the Society of Thoracic Surgery (STS) scale was 21.1%. The risk of stroke, prolonged ventilation, kidney failure, and repeat surgery was estimated at 1.4%, 13.6%, 3.6%, and 10%, respectively.

Because of the patient's elevated operative morbidity and mortality risk, and her favorable anatomy (venae cavae diameters between 16 and 42 mm, distance between the hepatic vein outlets and IVC outlet in the right atrium at least 1 cm, and absence of pacemaker leads implanted in the right ventricle), percutaneous treatment with the above-described endoprosthesis was indicated. The patient signed an informed consent form and elective implantation was scheduled.

The intervention was performed with the patient under general anesthesia, and monitoring by transesophageal echocardiography and right femoral venotomy. Venotomy was done for safety reasons, to avoid vascular complications and achieve better control of hemostasis and potential damage to the vein wall with the use of a 24-Fr catheter in this first case. After advancing a 0.032-inch vascular guidewire to the right subclavian artery, the endoprosthesis carrier system was inserted and positioned appropriately with its distal end in the superior vena cava. The device was then properly oriented with the radio-opaque markers facing the native tricuspid valve so that venae cavae anterograde flow would be toward the right ventricular inflow tract, and was gradually deployed under monitoring. Final release was carried out following expansion of the upper pillar of the valve component and after ensuring that the lower pillar was positioned at the junction of the IVC outlet and the right ventricle—and therefore, that the valve was in the right ventricle—and the lower anchor of the endoprosthesis was correctly positioned in the IVC without obstructing flow of the suprahepatic veins (Figure 1).

Following completion of the procedure and catheter withdrawal, hemostasis, femoral vascular closure, and extubation of the patient were carried out. The postprocedure clinical course was satisfactory. At the 1- and 3-month follow-up evaluations, the patient was in New York Heart Association functional class II and echocardiography depicted laminar flow through the prosthesis with no regurgitation to the venae cavae or periprosthetic leaks.

The first successful implantation of the Tricento valve prosthesis in Europe was performed by Toggweiler et al.[6] The case reported here is the second referred for publication in Europe. The valve has a simple design for percutaneous implantation and it is tailored to the patient's anatomy. Proper implantation of the device requires the following prerequisites: *a)* no interference with the hepatic veins at the proximal end, *b)* expansion of the nitinol support construct exceeding the dimension of the anchoring points in the venae cavae by 20% for proper fixation in the ideal position, *c)* prevention of periprosthetic leaks and prosthesis migration, and *d)* outlets of the suprahepatic veins at least 1 cm from the IVC outlet in the right atrium.

The limitations of the Tricento are as follows: *a)* made-to-order construction that requires at least 4 weeks, preventing its use in urgent cases; *b)* superior and inferior vena cava diameters must be between 16 and 42 mm; and *c)* uncertainty regarding whether the presence or need for a pacemaker may be a limitation to its use.

Implantation of the Tricento endoprosthesis was effective in the case described, and the patient's short-term clinical and echocardiographic status was satisfactory. A longer follow-up in broader series is needed to evaluate the effectiveness of this device at long-term.

CONFLICTS OF INTEREST

E. Abu-Assi is an Associate Editor of *Revista Española de Cardiología.*

APPENDIX. SUPPLEMENTARY DATA

Supplementary data associated with this article can be found in the online version, at http://dx.doi:10.1016/j.rec.2019.03.004.

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Treatment of Hypercholesterolemia With PCSK9 Inhibitors in Heart Transplant Recipients. First Experience in Spain

Tratamiento de la hipercolesterolemia con inhibidores de la PCSK9 en receptores de trasplante cardiaco. Primera experiencia en España

To the Editor,

Hypercholesterolemia continues to be an important comorbidity often seen in heart transplant (HT) recipients and is associated with a higher cardiovascular risk and with the appearance of graft vascular disease (GVD).[1] Statin therapy in this patient group has been shown to significantly reduce the incidence of acute graft rejection and GVD and to increase survival, benefits attributable not only to lower plasma cholesterol concentrations but also to the immunomodulatory effects of statins.[2] Consequently, clinical practice guidelines recommend long-term use in all HT recipients, regardless of low-density lipoprotein cholesterol (LDL-C) levels.[3]

Proprotein convertase subtilisin/kexin type 9 (PCSK9) selectively binds to LDL-C receptors in the hepatocyte membrane, enhancing

Table 1
Baseline characteristics and trend in LDL-C levels in HT recipients receiving treatment with a PCSK9i agent (alirocumab 75 mg/14 d)

Patient	Age, y	Time since HT, y	IS regimen	Initial statin	Final statin	Duration of treatment with PCSK9i, mo	Baseline LDL-C, mg/dL	Final LDL-C, mg/dL
1	68	9.1	TAC + EVL + corticosteroids	Rosuvastatin 40 mg/d	Rosuvastatin 20 mg/d	15	175	67
2	48	9	CsA + MMF + corticosteroids	Rosuvastatin 40 mg/d	Rosuvastatin 40 mg/d	5.6	180	98
3	58	10.5	TAC + EVL + corticosteroids	No	Pitavastatin 1 mg/d	21.4	129	69
4	73	13.4	CsA + EVL + corticosteroids	Pitavastatin 4 mg/d	Pitavastatin 4 mg/d	23.6	146	35
5	59	22.9	TAC + EVL + corticosteroids	Rosuvastatin 40 mg/d	Rosuvastatin 40 mg/d	12.3	146	38

