RESEARCH LINE 5. SECONDARY PREVENTION
RICORS ICTUS (2022-2024)

Line leaders: Mar Castellanos, Tomás Segura

The **general objective** of this line is to improve the identification of patients at the highest risk of stroke recurrence, so that the recurrence risk profile can be individualized in order to establish the most effective preventive strategy for each patient.

WP1. Identification of mechanisms related to the development of active (high risk) atherosclerotic plaques
WP2. Improvement of the management of patients diagnosed and suspected hidden atrial fibrillation
WP3. Identification of risk factors associated with stroke in children and young adults
WP4. Analysis of genetic factors associated with stroke risk

Collaborative Projects:

- **ATRIUM**
- **DESCUUBRE FA**
- **RECAST-II**

RESEARCH LINE 5. SECONDARY PREVENTION
RICORS ICTUS (2022-2024)

Objectives WP1

Identification of mechanisms related to the development of active (high risk) atherosclerotic plaques

1.- Description of **radiological techniques** to identify **high-risk intracranial atheroma plaques**

2.- Identification of **serum biomarkers** capable of **predicting instability of intracranial atheromatous plaques**

3.- Development of an **animal model of intracranial atheromatosis**

4.- Description of **predictive factors for complications after carotid angioplasty/stenting procedures**.

Participants:

Jordi Jiménez Conde (RG7)
Francisco Purroy (RG11)
Mónica Millán (RG 12)
Mar Freijo (RG 14)
Joan Salom (RG 15)
Joan Montaner (RG 17)
Ángeles Almeida (RG 19)
Juan Arenillas (RG 20)

Enrique Palacio-Portilla (CA 4)

RESEARCH LINE 5. SECONDARY PREVENTION
RICORS ICTUS (2022-2024)

Objectives WP2.
Improvement of the management of patients diagnosed and suspected hidden AF

1.- Selection of **patients with high risk of developing atrial fibrillation** from general population non-previously diagnosed with stroke who will be monitored with an EKG recording band system

2.- To develop a **computational system** able to non-invasively estimate **subtle changes in the atrial substrate predisposing to develop atrial fibrillation** after otherwise **cryptogenic stroke**

3.- To better understand the **risk factors for recurrence in patients with cardioembolic stroke** who are correctly anticoagulated.

Participants:

Blanca Fuentes (RG 2)
José A Vivancos (RG 3)
Mar Castellanos (RG6)
Jordi Jiménez Conde (RG 7)
Joaquín Serena (RG 8)
Joan Martí/I.Fernández (RG 9)
Mónica Millán (RG 12)
Mar Freijo (RG14)
Tomás Segura (RG 15)

Manuel Gómez-Choco (CA 1)
Enrique Palacio-Portilla (CA 4)
José María Ramírez (CA 5)
Juan Carlos López/Negrín (CA 6)
Ana Morales (CA 7)

RESEARCH LINE 5. SECONDARY PREVENTION
RICORS ICTUS (2022-2024)

Objectives WP3.

Identification of risk factors associated with stroke in children and young adults.

1.- To improve knowledge about cerebral vascular disease in the pediatric and young adult population

2.- To prospectively collect data on pediatric stroke and on young adult stroke.

Participants:

Blanca Fuentes (RG 2)
Francisco Purroy (RG 11)
Patricia Martínez (RG 18)
Ana Morales (CA 7)

RESEARCH LINE 5. SECONDARY PREVENTION
RICORS ICTUS (2022-2024)

Objectives WP4.

Analysis of genetic factors associated with stroke risk

1.- To find new genetic risk factors for ischemic stroke following the strategy of analyze homogeneous populations

2.- To use this information to generate clinical-genetic scores to stroke risk prediction

Participants:

Francisco Campos (RG 5)
Mar Castellanos (RG 6)
Joan Martí/ Israel Fernández (RG 9)
Francisco Purroy (RG 11)
Mar Freijo (RG 14)
Mónica Millán (RG 12)
Tomás Segura (RG 16)
Joan Montaner (RG 17)
Juan Arenillas (RG 20)
Elena López-Cancio (RG 22)
Cristófol Vives (RG 23)

Juan Carlos López/ Negrín (CA 6)
Ana Morales (CA 7)

