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Impact of chronic kidney disease on left atrial appendage occlusion for stroke prevention in patients with atrial fibrillation☆

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ABSTRACT

Background: Left atrial appendage occlusion (LAAO) using the Amplatzer cardiac plug (ACP) is a preventive treatment of atrial fibrillation related thromboembolism.
Aim: To assess the safety and efficacy of LAAO in patients with chronic kidney disease (CKD).
Methods: Among the ACP multicentre registry, 1014 patients (75 ± 8 yrs) with available renal function were included.
Results: Patients with CKD (N = 375, CHA2DS2-VASc: 4.9 ± 1.5, HASBLED: 3.4 ± 1.3) were at higher risk than patients without CKD (N = 639, CHA2DS2-VASc: 4.2 ± 1.6, HASBLED: 2.9 ± 1.2; $p < 0.001$ for both). Procedural (97%) and occlusion (99%) success were similarly high in all stages of CKD. Peri-procedural major adverse events (MAE) were observed in 5.1% of patients, 0.8% of death, with no difference between patients with and those without CKD (6.1 vs 4.5%, $p = 0.47$). In patients with complete follow-up (1319 patients years), the annual stroke + transient ischaemic attack (TIA) rate was 2.3% and the observed bleeding rate was 2.1% (62 and 60% less than expected, similarly among patients with and those without CKD). Kaplan–Meier analysis showed a lower overall survival (84 vs 96% and 84 vs 93% at 1 and 2 yrs. respectively; $p < 0.001$) among patients with an eGFR <30 ml/min/1.73 m^2.

☆ For all the authors: there are no conflicts of interest. The authors take the responsibility for all aspects of reliability and freedom from bias of the data presented and their discussed interpretation.

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Conclusion: LAAO using the ACP has a similar procedural safety among CKD patients compared to patients with normal renal function. LAAO with ACP offers a dramatic reduction of stroke + TIA rate and of bleeding rate persistent in all stages of CKD, as compared to the expected annual risk.

1. Introduction

Percutaneous left atrial appendage occlusion (LAAO) is an alternative therapeutic option for stroke prevention in patients with atrial fibrillation (AF). [1–5]. The first randomised trial PROTECT AF [6] showed that LAAO with the WATCHMAN device (Boston Scientific, Marlborough, MA, USA) reduced mortality and stroke rate compared to warfarin, at 5 years follow-up. As compared with the initial attempts [3,7–8], experienced operators have shown a significant reduction of serious periprocedural complication rate around 4–5% [5,9]. Recently, it has been demonstrated that LAAO using the Amplatzer Cardiac Plug (ACP; St. Jude Medical, St Paul, MN, USA), reduces the theoretical risk of both, stroke and bleeding [5] in patients with AF.

Renal failure patients are well known to be at high risk of procedural complications and to have a worse outcome after transcatheter interventions [10–11]. The risk of cardiovascular mortality increases in patients with chronic kidney disease (CKD) stage 3 [12]; recently, this category was subdivided in stage 3a and 3b [13]. The prevalence of AF in patients with CKD is high and renal failure represents a main risk factor for stroke, leading to a strong recommendation for anticoagulation therapy [14]. On the other hand, CKD significantly increases the risk of major bleeding in patients with AF [15–16]. Novel anticoagulants were approved for stroke prevention in AF [17–19] but their use is still controversial in the setting of CKD, especially among end-stage renal failure patients (eGFR <30 ml/min/m^2) [20]. LAAO, as a non pharmacological approach, could be a potential alternative in patients with AF and CKD.

The aim of the present study was to assess the procedural safety of LAAO in patients with AF and CKD, the efficacy on stroke and bleeding prevention, and finally to evaluate the impact of the stages of CKD on the clinical outcome after LAAO using the ACP.

2. Methods

Between December 2008 and November 2013, consecutive patients undergoing LAAO using the ACP in 22 centres, were prospectively included in the multicentre ACP registry, published elsewhere [5]. Demographics, baseline characteristics, indications for LAAO, CHA_2DS_2-VASc and HAS-BLED scores, antithrombotic medication, procedural details, periprocedural adverse events, clinical and echocardiographic follow-up were prospectively collected in a dedicated database. Among this cohort, patients with available serum creatinine and glomerular filtration rate values were included in the current substudy. An informed consent was obtained in each patient; the study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki.

