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4<sup>th</sup> International  
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the ESC Council  
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Heart and Brain Interaction - Antiphospholipid Antibodies: an important link

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## DIAGNOSTIC UTILITY AND PROGNOSTIC VALUE OF hs-cTnT, NT-Pro BNP AND COPEPTIN IN PATIENTS WITH ACUTE CARDIAC SYNCOPE

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**Background:** The diagnostic and the prognostic performance of hs-cTnT, NT-Pro BNP and Copeptin in patients presenting to an emergency department with acute syncope is unsettled.

**Purpose:** To assess the diagnostic performance of hs-cTnT, NT-Pro BNP and Copeptin for the discrimination of a cardiac versus non-cardiac reason of syncope, and to evaluate whether both biomarkers provide additional information on re-occurrence of syncope or on incident major cardiovascular events.

**Methods:** We prospectively enrolled patients with a history of syncope within 6 hours of presentation to the ED. The type of syncope was classified clinically, and patients were managed at the discretion of the attending physician. The type of syncope was re-adjudicated retrospectively by two physicians of all available records and the 30 days follow up findings. The spectrum included cardiac, neurogenic, vasovagal, orthostatic, other causes and unknown causes. Major cardiovascular events were defined as a composite of death, resuscitation, life-threatening arrhythmias, implantation of pacemaker/implantable cardioverter defibrillator, percutaneous coronary intervention or CABG, or acute myocardial infarction.

**Results:** Among 97 patients available for assessment, cardiac syncope was the adjudicated diagnosis in 20 patients (20.6%). Hs-cTnT and NT-Pro BNP were significantly higher in cardiac syncope vs. other causes  $p=0.012$  and  $p=0.024$ , respectively. The diagnostic accuracy of hs-cTnT for cardiac syncope, as quantified by the area under the curve (AUC), was 0.682 (95% CI: 0.557 – 0.806;  $p=0.013$ ). At a cut-off  $>7$  ng/L, hs-cTnT allows the discrimination of a cardiac syncope with a sensitivity and specificity of 85.0% and 45.45%, respectively. NT-Pro BNP showed an AUC for cardiac syncope of 0.687 (95% CI: 0.532 – 0.843;  $p=0.024$ ). At a cut-off  $> 767$  ng/L, NT-Pro BNP allows the discrimination of a cardiac syncope with a sensitivity and specificity of 58.82% and 77.27% respectively. Copeptin showed an AUC for cardiac syncope of 0.554 (95% CI: 0.403 – 0.705;  $P=0.457$ ). At cutoff of  $> 95$  pmol/L, Copeptin allows the discrimination of a cardiac syncope with a sensitivity and specificity of 30% and 88.31%, respectively. The prognostic accuracy of hs-cTnT, NT-Pro BNP and Copeptin for MACE were poor and showed the AUC of 0.592 (95% CI: 0.413 – 0.770;  $p=0.370$ ), 0.615 (95% CI: 0.359 – 0.871;  $P=0.303$ ) and 0.541 (95% CI: 0.350 – 0.732;  $P=0.688$ ), respectively. The prognostic accuracy of hs-cTnT, NT-Pro BNP and Copeptin for syncope re-occurrence were poor and showed the AUC of 0.668 (95% CI: 0.472 – 0.864;  $P=0.085$ ), 0.674 (95% CI: 0.444 – 0.905;  $P=0.138$ ). and 0.689 (95% CI: 0.495 – 0.882;  $P=0.053$ ), respectively.

**Conclusion:** hs-cTnT, NT-Pro BNP, and Copeptin poorly discriminate between a cardiac and non-cardiac reason of syncope, and confer little if any prognostic information on incident MACE or re-occurrence of syncope.

**Key words:** hs-cTnT, NT-Pro BNP, copeptin, cardiac syncope

# CARDIAC DYSFUNCTION AND INFLAMMATION ARE ASSOCIATED WITH HIGH-SENSITIVE TROPONIN T ELEVATION IN ACUTE ISCHEMIC STROKE: INSIGHTS FROM THE SICFAIL STUDY

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**Background:** Troponin elevation is frequently observed in patients with acute ischemic stroke (AIS). The pathophysiological mechanisms involved are only partially understood and comprise coronary as well as non-coronary causes such as autonomic dysfunction. We investigated determinants of troponin elevation in AIS patients including markers of autonomic dysfunction, assessed by heart rate variability (HRV) time domain variables.

**Methods:** Data were collected within the Stroke Induced Cardiac FAILure (SICFAIL) cohort study. Consecutive AIS patients admitted to the Department of Neurology, University Hospital Würzburg, Germany, underwent baseline investigation including previous history of cardiac disease, physical examination, standardized echocardiography, and blood sampling. High-sensitive troponin T (hs-TnT) level was determined at median 3 days (quartiles 2–4) after symptom onset. Four HRV time domain variables were calculated in patients undergoing electrocardiographic Holter monitoring: (1) standard deviation (SD) of normal-to-normal beats (SDNN, estimate of overall HRV), (2) SD of the averages of normal-to-normal intervals for all 5-min segments for 24 h (SDANN, estimate of long-term components of HRV), (3) mean of 5-min SDs of all normal-to-normal intervals for 24 h (SDNN index, estimate of HRV due to cycles shorter than 5 minutes), (4) root mean square of successive RR interval differences (RMSSD, estimate of short-term components of HRV). Multivariable logistic regression with corresponding odds ratios (OR) and 95% confidence intervals (CI) was used to investigate the determinants of hs-TnT  $\geq 14$  ng/L.

**Results:** In 430 (79%) of 543 AIS patients hs-TnT level was above the detection limit of 5 ng/L, and 203 (37%) patients had a hs-TnT  $\geq 14$  ng/L. hs-TnT elevation was independently associated with older age (OR per year 1.05; 95% CI 1.02–1.08), male sex (OR 2.65; 95% CI 1.54–4.58), lower estimated glomerular filtration rate (OR per 10 mL/min/1.73 m<sup>2</sup> 0.71; 95% CI 0.61–0.84), systolic dysfunction (OR 2.79; 95% CI 1.22–6.37), diastolic dysfunction in absence of systolic dysfunction (OR 2.29; 95% CI 1.29–4.02), atrial fibrillation (OR 2.30; 95% CI 1.25–4.23), and higher levels of C-reactive protein (OR 1.48 per log unit; 95% CI 1.22–1.79). HRV analysis was feasible in 196 patients. Of them, 42 patients (21.4%) had a hs-TnT level  $\geq 14$  ng/L. In univariate analyses, SDNN index was significantly reduced in patients with hs-TnT  $\geq 14$  ng/L (42.2 vs. 54.1 ms,  $p=0.008$ , OR 0.97; 95% CI 0.95–0.99) but this association became non-significant (OR 0.98; 95% CI 0.96–1.01) after adjustment for age. We found no association of SDNN, RMSSD, and SDANN with hs-TnT elevation.

**Conclusion:** Cardiac dysfunction and inflammation, but not a reduced HRV as a surrogate of autonomic dysfunction, were associated with increased levels of troponin in patients with AIS, independent of established cardiovascular risk factors.

Registration-URL: [https://www.drks.de/drks\\_web/](https://www.drks.de/drks_web/); Unique identifier: DRKS00011615

# IDENTIFICATION OF SUBCLINICAL MYOCARDIAL INJURY IN PATIENTS AFTER ACUTE STROKE

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**Background:** Patients after acute stroke frequently show signs of myocardial injury. The pathophysiology and exact incidence are not fully known yet.

**Purpose:** In our prospective observational study, we aimed to perform electrocardiogram analysis, transthoracic echocardiographic examination and determine dynamics of high-sensitive Troponin I (hs-cTnI), NT-proB-type Natriuretic Peptide (NT-proBNP) and marker of apoptosis - tumor necrosis factor-related apoptosis-inducing ligand (TRAIL) in patients after acute stroke to study possible impact of acute stroke on the heart.

**Methods:** Between August 2020 and February 2021, 47 consecutive patients after acute ischemic stroke and 11 patients after intracerebral hemorrhage were enrolled in our study. In included patients, we performed 12 lead electrocardiograms at admission, 24 hours and 48 hours later. We obtained blood samples at admission, 24 hours and 48 hours later to determine levels of hs-cTnI, NT-proBNP and TRAIL. Moreover, within first 5 days of hospitalization, we performed echocardiographic examination to evaluate regional wall motion abnormalities of left ventricle. Standard neurologic examinations, National Institutes of Health Stroke Scale (NIHSS) score and Intracerebral hemorrhage (ICH) score were performed at admission by neurologists.

**Results:** Fifty-eight patients of mean age 69.6±13.2 years, 33 men (58%) were included. Most common cardiovascular risk factors were arterial hypertension (82,8%), dyslipidemia (48%), smoking (41%), atrial fibrillation (22%), type 2 diabetes (20%) and coronary artery disease (7%). Nine patients died during hospitalization (3 patients with acute ischemic stroke, 6 patients with intracerebral hemorrhage). Increased hs-cTnI levels were presented in 24,1% and elevated NT-proBNP in 24% of the patients within first 48 hours. We found significant association between hs-cTnI and NT-proBNP levels at admission ( $p=0,02$ ) and after 48 hours ( $p=0,0002$ ). Mean level of TRAIL was 62.1± 32.9 pg/ml, 21% of patients presented with TRAIL levels below 30 pg/ml. We observed significant changes between TRAIL levels at admission comparing to levels after 24 hours ( $p=0,003$ ) and 48 hours ( $p=0,02$ ). Moreover, we found negative correlation between TRAIL and hs-cTnI levels, both after 24 hours ( $p=0,05$ ) and 48 hours ( $p=0,03$ ). We did not find association between stroke severity evaluated by NIHSS and ICH score and TRAIL, NT-proBNP and hs-cTnI levels. Out of 47 patients eligible for echocardiographic examination, five had regional wall motion abnormality, all of them presented with elevation in both hs-TnI and NT-proBNP and depression in TRAIL levels. Eleven patients (26,2%) without regional wall motion abnormality presented with elevation in one or more observation factors. In electrocardiographic analysis, 10 patients (17%) presented with ST segment depression. ST segment depression was significantly associated with TRAIL and hs-TnI levels ( $p<0,05$ ).

**Conclusion:** Subclinical myocardial injury in patients after acute stroke could be detected in almost one quarter of patients during acute phase. We found statistically significant changes in the levels of apoptosis inducing ligand TRAIL and negative correlation between TRAIL and hs-TnI levels in patients after acute stroke.

# VALIDATION OF THE AF-ESUS SCORE TO IDENTIFY PATIENTS WITH EMBOLIC STROKE OF UNDETERMINED SOURCE AND LOW RISK OF DEVICE-DETECTED ATRIAL FIBRILLATION

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**Background:** Atrial fibrillation (AF) is frequently detected after embolic stroke of undetermined source (ESUS) and therefore, cardiac rhythm monitoring is recommended. However, only a minority of ESUS patients receive prolonged cardiac monitoring, mainly due to limited availability of technical and human resources, and the considerable cost of some of the available monitoring options. The AF-ESUS score was recently developed for the identification of patients with low risk of new incident AF after ESUS.

