Supplementary material

Diseño de un registro de fibrilación auricular y riesgo embólico en México: CARMEN-AF

(Fibrilación Auricular y Riesgo de Tromboembolias EN Mexico)*

* This translation corresponds to the original article published in Spanish in: J.A. González-Hermosillo, M.F. Márquez, S. Ocampo-Peña, R.Y. Villanueva, E. Velázquez, J.M. Enciso, R. Robledo, J. Gómez, S. Lara, Design of an atrial fibrillation and embolic risk registry in Mexico: CARMEN-AF, Arch. Cardiol. Mex. 87 (2017) 5–12. doi:10.1016/j.acmx.2016.11.003.

Resumen

Objetivo: La fibrilación auricular (FA) es una de las arritmias más comunes y su prevalencia aumenta con la edad. Se asocia con alto riesgo de embolia cerebral. La prevención de dichas tromboembolías se realiza mediante anticoagulantes orales, que en nuestro país parecen estar subutilizados. El Registro CARMEN-AF tiene como objetivo primario determinar cuál es el estado actual de la tromboprofilaxis de la FA no-valvular en México. Como objetivo secundario pretende conocer la morbi-mortalidad asociada a la FA no-valvular en por lo menos un año de seguimiento.

Métodos: El Registro CARMEN-AF es un estudio observacional, longitudinal, multicéntrico y nacional, sobre el empleo de los anticoagulantes orales en pacientes con FA no-valvular, que pretende la inclusión de pacientes mayores de 18 años de edad diagnosticados con FA no-valvular durante los últimos 6 meses y con al menos un factor de riesgo para desarrollar una tromboembolia de acuerdo con la escala de CHA2DS2-Vasc. Serán recolectados datos demográficos y clínicos en las visitas clínicas habituales a lo largo de un seguimiento de dos años. El reclutamiento inició el 19 de septiembre de 2014 y se prevé la inclusión del último paciente el 18 de septiembre de 2016. Se estima la inclusión de 1,200 pacientes dada la incidencia de FA reportada a nivel mundial y tomando en consideración la población mexicana total.

Conclusiones: El registro de fibrilación auricular y riesgo embolico en Mexico (CARMEN-AF) permitirá conocer el estado actual de la tromboprofilaxis en pacientes con FA no-valvular, y
permitira obtener una panoramica del cumplimiento de las guias nacionales e internacionales de practica clinica en esta materia.

Conteo de palabras: 261

Palabras clave: Anticoagulante oral; Fibrilacion auricular; Registro; Tromboprofilaxis, Mexico
Objective: Atrial fibrillation (AF) is one of the most common arrhythmias, and its prevalence increases with age. It is associated with high risk of stroke. The prevention of such thromboembolism is accomplished with oral anticoagulants, which in our country seem to be underused. CARMEN-AF registry aims primarily to determine the current status of thromboprophylaxis of non-valvular AF in Mexico. A secondary objective is to know the morbidity and mortality associated with non-valvular AF in at least one year of follow-up.

Methods: CARMEN-AF registry is an observational, longitudinal, multicenter, and nationwide survey about the use of oral anticoagulants in patients with non-valvular AF. Patients 18 years old or older, diagnosed with AF during the last 6 months, and with at least one risk factor of thromboembolism based in the CHA2DS2-Vasc score are being selected. Demographic and clinical data will be collected during the visits to their usual clinic with a follow-up of two years. The recruitment began on September 19, 2014, and the inclusion of the last patient is expected on September 18, 2016. According to the reported incidence of AF globally and considering the total Mexican population, the inclusion of 1,200 patients is estimated.

Conclusions: The Atrial Fibrillation and Embolic Risk Registry (CARMEN-AF) will reveal the current status of thromboprophylaxis in patients with non-valvular AF and will allow to get an overview of the national and international clinical practice guidelines accomplishment in this area.

Word count: 236

Keywords: Atrial fibrillation; Oral anticoagulants; Registry; Thromboprophylaxis, Mexico
**Introduction**

Atrial fibrillation (AF) is the most common sustained arrhythmia encountered in clinical practice.\(^1\) It affects about 1-2% of the general population\(^3\), its prevalence increases with age, and it has multiple causes, among which are: heart failure, diabetes mellitus type 2, and hypertension\(^4\). AF is an important risk factor of stroke, as it is responsible for 25% of ischemic stroke, and 50% of cardioembolic stroke. Patients with AF have a cerebral ischemia incidence of 7% annually\(^5\). Besides, it is demonstrated that AF increases in-hospital mortality\(^6\), increases the number of hospitalizations, and decreases quality of life\(^7\). Thus, AF represents a public health problem with an associated high economic cost\(^8,9\).

