or VT storm or appropriate ICD shock after a 30-day treatment period, including as secondary outcomes all-cause mortality and hospital admissions for cardiac causes, among others. The ablation strategy was similar to that used in the postapproval THERMOCOOL VT trial. Catheter ablation demonstrated to be more effective than antiarrhythmic drug therapy in reducing the primary endpoint after 27.9 ± 17.1 months of follow-up, although mortality did not significantly differ between groups. With respect to mortality, it is likely that this study was underpowered. Large registries indicate that VT ablation, especially in postinfarction patients, appears to reduce mortality if successfully performed (Figure).[6]

The best of catheter ablation in 2016 provides the first evidence of improved outcomes with decreased hospitalizations and possibly also mortality after AF ablation in heart failure patients, and reduced death or VT storms or appropriate ICD shocks after VT ablation in patients with an infarct-related substrate. New imaging and mapping techniques for both substrates may further improve such outcomes and hopefully improve long-term success in the near future.

David Filgueiras-Rama,[a,b,e,*] Frank Bogun,[c] Nicasio Pérez-Castellano,[b,e] Fred Morady,[c] José Jalife,[a,d,e] and Julián Pérez-Villacastín[b,e]

[a]*Myocardial Pathophysiology Area, Fundación Centro Nacional de Investigaciones Cardiovasculares Carlos III (CNIC), Madrid, Spain*
[b]*Departamento de Cardiología, Hospital Universitario Clínico San Carlos, Madrid, Spain*
[c]*Department of Internal Medicine, Cardiology, University of Michigan, Ann Arbor, Michigan, United States*
[d]*Department of Internal Medicine, Center for Arrhythmia Research, University of Michigan, Ann Arbor, Michigan, United States*
[e]*Centro de Investigación Biomédica en Red de Enfermedades Cardiovasculares (CIBERCV), Spain*

*Corresponding author:
E-mail address: david.filgueiras@cnic.es (D. Filgueiras-Rama).

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Selection of the Best of 2016 in Mechanical Circulatory Support

Selección de lo mejor del año 2016 en dispositivos de asistencia mecánica circulatoria

To the Editor,

Heart failure (HF) is a major health problem that carries high mortality and morbidity.[1] Approximately 5% of patients are in advanced HF and prognosis remains poor. In a small proportion of patients, heart transplant (HT) is an option. Unfortunately, the number of donors is limited, resulting in 250 HT performed per year in Spain. Consequently, mechanical circulatory support with ventricular assist devices (VADs) has emerged as a treatment option for advanced HF. The type of VAD implanted will depend on the clinical situation defined by the Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) classification[2] (Table). The following article aims to select the most important work published in this field in 2015.

The annual report of the Spanish HT registry[3] shows a trend toward an increased use of emergency HT (40% in recent years), with an increasing use of VADs (20%). While long-term continuous-flow VADs are the preferred option in most countries, the most frequently used in Spain are short-term VADs. Peripheral venoarterial extracorporeal membrane oxygenation (ECMO) support is the preferred option in INTERMACS 1. In patients in

Table
Indications for Ventricular Assist Device Implantation

Chronology of heart failure	INTERMACS level	Type of VADs	Purpose of the implantation
Acute setting	INTERMACS 1-2	Short-term VADs	Bridge to decision Bridge to recovery Bridge to transplant Bridge to long-term VAD
Chronic heart failure	INTERMACS 2-4	Long-term VADs	Bridge to transplant Bridge to candidacy Destination therapy

VAD, ventricular assist device.

INTERMACS 1-2 but not in such a catastrophic situation, a short-term continuous-flow VAD is preferred, as it can provide longer support, with fewer long-term complications. However, the use of ECMO is clearly associated with worse survival and therefore, whenever possible, its use should be avoided before HT. It will be important to elucidate the reasons for this worse survival and to determine the outcomes with short- and long-term VAD as a bridge to transplant in Spain. An analysis of short-term VAD as a bridge to HT is currently underway in all HT centers in Spain and will soon provide some answers.

The INTERMACS database collects the outcome of VADs in the United States of America. Its seventh annual report[1] published data on more than 15 000 long-term VADs, with a rate of 2500 patients per year in the last 2 years. The dominance of continuous flow is noticeable, with $>$ 90% of patients receiving an intracorporeal pump, predominantly for left support. Within this group, the number of axial-flow VADs is still twice as high as that of centrifugal-flow VAD. Regarding the strategy, the increase in destination therapy (DT) is evident, with nearly 46% of implants, followed by bridge to transplant (30%) and bridge to candidacy (23%). Overall, survival at 1-year was 80%, but was worse in biventricular support (50%) and DT (76%). Several risk factors for mortality are described, such as increasing age, female sex, higher body mass index, ventilator use, INTERMACS levels 1-2, right VAD in the same operation and data suggestive of failure of other organs. The main causes of early death were right HF, neurologic events, and multisystem organ failure, while infection played an important role in late mortality.