**Purpose:** The aim of this study was to assess its performance in a previously published prospective cohort of consecutive ESUS patients with prolonged cardiac monitoring.

**Methods:** Consecutive ESUS patients admitted to the stroke unit of the Department of Neurology of the Evangelisches Klinikum Bethel between June 2013 and January 2015, were monitored with implantable loop recorders. AF-ESUS score was calculated for all ESUS patients. The sensitivity of AF-ESUS was defined as the probability that the AF-ESUS score will be >0 if AF is present and negative predicted value was defined as the probability that AF is not present if AF-ESUS ≤ 0 for various thresholds of AF duration.

**Results:** Among 123 patients (40% women, median age 66 years, IQR:59-73), 31 (25.2%) had AF-ESUS score ≤ 0. The overall follow-up period was 373 patient-years corresponding to a median of 36 months (IQR:36-42), and AF was detected in 52 (42.3%). The median AF-ESUS score was 2 (IQR:0-3) in the overall population. The sensitivity and NPV of the AF-ESUS threshold ≤ 0 were both 100% for the identification of ESUS patients with AF episodes lasting >10hours; 80% and 83.9% respectively for AF episodes >6 hours; and 76.6% and 64.5% respectively for AF episodes >6 minutes.

**Conclusion:** In this ILR-followed ESUS cohort, the threshold of AF-ESUS ≤ 0 showed high sensitivity and high NPV to identify a considerable proportion (25%) of the overall cohort who had low likelihood of AF.

# EVALUATING RISK OF PAROXYSMAL ATRIAL FIBRILLATION PRESENCE IN NON-CARDIOEMBOLIC ISCHEMIC STROKE USING ARTIFICIAL INTELLIGENCE-ENABLED ECG ALGORITHM

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## Background/Introduction

The TOAST classification defines five subtypes of ischemic stroke based on etiology. There is growing evidence that secondary prevention strategies should be differentiated according to the presence of atrial fibrillation (AF) in patients with non-cardioembolic ischemic stroke (NCIS). In 2019, a methodology was proposed for detecting such paroxysmal AF (PAF) during normal sinus rhythm (NSR) using artificial intelligence (the algorithm will be referred to as AIA).

## Purpose

Using AIA, we aimed at evaluating the risk of PAF presence in patients with NCIS when compared to the general population who visited the Ajou University Medical Center (AUMC).

## Methods

We extracted TOAST classification data from a pre-existing stroke database with manually entered clinical data of all patients with stroke admitted to AUMC. Using electrocardiogram data from AUMC, we developed AIA with a method almost identical to the study in 2019. After training AIA with the training/validation set, model inference outputs were obtained for the test set and NSRs of NCIS with large artery atherosclerosis (LAA), small artery occlusion (SAO), and cryptogenic etiology that were measured within a week before admission date. The inference output represented the relative probability of PAF presence in each NSR.

Multiple linear regression (MLiR) and multiple logistic regression (MLoR) analyses were conducted to evaluate the risk of PAF presence in patients with NCIS compared to the general population. Inference output (for MLiR) or the binary form (set at threshold=0.5, for MLoR) were used as dependent variables. Age, sex, and TOAST classification (LAA, SAO, cryptogenic, or test set) were used as predictor variables.

## Results

For AIA development, 398,202 NSRs were in the training/validation set, and 103,334 NSRs were in the test set. The number of NSRs inferred for LAA, SAO, and cryptogenic strokes were 153, 163, and 77, respectively. The area under the receiver operating characteristics curve for AIA was 0.807, indicating that the inference output and thus the relative probability of PAF presence could be deemed reliable.

There was an overall significance of both regression models ( $F[5,103721]=5847$ ,  $p<0.001$  for MLiR,  $\chi^2=154$ ,  $df=8$ ,  $p<0.001$  for MLoR). The predictor variables were significantly associated with the independent variable (MLiR: age [beta-coefficient=0.00707,  $p<0.001$ ]; male sex [beta-coefficient=0.0566,  $p<0.001$ ]; LAA [beta-coefficient=0.0514,  $p=0.002$ ]; SAO [beta-coefficient=0.0347,  $p=0.030$ ]; cryptogenic [beta-coefficient=0.0555,  $p=0.017$ ], MLoR: age [OR=1.067,  $p<0.001$ ]; male sex [OR=1.644,  $p<0.001$ ]; LAA [OR=1.404,  $p=0.049$ ]; cryptogenic [OR=1.787,  $p=0.018$ ]), except for SAO, in which MLoR was marginally significant (OR=1.322,  $p=0.091$ ), meaning that NCIS have higher risk/odds of having PAF compared to the general population after controlling for confounders (age, sex), with cryptogenic stroke having the highest risk/odds.

#### Discussion/Conclusion

After controlling for confounders, regression analyses showed that patients with NCIS had a higher risk of PAF than the general population. Since secondary prevention strategies should be differentiated according to the presence of AF in NCIS, our results imply the need for more vigorous Holter monitoring in these patients. Physicians can refer to each individual output of AIA as a guide to decide which patient should be monitored. Our study shows the potential and usability of artificial intelligence in clinical practice.

# ATRIAL HIGH-RATE EPISODES DURATION THRESHOLDS AND THROMBOEMBOLIC RISK: A SYSTEMATIC REVIEW AND META-ANALYSIS

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**Background:** The available evidence supports an association between atrial high-rate episodes (AHRE) burden and thromboembolic risk, but the necessary extent and duration of AHRE to increase the risk of thromboembolic events remains to be defined.

**Objectives:** The aim of this systematic review and meta-analysis was to identify the minimum AHRE burden associated with increased thromboembolic risk by deriving pooled estimates of the thromboembolic risk associated with various thresholds of AHRE burden.

**Methods:** We searched PubMed and Scopus until 01/09/2020 for literature reporting AHRE duration and thromboembolic risk in patients with implantable electronic devices. The outcome assessed was stroke or systemic embolism. Risk estimates in each study were reported as hazard ratio (HR) or relative risk (RR) alongside 95% confidence intervals (CI). We employed the Paule-Mantel estimator and heterogeneity was calculated with I<sup>2</sup> index.

**Results:** Among 27 studies including 61,919 patients, 23 studies reported rates according to the duration of the longest AHRE and 4 studies according to the cumulative day-level AHRE duration. In patients with cardiac implantable devices due to heart failure or severe dysrhythmias, AHREs lasting >30 seconds significantly increased the risk of stroke or systemic embolism (HR:4.41, 95%CI:2.32–8.39, I<sup>2</sup>:5.5%), which remained consistent for the thresholds of 5 minutes, 6 and 24 hours. Patients with previous stroke or TIA and AHREs lasting >2 minutes had a marginally increased risk of recurrent stroke or TIA.

**Conclusions:** This systematic review and meta-analysis suggests that the AHRE threshold of >30 seconds is associated with increased risk of stroke or systemic embolism.



## NEW-ONSET ATRIAL FIBRILLATION AS A PREDICTOR OF IN-HOSPITAL STROKE IN ACUTE CORONARY SYNDROME

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**Background:** Atrial fibrillation was long related to a higher risk of stroke. However, the presence of new-onset atrial fibrillation in the setting of acute coronary syndrome (ACS) can present other risk factors for in-hospital stroke.

**Objective:** Evaluate if new onset of atrial fibrillation was a predictor of in-hospital stroke in ACS patients.

**Methods:** Multicenter retrospective study, based on the Portuguese Registry of ACS between 1/10/2010-4/09/2019. New-onset AF was defined as the first episode of AF in patients without a history of AF and if occurred during the hospitalization for ACS. Logistic regression was performed to assess if new onset of atrial fibrillation was a predictor of in-hospital stroke in ACS patients. Kaplan-Meier test was performed to establish the survival rates and re-admission for all causes at one year of follow up.

**Results:** Both groups were similar regarding body mass index, arterial hypertension, valvular disease, previous history of heart failure, chronic kidney disease, neoplasia, chronic obstructive pulmonary disease, ST-segment elevation myocardial infarction, systolic blood pressure and multivessel disease. Patients without stroke had higher prevalence of smokers (26.7 vs 16.6%,  $p=0.005$ ), dyslipidemia (61.6 vs 53.5%,  $p=0.047$ ), and coronary artery disease (20.6 vs 12.7%,  $p=0.077$ ). On the other hand, patients with stroke during the hospitalization for ACS presented a higher medium age ( $67\pm 14$  vs  $72\pm 12$ ,  $p<0.001$ ), female gender (27.5 vs 53.2%,  $p<0.001$ ), diabetes (31.5 vs 43.9%,  $p<0.001$ ), peripheral vascular disease (5.5 vs 9.2%,  $p=0.044$ ), previous stroke (7.2 vs 13.3%,  $p=0.004$ ), dementia (1.7 vs 6.8%,  $p<0.001$ ), fatigue at admission (0.5 vs 2.6%,  $p=0.011$ ), cardiac arrest at admission (0.5 vs 2.6%,  $p=0.006$ ), heart rate at admission ( $77\pm 19$  vs  $84\pm 24$ ,  $p=0.001$ ), atrial fibrillation at admission (7.1 vs 16.4%,  $p<0.001$ ), Killip-Kimball classification  $> I$  (15.1 vs 28.0%,  $p<0.001$ ), and left ventricular ejection fraction (LVEF) $<30\%$  (5.3 vs 15.5%,  $p<0.001$ ). Logistic regression revealed that new onset of atrial fibrillation (odds ratio (OR) 1.865,  $p=0.024$ , confidence interval (CI) 1.085-3.205) was a predictor of in-hospital stroke in ACS patients. From 2024 patients with follow-up at 1 year, 1999 in group without stroke during the hospitalization for ACS and 25 patients that suffered stroke, stroke was associated with a poor outcome regarding readmission and death at 1 year follow up (OR 2.050,  $p<0.001$ , CI 1.382-3.041). Nonetheless, readmission at one year was not different (OR 1.549,  $p=0.234$ , CI 0.947-2.533) between the patients without stroke (1768 patients) and with stroke (16 patients) during the hospitalization for ACS. Death at one year follow up was significant higher (OR 3.331,  $p<0.001$ , CI 1.808-5.422) in the patients that presented stroke during the hospitalization (13 patients) comparing with non-stroke patients in ACS hospitalization (626 patients).

**Conclusions:** New onset of atrial fibrillation was a predictor of in-hospital stroke in hospitalized patients for ACS. Stroke during the hospitalization for ACS in patients that presented new onset of AF was not a predictor of re-admission or death, yet this group presented higher rates of mortality at 1 year of follow up.

## OUTCOMES OF ISCHEMIC STROKE IN PATIENTS WITH ATRIAL FIBRILLATION

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**Background.** Atrial fibrillation (AF) increases the risk of ischemic strokes (IS) and is associated with a more severe neurological impairment.