One of the main objectives of AF treatment is the prevention of thromboembolism with oral anticoagulants (OAC). The AF therapeutic guidelines\(^5,10\) provide recommendations about the suitability of a patient for OAC treatment according to different stroke risk stratification scores (CHADS\(_2\) y CHA\(_2\)_DS\(_2\)_VASc)\(^11\) and bleeding risk (HAS-BLED)\(^12\). The Mexican Clinical Practice Guideline follows these same recommendations but does not emphasize the benefits of OAC in the more long-lived patients or with a high risk, which are usually treated with antiplatelet drugs\(^13\).

Both direct OAC (DOAC), and vitamin K antagonists (VKA), have shown to be effective in preventing stroke in patients with AF\(^14-15\). However, adherence to vitamin K antagonists is highly variable, with a dropout rate in the first year of treatment that can reach up to 25%, and multiple drug interactions. Non-compliance with medication is associated with a poor perception by the patient about the need of taking medications or fear of adverse effects\(^16\). To improve the adherence more information is needed, so the patients be aware of the risk of their illness, consider it seriously, and get involved in essential prevention and treatment behaviors.

CARMEN-AF registry aims primarily to determine the current status of thromboprophylaxis of non-valvular AF in Mexico in order to identify the characteristics of the current use of OAC in Mexico. A secondary objective is to know the morbidity and mortality associated with this arrhythmia and the efficacy and safety in thromboprophylaxis of atrial fibrillation with the use of new and specific oral anticoagulants, in at least one year of follow-up.
Methods

The CARMEN-AF registry is an observational, longitudinal, multicenter, and nationwide survey about non-valvular AF. The CARMEN-AF registry is proposed as the first registry of the treatment of thromboembolic risk in non-valvular AF in Mexico that will have national representation. The participation of major health institutions, both public and private, of each state to ensure that the registry is representative of the country is planned. It seeks for wide geographical distribution to compare the quality of care between the different geographical areas of the country.

The follow-up period of each patient will be for a minimum of two years with periodic evaluations every three months. Data will be registered in an electronic case report form (Annex 2) stored in a centralized database in which all the necessary data for the study will be included. The study variables will be (1) demographic, (2) associated risk factors, (3) from diagnosis and characteristics of atrial fibrillation, as well as its clinical manifestations, (4) results of laboratory tests and cabinet examinations, and (v) clinical variables of important outcomes (morbidity-mortality). Data collection will be performed from the usual clinical practice through the participating researchers themselves and the patient's medical history at the time of inclusion in the study.

Inclusion and exclusion criteria

Candidates for the registry are those patients of any gender, older than 18 years who have documented by a 12-lead ECG, rhythm strip, Holter ECG monitoring or atrial electrograms of a pacemaker, at least one episode of AF in the last 6 months. All patients diagnosed with AF at the baseline visit must be eligible to receive antithrombotic prophylaxis with OAC and must have at least one risk factor for thromboembolism according to the CHA2DS2-VASc score. Female gender must be accompanied by some other risk factor, otherwise, it will not be coded for the risk score measured by CHA2DS2-VASc. Patients with AF of transient causes, AF onset in immediate postoperative or 3 months in cardiac surgery, terminal illness, mental inability to take anticoagulants, inability to fulfill the follow-up visits, already programmed for ablation of pulmonary veins, pregnant or lactating women, will be not eligible for inclusion in this registry (Table 1).
Data analysis

Descriptive and differential statistics will be used according to the observation obtained. For continuous variables, mean, standard deviation (SD), standard error of the mean (SEM), 95% confidence interval (CI 95%) minimum, percentile 25 (P25), median or percentile 50 (P50), percentile 75 (P75) and maximum, number of patients (n) and number of lost data will be obtained as descriptive statistics. For categorical variables, % will be obtained from the total and number of patients (n) in each category. Lost data will be treated as a new category.

Differences between continuous variables with normal distribution will be examined by Student’s t-test. The Wilcoxon Sum-Rank Test will be used when continuous variables have failed in normality tests. To analyze categorical variables, chi-square will be used by the Fisher exact test or Yates correction. A two-tailed test with a value of p <0.05 will be considered statistically significant. Logistic regression analysis will be used to select independent predictors in those variables in which a value of p <0.01 has been obtained through univariate regression analysis. Kaplan-Meier survival curves and the Cox proportional hazard model will be used to adjust the survival analysis. A p <0.05 will be considered statistically significant.

Results

The recruitment phase began on September 19, 2014 and will end on September 18, 2016. The participation of a total of 1,200 patients is estimated. A first preliminary analysis will be carried out with the first 1,000 patients. In September 2016, the cross-sectional analysis of all included patients will be performed (1,200 patients are calculated), and then one and two-year follow-up analysis will be performed.

