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LETTER TO THE EDITOR

New approach to the prevention of stroke in patients with non-valvular fibrillation in hemodialysis: percutaneous closure of left atrial appendage

Nuevo enfoque en la prevención del ictus en pacientes con fibrilación auricular no valvular en hemodiálisis: cierre percutáneo de orejuela izquierda

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Mr. Editor:

The prevention of cardioembolic episodes in patients with atrial fibrillation (AF) and high hemorrhagic risk entails a therapeutic challenge, inasmuch as advisability or not of anticoagulating should be assessed versus the risk of bleeding.

Patients with end-stage renal disease (ESRD) have a higher prevalence of AF than the general population (between 12% and 27%), higher tendency towards hypercoagulability and thrombotic phenomena and an increased risk of hemorrhage due to primary hemostasis alterations (platelet dysfunction)[1].

The most widely used compounds as anticoagulant treatment in nephropathic patients are anti-vitamin K drugs (warfarin and acenocoumarol). In patients with ESRD, their use is controversial, not only due to an increased risk of bleeding, but because of difficulties to maintain INR within limits[2], tissue calcification, calciphylaxis and increased arteriosclerosis, as well as an increased risk for hospitalizations of cardiovascular cause[3]. In addition, the use of new direct acting anticoagulants is limited because there is no scientific evidence to support their efficacy, since patients with ESRD were excluded from the clinical trials that have demonstrated their benefit versus warfarin[4].

For all the above, patients with ESRD represent an attractive scenario where left atrial appendage closure (LAAC) may derive a clear clinical benefit.

Six patients with ESRD on hemodialysis program, with diagnosis of AF and problems with oral anticoagulation (OAC), were jointly selected by the Nephrology and Cardiology Departments for LAAC, between June 2017 and December 2018. All patients gave their written consent. The exclusion criteria were having an OAC indication for a cause other than AF, severe pericardial effusion, prior atrial septal defect closure, intra-cardiac thrombus, severe chronic liver disease and express refusal of the patient. Clinical characteristics of the selected individuals are presented in table 1.

The device used in all cases was Watchman® (Boston Scientific Corporation, Marlborough, Massachusetts, USA). Implantation was successful in all cases and no complications related to the device or the procedure were recorded. All patients were discharged within 24 hours after the intervention. Table 2 summarizes the main technical details.

In the series of the authors, the success rate is absolute (100%) and the rate of complications during the procedure, nonexistent (0%), without losing sight that the number of patients was small. This refutes the

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Table 1. Clinical characteristics of included patients and at control three to six months of the intervention

Patient	1	2	3	4	5	6
Gender	Male	Male	Female	Male	Female	Male
Age	71	78	47	79	88	78
Cause: Nephropathy	DM + NAS	DM + NAS	PKD	Not established	NAS + PKD	Renal tumor
Time on dialysis (mo)	90.3	28.1	27.3	74.5	32.6	17.3
ChI	13	13	3	8	10	9
$CHA_2DS_2VAS_C$	6	5	3	4	4	3
HAS-BLED	6	5	4	6	6	5
AC for AF	Permanent	Paroxysmal	Paroxysmal	Paroxysmal	Paroxysmal	Paroxysmal
Previous treatment	LMWH + Clop	Clop	Acen	Acen + Clop	Warf	Acen
LAAC indication	Serious or recurrent hemorrhage	Labile INR	Serious or recurrent hemorrhage	Serious or recurrent hemorrhage	Serious or recurrent hemorrhage	Serious or recurrent hemorrhage
3-6 m control TEE	No leakage or thrombi on device	No leakage or thrombi on device	No leakage or thrombi on device	No leakage or thrombi on device	Leakage < 5 mm	No leakage or thrombi on device
Treatment	None	ASA	ASA	ASA	ASA	ASA
Episodes	Withdrawal due to sepsis	No episodes	No episodes	No episodes	No episodes	Sudden death at 12 Months

DM: diabetes mellitus; NAS: nephroangiosclerosis; PKD: polycystic kidney disease; ChI: Charlson index; LMWH: low molecular weight heparins; Clop: clopidogrel; Acen: acenocoumarol; Warf: warfarin; LAAC: left atrial appendage closure; TEE: transesophageal echo; ASA: acetylsalicylic acid; AC: anticoagulation; AF: atrial fibrillation.

