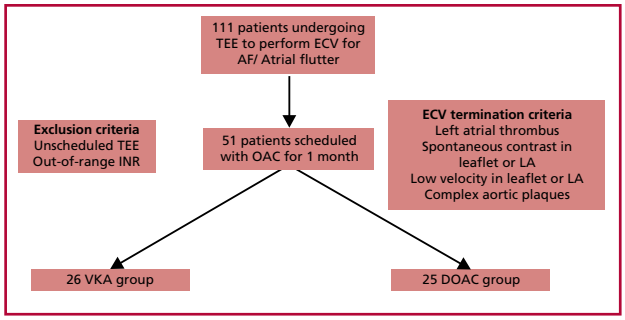
Comparison of the Use and Efficacy of Oral Anticoagulation in Patients Undergoing Transesophageal Echocardiography and Possible Electrical Cardioversion for Atrial Fibrillation: An Initial Report.

Atrial fibrillation (AF) is the most common sustained arrhythmia encountered in clinical practice, and with increasing prevalence. (1) A CHA_2DS_2-VASc score ≥2 in men and ≥3 in women indicates increased risk of stroke and determines who should receive oral anticoagulation (OAC) as IA indication. (1) Both vitamin K antagonists (VKA) and direct oral anticoagulants (DOAC) have been shown to reduce the incidence of stroke, and comparison of both groups of drugs have revealed similar efficacy and safety for stroke prevention. (2)

Cardioversion is a class I indication in patients with symptomatic AF, and electrical (ECV) or pharmacological cardioversion is a common procedure performed worldwide. Anticoagulation is recommended for at least 3 weeks prior to ECV, or transesophageal echocardiography (TEE). (1) There is little information about DOAC success in patients undergoing ECV and their comparison with VKA in terms of efficacy and safety. (3)

The purpose of our study was to assess OAC in patients undergoing ECV in the routine clinical practice of an Argentine center, analyzing the efficacy of the different types of anticoagulants and the incidence of immediate adverse events after the procedure.

All consecutive patients undergoing scheduled ECV for AF/atrial flutter who had previously been submitted to TEE between August 2014 and March 2019 were retrospectively evaluated using our center's database (Figure 1). Demographic, clinical and echocardiographic characteristics were evaluated at the time of the procedure. Inclusion criteria were broad, and all patients signed an informed consent for the procedure. The primary efficacy endpoint was the presence of thrombus during TEE; ECV was cancelled if there was evidence of left atrial thrombus through visualization during the procedure of turbulent flow, spontaneous contrast, complex aortic plaques, or any other reason suggesting risk of embolization, based on the operator's criteria. All the patients in the VKA group received acenocoumarol, while those in the DOAC group received one of the three drugs available in the local market (apixaban, rivaroxaban, or dabigatran). Patients on VKA should have a therapeutic INR range of 2-3.



TEE: transesophageal echocardiography; ECV: electrical cardioversion; AF/Atrial flutter: atrial fibrillation/atrial flutter; INR: international normalized ratio; OAC: Oral anticoagulation; LA: left atrium; VKA: vitamin K antagonists; DOAC: direct oral anticoagulants.

Fig. 1. Study design

Categorical variables were expressed as percentage and continuous variables as mean and standard deviation. Chi square test was used to compare categorical variables, and Student t test or one way ANOVA, as appropriate, to compara continuous variables. SPSS V11.7 statistical package (IBM, USA) was used for statistical analysis.

During the assessment period, 111 patients underwent TEE prior to scheduled ECV for AF or atrial flutter. Among them, all subjects who received properly documented OAC for at least one month prior to the procedure were selected. A total of 51 patients meeting this requirement were included. Subsequently, 3 patients in the VKA group were excluded from the analysis because they had no therapeutic INR range at the time of the procedure.