The participating medical societies that support this Registry are, in alphabetical order: Asociacion Mexicana para la Prevencion de la Aterosclerosis y sus Complicaciones (AMPAC), Asociacion Nacional de Cardiologos al Servicio de los Trabajadores del Estado (ANCISSSTE), Asociacion Nacional de Cardiologos del Centro Medico La Raza A.C., Asociacion Nacional de Cardiologos de Mexico A.C. (ANCAM), Instituto Nacional de Cardiología “Ignacio Chavez”
Currently, there are 51 participating centers confirmed by the time being to include patients in the registry (Table 2).

Discussion

As in the rest of the world, in Latin America, the increase of life expectancy of population increases the incidence of ischemic stroke, and it is feared that its mortality will increase in the coming years\(^\text{17,18}\). Between 2003 and 2005 stroke occurred in 6.9% of the Mexican population, and it was the main cause of mortality in urban areas, affecting 14.9% of the mentioned population\(^\text{19}\). In 2010, 0.9% of the expenses of the Mexican public health sector were registries of acute stroke, of which 20,298 (43.9%) were ischemic\(^\text{20}\). On the other hand, the epidemiology of AF in Latin America is little known. In 2007, it was estimated that 60.7% of arrhythmias in Mexico were due to AF, of which 65.7% were non-valvular.

An important part of AF treatment is the prevention of thromboembolism. Anticoagulant therapy is highly effective in reducing the risk of stroke in these patients\(^\text{21}\); however, each patient must be assessed individually to determine the risks and benefits of antithrombotic therapy. Current clinical practice guidelines recommend administering anticoagulants according to the different risk stratification scores, in order to make treatment decisions according to the score obtained\(^\text{22}\). Thus, the Canadian guidelines advise the use of the CHADS\(_2\) score to assess the risk of stroke, and the HAS-BLED score to assess the risk of bleeding, and the use of DOAC (dabigatran, rivaroxaban or apixaban) against VKA\(^\text{23}\). The USA guideline recommends the use of antithrombotic agents as a rule, except in contraindicated cases\(^\text{24}\). Finally, the European guidelines recommend the use of the CHA\(_2\)DS\(_2\)-VASc and the HAS-BLED scores to measure the risks of stroke and bleeding, respectively, and the use of DOAC against aspirin and VKA\(^\text{10}\). All these recommendations are based on the results obtained in phase III studies such as ARISTOTLE, RE-LY or ROCKET AF\(^\text{25-28}\), which have shown advantages in the safety, efficacy,
and management of DOAC compared to VKA\textsuperscript{29}. The recommendations of the Mexican clinical practice guideline also favor treatment with oral anticoagulants\textsuperscript{5}.

Despite the existing recommendations and the evidence in favor of treatments with OAC, it is estimated that only between 15\% and 79\% of patients receive this treatment properly\textsuperscript{30}. VKA have complex pharmacokinetics that requires continuous monitoring of prothrombin time, frequent dose adjustments, with a high risk of bleeding, in addition to multiple interactions with other drugs and foods\textsuperscript{30}. Ease of administration, low interaction with other drugs and reduced need for surveillance of DOAC, make an expected increase in the use of anticoagulant therapy in patients with AF\textsuperscript{31}.

Adherence to VKA is very variable. The ATRIA study documented a 25\% dropout in the first year in patients treated with VKA\textsuperscript{32}, while the IN-RANGE study documented that 92\% of patients missed a dose and 36\% missed more than 20\% of treatment\textsuperscript{33}. This lack of adherence is one of the main causes of embolic events. On the other hand, there is no information on DOAC adherence, although it is expected to be greater than with VKA because of their fixed dosage, ease of administration, unnecessary monitoring, greater efficacy, and safety. To obtain a good follow-up in medication it is necessary to reduce the asymmetry of information, but it is also important to follow the recommendations of the international clinical practice guidelines.

**Conclusion**

The CARMEN-AF study will allow obtaining information about the current status of thromboprophylaxis in patients with non-valvular AF in Mexico. Anticoagulant treatment strategies in a total of 1,200 patients will be analyzed and their effectiveness will be evaluated. In addition, the degree of compliance with the clinical practice guidelines may be assessed, which will allow the development of an educational strategy to improve adherence to this type of treatment.
Ethical disclosures

Protection of human and animal subjects. The authors state that for this investigation no experiments have been performed on humans or animals.

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

Right to privacy and informed consent. The authors state that in this article there are no patient data.

Funding

Bayer, Boehringer-Ingelheim, and Pfizer unrestrictedly support the CARMEN-AF Registry, only for academic purposes.

Conflicts of interest

The Registry has unrestrictedly support from the Pharmaceutical Industry. They did not intervene in the development or the design of the CARMEN-AF Registry. Data collection will be performed by a specialized agency, independent of the sponsoring industry. Data analysis will be the responsibility of the Scientific Committee members who will be also in charge of coordinating the publications that may be generated from these analyses.