**Aims.** We sought to investigate whether AF also impacts the neurological recovery and whether patients with AF have a different response to the treatment.

**Methods.** Data of patients admitted for an ischemic stroke to the Stroke Unit of our institution from January to December 2020 were retrieved from the local database. The stroke severity was calculated by mean of the National Institute of Health Stroke Scale (NIHSS) at hospital admission (NIHSSad), at 24 hours (NIHSS24) and at discharge (NIHSSdis). The functional capacity was assessed by the modified Rankin score (mRS). As for the neurological recovery, this was assessed by the delta NIHSS at 24 hours ( $\Delta 24 = \text{NIHSS}_{24} - \text{NIHSS}_{ad}$ ) and at discharge ( $\Delta \text{dis} = \text{NIHSS}_{dis} - \text{NIHSS}_{ad}$ ).

**Results.** Out of 545 patients with IS 64 had known history of AF or were admitted with AF. Patients with AF had higher NIHSSad ( $13.9 \pm 7$  vs  $8.5 \pm 7$ ;  $p < 0.001$ ) and NIHSS24 ( $9.6 \pm 8$  vs  $6.4 \pm 7$ ;  $p = 0.007$ ) than patients without, however the neurological improvement was greater ( $\Delta \text{dis} -7.4 \pm 9$  vs  $-3.4 \pm 6$ ;  $p = 0.002$ ), indeed the NIHSSdis was similar ( $4.2 \pm 5$  vs  $4.2 \pm 6$ ;  $p = 0.98$ ). Patients with AF also had a more impaired mRS before the ischemic event and at discharge ( $2.4 \pm 1.9$  vs  $1.6 \pm 1.7$ ,  $p = 0.02$ ;  $1.2 \pm 1.2$  vs  $0.4 \pm 0.9$ ,  $p < 0.001$ ). Amongst AF patients with CHADVASC  $\geq 3$ , 34% of them were taking antiplatelet therapy, 31% anticoagulants and 35% didn't take any therapy. Of interest, no differences in the NIHSSad nor in the NIHSSdis were found between them and neither in the  $\Delta \text{dis}$ . As for the treatment of AF patients, no differences in the neurological recovery were observed between those treated with intravenous thrombolysis and those not treated at all ( $\Delta \text{dis} 2.8 \pm 5$  vs  $2.8 \pm 8$ ,  $p = 1$ ), whereas the  $\Delta \text{dis}$  was significantly higher in patients treated with mechanical thrombectomy ( $-11.7 \pm 7$ ,  $p = 0.007$ ).

**Conclusion.** Patients with AF experience more severe stroke, however the neurological recovery is greater than in patients without the arrhythmia. The treatment with antiplatelets or anticoagulants before the event does not reduce the severity of the stroke and does not influence the improvement of the NIHSS at discharge. The mechanical thrombectomy is more effective in reducing the neurological impairment.

## PREDICTING FACTORS OF ATRIAL FIBRILLATION IN PATIENTS WITH CRYPTOGENIC STROKE

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**Background.** Paroxysmal AF(PAF) is a cause of cryptogenic stroke(CS) in every third patient. PAF often remain undiagnosed due to their short duration and asymptomatic nature. A number of devices for continuous monitoring of the heart rate are used. However, the largest proportion of detection of latent atrial fibrillation can be obtained when using the preliminary selection of patients by risk factors. **Purpose.** Invention of a model for predicting atrial fibrillation in patients with CS. **Materials and methods.** The study included 981 patients with ischemic stroke. In order to identify the factors influencing the likelihood of AF in patients, crude odds ratios COR (CI 95%) were calculated for the following factors: gender, history of stroke, history of thromboembolism, presence of diabetes mellitus (DM), degree of arterial hypertension (AH), functional class of chronic heart failure (FC CHF), age, biochemical blood test data, coagulogram data. For further analysis, factors with a significance of  $p < 0.05$  were used. Binary logistic regression was used to build the predictive model. The critical level of p-value when testing statistical hypotheses in our study was taken equal to 0.05. **Results.** The predictive model is the following:

$$P = 1 / (1 + e^{-z})$$

$$z = -3.51 + 1.709 * X_{FC\ CHF} + 0.526 * X_{stroke} + 0.053 * X_{age} - 0.016 * X_{XPI} - 0.382 * X_{Xhol} - 0.888 * X_{sex}$$

where P is the probability of AF, X<sub>FC CHF</sub> - functional class of chronic heart failure (0-no CHF, 1-I class, 2-II class, 3- III class, 4-IV class), X<sub>stroke</sub> - history of stroke (0-absence, 1 - presence), X<sub>age</sub> - age (years), X<sub>XPI</sub> - prothrombin index (%), X<sub>hol</sub> - cholesterol level (mmol / l), X<sub>sex</sub> - gender (0 - female, 1-male).

The resulting predictive model was statistically significant ( $p < 0.001$ ). Based on Nagelkirk's coefficient of determination R<sup>2</sup>, 53.8% of the factors influencing the likelihood of AF were taken into account in it. The model we obtained had the following characteristics: sensitivity - 74%, specificity - 89.9%, positive predictive value of the model - 54.7% and negative predictive value - 95.5%. **Conclusion.** The invention of a predictive model to identify the likelihood of atrial fibrillation will significantly increase the proportion of detected AF, since monitoring will be carried out in a target group of patients.

# POPULATION TRENDS IN PREVALENCE, RISK STATUS, ANTITHROMBOTIC THERAPY, AND HOSPITALISATION WITH THROMBOEMBOLIC EVENTS IN NON-VALVULAR ATRIAL FIBRILLATION: SAIL COMPARATIVE ANTICOAGULATION OUTCOMES RISK EVALUATION STUDY (SCORE-AF)

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## Background

Atrial fibrillation (AF) can occur at any age but is more common in older persons and in those with cardiovascular disease, obesity, diabetes mellitus, or chronic kidney disease. In the UK, increasing AF prevalence can be attributed both to better detection of silent AF, alongside increasing incidence in an ageing population. AF is associated with an increased risk of stroke and systemic embolism (SSE), which can be reduced by effective antithrombotic therapy.

Historically the mainstay of antithrombotic treatment has been with an oral vitamin K antagonist (VKA), or an antiplatelet (APT) agent such as aspirin. From 2014 in the UK the AF management NICE Clinical Guideline 180 has recommended that patients with AF have their stroke risk assessed using the CHA2DS2-VASc score and, based on their CHADS-VASc score and bleeding risk, are offered oral anticoagulation in preference to antiplatelet therapy.

## Purpose

To evaluate the overall impact of changes in the prevalence of non-valvular AF (NVAf), associated SSE risk, and evolving trends in antithrombotic treatment strategy on hospitalisation for SSE at a population level.

## Method

Patients with NVAf were identified from routinely-collected, longitudinal, primary and secondary care data in the All-Wales Secure Anonymised Information Linkage (SAIL) Databank. Temporal trends of prevalence, CHA2DS2-VASc risk scores, antithrombotic treatment status (oral anticoagulation [OAC], anti-platelet therapy [APT], and no therapy [NT]), and hospital admissions for SSE were reported for NVAf patients over the study period 2010 to 2019.

## Results

During the study period the numbers of patients with NVAf increased from 39,049 to 65,533, reflecting an increase in population prevalence from 1.2% to 2.0%. Mean CHA2DS2-VASc score increased from 2.6 ( $\pm 1.5$ ) to 2.8 ( $\pm 1.5$ ) ( $p < 0.001$ ).

Numbers prescribed OAC increased from 18,434 (47.2% of the population) to 46,772 (71.4%); numbers prescribed APT decreased from 12,244 (31.4%) to 4,001 (6.1%); the proportion of patients not prescribed any antithrombotic treatment remained stable over the study period 8,371 (21.4%) to 14,760 (22.5%).

In 2010 there were 844 admissions with SSE increasing over the decade to 944 in 2019. This equates to a reduction in admission rates for SSE (per 100 patients/year) from 2.2 in 2010 to 1.4 in 2019. (Figure).

### Conclusions

NVAF prevalence increased progressively in Wales over the period 2010-19, accompanied by a modest increase in SSE risk. The proportion of the population prescribed anticoagulation increased substantially as the prescribing of antiplatelet therapy fell over the same period. This was associated with a progressive year on year fall in SSE hospitalisation rates equating to a hospitalisation rate in 2019 of less than two thirds of the rate.

### Funding

This study was sponsored by Pfizer and Bristol Myers Squibb.

### Conflict of interest

DH: paid for delivering educational presentations for both Bristol Myers Squibb & Pfizer

JH: received personal fees from Bristol Myers Squibb, Pfizer, Boehringer Ingelheim, and Bayer outside the submitted work and received research funding from BMS & Pfizer

RA: received fees for consulting work from Bristol Myers Squibb, Pfizer, Bayer & Daiichi

SL, SG and KP: employees of Bristol-Myers Squibb Ltd.

LM: employee of Pfizer Ltd.

# NON-VALVULAR ATRIAL FIBRILLATION AND ORAL ANTICOAGULATION ASSOCIATED HOSPITALISATION DUE TO BLEEDING: A 10 YEAR RETROSPECTIVE STUDY IN WALES, UK (SCORE AF)

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## Background

Oral anticoagulation (OAC) reduces the risk of stroke and systemic embolism (SSE) in patients with non-valvular atrial fibrillation (NVAF). However, concern regarding the risk of bleeding is a commonly cited reason for not prescribing OAC. The 2014 UK NICE Clinical Guidelines 180 for management of AF recommended OAC with a direct oral anticoagulant (DOAC) or a vitamin K antagonist (VKA) for SSE prevention and advised against antiplatelet therapy (APT). As part of the stroke delivery plan for Wales and the Stop A Stroke campaign [www.stopastroke.co.uk](http://www.stopastroke.co.uk) in conjunction with the Wales Cardiac Network, British Heart Foundation and Stroke Association, a series of initiatives were launched in primary and secondary care to increase the awareness of AF related stroke risk and to encourage OAC prescribing while remaining mindful of the risk of bleeding.

## Purpose

To describe relationships between changes in antithrombotic prescribing and the rate of hospitalisation due to bleeding in patients with NVAF.

## Methods

Retrospective, observational study using linked anonymised population health records in patients with NVAF from 1st Jan 2010 – 31 Dec 2019 in Wales, UK.

## Results

At the end of 2010, only 47% of the NVAF population in Wales was anticoagulated, all with a VKA. There was little prescribing of DOACs prior to 2015 (<5% of the NVAF population). Between 2012 – 2015 there was a year-on-year increase in patients prescribed VKA peaking at 27,170 (51%) with 5,518 prescribed a DOAC (10%). During this time there was an increase in the rate of hospitalisation with bleeding from 2.7 to 3.1 per 100 patients / year.