Table 1 shows the most relevant baseline clinical and echocardiographic data. Among a total of 51 patients, 26 received VKA and 25 DOAC (16% with dabigatran, 24% with rivaroxaban, and 60% with apixaban). In the VKA group, INR on the TEE day was 2.1±0.4, and in the DOAC group all patients received the full dose of the selected drugs. In the VKA group, 15.4% of patients also received aspirin, compared with the DOAC group where only 4% were treated with this agent (p=0.01). In addition, 2 patients in the VKA group and one patient in the DOAC group were on a triple regimen with clopidogrel, aspirin and an anticoagulant (p=ns). The atrial area was significantly greater in VKA patients: 30.5±5.6 cm^2 vs. 29.0±3.9 cm^2 in DOAC patients, p=0.02. There were no intraprocedural adverse events, and no significant differences were found in terms of ECV termination due to thrombus in VKA (8.3%) vs. DOAC (4.0%) patients (p=0.51).

Electrical or pharmacological cardioversion for AF or atrial flutter is common and, although there are limited data in Argentina, international registries report that 1 out of 5 patients with AF/atrial flutter undergoes ECV, with low incidence of intraprocedural adverse events (<1%). The ORBIT-AF II registry reported 0.3% asystole and 0.1% ventricular arrhythmias, (4) and similar outcomes were found in other registries, with around 1% intraprocedural events. (5)

Table 1. Baseline clinical and echocardiographic characteristics

	VKA	DOAC	p value
n	26	25	
Age (years)	70.6±9.2	71.4±9.4	0.50
Male sex (%)	69.2	72.0	0.53
Hypertension (%)	80.8	65.2	0.09
Diabetes (%)	19.2	20.0	0.81
Chronic kidney disease (%)	0.0	4.0	0.67
Creatinine (mg/dL)	1.2±0.5	1.0±0.24	0.71
Previous stroke (%)	0.0	0.0	NS
INR	2.1±0.4	NA	
CHA2DS2-VASc	3.2±1.1	2.7±1.3	0.55
LA area (cm^2)	30.5±5.6	29.0±3.9	0.02

VKA: vitamin K antagonist; DOAC: direct oral anticoagulants; INR: international normalized ratio; LA: left atrial.

A meta-analysis reported evidence of similar efficacy and safety when comparing VKA and DOAC, (5, 6) and even a reduction in mortality for DOAC patients. (2) At present, treatment guidelines recommend the use of DOAC over VKA for stroke prevention in patients with nonvalvular AF/atrial flutter. (2) While the use of DOAC in Argentina has been increasing, their use over traditional anticoagulants is limited, possibly due to their high cost and lack of access to the antidote in case of emergency.

This analysis has significant limitations. Firstly, it is a small observational registry. As such, no final conclusions can be drawn; it is only an approach to what happens in daily practice. Secondly, it is a retrospective analysis; the original registry was not conducted to evaluate the efficacy of anticoagulant agents; therefore, confounding causes that might increase or reduce their efficacy were not evaluated. Thirdly, operators were not blinded to the medication the patient had received, so some bias in evaluating TEE outcomes cannot be excluded. And fourthly, it is a single-center registry in the City of Buenos Aires. In many other parts of the country, TEE is not performed along with scheduled ECV, and there is no access to DOAC.

Despite these limitations, the registry also has its strengths, as it is the first study of its kind presented in our country and all patients were included consecutively, turning it into a "real world" observation.

In our experience, there were no differences between DOAC and VKA in the incidence of thrombus detected by TEE in patients scheduled for ECV due to AF, showing similar safety results for both drugs.

Conflicts of interest

None declared.

(See authors' conflicts of interest forms on the website/ Supplementary material).

Ethical considerations

Not applicable.

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Combined Pulmonary Hypertension

Pulmonary hypertension (PH) is a pathophysiological disorder that can occur in the presence of cardiac and respiratory conditions, worsening its prognosis and increasing morbidity and mortality. (1, 2) Depending on its etiology, PH is classified into five groups. (3) Group 2 consists of PH secondary to left-heart diseases, and represents about 70% of patients with PH. (4)

Use of specific drugs is exclusive to treat pulmonary artery hypertension (group 1) and chronic thromboembolic pulmonary hypertension (group 4), in contrast with the rest of the groups —in which therapy is based on the underlying condition and the use of specific treatment is not indicated (class of recommendation and level of evidence III C ESC/ERS 2015 Guidelines for the Diagnosis and Treatment of Pulmonary Hypertension).