2.1. Renal failure

The estimated glomerular filtration rate (eGFR) was calculated with the CKD-EPI formula [21]. By using the creatinine serum level, the age, the gender and the race of the patient, the CKD-EPI equation was expressed as:

$$\mathrm{GFR} = 141 \times \min(\mathrm{Scr}/\kappa, 1)^{\alpha} \times \max(\mathrm{Scr}/\kappa, 1)^{-1.209} \times 0.993^{\mathrm{Age}} \times 1.018\ [\text{if female}] \times 1.159\ [\text{if black}].$$

According to the guidelines [22], CKD was defined as eGFR <60 ml/min per 1.73 m^2 and CKD stages were classified based on the eGFR values: stage 1 = ≥90 ml/min/1.73 m^2, stage 2 = 60 to 89 ml/min/1.73 m^2, stage 3a = 45 to 59 ml/min/1.73 m^2, stage 3b = 30 to 44 ml>/min/1.73 m^2, stage 4 = 15 to 29 ml/min/1.73 m^2 and stage 5 = <15 ml/min/1.73 m^2.

In addition, patients on dialysis and those with previous renal transplantation were noted.

2.2. Procedural success

Procedural success was defined as successful implantation of the ACP in the left atrial appendage (LAA).

2.3. Periprocedural complications

Periprocedural complications (occuring during 0–7 days after procedure or before hospital discharge, whichever last) included death, myocardial infarction, stroke, transient ischaemic attack (TIA), systemic embolism, air embolism, device embolisation, major bleeding (requiring surgery or transfusion) and cardiac tamponade.

Periprocedural major adverse events (MAE) included death, stroke, systemic embolism and complication requiring major surgical or endovascular intervention (major bleeding, tamponade, device migration treated by snare or surgery) occurring between 0.7 days post procedure or before hospital discharge, whichever latest.

2.4. Clinical follow-up

Patient survival and occurrence of clinical events during the follow-up were determined by review of medical records or phone contact of patients implanted successfully. Adverse events during follow-up included death (cardiovascular or non-cardiovascular), stroke, TIA, systemic embolism and major bleeding. Antithrombotic medication was recorded at the admission date and at last follow-up visit. The recommendation by the manufacturer is to give a low dose of acetylsalicylic acid for a long period with clopidogrel (75 mg/d) for at least 1 month. So, a successful LAAO implies the absence of anticoagulant therapy. Nevertheless, the choice and the duration of antithrombotic therapy was individualised, depending on the patient characteristics and physician preference.

2.5. Efficacy on stroke, TIA and systemic embolism prevention

LAAO efficacy on stroke, TIA and systemic embolism prevention was tested by comparing the actual event rate at follow-up with the predicted event rate by the CHA_2DS_2-VASc score [23]. Individual patient annual risk was recorded and the average annual risk for the whole study population was calculated. The total number of thromboembolic events (stroke, TIA and systemic embolism) during both the periprocedural and follow-up periods was divided by the total patient-years of follow-up and was multiplied by 100 in order to get the actual annual rate of thromboembolism. Thromboembolism reduction was calculated as follows (estimated % − actual% event rate) / estimated % event rate.

2.6. Efficacy on bleeding prevention

The total number of major bleeding events during both the periprocedural and follow-up periods was compared with the events predicted by the HAS-BLED score [24]: bleeding reduction was calculated as follows: (estimated% − actual% event rate) / estimated% event rate.

2.7. Echocardiographic follow-up

Implanted patients underwent a transoesophageal echocardiography (TOE) at follow-up. Residual leak was graded using the width of the Doppler colour jet as trivial (<1 mm), mild (1–3 mm) or significant (>3 mm). Occlusion success was defined as a procedural success without a significant residual leak. The presence of thrombus on the device was noted as well.

2.8. Statistical analysis

Continuous variables are presented as mean ± 1 standard deviation. Categorical variables are presented as counts and percentages. Continuous variables were tested by using the independent samples t-test and categorical variables by using the Fischer's exact test.

Univariate analysis was done using the Cox proportional-hazards method. Estimates for freedom from the composite of death and MAE were obtained by the Kaplan–Meier estimation method. A p value <0.05 was considered statistically significant. Analyses were performed using the SPSS version 15.0 (SPSS Inc., Chicago, Illinois).

3. Results

3.1. Patients

Of the cohort of 1053 patients enrolled in the ACP multicentre registry, serum creatinine and eGFR values were available in 1014 and they were included in the study. Baseline characteristics are listed in Table 1. There were 183 patients categorised in stage 1, 456 in stage 2,