From 2016, the number and proportion of NVAF patients prescribed OAC continued to increase, but the number and proportion of those treated with VKA fell steadily, along with a concomitant increase in the number and proportion prescribed a DOAC. In the final year, 26.3% of NVAF patients were prescribed a VKA and 45.7% a DOAC. This represents an increase in the proportion of the NVAF population that was anticoagulated rising from 61% in 2015 to 72% in 2019. Over this period the rate of hospitalisation with bleeding fell to a rate of 2.7 per 100 patients per year.

## Conclusion

This study demonstrated that increasing OAC prescriptions between 2010 – 2019 did not significantly change the rate of hospitalisation due to bleeding in patients with AF.

However, between 2010 – 2015 an increasing number and proportion of patients with NVAF were prescribed VKA with a small increase in the proportion prescribed a DOAC; over this period the rate of

hospitalisation due to bleeding increased. Since 2016, increasing numbers of NVAF patients were anticoagulated, with an increasing proportion prescribed a DOAC; over this period the rate of admission with bleeding fell to similar rates to those observed in 2010. Thus, the temporal patterns in rates of hospitalisation with bleeding between 2010-19 reflect changing patterns VKA and DOAC prescribing in NVAF patients at a population level. Causal relationships cannot be confirmed in a study of this type.

## THE HEART-BRAIN AXIS IN EXPERIMENTAL SUBARACHNOID HEMORRHAGE

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**Objective:** Cardiac pathologies occur in up to 30% after subarachnoid hemorrhage (SAH), significantly contributing to complications and outcome. The underlying pathology of the interplay between cerebral hemorrhage and cardiac dysfunction is poorly understood. We sought to describe an in-vivo mouse model to investigate the systemic role of extracellular RNA known to be released in the injured brain in SAH and its effects on cardiac function.

**Methods:** Experimental SAH was induced in male C57Bl/6 mice via a filament perforation model and confirmed via MRI, while sham operation was conducted for the control group. Transthoracic echocardiography (TTE) was performed to elicit diastolic and systolic function on three timepoints: day 1, 7 and 14 (ntotal=72). Invasive pressure volume measurements were used for cardiac functional testing at day 14. Diastolic function was assessed by determining early and late atrial transmitral flow velocity (E/A ratio). Left ventricular ejection fraction (LVEF) was used as a measure for systolic function. Cardiomyocyte size was quantified using Hematoxylin/Eosin staining. Masson Trichrome staining was performed to determine percentage of fibrotic tissue. Extracellular RNA (eRNA) was determined by triple immunofluorescence staining of F-actin, ribosomal RNA (rRNA), and DAPI.

**Results:** While there were no significant differences in cardiac function on d1 and d7 after induction of SAH, mice had impaired diastolic function demonstrated by reduced E/A ratio (Sham vs. SAH: 1.60 vs. 1.05;  $p=0.023$ ) 14 days after SAH with preserved systolic function (LVEF: Sham vs. SAH: 68% vs. 64%,  $p=n.s.$ ). Diastolic dysfunction was accompanied by cardiac hypertrophy assessed by increased heart weight by 11.7% (Sham vs. SAH: 136 mg vs. 152 mg;  $p<0.05$ ) and increased cardiomyocyte size (Sham vs. SAH:  $354.2\mu\text{m}^2$  vs.  $412.2\mu\text{m}^2$ ;  $p=0.017$ ). Furthermore, we observed increased perivascular (Sham vs. SAH: 24.4% vs. 41.6%;  $p=0.008$ ) and interstitial fibrosis (1.31% vs. 2.09%;  $p=0.033$ ) in the myocardial tissue. This was accompanied by increased eRNA levels in cardiac tissue (Sham vs. SAH:  $18.32$  vs.  $103.3 * 103\mu\text{m}^2$  eRNA/ $\text{mm}^2$  tissue,  $p<0.001$ ). Interestingly, diastolic dysfunction as well as cardiomyocyte hypertrophy was reversed by inhibiting endogenous eRNA via RNase1 treatment after 14 days (SAH vs. SAH+RNase1: 1.05 vs. 1.5;  $p=0.028$ ) and  $412.2\mu\text{m}^2$  vs.  $353.9\mu\text{m}^2$ ;  $p=0.013$ ).

**Conclusion:** We describe a model that can be utilized to study the heart-brain axis in the setting of SAH. In SAH mice, a significant impact on diastolic dysfunction is observed 14 days after inducing SAH, paralleled by cardiac hypertrophy, and RNase application rescues this phenotype. Hence, eRNA could represent a novel and potentially modifiable mediator in the brain-heart axis in SAH.



## AORTOGENIC ISCHEMIC STROKE DIAGNOSED BY NON-OBSTRUCTIVE GENERAL ANGIOSCOPY

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**Background:** Aortogenic embolization is one of the major mechanisms of cryptogenic stroke. Prior studies evaluated by transesophageal echocardiography (TEE) have reported that the extent of atherosclerosis in the aortic arch and descending aorta predicts ischemic stroke. However, the TEE is relatively insensitive for the detection of aortic plaques and are limited in their ability to assess plaque characteristics that may predict subsequent clinical events. Non-obstructive general angiography (NOGA), which is a newly developed method to evaluate aortic atheromatous plaques with real-time and high spatial resolution images, can clearly detect the atherosclerotic vulnerability of the aortic wall in more detail than TEE. We, herein, present 2 ischemic stroke cases of aortic arch observation using NOGA.

**Case 1:** A 71-year old man was admitted to our hospital because of the sudden onset of left incomplete paralysis. Magnetic resonance imaging of the brain indicated an acute ischemic stroke at the right striatum. Furthermore, immediately after hospitalization, an electrocardiogram showed ST elevation in the III and aVF lead, and echocardiography revealed hypokinesis of the left ventricular inferior wall. Serum troponin I test was positive. Under the diagnosis of ST-elevation myocardial infarction, emergent coronary angiography was carried out, and the left circumflex artery was obstructed. We performed percutaneous coronary intervention (PCI) to the obstructed lesion. Following PCI, NOGA was performed to identify the etiology of the stroke and showed lots of atheromatous plaques throughout the aorta. Especially, spontaneously rippled thrombi on the ruptured plaques was observed in the aortic arch by NOGA. Embolization of the thrombi in the aortic arch could cause an ischemic stroke.

**Case 2:** An 82-year-old man had sudden right incomplete paralysis. Brain magnetic resonance imaging indicated an acute ischemic stroke in the left striatum. He underwent catheter ablation of paroxysmal AF 15 years before the stroke. No recurrence of AF had been detected until or during hospitalization. His CHADS2 score was low (1: age), and he was taking an anticoagulant. TEE showed no thrombus in the left atrium and appendage and no atheromatous plaques the aortic arch. There were no significant lesions in the carotid or intracranial arteries. For seeking the etiology of the stroke, NOGA revealed several atheromatous plaques in the aortic arch. Remarkably, some ruptured plaques scattered atheromatous materials, which could become the cause of his embolic stroke, although TEE detected no atheromatous plaque.

### Conclusions:

We report 2 cases of acute stroke with NOGA-derived atheromatous plaques in the aortic arch. NOGA might help to diagnose atheromatous plaques and embolic materials in the aortic arch.

# BI-ATRIAL THROMBUS STRADDLING A PATENT FORAMEN OVALE WITH BILATERAL EMBOLISATION

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## Introduction

Stroke is a leading cause of morbidity and mortality. Cardioembolic stroke as a result of intra-cardiac thrombus is a difficult entity to manage due to the risk of haemorrhagic transformation during the acute phase of an ischaemic stroke as well as the need for anticoagulation to prevent further embolisation. The scenario lacks clear guidelines and it is therefore important to highlight such difficult cases and the rationale behind the multidisciplinary decisions made, in order to further progress research and interest in these cases.

## Case Presentation

A 55-year-old male presented with sudden onset speech disturbance. Examination revealed an expressive dysphasia. A CT head was performed which showed hypodensity in the left insular cortex and temporoparietal lobe suggesting acute ischaemia. An MRI head showed a moderate-sized acute left MCA territory infarct involving the left frontal operculum, insular cortex and temporoparietal regions with mild local mass effect. A CT angiogram demonstrated a filling defect within the left MCA suggesting thrombus.

A transthoracic echocardiogram (TTE) demonstrated a large mobile mass within the right atrium measuring at least 6.0cm x 0.9cm. A transoesophageal echocardiogram (TOE) confirmed a large thrombus within the right atrium that prolapsed into the right ventricle as well as through a patent foramen ovale (PFO) into the left atrium. He also underwent a CT pulmonary angiogram which demonstrated multiple bilateral pulmonary emboli.

## Discussion

We present a case of a patient with a cardioembolic stroke due to a large thrombus across a patent foramen ovale, which required a multidisciplinary approach between the cardiology, cardiac surgical, stroke and haematology teams. The size, position and mobility of the thrombus and the presence of bilateral pulmonary emboli and a PFO made our patient high-risk of further emboli. Although anticoagulation would increase the risk of haemorrhagic transformation of his ischaemic infarct, it was felt across the teams that the benefit of preventing further emboli outweighed the risks. He was, therefore, started on intravenous unfractionated heparin, providing rapid onset of action and allowing careful control guided by the APTT ratio. This also provided a means of immediate withdrawal of anticoagulation in the event of significant haemorrhagic transformation. The risks of cardiac surgery to extract the thrombus were deemed excessive in the context of a recent stroke with concerns that manipulation of the heart during surgery may have also exposed the patient to an embolic shower.

As he remained on the heparin infusion following a recent infarct, a repeat CT head with contrast was performed on day 8 which showed mild haemorrhagic transformation. The patient, however, remained well neurologically and continued to make a good recovery with intravenous heparin.

A subsequent TOE confirmed complete resolution of the thrombus. The patient was switched to apixaban therapy and underwent neuro-rehabilitation. Following discharge there have been no further embolic episodes. He has made good neurological progress and has been referred for PFO closure.

## A SEQUENCE OF UNUSUAL FINDINGS IN A “CARDIOCEREBRAL INFARCTION” - A CASE REPORT

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The acute complications of myocardial infarction (MI) may include cerebrovascular events. The expression of “cardiocerebral infarction” was first described by Omar et al., and can be classified as “synchronous” or “metachronous”. In-hospital stroke after an acute coronary syndrome is estimated around 0.9% with the highest incidence for ST-segment elevation myocardial infarction (STEMI).

The authors describe the case of a 46-year-old woman, smoker, admitted to the emergency room due to syncope, with fast recovery. She also experienced transient acute chest pain during transport. Her mother had a MI and several strokes, one of which was fatal at the age of 55.

On admission, she was asymptomatic, with a normal physical examination. The electrocardiogram (ECG) revealed non-significant ST-segment changes. During the examination, she initiated slight chest pain and suffered from three episodes of polymorphic ventricular tachycardia (PVT). Cardiopulmonary resuscitation with electrical defibrillation was performed and she recovered immediately.