To date, the available evidence of specific therapy in patients with group 2 PH has not shown clinical improvement, and in many cases the prognosis has

worsened. Studies are currently underway, but have not been completed yet. (5)

In daily practice, we see patients with PH secondary to left-heart diseases who, despite adequate treatment according to guidelines and recommendations, develop a predominant precapillary component with signs of right heart failure, constituting a real medical challenge. We report a representative case of this situation.

This is the case of a 17-year-old male patient with a history of Alström syndrome due to a mutation of the AMLS1 gene on chromosome 2p. As part of this syndrome, the patient presented hypothyroidism, hypogonadotrophic hypogonadism, growth retardation, retinitis pigmentosa and chronic heart failure secondary to restrictive cardiomyopathy since the age of two months, severe group 2 pulmonary hypertension and also permanent atrial flutter

From childhood he was treated in various centers in the country, with different standard therapeutic schemes for heart failure. He consulted our team three years ago after ruling out the possibility of cardiopulmonary transplantation, with clinical deterioration despite the established treatment.

At the first visit, in 2018, he presented clinical signs of right heart failure, and was medicated with: spironolactone 12.5 milligrams (mg) per day, furosemide 20 mg per day, digoxin 0.25 mg per day, acetylsalicylic acid 50 mg per day, acenocoumarol according to hematological scheme, levothyroxine 50 micrograms (mcg) per day, bosentan 62.5 mg once a day and tadalafil 5 mg every 12 hours. He had a previous right catheterization that showed findings compatible with severe combined pre- and post-capillary pulmonary hypertension. (Table 1 A)

It was decided to perform a negative fluid balance by increasing the dose of oral furosemide to 60 mg per day and spironolactone to 25 mg per day; the specific medical treatment brought by the patient was not withdrawn, adjusting the dose of bosentan to 62.5 mg every 12 hs, tadalafil 10 mg every 24 hours and bisoprolol 2.5 mg per day was added.

A Doppler echocardiogram was performed, which reported: right chamber dilation with decreased right ventricular systolic function, severe left ventricular dysfunction (LVEF 28%), severe tricuspid regurgitation.

The admission laboratory showed as positive data a brain natriuretic peptide (BNP) of 558 pg / mL (normal value less than 100 pg / mL), and iron deficiency, for which an intravenous iron supplement was added.

A 6-minute walk test was performed, walking 131 meters (m), with a 7-point drop in oxygen saturation and Borg 7-8, so it had to be suspended after 3 minutes.

Two months after the changes introduced, the patient improved his functional class, and did not present clinical signs of right heart failure; a new 6-minute walk test was performed where he traveled 324 m, without a drop in oxygen saturation and with a score of 3 in Borg Scale.

Months later, he was hospitalized for decompensated right heart failure, Doppler echocardiogram with right ventricular dilation, and passive collapse of the secondary interventricular septum. Medical treatment with negative fluid balance and inodilator support (dobutamine) was decided. A new right catheterization was performed. (Table 1 B). Assessing the prevailing pre-capillary component of his pulmonary hypertension, a therapeutic trial with subcutaneous treprostinil was started, starting with 4 ng / Kg / min, and titrated up to 40 ng / Kg / min; the dose of tadalafil was increased to 30 mg per day; bosentan was discontinued and dapagliflozin 10 mg per day was started. The patient had a good evolution and was discharged.

At three months of evolution with the new therapy, he was in functional class II of the New York Heart Association (NYHA), with no signs of heart failure. Ambrisentan 5 mg per day was added to the specific therapy and tadalafil was optimized to 40 mg per day.

Once the therapeutic changes were established, a new BNP was requested: 224 pg / mL with a frank decrease compared to the previous one and a 6-minute walk test where he walked 400 m, with Borg 3, without a drop in oxygen saturation.