RESEARCH LINE 5. SECONDARY PREVENTION
RICORS ICTUS (2022-2024)

Collaborative projects

ATRIUM *(led by Albacete University Hospital)*

"Risk stratification of occult atrial fibrillation based on advanced electrocardiographic analysis to improve secondary prevention after Cryptogenic Stroke and Embolic Stroke of Undetermined Source"

This study aims to develop and validate a computational tool for accurately estimating the risk of paroxysmal atrial fibrillation. Development of a novel ECG-based predictors of occult atrial fibrillation (OAF) after CS and ESUS by performing a beat-to-beat analysis of the P-wave and QRS-complex over several hours, at least, over a full day.

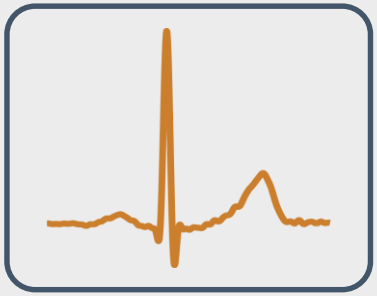
Current status and results:

+ Clinical, echocardiographic, and analytical variables have already been collected for approximately 200 patients from 7 hospitals: Albacete, Ciudad Real, Toledo, Leon, Salamanca, Valladolid, Oviedo. All patients received continuous, high-resolution ECG monitoring for 48 hours on admission to the stroke unit and for at least 30 days immediately thereafter.
+ After this monitoring and conventional follow-up of about one year, OAF was detected in about 30% of the patients.
+Approximately 100 additional patients are expected to be enrolled over the next 6-12 months. Later, novel ECG-based predictors will be developed, and established statistical tools as well as novel machine and deep learning techniques will be used to generate predictive models of OAF

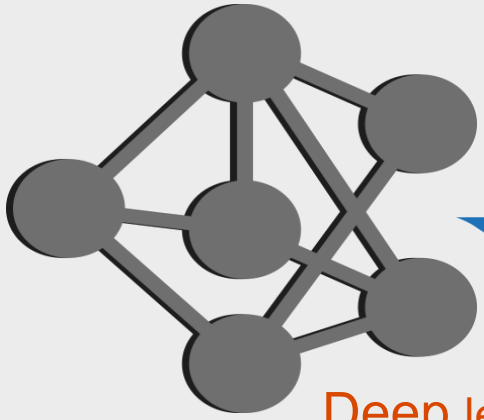
ATRIUM

MATLAB App

Novel ECG-based predictors



Machine learning



AF risk

Deep learning

Common clinical, serological, echocardiographic predictors

Sexo

Edad

RESEARCH LINE 5. SECONDARY PREVENTION
RICORS ICTUS (2022-2024)

Collaborative projects

DESCUUBRE-AF *led by IIS-La Princesa-Madrid*

"Detection of hidden atrial fibrillation in primary care using a long-term band-based ECG registration system"

The objective of the study is to establish the prevalence of undiagnosed atrial fibrillation in the at-risk population within a primary care setting, using prolonged band-based EKG recording systems (textile device). This study also aims to identify a profile of patients at risk of developing atrial fibrillation and evaluate the usefulness of these devices as a screening tool.

Current status and results:

+ In a primary prevention setting, within an elderly population at risk of AF, a band-based EKG monitoring strategy using the Nuubo wearable device (2-lead EKG) applied for only two weeks identified approximately 3% of new AF cases, leading to adjustments in antithrombotic therapy.

+ Variables potentially associated with a higher risk of developing AF included a higher frequency of supraventricular extrasystoles, episodes of supraventricular tachycardia, and prolonged P wave duration.

+Most participants found the device easy to use and comfortable, reporting no significant limitations in daily activities during the two-week study period

→FINDINGS published under DOI: 10.1016/j.jstrokecerebrovasdis.2022.106642

+ Next steps: Include new centres belonging to the RICORS network. identify differences and develop an Artificial Intelligence model that can, with just a few minutes of monitoring, classify whether a patient is likely to develop cardiac abnormalities, enabling personalized follow-up before the need for specialized medical consultations

RESEARCH LINE 5. SECONDARY PREVENTION
RICORS ICTUS (2022-2024)

Collaborative projects

RECAST-II *led by IBIS-Sevilla*

"Restenosis after Carotid Angioplasty and Stenting (RECAST) registry: External Validation of RECAST score."