None of the authors involved in this research have a conflict of interest of any kind with Bayer, Boehringer-Ingelheim, Pfizer, Medicaweb or with any of the participating medical societies.

Acknowledgements

The authors would like to thank the Mexican Society of Cardiology for their endorsement, and MedicaWeb for the technical support provided in the development of this nationwide Registry.
References

1. Kakkar AK, Mueller I, Bassand JP, et al. International longitudinal registry of patients with atrial fibrillation at risk of stroke: Global Anticoagulant Registry in the FIELD (GARFIELD). Am Heart J. 2012; 163:13-9.

2. Iturralde-Torres P, Lara-Vaca S, Cordero-Cabra A, et al. Diseño de un registro multicentrico para evaluar control de ritmo contra control de la frecuencia en fibrilación auricular: Registro Mexicano de Fibrilación Auricular (ReMeFA). Arch Cardiol Mex 2011; 81:13-7.

3. Go AS, Hylek EM, Phillips KA, et al. Prevalence of diagnosed atrial fibrillation in adults: national implications for rhythm management and stroke prevention: the Anticoagulation and Risk Factors in Atrial Fibrillation (ATRIA) Study. JAMA 2001; 285:2370-5.

4. Benjamin EJ, Levy D, Vaziri SM, et al. Independent risk factors for atrial fibrillation in a population-based cohort. The Framingham Heart Study. JAMA 1994; 271(11):840-4.

5. Castaño-Guerra RJ, Franco-Vergara BC, Baca-Lopez FM, et al. Guia de practica clinica. Diagnostico y tratamiento de la fibrilacion auricular. Rev Med Inst Mex Seguro Soc. 2012; 50:213-31.

6. Gonzalez-Pacheco H, Marquez MF, Arias-Mendoza A, et al. Clinical features and in-hospital mortality associated with different types of atrial fibrillation in patients with acute coronary syndrome with and without ST elevation. J Cardiol. 2015; 66:148-54.

7. Rivero-Ayerza M, Scholte op Reimer W, Theuns DAMJ, et al. New-onset atrial fibrillation is an independent predictor of in-hospital mortality in hospitalized heart failure patients: results of the EuroHeart Failure Survey. Eur Heart J 2008; 29:1618-24.

8. Go AS, Mozaffarian D, Roger VL, et al. Heart disease and stroke statistics- 2013 update: a report from the American Heart Association. Circulation 2013; 127:e6-e245.

9. Fuster V, Ryden LE, Cannon DS, et al. ACC/AHA/ESC 2006 guidelines for the management of patients with atrial fibrillation: full text: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines and the European Society of Cardiology Committee for Practice Guidelines (Writing Committee to Revise the 2001 guidelines for the management of patients with atrial fibrillation) developed in collaboration with
the European Heart Rhythm Association and the Heart Rhythm Society. Europace 2006; 8:651-745.

10. Camm J, Kirchhof P, Lip GYH, et al. Guidelines for the management of atrial fibrillation. Eur Heart J 2010; 31:2369–429.

11. Olesen JB, Torp-Pedersen C, Hansen ML, et al. The value of the CHA2DS2-VASc score for refining stroke risk stratification in patients with atrial fibrillation with a CHADS2 score 0–1: A nationwide cohort study. Thromb Haemost 2012; 107:1172–9.

12. Pisters R, Lane DA, Nieuwlaat R, et al. A novel user-friendly score (HAS-BLED) to assess 1-year risk of major bleeding in patients with atrial fibrillation: the Euro Heart Survey. Chest 2010; 138:1093-100.

13. Martínez-Flores JE. Reflexiones sobre la guía clínica en fibrilación auricular. Rev Med Inst Mex Seguro Soc 2012; 50 (2): 117-22.

14. Hart RG, Pearce LA, Aguilar MI. Meta-analysis: antithrombotic therapy to prevent stroke in patients who have nonvalvular atrial fibrillation. Ann Intern Med 2007; 146(12):857-67.

15. Laupacis A, Dalen J, Feinberg W. Antithrombotic therapy in atrial fibrillation. Chest 1995; 108:352S-359S.

16. Kimmel SE, Chen Z, Price M, et al. The influence of patient adherence on anticoagulation control with warfarin. Results from the International Normalized Ratop Adherence and Genetics (IN-RANGE) study. Arch Intern Med 2007; 167:229-35.

17. Hart RG, Benavente O, McBride R, et al. Antithrombotic therapy to prevent stroke in patients with atrial fibrillation: a meta-analysis. Ann Intern Med 1999; 131:492-501.

18. Demographics and Retirement Policy in Brazil, Chile, and Mexico. Global Aging Initiative. Center for Strategic and International Studies. 2009. http://csis.org/files/media/csis/pubs/090324_gai_english.pdf Accessed March 21, 2013.