A new ECG revealed moderate ST-segment elevation in precordial and inferior leads. An emergent coronary angiography showed a proximal occlusion of the right coronary artery, with thrombus embolization during contrast injection. The lesion was treated with thrombus aspiration, predominantly white, and balloon dilatation. Finally, due to a proximal dissection flap, a drug stent was implanted. During the procedure, she suffered from two episodes of PVT, initiated by the “R-on-T” phenomenon, reverted with electrical defibrillation.

About 4 hours after, she started a sudden onset of dysarthria, facial palsy and mild right hemiparesis (National Institutes of Health Stroke Score [NIHSS] 11). The cervical and cranial computed tomography (CT) angiography revealed a total proximal occlusion of the left internal carotid artery (ICA) since cervical planes up to the cavernous planes, suggestive of thrombosis. The cranial CT showed slight signs of left ischemic stroke.

It was considered that there was no indication for thrombolysis or thrombectomy, taking into account the location of the occlusion, the existence of signs of cerebral infarction and the high hemorrhagic risk. She evolved with global aphasia, dysphagia, right facial paralysis, right homonymous hemianopsia, right hemiplegia and hypoesthesia (NIHSS 21). 24-hours cranial CT showed an extensive left cortico-subcortical temporoparietal infarction and midline shift. The carotid-vertebral Doppler showed dissection and subocclusion of the left ICA due to an extensive organized thrombus, occlusion in the distal M2 segment and ineffective collateral circulation. A decompressive craniectomy wasn't necessary.

The analytical study revealed dyslipidemia, hyperthyroidism, heterozygosity for MTHFR mutation A1298C and positive lupus anticoagulant (in the acute phase). During hospitalization, she attended a rehabilitation programme with dysphagia resolution and motor improvement. After one month, she was discharged to a Physical Rehabilitation Hospital.

In conclusion, the authors reported a case of a “metachronous cardiocerebral infarction”, possibly related to cardiac catheterization and/or to the thrombotic risk of this patient. Despite its rarity, it is a severe complication with a challenging and unclear management. Some evidence suggests that direct oral anticoagulants may reduce the risk of cerebrovascular events in patients with a recent STEMI. Further studies would be important in order to improve the associated prognosis.

# THE CAPABILITIES OF THE REMOTE MONITORING SYSTEM FOR STROKE PREVENTION

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**Background.**The remote patient monitoring system became most relevant during the COVID-19 pandemic, as the doctor was able to invite only patients with emergency conditions and reduce unnecessary visits.

**Purpose.**The case describes the detection and management of atrial fibrillation using an implanted cardiac device in a patient suffering from heart failure and no previous arrhythmias.

## Patient presentation

A 56 year old man presented to the clinic with shortness of breath when climbing the 2nd floor, moderate nonspecific fatigue, general weakness, a decrease in exercise tolerance. Past medical history-arterial hypertension for 10 years with maximum BP 200/100 mm Hg, myocardial infarction 8 years before, right coronary artery stenting, circumflex coronary artery bypass grafting, mammary coronary artery bypass grafting of the anterior interventricular branch. Physical examination on admission showed obesity with BMI - 35.0 kg / m<sup>2</sup>. No edema. Pulse was regular with an average rate of 76 beats per minute. BP 90/60 mm Hg. The patient received standard treatment for HF for at least 3 months (ACEI, beta blockers and MR antagonists) in individually selected doses.

## Initial work up

ECG on admission. Sinus rhythm with a heart rate of 81 beats per minute, QRS 150 ms. LBBB. Biochemical blood test cholesterol - 5.25 mmol / l, triglycerides - 1.18 mmol / l, LDL chol - 3.25 mmol / l, HDL chol - 1.93 mmol / l, glucose - 100.6 mg / dl, Na - 138 mmol / L, K - 4.3 mmol / L. Pro-BNP-1512 pg / ml. 6 minutes walk test -320m. Echo showed dilation of all heart chambers. Diffuse wall hypokinesis. Akinesis of the apical, middle anterior segments of the LV. Hypokinesis of the basal, middle apical septal, anterior septal segments of the LV. Global myocardial contractility is reduced. Ejection fraction 35 %. Mitral regurgitation (+1.5). Tricuspid regurgitation (+). RV function is reduced.

## Diagnosis and Management

According to indications for cardiac resynchronization therapy in patients in sinus rhythm from ESC Guidelines CRT is recommended in chronic HF patients and LVEF  $\leq$ 35% who remain in NYHA functional class II, III and ambulatory IV despite adequate medical treatment. This is particularly true for patients with LBBB with QRS duration 120–150 ms. After a detailed discussion with the team, it was decided to do implantation of a cardioverter-defibrillator with resynchronization function, with a primary endocardial system. Medicines were prescribed according to the guidelines

## Follow-up

ECG at discharge. Atrial-synchronized biventricular stimulation with HR-74 beats / min. QRS-120ms. Routine follow-ups did not reveal any heart rhythm disturbances in the patient. As the patient was connected to the remote monitoring system only after 1 year and 11 months, he was diagnosed with asymptomatic atrial fibrillation. The episode lasted 1 min 22 sec. On the following days of monitoring, episodes of atrial fibrillation were also recorded.

Patient's risk of stroke was 4 when assessed using the CHA2DS2VASc scale. It was recommended to add antiarrhythmic drugs and oral anticoagulants.

Two weeks later periodic IEGM showed absence of atrial fibrillation.

## Conclusion.

Remote monitoring allows immediately identify AF and prevent stroke.

## TREATING MAY HAVE ITS SETBACKS

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**Introduction:** Stroke is an important complication after cardiac catheterization procedures, with reported rates ranging from 0.07 to 7%, resulting in death and disability. Common risk factors include advanced age, vascular comorbidities, and complicated procedures. They are likely embolic, either from a dislodged clot or atheromatous debris off the aortic arch or from thrombus formation on the tip of a guide catheter.

**Case Report:** Male patient, 73 years old, with history of hypertension, heavy smoking and ethanolic habits, presented with an inferior myocardial infarction, so emergent coronariography was made. It revealed a 95% lesion on the proximal segment of the right coronary artery, so angioplasty with a drug eluting stent was performed. Transthoracic echocardiogram showed preserved left ventricular systolic global function with hypokinesia of mid- basal segments of the inferior wall. On the next morning, he was found presenting with muscle strength impairment grade 3 on the right inferior limb, right hemiparesthesias and expression aphasia (NIHSS 6). Consequently, the patient did a brain CT, which did not showed any changes.

Neurological deficits improved after two days. During this time, neither arrhythmias, nor heart failure symptoms were observed. Brain MRI was performed. It revealed hydric diffusion restriction of corona radiata, globus pallidus, peri-atrial region, and parietal cortex on the left side. These were compatible with recent ischemic lesions of left middle and posterior cerebral arteries territories. Absence of left internal carotid artery contrast fill from its origin until subarachnoid segment. Posterior communicating arteries, two segments of A2 and left vertebral artery V4 segment were not observed (it was not possible to exclude occlusion vs anatomical variant). The case was discussed with Interventional Neuroradiology of the reference center. It was decided not to intervene, as it was considered that the risk outweighed the benefit, due to the presence of non-acute right internal carotid artery occlusion. Patient was discharge seven days after stroke without any neurological deficits (NIHSS 0), nor cardiac symptoms or arrhythmias.

**Conclusion:** This patient only presented with mild neurological symptoms, which fully reverted, although targeted treatment was not performed. Despite that, stroke caused by coronariography increased patient's in-hospital stay.

## STROKE AS COMPLICATION IN CORONARY ANGIOGRAPHY AND PERCUTANEUS CORONARY INTERVENTION

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**Background :** Stroke is serious complication of percutaneous coronary interventions. It is reported to occur in 0,05 – 0,1% of diagnostic cardiac catheterizations and 0,18-0,4% of patient treated with percutaneous coronary interventions. Reported rates including ischemic and hemorrhagic types of stroke. Risk factors for periprocedural stroke are: age, arterial hypertension, diabetes mellitus, emergency coronary procedure, renal failure and others.

**Methods and results:** We will present a series of three case studies of stroke after cardiac catheterization. **Case1.** 78-year-old male patient admitted to the coronary unit as an acute myocardial infarction of the posterolateral wall NSTEMI. After admission, coronary angiography and percutaneous coronary angioplasty with stent implantation in SVG-OM2 are performed. "During the intervention, the patient feels dysphasia and weakness of the right arm and leg. A CT scan of the head is performed to diagnose an acute ischemic lesion of the insula and the external capsule. In the history of the disease, the patient had earlier myocardial infarction, triple coronary artery bypass grafting and arterial hypertension.

**Case 2.** A 46-year-old male patient was admitted to the coronary unit due to STEMI anteroseptal localization. Percutaneous coronary angioplasty with stent implantation in LAD was performed. After 24 hours of the procedure, the patient feels weakness in the right arm and leg. A CT scan of the head is performed and diagnose acute ischemic lesion in the medulla oblongata. The patient had a history of chronic renal failure and arterial hypertension.

**Case 3.**

A 56-year-old male patient was admitted due to an acute myocardial infarction of the anterior wall STEMI. Percutaneous coronary angioplasty is performed with stent implantation in the LAD. 24 hours after the intervention, the patient complains of severe dizziness. A CT scan of the head is performed to diagnose a hematoma in the right temporal region. The patient's treatment was completed successfully with hematoma withdrawal and without thrombosis and stent stenosis. In the history of the disease, the patient has arterial hypertension and diabetes mellitus.

**Conclusions:** Peri-interventional stroke is still associated with an exceedingly high in-hospital mortality rate. Intra-arterial thrombolysis and mechanical embolectomy seem to be promising and relatively safe approaches in the treatment of periprocedural ischemic stroke. Most predictors for periprocedural stroke are not modifiable and cannot be diminished before PCI. Treatment of patients with stroke after PCI needs further research.

**Abbreviations:** NSTEMI-non ST elevation myocardial infarction  
SVG-OM2- safena vena graft-obtuse marginal branch 2 coronary artery  
CT- computed tomography  
STEMI- ST elevation myocardial infarction  
LAD- left anterior descedens coronary artery  
PCI-percutaneous coronary intervention

## STROKE IN ACUTE CORONARY SYNDROME

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**Background:** Acute coronary syndromes (ACS) are frequent and are associated with high levels of comorbidities and complications. Stroke is one of the several complications described that can occur and affect the patient's recovery.

**Objective:** Evaluate predictors of stroke in ACS.

**Methods:** Multicenter retrospective study, based on the Portuguese Registry of ACS between 1/10/2010-4/09/2019. Patients were divided in two groups: A – patients without stroke, and B – patients that presented stroke during the hospitalization for ACS. Were excluded patients without a previous cardiovascular history or clinical data. Logistic regression was performed to assess predictors of stroke in ACS patients.