Table 2. Technical characteristics of the procedure

Appendage morphology (%)	
"Chicken wing" "Windsock" "Cauliflower"	4 (66.6) 1 (16.7) 1 (16.7)
Ostium largest diameter (mm)	22.2 ± 1.3
Ostium smallest diameter (mm)	17.7 ± 1.5
Depth (mm)	23.5 ± 3.7
Device size (mm)	26.5 ± 1.2
Endoscopy time (min)	23.75 ± 3
Implantation total duration (min)	75 ± 38
Amount of contrast (ml)	72.5 ± 15
Implant success (%)	6 (100)
Complications during the procedure (%)	0
Treatment after implantation (%)	
Double anti-aggregation	5 (93.3)

belief that patients with ESRD who undergo interventional cardiology procedures have a higher risk for complications, given that they are more fragile than the general population and have larger numbers of comorbidities[5]. Chak et al. reported a series of 196 patients undergoing LAAC where they compared two groups, with and without CKD, with a higher rate of peri-procedural complications (9.9% vs. 2.4%, p = 0.04) being found in the group with renal function deterioration, at the expense of cardiac tamponade (8.5% vs. 0.8%, p = 0.01)[6]. Genovesi et al. recently published data from the largest series reported thus far, and showed in 50 patients that, despite advanced age and multiple comorbidities suffered by patients with ESRD, implantation of the device is feasible and safe, with a high rate of success (100%) and a low complication rate during and after the procedure (only three minor complications were described[7]). In turn, Kefer et al. published a series where the effect CKD has on the prevention of stroke is analyzed in patients undergoing LAAC; in this series, patients with varying degrees of CKD were considered, including those with ESRD (stage V). In them, the success rate in the procedure was also high (> 98%) and that of complications low (5.1%), with no differences being observed between patients with and without impaired renal function, or between those who showed mild deterioration or ESRD[8]. Higher knowledge on LA

anatomy, rational use of imaging techniques, larger accumulated experience in the implant of this type of devices, as well as proctoring software programs provided by the manufacturers, make this type of procedures to be safe even when the hemodynamics unit is in the "learning curve" as in this case.

During a median follow-up of 272 days, and with controls with transesophageal echocardiography (TEE) at three, six and 12 months, no device-related thrombi have been found in any case, and only a small leak in one of them, which did not require intervention, since it was lower than 5 mm. Moreover, no cardioembolic episode or significant bleeding (BARC > 2) have been recorded so far.

Although procedure-related mortality has been null, two patients have died, one due to sepsis and then other due to sudden death; although it cannot be ruled out that the latter was of embolic cause, it most likely was due to the advanced underlying heart disease the patient had.

Clinical complexity of these patients is very high and measuring it with Charlson comorbidity index (ChI) has been tried, not so much to evaluate the patients but to compare them with those of other series in the future. The ChI was resorted to because it has been widely used as a variable of adjustment in different prognostic models[9]. The ChI of the authors' patient series is considerably high (mean of 9.3): both deceased subjects were among those with the highest scores (13 and 9). It is possible that in the future this index will be able to help select, within this population of patients, those can benefit more from this preventive measure in the medium and long term.

Although this series includes a reduced number of patients and statistical conclusions cannot be inferred, the perspectives for the technique are highly promising. However the "Left atrial appendage occlusion vs. usual care in patients with atrial fibrillation and severe chronic kidney disease" (WatchAFIB) and "Strategy to prevent hemorrhage associated with anticoagulation in renal disease management" (STOP HARM) clinical trials were terminated by the end of 2018 due to problems in patient recruitment. The Registry of left appendage percutaneous closure with the Watchman® device in patients with non-valvular atrial fibrillation and chronic kidney disease on hemodialysis (NCT NCT03446794) is currently underway, which is a Spanish multi-center registry that has a combined endpoint that includes stroke or transient ischemic attack, BARC-2 bleeding and systemic embolism at 24 months, as well as safety secondary endpoints related to the procedure and echocardiographic follow-up.

It is clear that the nephrologist is for the moment reluctant to use an invasive technique as a preventive measure, even if it means withdrawing OAC and its known benefits from patients, and also the cardiologist, who is *a priori* reluctant to treat patients with considerable comorbidity. Therefore, the authors highlight the need to establish communication channels between both specialties, in order to enable a correct selection of patients and thus optimize the benefit offered by this technique.

Conflict of interests

None.

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Ethical disclosures

Protection of people and animals. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors declare that no patient data appear in this article.

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