ROADMAP[4] is the first study to assess the use of long-term VADs in patients with ambulatory HF (INTERMACS 4-7). All patients met indications for VAD as DT, had $\geq$ 1 hospitalization in the last year, and 6-minute walk distance $<$ 300 meters. Two hundred patients were included and assigned to medical treatment vs VAD on the basis of patient or physician choice, not randomization. Survival on original therapy with improvement in 6 minutes walking test $>$ 75 m at 1 year, was better in the VAD group (39%) compared with medical treatment (21%), P = .012. The difference was driven by delayed VAD implant in the medical treatment group. Health-related quality of life and depression improved more significantly with mechanical circulatory support. However, a composite of adverse events that included bleeding, infection, thrombus, stroke, arrhythmias, and worsening HF was twice as common in the VAD group (1.89 events/patient-year). Although the authors conclude that this study supports the use of VAD in INTERMACS 4-7, the high incidence of adverse events and the costs of VAD indicate the need for caution regarding too early VAD placement.

Stroke and bleeding still remain major adverse events and the TRACE study[5] is interesting because it analyzed 100 HeartMate II patients with reduced antithrombotic therapy, which included warfarin only (38%), aspirin only (28%), or no antithrombotic agent (34%). While the rate of device thrombosis (0.08 patients-per-year) was higher than in clinical trials, subsequent bleeding occurred in 52%, despite reduced antithrombotic therapy. Therefore, although reduced antithrombotic therapy may be necessary when bleeding occurs, it should not be the standard strategy for all patients.

Finally, we must mention the first report on the initial experience with a new magnetically levitated continuous-flow VAD (Heartmate 3), which shows similar short-term results to the existing VAD technology.[6] Further studies, such as the MOMENTUM 3 (NCT02224755), will compare outcomes with this new technology with those of the most commonly used axial-flow VAD.

In conclusion, VADs save lives and their use as a bridge to transplant or candidacy is unquestionable. However, their costs and rate of adverse events limit their potential as DT. The use of VADs in Spain is increasing and the management of these patients with advanced HF remains a challenge.

CONFLICTS OF INTEREST

None declared.

Cristina Sánchez-Enrique,[a] José González-Costello,[a,*] Albert Ariza-Solé,[b] Albert Miralles,[c] Nicolás Manito,[a] and Angel Cequier[a,b]

[a]*Unidad de Insuficiencia Cardiaca Avanzada, Área de las Enfermedades del Corazón, Hospital Universitari de Bellvitge, L'Hospitalet de Llobregat, Barcelona, Spain*
[b]*Unidad Cuidados Agudos Cardiológicos, Área de las Enfermedades del Corazón, Hospital Universitari de Bellvitge, L'Hospitalet de Llobregat, Barcelona, Spain*
[c]*Servicio de Cirugía Cardiaca, Área de las Enfermedades del Corazón, Hospital Universitari de Bellvitge, L'Hospitalet de Llobregat, Barcelona, Spain*

* Corresponding author:.
E-mail address: jgcostello@hotmail.com (J. González-Costello).

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Selection of the Best of 2016 in the Treatment of Pulmonary Hypertension

Selección de lo mejor del año 2016 en el tratamiento de la hipertensión pulmonar

To the Editor,

Pulmonary hypertension (PH) is a pathophysiological disorder that can coexist with numerous clinical entities and can complicate most cardiovascular and respiratory diseases. PH is defined as a mean pulmonary arterial pressure (PAPm) increase $\geq$ 25 mmHg at rest, calculated using right heart catheterization.

There have been a number of significant developments in the PH field in the last 2 years, particularly in available treatments. These advances include the approval of new drugs, new tests for the use of initial drug combination therapies in pulmonary arterial hypertension (PAH), and the approval of drugs for use in chronic thromboembolic PH that is not amenable to surgical thromboendarterectomy.

The field continues to evolve and it is hoped that ongoing clinical trials will identify drugs that can effectively treat PH due to left heart disease and chronic hypoxia. This article highlights the most significant recent advances in PH management.