**Results:** Both groups were similar regarding arterial hypertension, dyslipidemia, valvular disease, previous history of heart failure, peripheral vascular disease, chronic kidney disease, neoplasia, chronic obstructive pulmonary disease, ST-segment elevation myocardial infarction and systolic blood pressure. Group A had higher index of smokers (29.9 vs 18.9%,  $p=0.008$ ). On the other hand, group B had higher median age ( $66\pm 14$  vs  $71\pm 13$ ,  $p<0.001$ ), female gender (28.8 vs 53.8%,  $p<0.001$ ), body mass index ( $27.4\pm 4.4$  vs  $26.7\pm 4.4$ ,  $p<0.0019$ ), diabetes (27.2 vs 38.8%,  $p=0.004$ ), previous stroke (6.1 vs 12.9%,  $p=0.002$ ), dementia (1.8 vs 7.4%,  $p<0.001$ ), chest pain at admission (92.3 vs 75.8%,  $p<0.001$ ), heart rate at admission ( $78\pm 19$  vs  $83\pm 23$ ,  $p<0.001$ ), atrial fibrillation at admission (6.7 vs 17.1%,  $p<0.001$ ), Killip-Kimball classification  $> I$  (13.6 vs 24.0%,  $p<0.001$ ), left bundle branch block (3.0 vs 6.6%,  $p=0.033$ ) and left ventricular ejection fraction (LVEF) $>50\%$  (64.0 vs 48.3%,  $p<0.001$ ). Logistic regression revealed female gender (odds ratio (OR) 1.891,  $p=0.005$ , confidence interval (CI) 1.208-2.959), age  $>75$  years old (OR 1.691,  $p=0.029$ , CI 1.055-2.710), dementia (OR 2.489,  $p=0.022$ , CI 1.140-5.434), atrial fibrillation at admission (OR 1.944,  $p=0.023$ , CI 1.097-3.445) and LVEF  $<40\%$  (OR 2.161,  $p=0.002$ , CI 1.334-3.501) as predictors of stroke in ACS.

**Conclusions:** Female gender, Age  $> 75$  years old, dementia, atrial fibrillation at admission and LVEF $<40\%$  were predictors of stroke in ACS.

## FACTORS ASSOCIATED WITH HOSPITAL ARRIVAL TIME OF ACUTE STROKE PATIENTS IN RURAL INDIA

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**Background:** Delays in the treatment of acute stroke leads to unfavorable prognosis. Shortening the delay time in the health care of these patients is essential in order to reduce the morbidity and mortality rates of this disease. Eligibility for acute stroke interventions depends on the time from symptom onset to hospital arrival. The socio-cultural profile in rural India is different from that in urban India. Lot of people in rural India prefer living in joint families, general level of education and awareness is low and they opt for alternative modalities of treatment for stroke. There is lack of adequate and fast transport facilities that worsen the scenario. Delay in arrival of acute stroke cases may be caused by organizational, educational, socioeconomic and demographic factors.

**Purpose:** This study was conducted to understand the factors associated with hospital arrival time of acute stroke patients in Rural India.

**Materials and Methods:** Hospital data of 27 acute stroke patients admitted to Samarpan Clinic from January 2019 to December 2019 was retrospectively studied. Stroke was defined, according to the WHO definition, as 'rapidly developing clinical sign of focal (or global) disturbance of cerebral function, lasting more than 24 hours or leading to death with no apparent cause other than of vascular origin'. Chi square test and Mann Whitney U tests were used to analyze the data.

**Results:** Only 8 (29.62%) patients arrived within 3 hours of stroke onset whereas 3 (11.11%) patients arrived after 12 hours. Mean and standard deviation of hospital arrival time in minutes for patients < 50 years was 125±116, for 51-60 years was 279±127, for 61-70 years was 379±191 and for >70 years was 1127±716. Younger patients reported significantly earlier than older ones ( $p < 0.001$ ). Males reported earlier than females ( $p: 0.032$ ). Patients with stroke onset in the night time arrived significantly late compared to stroke onset in the day time ( $p: 0.001$ ). Prior ayurvedic treatment delayed hospital arrival ( $p < 0.001$ ).

**Conclusions:** A nationwide public awareness campaign is needed to improve the public awareness of stroke and importance of timely treatment when acute stroke symptoms are suspected. Lot of patients in rural India still delay emergency treatment of acute stroke due to preference to ayurvedic remedies which should be strongly discouraged. Gender and age bias need to be further studied and strategies to reduce the bias should be considered. This study shows that there is substantial room for reducing the time from symptom onset to hospital arrival in acute stroke. Strategies to improve stroke awareness and referral protocols together with the use of tele-medicine and mobile stroke unit should be considered to reduce the hospital arrival time.



## ATRIOVENTRICULAR BLOCK IN THE SETTING OF ACUTE CORONARY SYNDROME PREDICTS STROKE

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**Background:** The atrioventricular block (AVB) is a life-threatening complication in the setting of acute coronary syndrome (ACS) associated to worst prognosis to short and long-term follow-up. Stroke during an ACS is a well documented complication, that can be influenced by the presence of other comorbidities. **Objective:** Evaluate if AVB in the setting of ACS was a predictor of stroke.

**Methods:** Multicenter retrospective study, based on the Portuguese Registry of ACS between 1/10/2010-3/05/2020. Patients were divided into two groups: A – patients without AVB, and B – patients that presented AVB. Were excluded patients without a previous cardiovascular history or clinical data regarding AVB and stroke occurrence. Logistic regression was performed to assess if AVB was a predictor of stroke in ACS patients.

**Results:** From 23774 patients, 23148 in group A (97.4%) and 626 in group B (2.6%). Groups A and B were comparable regarding the prevalence of smokers ( $p=0.222$ ), arterial hypertension ( $p=0.776$ ), diabetes mellitus ( $p=0.508$ ), peripheral artery disease ( $p=0.479$ ), chronic kidney disease ( $p=0.467$ ), onset of symptoms until the first medical contact ( $p=0.410$ ) and in-hospital re-infarction during the hospitalization ( $p=0.145$ ). Patients that had AVB in the setting of ACS presented higher medium age ( $66\pm 13$  vs  $71\pm 13$ ,  $p<0.001$ ), female gender (27.4 vs 32.4%,  $p<0.001$ ), previous stroke history (6.9 vs 10.9%,  $p<0.001$ ), neoplasia history (4.9 vs 6.8%,  $p=0.031$ ), ST-segment elevation myocardial infarction as diagnosis at presentation (46.2 vs 75.4%,  $p<0.001$ ), syncope as major symptom (1.3 vs 10.0%,  $p<0.001$ ), Killip-Kimball class >I (15.4 vs 31.6%,  $p<0.001$ ), multivessel disease (52.1 vs 61.4%,  $p<0.001$ ), in-hospital heart failure complication (15.5 vs 40.6%,  $p<0.001$ ), in-hospital cardiogenic shock complication (3.8 vs 24.6%,  $p<0.001$ ), in-hospital new-onset of atrial fibrillation (4.2 vs 14.1%,  $p<0.001$ ), in-hospital ACS mechanical complication (0.6 vs 3.2%,  $p<0.001$ ), in-hospital sustained ventricular tachycardia (1.3 vs 10.0%,  $p<0.001$ ), in-hospital cardiac arrest (2.7 vs 13.3%,  $p<0.001$ ), in-hospital stroke complication (0.6 vs 1.9%,  $p<0.001$ ), length of in-hospital stay ( $5\pm 4$  vs  $7\pm 4$ ,  $p<0.001$ ) and in-hospital death (3.5 vs 19.0%,  $p<0.001$ ). On the other hand, patients without AVB presented higher body mass index ( $27.4\pm 4.4$  vs  $26.9\pm 4.6$ ,  $p=0.005$ ), higher rates of dislipidaemia (59.6 vs 51.4%,  $p<0.001$ ), coronary artery disease (18.9 vs 13.0,  $p<0.001$ ), heart rate at admission ( $78\pm 19$  vs  $65\pm 25$ ,  $p<0.001$ ), systolic blood pressure at admission ( $139\pm 29$  vs  $119\pm 32$ ,  $p<0.001$ ) and left ventricular ejection fraction (LVEF) >50% ( $60.1$  vs  $51.7\%$ ,  $p<0.001$ ). Logistic regression revealed that AVB in the setting of ACS was a predictor of in-hospital stroke (odds ratio (OR) 2.231,  $p<0.001$ , confidence interval (CI) 1.779-5.852). **Conclusions:** ACS patients was a predictor of stroke complication during the hospitalization for ACS.

# ASSOCIATIONS OF MATERNAL HYPERTENSIVE DISORDERS DURING PREGNANCY WITH OFFSPRING RISKS OF ISCHEMIC HEART DISEASE AND STROKE: A NORDIC COHORT STUDY

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## Background:

A substantial body of evidence suggests that children exposed to maternal hypertensive disorders during pregnancy (HDP) have increased risks of preterm birth, fetal growth restriction and several cardiovascular risk factors (e.g., hypertension, obesity, diabetes) later in life. However, the direct evidence on the link between maternal HDP and the risk of severe cardiovascular diseases such as ischemic heart disease (IHD) and stroke in the offspring is very limited.

## Objective:

To investigate the associations between maternal HDP and the risk of IHD and stroke in the offspring.

## Methods:

We conducted a population-based cohort study by linking several national registers in Sweden and Finland. Live singleton births from the Swedish Medical Birth Register (1973-2014) and the Finnish Medical Birth Register (1987- 2014) were followed for IHD and stroke until 2014 by the national patient and cause of death registers. We performed Cox regression models to examine the association between maternal HDP and its subtypes, i.e., pre-existing chronic hypertension, gestational hypertension, and preeclampsia, and the risk of IHD, and stroke in the offspring while adjusting for relevant maternal and pregnancy-related confounders. We conducted sibling analyses to control for unmeasured shared familial (genetic and/or environmental) risk factors.

## Results:

Among the 5,807,122 singletons included in the study, 218,322 (3.76 %) children were born to mothers with HDP. During the up to 41 years of follow-up, 2,340 (0.04%) offspring were diagnosed with IHD and 5,360 (0.09%) were diagnosed with stroke. Offspring exposed to maternal HDP had an increased risk of IHD (adjusted hazard ratio (aHR), 1.29; 95% confidence interval (CI), 1.01-1.63), and stroke (aHR, 1.33; 95% CI, 1.14-1.56). Significantly increased rates of stroke were also observed in children exposed to the subtypes of maternal HDP: pre-existing chronic hypertension (aHR, 1.64; 95% CI, 1.03-2.60), gestational hypertension (HR, 1.38; 95% CI, 1.08-1.77), and preeclampsia (HR, 1.26; 95% CI, 1.02-1.55). The associations between maternal HDP and offspring's IHD and stroke were independent of preterm birth and small for gestational age at birth. Maternal HDP remained associated with stroke in the offspring (aHR, 1.94; 95% CI, 1.16-3.22), but not with IHD (aHR, 0.89; 95% CI, 0.47-1.67) in the sibling analyses.

## Conclusion:

Children to mothers with HDP have increased rates of IHD and stroke from childhood to young adulthood. While the link between maternal HDP and IHD in the offspring seemed to be attributed to confounding by familial factors, the relation between maternal HDP and stroke persisted even when considering such confounding. Persons born to mothers with HDP may benefit from early screening and prevention efforts to reduce the risk of IHD and stroke later in life.