CsA, cyclosporin A; EVL, everolimus; HT, heart transplantation; IS, immunosuppression; LDL-C, low-density lipoprotein cholesterol; MMF, mycophenolate mofetil; PCSK9i: proprotein convertase subtilisin/kexin type 9 inhibitor; TAC, tacrolimus.

receptor breakdown and indirectly raising plasma LDL-C concentrations. The PCSK9 inhibitors (PCSK9i) known as alirocumab and evolocumab are monoclonal antibodies that block the activity of this protein, and they have been shown to significantly reduce LDL-C and the risk of cardiovascular events.[4] Furthermore, PCSK9 metabolism does not involve cytochrome P450 or certain hepatic carriers, such as organic anion transporting polypeptide C (OATP-C), which play a key role in the process that breaks down statins and common immunosuppressant drugs, thereby dramatically reducing the likelihood of drug interactions and adverse reactions. Hence, this pharmacological group is an interesting therapeutic alternative for the treatment of hypercholesterolemia in HT recipients, although there is currently little evidence on its safety and efficacy in this population.

We describe a series of 5 HT recipients who began taking PCSK9i due to LDL-C $>$ 100 mg/dL despite ezetimibe therapy and, when tolerated, the highest dose of a statin, as recommended in the therapeutic positioning report published by the Ministry of Health, Consumer Affairs and Social Welfare of the Government of Spain. All patients were men, the mean age was 58.8 $\pm$ 8 years, and the mean post-HT time was 13 $\pm$ 5.2 years. In all patients, the immunosuppressant regimen included 3 drugs, and in 3 patients (patients 3, 4, and 5), the presence of GVD had been previously confirmed. Patients 1, 2, and 5 were receiving a combination of rosuvastatin 40 mg/d and ezetimibe 10 mg/d; patient 3 was receiving only ezetimibe 10 mg/d due to a history of liver and muscle toxicity with several statins, and patient 4 was receiving a combination of pitavastatin 4 mg/d and ezetimibe 10 mg/d following muscular toxicity with other, more potent statins (Table 1).

The PCSK9i administered to all patients was subcutaneous alirocumab 75 mg/14 d, for a mean of 15.6 $\pm$ 6.5 months. Mean baseline levels for total cholesterol, LDL-C, high-density lipoprotein cholesterol (HDL-C), and triglycerides were 262 $\pm$ 21, 155 $\pm$ 19, 60 $\pm$ 14, and 227 $\pm$ 41 mg/dL, respectively, and dropped to 150 $\pm$ 33, 61 $\pm$ 23, 58 $\pm$ 19, and 153 $\pm$ 63 mg/dL by the end of follow-up. All patients reached the target of LDL-C $<$ 100 mg/dL, with percent reductions of 45% to 76% (Figure 1).

There were no reports of drug-related specific adverse reactions, such as injection site reactions or pruritus, and no abnormalities were observed in the liver panel or in creatine kinase levels. None of the patients had unexplained fluctuations in blood concentrations of immunosuppressant drugs, episodes of graft rejection, or infections. Treatment was discontinued in only 1 patient, at the patient's own request (patient 2). Patient