19. Ferri CP, Acosta D, Guerra M, et al. Socioeconomic factors and all cause and cause-specific mortality among older people in Latin America, India, and China: A population-based cohort study. PLoS Med 2012; 9(2): e1001179. doi:10.1371/journal.pmed.1001179
20. Chiquete E, Ruiz-Sandoval JL, Murillo-Bonilla LM, et al. Egresos por enfermedad vascular cerebral aguda en instituciones publicas del sector salud de Mexico: Un analisis de 5.3 millones de hospitalizaciones en 201. Rev Mex Neuroci 2012; 13:252-8.

21. Lip GYH. Recommendations for thromboprophylaxis in the 2012 focused update of the ESC guidelines on atrial fibrillation: a commentary. J Thromb Haemost 2013; 11: 615-26.

22. Camm AJ, Lip GY, De Caterina R, et al. 2012 focused update of the ESC guidelines for the management of atrial fibrillation: an update of the 2010 ESC guidelines for the management of atrial fibrillation—developed with the special contribution of the European Heart Rhythm Association. Europace 2012; 14:1385-413.

23. Skanes AC, Healey JS, Cairns JA, et al. Focused 2012 update of the Canadian Cardiovascular Society atrial fibrillation guidelines: recommendations for stroke prevention and rate/rhythm control. Canadian J Cardiol 2012; 28:125-36.

24. Anderson JL, Halperin JL, Albert NM, et al. Management of patients with atrial fibrillation (compilation of 2006 ACCF/AHA/ESC and 2011 ACCF/AHA/HRS recommendations). A report of the American College of Cardiology/American Heart Association task force on practice guidelines. Circulation 2013; 127:1916-26.

25. Granger CB, Alexander JH, McMurray JJ, et al. Apixaban versus warfarin in patients with atrial fibrillation. N Engl J Med 2011; 365:981-92.

26. Connolly SJ, Ezekowitz MD, Yusuf S, et al. Dabigatran versus warfarin in patients with atrial fibrillation. N Engl J Med 2009; 361(12):1139-51.

27. Patel MR, Mahaffey KW, Garg J, et al. Rivaroxaban versus warfarin in nonvalvular atrial fibrillation. N Engl J Med 2011; 365(10):883-91.

28. Tendera M, Syzdol M, Parma Z. ARISTOTLE RE-LYs on the ROCKET. What’s new in stroke prevention in patients with atrial fibrillation? Cardiol J 2012; 19:4–10.

29. Buckingham TA, Hatala R. Anticoagulants for atrial fibrillation: why is the treatment rate so low? Clin Cardiol 2002; 25:447-54.

30. Michota F. Transitions of care in anticoagulated patients. J Multidiscip Healthc 2013; 6:215-28.
31. Singer DE, Chang Y, Fang MC, et al. The net clinical benefit of warfarin anticoagulation in atrial fibrillation. Ann Intern Med 2009; 151(5):297-305.

32. Ferguson C, Inglis SC, Newton PJ, et al. Atrial fibrillation and thromboprophylaxis in heart failure: the need for patient-centered approaches to address adherence. Vasc Health Risk Manag 2013; 9:3–11.

33. Horne R. Patients’ beliefs about treatment: the hidden determinant of treatment outcome? J Psychosom Res 1999; 47:491-5.
Table 1. Inclusion and exclusion criteria.

**Inclusion criteria**

- Sex: Male or female.
- Age: ≥ 18 years old.
- Patient with diagnosis of chronic AF (permanent) documented by at least 2 electrocardiogram tracings taken on different days in the last 6 months. Tracings can be by 12-lead electrocardiogram, rhythm strip, or 24-hour Holter monitoring.
- Patient with diagnosis of paroxysmal/persistent AF documented for at least 30 seconds by 12-lead electrocardiogram, rhythm strip, 24-hour Holter monitoring, or atrial electrograms from a pacemaker. It is required that at least one episode has occurred and documented in the last 6 months.
- Patient with at least one risk factor for thromboembolism evaluated by CHA\textsubscript{2}DS\textsubscript{2}-VASC score.