After two years of initiating triple therapy, the patient is in NYHA functional class I / II, with no clinical signs of heart failure, with a BNP of 134 pg / mL; in the last control he traveled 400 m in the test of a 6-minute walk with a LVEF that reached 45%. (Table 1 C)

Table 1. Hemodynamic parameters of right catheterization in the course of treatment

PARAMETERS	VALUES		
	A Previous to visit 2018	B 2019	C 2021
RAP mmHg	21	18	9
SVRI UW/m²	17.9	32.35	14.84
CO L/min	2.8	2.05	4.73
CI L/min/m²	2.1	1.89	4.11
SPP mmHg	72	ND	35
DPP mmHg	44	ND	15
MPP mmHg	51	45	26
PVR UW	9.15	16.37	6.89
TPG mmHg	27	31	18
DPG mmHg	20	ND	7
PCP mmHg	24	14	8
SvO2 %	ND	70	70

Comparison in right catheterization. RAP: right atrial pressure; SVRI: systemic vascular resistance index; CO: Cardiac output CI: cardiac index; SPP: systolic pulmonary pressure; MPP: mean pulmonary pressure; PVR: pulmonary vascular resistance; TPG: transpulmonary pressure gradient; DPG: diastolic pulmonary gradient; PCP: pulmonary capillary pressure; SvO2: venous oxygen saturation; ND: no data.

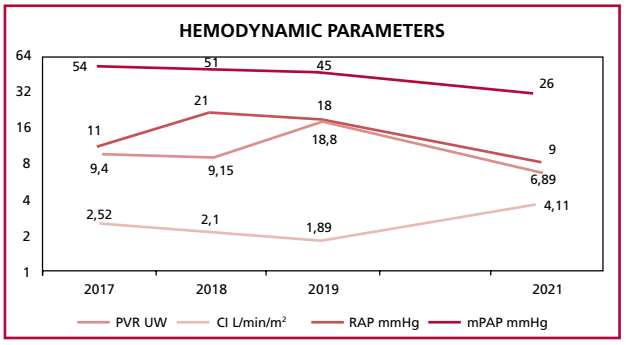

Fig. 1. Comparison of hemodynamic data. PVR: pulmonary vascular resistance; CI: cardiac index; RAP: right atrial pressure; mPAP: mean pulmonary arterial pressure

Figure 1 illustrates the successive hemodynamic changes according to the clinical picture and the established therapy.

We report a clinical case of group 2 PH due to restrictive cardiomyopathy with heart failure, severely impaired LVEF, secondary to genetic syndrome, and with a combined pre- and post-capillary component.

Considering the currently available evidence and according to the latest recommendations, a specific drug therapy for pulmonary arterial hypertension, such as endothelin receptor antagonists, prostanoids and IP agonists, phosphodiesterase-5 inhibitors, and soluble guanylate cyclase stimulators would be contraindicated in this group, since in many cases there would be no clinical and hemodynamic improvement, and in other cases prognosis would worsen. Therefore, specific therapy is used exclusively in groups 1 and 4. However, a subgroup of patients would have genetic susceptibility to develop pulmonary arterial remodeling, similar to group 1 PH, i.e., these patients have a disproportionate increase in mean pulmonary pressure compared to the increase of filling pressures. Given the non-response to the standard options for heart failure, it was decided to optimize specific off-label treatment targeting the prevalent precapillary component, resulting in a good and sustained hemodynamic and clinical response.

There are certain selected patients who could share the pathophysiological characteristics of various groups of PH and receive a specific therapy, since they would have a certain predisposition to a behavior similar to that of group 1, with a disproportionate increase in remodeling of the pulmonary bed. In the case reported, the improvement in clinical and hemodynamic parameters and in left ventricular ejection fraction demonstrate that by using a specific treatment with emphasis on this prevalent precapillary component, a clinical and hemodynamic benefit is obtained. It should be pointed out that the treatment of the underlying condition was insufficient in our patient, and future therapeutic options are limited by the available evidence.