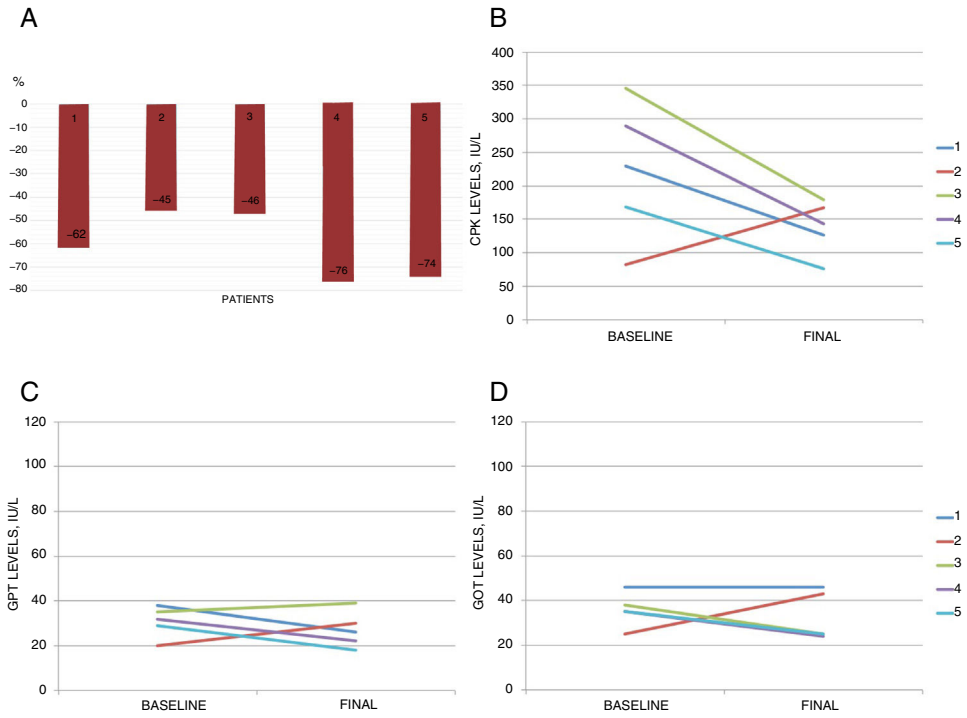

Figure 1. A, percent reduction in low-density lipoprotein cholesterol after the start of treatment with a proprotein convertase subtilisin/kexin type 9 inhibitor (PCSK9i) (alirocumab 75 mg/14 d). B-D, trend for creatine kinase (CPK), glutamic-pyruvic transaminase (GPT), and glutamic-oxalacetic transaminase (GOT) levels (baseline and end of follow-up) during PCSK9i therapy.

3 experienced 2 acute non–Q-wave myocardial infarctions at 2 and 7 months after starting PCSK9i and an ischemic stroke at 12 months. The same patient had been hospitalized 3 years earlier due to unstable angina, and coronary angiography revealed GVD affecting 1 vessel, which was revascularized. Additionally, from the time the patient started alirocumab 75 mg/14 d, he had been taking only ezetimibe 10 mg/d due to statin intolerance, with LDL-C levels > 100 mg/dL persisting until the third cardiovascular event. At that time, pitavastatin 1 mg/d was started; 4 months later, the patient reached the target of LDL-C < 100 mg/dL, experiencing good tolerance and no new adverse events.

In summary, this is the first series in Spain of HT recipients treated with a PCSK9i. To date, only 2 similar series have been published, one with 6 patients and a mean follow-up of 9 months[5] and another with 10 patients and a mean follow-up of 10 months.[6] Our series contributes further data with a longer follow-up (nearly 16 months).

These results indicate the potential safety and efficacy of PCSK9i for treating hypercholesterolemia in HT recipients, although larger studies with longer follow-up are needed to confirm this hypothesis and to evaluate the effects in terms of cardiovascular morbidity and mortality.

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Transthyretin Cardiac Amyloidosis Due to Homozygous Val122Ile Mutation in a Caucasian Man

Amiloidosis cardiaca por transtiretina causada por la mutación Val122Ile en homocigosis en varón de raza blanca

To the Editor:

A 57-year-old man with spinal arthropathy and treated bilateral carpal tunnel syndrome consulted for anorexia, weight loss, and occasional episodes of epigastric pain, nausea, and vomiting. Over the last year he had experienced dyspnea on exertion. The physical examination was unremarkable.

The electrocardiogram showed low voltages, and the echocardiogram depicted severe, asymmetrical left ventricular hypertrophy with septal predominance (19 mm); the left ventricular cavity size was normal, with preserved systolic function (left ventricular ejection fraction, 54%) and a pseudonormal diastolic filling pattern (Figure 1A-B).

On analytic study, performed to investigate a suspected deposit disease, blood count and biochemical findings were normal, with no proteinuria. The serum electrophoretic pattern was normal and free kappa and lambda chains tested negative. Gadolinium cardiac magnetic resonance imaging showed large areas of subendocardial enhancement in both ventricles and the left atrium, consistent with amyloidosis (Figure 1C). On scintigraphy with 99mTc-3,3-diphosphono-1,2-propanedicarboxylic acid, radiotracer deposit in the left ventricle was greater than bone intensity (Figure 1D). Amyloid was not detected in subcutaneous fat or rectal biopsies. The neurological evaluation and sensory-motor nerve conduction studies showed no abnormalities, except for bilateral median nerve involvement.

Five months later, the patient was admitted to the emergency room with acute pulmonary edema. On electrocardiography, the non-dilated left ventricle showed moderate dysfunction and (left ventricular ejection fraction, 38%) and diastolic function had a restrictive pattern. The N-terminal pro-brain natriuretic peptide fraction was 14,879 pg/mL.

Genetic study, carried out to determine whether the amyloidosis resulted from wild-type transthyretin deposit or a hereditary form of the disease, found a homozygous mutation, Val142Ile (classically, Val122Ile), in the transthyretin gene (Figure 2A). In the family evaluation (Figure 2B) there were no known black ancestors, and the deceased parents were cousins. The mother had no known cardiologic history, but the father had an unspecified cardiac condition since the age of 40 years and died suddenly at 65 years. On study of 7 of the 8 siblings, 2 homozygotes were found and all siblings were asymptomatic. Electrocardiography and echocardiography findings were normal in all, except for 1 sister who had the mutation in homozygosis and showed the following: normal electrocardiography findings, bilateral carpal tunnel syndrome,