## OUTCOMES IN PATIENTS WITH CORONARY ARTERY DISEASE AND CONCOMITANT CAROTID ATHEROSCLEROSIS AFTER CORONARY ARTERY BYPASS GRAFTING

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**Background:** concomitant carotid atherosclerosis (CAS) is associated with poor outcomes in patients (pts) with coronary artery disease (CAD). The impact of CAS on long-term survival in pts undergoing coronary artery bypass grafting (CABG) is not well established.

**Purpose:** to evaluate the prognosis after CABG in pts with concomitant CAS.

**Methods:** 140 CAD pts (77,4% males, median age was 64 [IQR 60; 71] yrs) after successful CABG with carotid artery stenosis  $\geq 50\%$  were enrolled in the single center prospective Registry of Long-term Antithrombotic Therapy (REGATTA-1 NCT04347200). Frequency of diabetes mellitus was 31,4%, lower extremity arterial disease—17,9%, history of ischemic stroke or transient ischemic attack—22,9%. Exclusion criteria was need for chronic oral anticoagulation due to atrial fibrillation, valvular heart disease and recent venous thromboembolism. The primary outcome was the sum of cardiovascular events (CVE): cardiovascular death, acute coronary syndrome (ACS), ischemic stroke (IS), urgent coronary or carotid arteries revascularization, acute limb ischemia.

**Results:** 27,9% pts had clinical and/or imaging features associated with high risk of stroke. For them carotid endarterectomy was performed (simultaneously with CABG in 84,6%). According to physicians decision acetylsalicylic acid (ASA) monotherapy was prescribed in 47,7% of pts on discharge. Other pts were discharged on dual antithrombotic therapy – DATT (ASA with either clopidogrel or oral anticoagulant) at least for 3-12 months. More risk factors (especially diabetes and previous myocardial infarction) were revealed in DATT group. Median duration of follow up period was 35 [IQR 23; 43] months. Frequency of CVE during follow up period was 10,7% (cardiovascular death 7; ACS 1; IS 1; urgent coronary revascularization 3; urgent carotid revascularization 1, acute limb ischemia 2). Incidence of CVE was 2,7% and 4,6% in DATT and ASA groups respectively during 1st yr of follow-up. Withdrawal of the second antithrombotic drug was associated with adverse prognosis and cumulative incidence of CVE achieved 10,8% in initial DATT group vs 3% in ASA group.

**Conclusions:** Despite complete revascularization of coronary and carotid arteries high risk of CVE was observed. Most of CVE occurred in the DATT group after switching to ASA monotherapy. We supposed that more potent antithrombotic therapy can improve cardiovascular outcomes in CAD patients with concomitant carotid atherosclerosis.

## BENCHMARKING ANALYSIS OF A SINGLE CENTRE PFO CLOSURE PROGRAM: COMPARATIVE STUDY USING THE REDUCE TRIAL DATA

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**Introduction:** 30-40% of ischaemic strokes are cryptogenic in origin with unknown aetiology. Nearly half of them are attributed to persistent foramen ovale (PFO). Transcatheter closure of PFO significantly reduces the risk of recurrent stroke. Our centre has been routinely performing percutaneous PFO closures since January 2015.

**Purpose:** Our aim was to perform a comparative analysis of the baseline clinical data and follow up results from our PFO closure patients with the corresponding data from the largest randomized trial on PFO with 441 patients.

**Methods:** We prospectively enrolled 105 consecutive patients in our single-centre registry who underwent PFO-closure between January 2018 and March 2021. We analysed retrospectively their baseline clinical data, PFO anatomy and procedural outcome. Arrhythmias, device-related complications, and recurrent stroke events were assessed during a median clinical follow-up time of 585 days. Data was compared to the published data from the interventional arm of the REDUCE study.

**Results:** The mean age of the patients was not different between our cohort and REDUCE population ( $45\pm 10.6$  vs.  $44.4\pm 9.3$  ( $p=0.563$ ); and the distribution of genders was equally similar (males 64 % 67/105 vs. 59.2% 261/441;  $p=0.440$ ). More patients had hypertension in our group (42.9% 45/105 vs. 25.4% 112/441  $p=0.0007$ ), and more of them were smokers (36.2% 38/105 vs 14.3% 63/441  $p=0.001$ ), while the prevalence of diabetes was similar (4.7% 5/105 vs. 4.1% 18/441 ( $p=0.800$ )). The proportion of complex PFO-s was similar between the two groups (57,2% 57/105 vs 42.8% 268/441  $p=0.230$ ). The success rate of closure was also similarly high: 91.4% 96/105 vs. 93.7% 413/441  $p=0.400$  respectively. Device dislocation occurred in one patient in our group while 3 cases were recorded in REDUCE (0.9% 1/105 vs. 0.6% in 3/441 patients  $p=0.580$ ). During our median follow-up of 585 days no recurrent ischaemic stroke event occurred in our cohort, while 5 patients (1.2%) had clinical ischaemic stroke in REDUCE in the first 24 months follow-up period, this difference is non-significant. One of our patients (0.9%) developed paroxysmal atrial fibrillation within 15 days after the implant, while 29 patients (6.6%) in the REDUCE cohort, however their follow up time for arrhythmias was significantly longer, therefore this data is not comparable directly.

**Conclusion:** The short and midterm outcome of our PFO program yielded similar results to the largest prospective randomized trial, despite the treatment of a patient population of higher cardiovascular risk. Further follow up is needed to determine the long-term prevalence or atrial fibrillation in our patient population.

## SAFETY, EFFECTIVENESS AND LONG-TERM DURABILITY OF CAROTID ARTERY STENTING: A SINGLE-CENTER TEN-YEAR EXPERIENCE OF TAILORED APPROACH FROM A TERTIARY HOSPITAL IN GREECE

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**Background:** Although carotid endarterectomy remains the treatment of choice for the revascularization of carotid artery stenosis, recent evolution in stents, cerebral protection devices as well as in carotid stenting techniques resulted in a significant decrease in stroke rate in specially selected patients undergoing carotid artery stenting (CAS).

**Purpose:** We aim to evaluate safety, success and long-term durability in both symptomatic and asymptomatic patients undergoing CAS managed with so called "tailored approach" to intervention, which lays on selecting the appropriate materials and techniques for the right patient.

**Methods:** Between 2010 and 2020, 188 patients [156 men; mean age (SD) 68.2 (7.1) years] were prospectively enrolled in a safety and efficacy study of tailored approach CAS by experienced operators. Nearly half of the patients (49.9%) were symptomatic. Indications for symptomatic patients included stenoses  $\geq 50\%$  and increased surgical and post-surgery complications risk. Eligible asymptomatic patients had stenoses  $\geq 80\%$  accompanied by decreased peri-procedural risk for major complications and increased risk of stroke with medical therapy alone. The tailored approach protocol included carotid computed tomography angiography (CCTA) in all patients in order to select the appropriate access site, the suitable stent regarding type as well as size and dimensions and finally the best type of cerebral protection device. **Results:** Procedural success rate was 100%. All CAS procedures were performed under distal cerebral protection and all patients received closed-cell stents with almost half of them (48.9%) being tapered stents. Preprocedural imaging determined the preferred technique of carotid cannulation. Telescopic approach was used in 16 patients (8.5%) whereas anchoring technique was used in 24 patients (12.8%). In-hospital complications included 1 (0.53%) hyperperfusion syndrome which was fatal and 1 (0.53%) transient ischemic attack (minor stroke). The event free survival rates from all strokes or stroke-related deaths at one year of follow-up was 98.9%.

**Conclusions:** Tailored approach CAS guided by pre-procedural carotid CTA appeared to be a safe and effective method of carotid artery stenosis revascularization, resulting in excellent outcome considering a thorough non-invasive, diagnostic work-up. In order to decrease periprocedural risk for major complications the right selection of patients is of great priority. Future improvements in CAS procedural safety accompanied by preprocedural imaging helping the operator to select the right materials for the right patient might provide similar outcomes between surgical and endovascular treatment.

# SHOULD PATIENTS WITH BICUSPID AORTIC VALVE BE SCREENED FOR AN INTRACRANIAL ANEURYSM? A CASE REPORT AND LITERATURE REVIEW

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## Background:

Bicuspid aortic valve (BAV) is the commonest congenital heart condition affecting up to 1.4% of the general population. BAV is associated with systemic arteriopathy involving different organs. 10% of patients with BAV are found to have Intracerebral aneurysm (IA). Subarachnoid hemorrhage is the most serious complication in such cases. As it is a frequent occurrence, we reviewed literature about screening guidelines after managing a case of SAH who previously had a successful BAV replacement.

## Purpose:

Literature search about screening policy for IA in BAV cases.

## Methods:

Case report followed by

PubMed search 1950 to 2021, guidelines review of major cardiothoracic societies, case reports of SAH in BAV cases.

## Case Report:

43-year Asian male was repatriated to our stroke unit after coiling of anterior communicating artery aneurysm. He had a significant cognitive deficit, urinary incontinence, and apraxia of speech. Prior to the stroke, he worked as a shopkeeper and functionally independent for activities of daily living. He had tissue valve replacement for the bicuspid aortic valve. His mother also had BAV and was repaired in her native country.

In short, he made a full recovery from his heart condition but IA rupture caused a significant disability.

## Literature review;

A recent meta-analysis showed an 8% Prevalence of IA in BAV cases. A few case series and retrospective studies showed approximately up to 9-10% prevalence. We conclude that patients with aortopathy and BAV are at higher risk of IA and at this stage, there is no prediction model available for estimating the risk of rupture. None of the guidelines have a clear recommendation on screening for IA.

## Conclusion;

This association should be kept in mind by stroke physicians, cardiothoracic surgeons, neurosurgeons, and intensivists. In case of peri-operative neurological decline, IA rupture should be considered. Aggressive hypertension control and smoking cessation should be emphasized to reduce risk of rupture.

## LONG-TERM FOLLOW-UP DATA FROM THE LEFT ATRIAL APPENDAGE CLOSURE BY SURGERY (LAACS) RANDOMIZED CLINICAL TRIAL

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### Background

The risk of stroke after open heart surgery is 1-5% per year. Thrombi formation in the left atrial appendage (LAA) occurring during atrial fibrillation (AF) subsequently travelling to the brain is a likely explanation for the elevated stroke risk. AF occurs – and recurs – frequently in patients that have undergone open heart surgery. Nonetheless, prophylactic anticoagulants are not recommended in the current guidelines. Systematic closing of the LAA, on occasion of open-heart surgery, could reduce the likelihood of thrombi formation in the heart, thus reducing the stroke risk. The Left Atrial Appendage Closure by Surgery (LAACS) study was the first randomized clinical trial to investigate the effect of systematic LAA closure concomitant to elective open-heart surgery in both patients with – and without – known AF. Here we present follow-up data 10 years after inclusion of the first patient.