PAH (group 1) encompasses idiopathic PAH, heritable PAH, and PAH associated with disease, such as connective tissue diseases, HIV infection, portal hypertension, congenital heart disease, schistosomiasis, and that induced by drugs or toxins.[1] Despite the considerable effort expended into the research and development of therapeutic agents in the last 20 years, the disease is largely incurable and the general prognosis remains poor. The median survival for an untreated patient is 2.8 years. In the last 3 decades, spectacular advances have been made in the understanding of the molecular mechanisms and signaling pathways involved in the disease, which have resulted in the development of new treatment strategies.

Regarding the new drugs acting on the nitric oxide pathway, whereas phosphodiesterase type 5 inhibitors (PDE-5is) such as sildenafil and tadalafil activate the nitric oxide-cyclic guanosine monophosphate (cGMP) pathway to inhibit cGMP breakdown, its production is promoted by soluble guanylate cyclase stimulators. Treatment of 443 PAH patients (44% and 6% receiving baseline treatment with endothelin receptor antagonists [ERAs] and prostanoids, respectively) with up to 2.5 mg riociguat 3 times a day obtained positive results in terms of exercise capacity, hemodynamic parameters, World Health Organization functional class (WHO FC), and time to clinical worsening.[2] Exercise capacity increased in both the riociguat and placebo groups. These beneficial effects were maintained for at least 2 years of open follow-up.

The dual ERA antagonist macitentan was evaluated in an event-driven clinical trial that randomized 742 patients to treatment with 3 or 10 mg macitentan or placebo during a mean treatment period of 100 weeks.[3] The primary endpoint was the time from the initiation of treatment to the first occurrence of a composite endpoint of death, atrial septostomy, lung transplantation, initiation of treatment with intravenous or subcutaneous prostanoids, or worsening of PAH. Macitentan significantly reduced the composite endpoint of morbidity and mortality of patients with PAH and increased exercise capacity. Benefits were seen both in patients not previously receiving therapy for PAH and those receiving additional PAH therapy.

Regarding drugs targeting the prostaglandin pathway, selexipag is an oral selective IP prostacyclin receptor agonist. Although selexipag and its metabolite have similar mechanisms of action to endogenous prostacyclin (IP receptor agonists), they are chemically distinct and have different pharmacological characteristics. A controlled, randomized, event-driven, phase III study including 1156 patients[4] showed that selexipag, alone or added to single or dual treatment with ERA or PDE-5i, obtained a 40% reduction (hazard ratio, 0.60; $P < .001$) in the composite endpoint of morbidity and mortality (which included death from any cause, hospitalization due to worsening of PAH, worsening of PAH that resulted in lung transplantation or atrial septostomy, initiation of parenteral prostanoid therapy or oxygen therapy due to worsening of PAH, and disease progression).

Combination therapy is defined as the simultaneous use of 2 or more classes of drugs. A recent multicenter study, with blinding and a placebo control group, compared initial monotherapy with tadalafil or ambrisentan to initial combination therapy with tadalafil and ambrisentan in patients with de novo PAH and WHO FC II-III.[5] The primary composite endpoint was the first event of clinical failure (death, hospitalization, PAH progression, and unsatisfactory clinical response). Positive results were obtained, with a 50% reduction in events in the combination therapy group. In addition, improvements were seen in exercise capacity, rates of a satisfactory clinical response, and the plasma concentration of N-terminal pro–B-type natriuretic peptide.

The figure shows a treatment algorithm for patients with PAH that follows the directives of the latest PH guidelines of the European Respiratory Society/European Society of Cardiology.[1]

The first treatment objective for PH caused by left heart disease (group 2 PH) is to improve the overall treatment of the underlying entity before considering specific measures for PH treatment. Two ongoing multicenter studies are evaluating the treatment of PH caused by left heart disease, the SilHF trial (NCT01616381) with sildenafil and the Melody-1 trial (NCT02070991) with macitentan; the latter study is the only one to require evaluation using right heart catheterization.

Nonetheless, there is no new evidence permitting recommendation of the use of specific treatments for PAH for PH caused by left heart disease, and this is partly due to the absence of studies specifically stratifying patients with PH or specifically targeting this entity.

There is currently no specific treatment for PH associated with chronic pulmonary diseases or hypoxia (group 3 PH). Long-term oxygen therapy partially reduces PH progression in chronic obstructive pulmonary disease. Few data have been published on the specific treatment of PAH and there is still no evidence from controlled studies of drugs for PAH showing symptom or outcome improvements in patients with pulmonary disease.