Wp-1. The objective of the study is to conduct an external validation of the scale predictor of restenosis ≥ 70% post-angioplasty and stenting

Current status and results:

→PREVIOUS FINDINGS (Unicenter Project): Development of a Risk Prediction Nomogram for Carotid Restenosis in the One Year RECAST Registry. Eur J Vasc Endovasc Surg. 2024 May 25:S1078-5884(24)00460-X.

→FINDINGS published under DOI: 10.1016/j.ejvs.2024.05.033

Next steps:
+ Pending ethical committee approval to begin study
+ Participation of 8 Hospitals: Vall d´Hebrón, Asturias, Clínico (Madrid), Murcia, Sabadell, Toledo, Son Espases (Baleares), La Fe (Valencia)
+ Patients are expected to be enrolled over the next 24 months

RESEARCH LINE 5. SECONDARY PREVENTION
RICORS ICTUS (2022-2024)

PUBLICATIONS

WP1. Identification of mechanisms related to the development of active (high risk) atherosclerotic plaques

- Plaque vulnerability biomarkers in patients with carotid stenosis (Carballo-Perich et al., Int J Mol Sci. 2022)
- Prevention of recurrences (Gil-Nuñez et al., Neurologia (Engl Ed). 2022; McCabe et al., Stroke 2023)
- Atherosclerosis (Gómez-Vicente et al., Clin Neuroradiol. 2023; Psychogios et al., Eur Stroke J 2022)
- Treatment with endarterectomy or angioplasty for carotid occlusion (García- Pastor et al. AJNR Am J Neuroradiol 2022)

WP2. Improvement of the management of patients diagnosed and suspected hidden atrial fibrillation

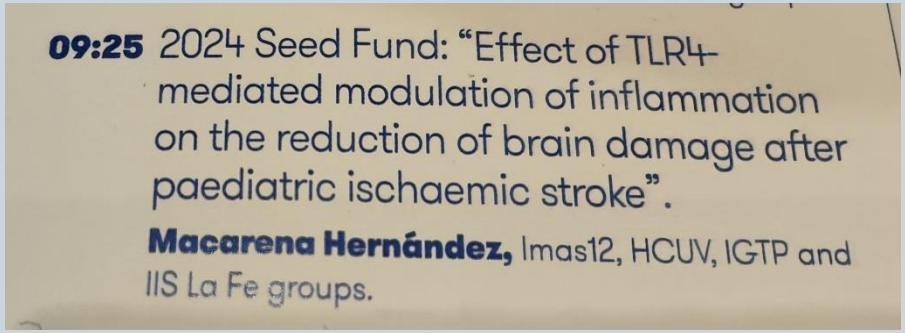
- Plasma and radiological biomarkers for the diagnosis of atrial fibrillation in asymptomatic patients with and without dementia (Pala et al., Front Cardiovasc Med 2022. J Stroke Cerebrovasc Dis 2022; Plos One 2022; Schweizer et al., J Am Coll Cardiol. 2022)

- Atrial fibrillation (Vera et al., Am J Cardiol. 2022; Ximenez-Carrillo et al., J Stroke Cerebrovasc Dis 2022; Caso et al., Heart 2023; Escudero-Martnez et al., Trends Cardiovasc Med. 2023; Rivard et al., Circulaton 2022)

RESEARCH LINE 5. SECONDARY PREVENTION
RICORS ICTUS (2022-2024)

PUBLICATIONS

WP3. Identification of risk factors associated with stroke in children and young adults



WP4. Analysis of genetic factors associated with stroke risk

- Genetics of stroke and drugs (Mishra et al., Nature 2022)
- Polygenic risk in cardioembolic stroke (Cárcel-Márquez et al., Front Cardiovasc Med. 2022)
- Genetic variants of ApoE and amyloid angiopathy (Bonaterra-Pastra et al., Front Aging Neurosci. 2023).
- Connectomics and genetics in small vessel disease (Gutiérrez-Zúñiga et al., Neurobiol Dis. 2022)
- DNA methylation and risk (Cullel et al., Thromb Haemost. 2022)
- Genes and COVID (Cruz et al., Hum Mol Genet. 2022)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