**Exclusion criteria**

- AF of transient causes (thyrotoxicosis, alcohol intoxication, myocardial infarction in acute phase, pericarditis, myocarditis, electrocution, pulmonary embolism or other lung disease, electrolyte or metabolic disorder, etc.).
- AF onset in immediate postoperative or 3 months in cardiac surgery.
- Terminal illness.
- Mental inability to take anticoagulants.
- Inability to fulfill the follow-up visits.
- Patient already programmed for ablation of pulmonary veins.
- Pregnant or lactating women.
- Contraindication for oral anticoagulation (anemia, thrombocytopenia, severe liver or kidney damage, etc.).
| STATE                        | CITY                  | CENTER                                                                 |
|------------------------------|-----------------------|------------------------------------------------------------------------|
| AGUASCALIENTES              | Aguascalientes        | Cardiologica Aguascalientes                                            |
| BAJA CALIFORNIA             | Tijuana               | Hospital Angeles de Tijuana                                            |
|                              |                       | ISSSTECALI                                                             |
| BAJA CALIFORNIA SUR         | La Paz                | Hospital General La Paz, ISSSTE                                        |
| CAMPECHE                     | Campeche              | Hospital General de Especialidades INDESALUD                            |
| CHIAPAS                      | Tuxtla Gutierrez      | Hospital General de Zona No.1, IMSS                                    |
| CHIHUAHUA                    | Chihuahua             | Policlinica de especialidades                                          |
| CIUDAD DE MEXICO            | Mexico City           | Centro Medico Nacional "20 de noviembre", ISSSTE                       |
|                              |                       | Centro Medico Nacional "La Raza", IMSS                                  |
|                              |                       | Hospital ABC                                                            |
|                              |                       | Hospital Central de Alta Especialidad Norte, PEMEX                      |
|                              |                       | Hospital de Cardiologia, Centro Medico Nacional "Siglo XXI", IMSS       |
|                              |                       | Hospital General de Mexico                                            |
|                              |                       | Instituto Nacional de Cardiologia "Ignacio Chavez"                     |
|                              |                       | Instituto Nacional de Ciencias Medicas y Nutricion "Salvador Zubiran"  |
| COAHUILA                     | Torreon               | Unidad Medica de Alta Especialidad No. 71, IMSS                       |
| COLIMA                       | Colima                | Centro Medico “Puerta de Hierro”                                      |
| DURANGO                      | Durango               | Hospital General de Durango                                            |
| ESTADO DE MEXICO            | Toluca                | ISSEMYM Toluca                                                         |
| GUANAJUATO                   | Guanajuato            | Unidad Medica de Alta Especialidad No. T-1, IMSS                       |
| GUERRERO                     | Leon                  | Hospital Angeles de Leon                                               |
|                              | Acapulco              | Hospital General de Acapulco                                           |
|                              | Iguala                | Hospital General de Iguala                                             |
| HIDALGO                      | Pachuca               | Consultorio privado, Dr. Lechuga                                       |
|                              |                       | Hospital General de Pachuca                                           |
| JALISCO                      | Guadalajara           | Centro Medico Nacional de Occidente, IMSS                               |
|                              |                       | Hospital Civil de Guadalajara                                         |
| MICHOACAN                    | Uruapan               | Hospital General de Uruapan, SSA                                       |
| MORELOS                      | Cuernavaca            | Instituto Mexicano de Trasplantes                                      |
| NAYARIT                       | Tepic                 | Consultorio privado, Dr. Varela                                       |
| NUEVO LEON                   | Monterrey             | Hospital San Jose                                                      |
| OAXACA                       | Oaxaca                | Clinica Molina                                                         |
| PUEBLA                       | Puebla                | Hospital Angeles de Puebla                                             |
|                              |                       | Hospital General del Sur de Puebla, SSA                               |
| Estado       | Ciudad          | Hospital                                             |
|--------------|-----------------|------------------------------------------------------|
| QUERETARO    | Queretaro       | Instituto Corazon de Queretaro                       |
| QUINTANA ROO | Cancun          | Hospital General de Zona No.3, IMSS                 |
| SAN LUIS POTOSI | San Luis Potosi | Hospital Angeles de San Luis Potosi                  |
|              |                 | Hospital Central "Morones Prieto"                   |
| SINALOA      | Culiacan        | Hospital Angeles de Culiacan                         |
|              |                 | Hospital Civil de Culiacan                           |
| SONORA       | Obregon         | Centro Medico Nacional del Noroeste, IMSS            |
| TABASCO      | Villahermosa    | Hospital Regional de Alta Especialidad, Villahermosa, SSA |
| TAMAUlipas   | Tampico         | Hospital Angeles de Tampico                          |
|              |                 | Hospital Regional Tampico, PEMEX                     |
| VERACRUZ     | Veracruz        | Unidad Medica de Alta Especialidad No. 14, IMSS      |
| YUCATAN      | Merida          | Star Medica Merida                                   |
| ZACATECAS    | Zacatecas       | Hospital General No. 26, ISSSTE                      |
|              |                 | Hospital San Agustin                                |
ANNEX 1

Study participants

Scientific Committee: Dr. J Antonio Gonzalez- Hermosillo (National Coordinator); Dr. Manlio F. Marquez Murillo (President); Dr. Salvador Ocampo Peña (Secretary); Dr. Guillermo Ceballos; Dr. Alejandro Cordero; Dr. Marcelo Jimenez; Dr. Armando Garcia; Dr. Efrain Gaxiola; Dr. Jorge Gomez; Dr. Enrique Martinez; Dr. Luis Molina; Dr. Gerardo Rodriguez-Diez; Dr. Humberto Rodriguez; Dr. Juan Pablo Benitez.