At present, there is absence of scientific papers on this subject, and the few available lack statistical significance in hard points; therefore, further research in this field is needed, as this may lead to a change in the complex management of certain patients that represent a new phenotype in heart failure.

Conflicts of interest

None declared.

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Ethical considerations

Not applicable

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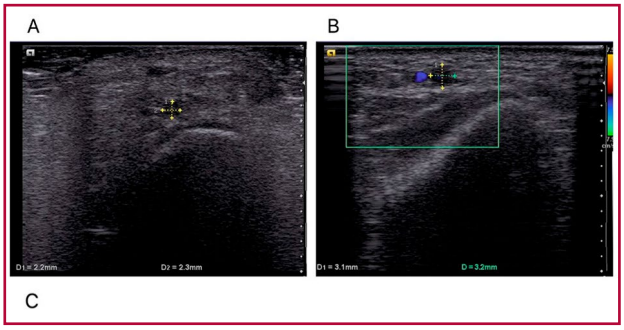
Use of Bushido Technique in Percutaneous Coronary Intervention for Chronic Total Occlusion of the Right Coronary Artery

We present the case of a 66-year-old male patient with several cardiovascular risk factors: dyslipidemia, systemic arterial hypertension, type 2 diabetes mellitus, and smoking.

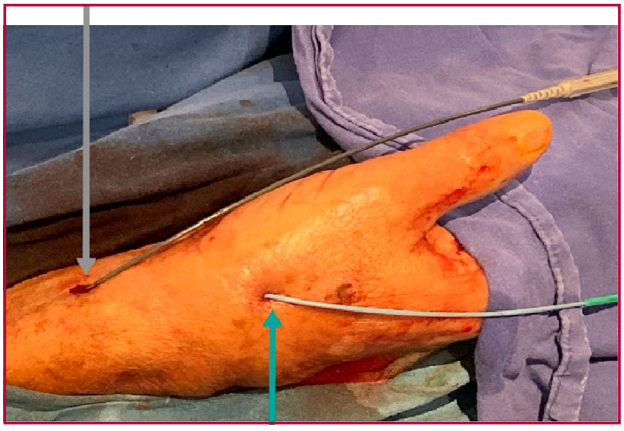
His cardiovascular history started with dyspnea in

May 2019. In June 2019, he suffered a non-ST-segment elevation myocardial infarction (NSTEMI), and underwent a percutaneous coronary intervention (PCI) of the left anterior descending and circumflex arteries. A stratification study was carried out by means of technetium-99m myocardial perfusion and pharmacological stress with dipyridamole to perform PCI for chronic total occlusion (CTO) of the right coronary artery (RCA).

Percutaneous coronary intervention was performed through the right radial artery as the only vascular access using the Bushido technique. The distal and proximal radial artery was measured preoperatively with Doppler ultrasound (USG) (Figures 1 A & B). Punctures were performed with Seldinger technique, inserting a sheathless Ikari 5Fr (TERUMO®) left guiding catheter in the proximal radial artery, and a Terumo Radial TIG 5Fr catheter in the distal radial artery (Bushido technique) (Figure 1 C). Its advancement was performed using the balloon-assisted



Proximal radial artery. sheathless, catheter Ikari left 5Fr, Balloon-Assisted Tracking technique



Distal radial artery. sheathless, catheter TIG 5Fr, Balloon-Assisted Tracking technique

Fig. 1. Vascular ultrasound of the right radial artery. A. The distal radial artery measures 2.2 x 2.3 mm in diameter. B. Proximal radial artery measures 3.1 x 3.2 mm in diameter. C. Bushido technique. A. Right coronary cannulation, sheathless Ikari 5Fr left catheter, Balloon-assisted tracking technique. B. Left coronary cannulation, sheathless TIG 5Fr catheter, Balloon-assisted tracking technique.