Financial Committee: Dr. Luis Molina; Dr. Bernardo Quintana; Dr. Ruben Yza Villanueva, AMPAC; Dr. Enrique Velazquez, ANCCMN “LA RAZA”; Dr. Jose Manuel Enciso, ANCAM; Dr. Rogelio Robledo, ANCISSSTE; Dr. Jorge Gomez (temporally), SMC; Dr. Susano Lara, SOMECC.

Pharmaceutical Industry Representatives: Dra. Alejandra Meaney, Bayer; Dra. Yuriria Valle, Boehringer-Ingelheim; Dra. Ma. Eugenia Pastrana, Pfizer.

Contract Research Organization: Medicaweb, S. A. de C. V.
ANNEX 2

Case Report Form

Institution: ______________________

Variables Demográficas

Iniciales: ______________________

Fecha de nacimiento: __/__/______

Sexo: ( ) Masculino ( ) Femenino

Número de Registro Institucional: ______________________

Fecha de Recubrimiento (dia/mes/año): / / 

Cobertura de salud: ( ) Privado ( ) Sector Salud ( ) IMSS ( ) ISSSTE ( ) PEMEX ( ) Otro

Lugar de Residencia (Estado): ______________________

Tipo de residencia: ( ) Urbana ( ) Rural

Medico responsable (Especialidad): ______________________

Cardiologo ( ) Neurologo ( ) Hematologo

( ) Medicina Interna ( ) Medico General ( ) Otro, especificar: ______________________

Lugar de reclutamiento: ______________________

Urgencias ( ) Hospitalización ( ) Consulta externa

Elegibilidad: ( ) si ( ) no

Factores de Riesgo

Peso: Kg. ______________________

Estatura: m. ______________________

( ) Diabetes Melito ( ) Complicaciones ( ) Retinopatia ( ) Neuropatia

( ) Distres Diastolico: ( ) Hipertensión ( ) Hipotensión

( ) Insuficiencia Cardiaca: ( ) Tumor Cardiaco ( ) Enfermedad Arterial Coronaria

Class Functional: ( ) I ( ) II ( ) III ( ) IV

( ) Otras Insuficiencias: ( ) Diafragma ( ) Especifico:

( ) Evento Cardiovascular Previo: ______________________

( ) Disfunción del Nodo Sinoauricular

( ) Enfermedad Pulmonar:______________________________

Exacerbación COPD ( ) Asma ( ) SAHOS ( ) HAIPalm

( ) Insuficiencia Renal Crónica: ( ) E( ) I( ) III( ) IV( ) ECV

( ) Trombocitopenia: ______________________

( ) Hipertensiòn Arterial: ______________________

( ) Enfermedad Hepática: ______________________

( ) Enfermedad Trombótica: ______________________

( ) Anemia: ______________________

( ) Alcoholismo: ______________________

Variables Diagnósticas de Fibrilación Auricular

Metodo diagnóstico de fibrilación auricular (selecte uno): ______________________

( ) Electrocardiograma de 12 derivaciones ( ) Monitor electrocardiográfico de 24 horas

Tipo: ( ) Paroxístico ( ) Permanente ( ) Persistente

Manifestaciones Clínicas

- Dolor Torácico ( ) Palpitaciones ( ) Presincope

- Mareos ( ) Díseña ( ) Sincope

- Descompensación de insuficiencia cardiaca ( ) Fatiga ( ) Edema

- Desencadenamiento de angina ( ) Asintomático

Electrocardiograma

Ritmo: ______________________

( ) FA ( ) Sinusal

( ) Tira de Ritmo

( ) Monitor electrocardiográfico de 24 horas ( ) Monitorización de marcapaso permanente

Duración QRS: __________ ms

Duración onda P*: __________ ms

( ) Bloqueo de rama derecha Intervalo PR*: __________ ms

( ) Bloqueo de rama izquierda Intervalo QT*: __________ ms

Frecuencia cardíaca: ______________________

Frecuencia ventricular media*: ______________________

Ecocardiografía Básica

Aurícula derecha: Dimensiones vista apical de 4 cámaras (Fin de la sistole ventricular):

Longitudinal mm Transversal mm

Aurícula izquierda: Dimensiones vista apical de 4 cámaras (Fin de la sistole ventricular):