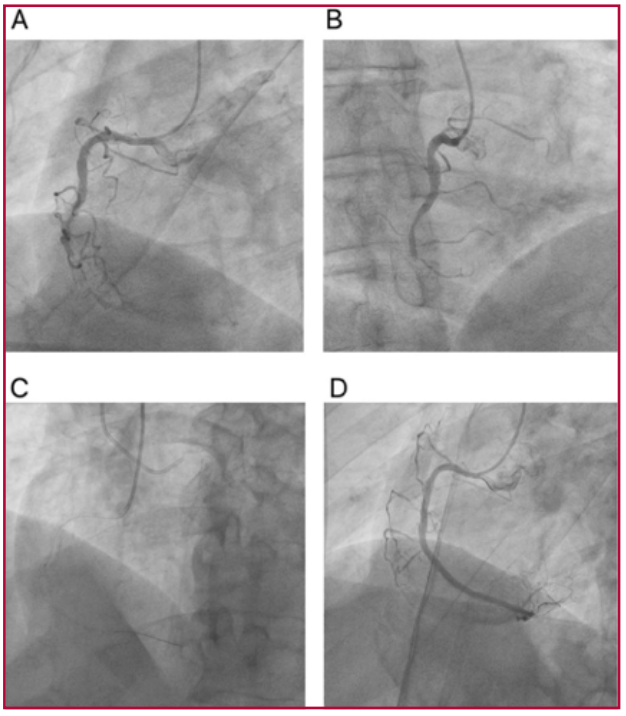


Fig. 2. Coronary angiography showing chronic total occlusion of the right coronary artery in the mid segment, TIMI flow 0, J-CTO SCORE: 2 points. A. 40° left anterior oblique view. B. 30° right anterior oblique view. Coronary angiography. C. CTO crossing with 0.014 Pilot 150 coronary guidewire with microcatheter support. D. Final angiography in 40° left anterior oblique projection of the right coronary artery with TIMI 3 flow.

tracking (BAT) technique. Coronary angiography using double coronary cannulation was performed, observing CTO with a 2-point J-CTO score (Figures 2 A & B). The crossing of the occlusion was achieved in 20 minutes, using the antegrade technique with wire escalation. Predilation was performed with the following balloon sizes: 1.0 x 5 mm, 1.25 x 10 mm, 1.5 x 10 mm, 2.0 x 20 mm, and 2.5 x 10 mm. In the presence of a non-dilatable calcified plaque, a 2.5 x 10 mm cutting balloon was used. Then, dilation was performed with the following balloons: 2.5 x 15 mm and 3.0 x 20 mm. A 2.5 x 38 mm and 3.0 x 38 mm drug-eluting stent (DES) was placed from the distal and middle segment of the artery, ending with proximal optimization technique (POT) using a non-compliant 3.5 x 15 mm balloon. The procedure was completed without complications, and the control angiography showed TIMI 3 epicardial flow, presenting no-reflow phenomenon, dissection, perforation or thrombosis (Figures 2 C & D). Angiography was performed in the radial artery without complications, and hemostasis was carried out with a distal and a proximal radial band.

In chronic total occlusions, the advancement technique can be performed using an antegrade approach with wire escalation and reentry dissection or a retrograde approach with wire escalation and hybrid re-

entry dissection; in these cases, double coronary cannulation through two arterial accesses is performed. (1) Few cases of PCI-CTO with a single radial access using the Bushido technique have been reported. The first case was described by Fuminobu Yoshimachi, et al. (2) The safety of the radial approach using a hydrophilic sheathless catheter is associated with lower rates of complications in vascular access. (3) The use of distal radial access for PCI currently shows a lower rate of complications and better hemostasis versus other vascular accesses. (4) Adequate ultrasound evaluation of the size of the radial artery is important to select the size of the introducer or catheter to be used, thus reducing complications during the procedure. (5)

In the present case, the use of a single access through the radial artery, after ultrasound evaluation of the diameters and using a sheathless guide catheter with simultaneous proximal and distal radial access (Bushido technique), is feasible and safe for successful PCI in complex coronary disease, in this case, CTO.

Conflicts of interest

None declared.

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Ethical considerations

Not applicable

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