Longitudinal mm Transversal mm

( ) Enfermedad Espontánea: ( ) Leve ( ) Moderada: ( ) grave

( ) Enfermedad Hipertrófica de la Ventrícula: ( ) Fatiga: ( ) Edema

Imagen ecocardiografía: ( ) No ( ) Sí_____________________

Sugerente de trombo ( ) Sí ( ) No Describir: ______________________

( ) Aneurisma del Septum interauricular: __________ mm

Se realizó estudio contrastado (Solución salina agitada): ( ) No ( ) Sí

El estudio sugiere permeabilidad de foramen oval: ( ) No ( ) Sí

( ) Comunicación interauricular (Este es un criterio de eliminación, el paciente no puede ser incluido si la FA puede estar relacionada con una enfermedad valvular)

Ventriculo derecho

Dilatado ( ) Sí ( ) No Diametro antero-posterior (en diastole): __________ mm

Ventriculo izquierdo

Dilatado ( ) Sí ( ) No Diametro antero-posterior (en diastole): __________ mm

Grosor LV __________ mm Fracción de expulsión __________%

( ) Enfermedad Valvular Mitral: ( ) Funcional: ( ) Orgánica: ( ) Leve ( ) Moderada ( ) Severa

( ) Enfermedad Valvular Aórtica: ( ) Funcional: ( ) Orgánica: ( ) Leve ( ) Moderada ( ) Severa

( ) Enfermedad Valvular Tricúspide: ( ) Funcional: ( ) Orgánica: ( ) Leve ( ) Moderada ( ) Severa

Antiagregantes

Terapia de antiagregación oral: ( ) No ( ) Sí Tipo: ______________________

( ) Acenocumarina ( ) Warfarina ( ) Prasugrel ( ) Dosis X día ______________________

M V S D

Valor de INR Inicial: ______________________

( ) Atriptel ( ) Nattprotel ( ) Apixaban Dosis: ______________________

Variables de Riesgo

( ) Insuficiencia Cardiaca ( ) Mareos ( ) Palpitaciones ( ) Dificultad respiratoria ( ) Fatiga

Tipo: ( ) Paroxístico ( ) Permanente

( ) Enfermedad Pulmonar: ______________________

( ) Enfermedad Osteoarticular: ______________________

( ) Enfermedad Arterial Periférica: ______________________

( ) Enfermedad Trombótica: ______________________

( ) Marcapaso: ______________________

( ) Marcapaso Fijo ( ) Sí ( ) No Describir: ______________________

( ) Enfermedad Hemotrófica: ______________________

( ) Enfermedad Renal Crónica: ______________________

( ) Enfermedad Hepática: ______________________

( ) Enfermedad Trombocitopenica: ______________________

( ) Enfermedad Pulmonar: ______________________

( ) Enfermedad Cardíaca: ______________________

( ) Enfermedad Trombótica: ______________________

( ) Enfermedad Hemotrófica: ______________________

( ) Enfermedad Renal Crónica: ______________________

( ) Enfermedad Arterial Periférica: ______________________

( ) Enfermedad Trombocitopenica: ______________________

( ) Enfermedad Cardíaca: ______________________

( ) Enfermedad Trombótica: ______________________

( ) Enfermedad Hemotrófica: ______________________

( ) Enfermedad Renal Crónica: ______________________

( ) Enfermedad Arterial Periférica: ______________________

( ) Enfermedad Trombocitopenica: ______________________

( ) Enfermedad Cardíaca: ______________________

( ) Enfermedad Trombótica: ______________________

( ) Enfermedad Hemotrófica: ______________________

( ) Enfermedad Renal Crónica: ______________________

( ) Enfermedad Arterial Periférica: ______________________

( ) Enfermedad Trombocitopenica: ______________________
Ticagrelor ( ) dosis mg/día
Otro antiplaquetario ( ) dosis mg/día

| Procedimientos Previos | Ritmo sinusal final: | No | Si |
|-----------------------|----------------------|----|----|
| Cardioversión Electrónica |                      |    |    |
| Aislamiento de Venas Pulmonares |                   |    |    |
| Cirugía de laborinto (maze) |                   |    |    |
| Abolición del nodo AV o implantación de Marcapaso | Disfunción del nodo sinusal ( ) | Disfunción del Nodo auriculo-ventricular ( ) | FA lenta ( ) |

| Pruebas de Laboratorio: | Fecha: | / | / |
|-------------------------|---------|---|---|
| Hemoglobina | g/dl | Acido urico | mg/dl |
| Hematocrito | % | Colesterol | mg/dl |
| Plaquetas | /mm³ | Triglicéridos | mg/dl |
| Tiempo parcial de tromboplastina | _____ seg | Peptido natriuretico tipo B | |
| Testigo | _____ seg | Nitrogeno ureico (BUN) | mg/dl |
| Tiempo de trombina | _____ seg | Alanina transaminasa (TGP)mg/dl | |
| Testigo | _____ seg | Gamma glutamiltransferasa | mg/dl |
| Potasio mEq/l | | Proteínas totales g/dl | |
| Leucocitos | /μl | Magnesio | mg/dl |
| | | Albumina | g/dl |

Llenado por: ____________________________