### Purpose

To provide evidence – in long-term data – that primary prevention of ischemic brain damage in patients undergoing open-heart surgery is possible through systematic closure of the LAA.

### Methods

Long-term follow-up data of patients enrolled in the prospective, randomized, open-label, blinded evaluation (PROBE) trial entitled LAACS (NCT02378116). Patients were originally randomized to LAACS in addition to elective open-heart surgery vs. standard care and stratified by usage/ planned usage of oral anticoagulation. We have performed a thorough chart review on all randomized patients. All cerebral events were adjudicated by two neurologists blinded for randomization. The primary endpoint was a composite of symptomatic ischemic stroke, transient ischemic attack or imaging findings of silent cerebral ischemic (SCI) lesions occurring after index surgery. Cumulative incidence plots with death as competing risk (Aalen-Johansen) and Gray's tests were performed.

### Results

Electronic patient charts from 186 patients (82% males) were reviewed. At study entry, mean (SD) age was 68 (9) years, mean CHA2DS2VASc was 2.9 (1.5) and 48 of 186 (25.9%) patients were receiving anticoagulant medication. The randomization groups were comparable on all parameters. After a mean follow-up of 6.2 (2.5) years, the primary endpoint remained in favour of the group randomized to LAACS in the intention-to-treat analyses 11 (12.8%) vs 19 (19%) events,  $p=0.033$ . In the per protocol analyses ( $n=141$ ), we observed 9 (14.1%) events in the LAACS group vs 17 (22.1%) in the control group ( $p=0.186$ ). Mortality rates did not vary between groups. Analyses of symptomatic cerebral events (i.e. stroke and TCI without

SCI) showed parallel cumulative incidence curves, with lower incidence for the LAACS group throughout the follow-up time, though not reaching the predefined significance level ( $p=0.252$ ).

#### Conclusion(s)

The long-term follow-up data of the LAACS study, confirms that systematic LAACS in addition to open-heart surgery, regardless of AF and oral anticoagulation status pre-surgery, reduces the risk of post-operative ischemic brain injury. Larger randomized trials are warranted to determine the effect of LAACS on symptomatic ischemic brain damage.



## INVESTIGATION OF NICKEL SENSITIZATION AFTER PERCUTANEOUS IMPLANTATION OF PATENT FORAMEN OVALE OCCLUDER; A RANDOMIZED TRIAL (INSPIRE). RATIONALE AND DESIGN

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**Background:** Percutaneous Patent Foramen Ovale (PFO) closure has been established as a first-line invasive treatment for preventing recurrent strokes in selected patients. The devices used for the specific purpose contain and release nickel, which is considered as the most allergen metal in nature. While the allergic contact dermatitis has been well described, existing literature cannot explain adequately the effect of systematic nickel release on the clinical manifestations of patients implanted with such devices. Allergic dermatitis is currently diagnosed by performing of specific skin patch tests.

**Purpose:** Our trial will prospectively investigate the impact of device placement to nickel skin patch test results and the correlation with the clinical manifestations.

**Methods:** Consecutive adult patients indicated for transcatheter PFO occlusion will participate in our study. Skin patch tests using the European standard series and an extended metal and isocyanates series will be performed in all included patients, 14 days prior and 90 days after the procedure. The patients will be randomized to receive either Amplatzer® or Gore® device, with parallel assignment and randomization 1:1. During follow-up, clinical manifestations and transthoracic echocardiographic findings will be evaluated and associated with patch skin tests. The time frame of 90 days has been selected, due to the duration of device's endothelization and nickel release.

**Results:** During the next three years, our trial plans to include a total of 100 patients. The primary endpoint of our study is to investigate the possible change (either as continuous or dichotomous outcome) of nickel skin patch test, after the device implantation. Secondary endpoints include the investigation of patients implanted with Amplatzer and Gore device, who develop nickel sensitization, evaluation of residual interatrial leakage, by performing transthoracic echocardiographic and evaluation of the possible additional sensitizations to any metals or isocyanates.

**Conclusion:** Our trial aims to provide an improved comprehension of the impact of the PFO occluders' implantation in nickel skin patch test results and the clinical manifestations of patients.

# PERIPHERAL VASCULAR DISEASE INDEPENDENTLY PREDICTS PERIPROCEDURAL ADVERSE CEREBROVASCULAR EVENTS AMONG PATIENTS WITH ACUTE MYOCARDIAL INFARCTION UNDERGOING PERCUTANEOUS REVASCULARIZATION: ANALYSIS OF 2,810,728 HOSPITALIZATIONS IN THE US

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**Background:** Peripheral vascular disease (PVD) is in tight association with atherosclerosis of cerebral and coronary vascular territories and portends a poor prognosis. Complications of PVD might result in limb ischemia and amputation, coronary artery disease (CAD), and stroke. The association of existing PVD with adverse periprocedural cerebrovascular events in patients with acute myocardial infarction (AMI) undergoing percutaneous coronary intervention (PCI) is poorly understood.

**Purpose:** In the present study, we underwent to 1) examine the incidence of PVD in patients with AMI undergoing PCI, 2) examine the rates of adverse periprocedural cerebrovascular events in patients with PVD vs. without PVD, and 3) quantify the predictive role of PVD concerning periprocedural adverse cerebrovascular events after adjustment for relevant baseline covariates in the multivariable regression model.

**Methods:** We retrospectively analyzed 2,810,728 patients hospitalized for ST-elevation myocardial infarction (STEMI) and non-ST-elevation myocardial infarction (NSTEMI) who were treated with PCI during the 2004-2014 period. Data were obtained from the United States National Inpatient Sample (NIS) database by using International Classification of Diseases, Ninth Revision (ICD-9) diagnostic and procedural codes. The primary endpoint of interest was the in-hospital composite of periprocedural adverse cerebrovascular events consisting of ischemic/hemorrhagic stroke and transient ischemic attack (TIA) events. Multivariable regression analysis robustly adjusted for baseline covariates was used to determine the relationship of PVD with the adverse periprocedural cerebrovascular events. The regression model was adjusted for prespecified covariates including age, sex, emergent PCI setting, type of ACS, atrial fibrillation (AF), diabetes mellitus (DM), arterial hypertension (AH), smoking, hypercholesterolemia, chronic kidney disease (CKD), history of stroke/TIA, and history of myocardial infarction (MI). For this analysis, odds ratios (OR) and 95% confidence intervals (95% CI) were reported.

**Results:** The mean age of the analyzed population was  $62.9 \pm 13.1$  years and 68% were men. A total of 1,439,607 patients (51.2%) were admitted for NSTEMI while 1,371,121 (48.8%) were admitted for STEMI. A vast majority (91.9%) of PCI procedures were done in the emergent setting. About 10% of the whole sample had AF, 30.2% had DM, 65.4% had hypertension, 9.1% had a positive history for MI while 2.9% had a positive history of the cerebrovascular event (previous ischemic/hemorrhagic stroke or TIA). The average incidence of PVD during the examined period was 8.6% (N=242,994) while the crude rate of in-hospital periprocedural stroke/TIA was 2.4%. The rate of periprocedural stroke/TIA was significantly higher in patients with PVD vs. patients without PVD (7.5% vs. 1.9%,  $p < 0.0001$ ). Likewise, patients with AF had a two-fold increase in the rate of adverse cerebrovascular events compared to non-AF patients (4.4% vs. 2.2%,  $p < 0.0001$ ). In the multivariable regression model adjusted for prespecified covariates, the presence of PVD was independently associated with a threefold increase in the likelihood of periprocedural stroke or TIA (OR 2.99, 95% CI 2.90-3.11,  $p < 0.0001$ ).

**Conclusion:** Among patients with AMI undergoing PCI, those with peripheral vascular disease are three times more likely to experience adverse periprocedural cerebrovascular events during the hospital stay.

# STENT RETRIEVER VERSUS DIRECT ASPIRATION THROMBECTOMY AS ENDOVASCULAR TREATMENT OF ACUTE ISCHEMIC STROKE, SINGLE CENTRE EXPERIENCE FROM 2012-2020

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## Introduction

Mechanical thrombectomy of large-vessel occlusion results in better outcomes than medical therapy alone in patients with acute ischemic stroke. The optimal technique (stent retriever versus aspiration catheter) remains to be established.

## Purpose

To evaluate the efficiency and safety of these two main thrombectomy techniques.

## Methods

Retrospective analysis of 298 consecutive patients who were treated by mechanical thrombectomy or direct aspiration in a comprehensive stroke center between 2012 and 2020 was used to compare the revascularization rates, peri and post-procedural complications and clinical outcomes of the patients. Patients with ischemic stroke of posterior circulation were excluded from this analysis.

## Results

In total 237 patients underwent mechanical thrombectomy using stent retriever and 24 patients were treated by direct aspiration. Angiographic recanalization characterized by thrombolysis in cerebral infarction (TICI) 2b/3 was achieved in 84,39% patients in the stent retriever group and 79,17% in the aspiration group. Clinical endpoint of a modified Rankin Score (mRS) of 0–2 at 90 days was observed in 51,75% patients treated by stent retriever and 57,14% by direct aspiration. Symptomatic intracranial hemorrhage (sIH) occurred in 7,17% patients in stent retriever group vs. 4,17% in direct aspiration group. In stroke patients treated with direct aspiration there were no embolization to new vascular territory observed and in stent retriever the occurrence was 2,53%.

Conversion from one technique to another during endovascular treatment had to be done in 37 patients. These patients had the lowest revascularization rates (67,57%) and only 26,47% of them achieved at 90 days functional independence characterized by mRS 0-2. In this group there were the highest rates of adverse events – sIH 8,11% and embolization to new vascular territory occurred in 8,11% of them.

## Conclusion

Both techniques of thrombectomy are effective in acute ischemic stroke. Rates of successful recanalization are slightly in favor of stent retrievers. Direct aspiration tends to be associated with lower risk of adverse events. Complicated lesions, where conversion from one technique to another has to be done, may predict worse functional outcome.

## PATIENTS WITH HISTORY OF STROKE AND CORONARY HEART DISEASE IN CLINICAL PRACTICE: DEMOGRAPHIC CHARACTERISTICS, COMORBIDITY AND OUTCOMES (STROKE REGISTRY DATA)

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**Aim.** To evaluate demographic characteristics, comorbidity and outcomes in patients with history of stroke (STR) with/without diagnosed concomitant coronary heart disease (CHD) based on STR registry.

**Methods.** 986 patients with history of STR were enrolled in the registry. 702 patients had a diagnosed CHD (STR+CHD group) and 284 had no CHD (STR without CHD group). We analyzed the incidence of cardiovascular diseases, chronic non-cardiac diseases and outcomes during 4-year follow-up.

**Results.** The age of patients in STR+CHD group was significantly older than in STR without CHD group (73.5±9.6 and 63.4±10.6 years; p<0.01). Women prevailed in both groups (59.3% and 51.9%, respectively). 97% and 84% of strokes in these groups were ischemic (p<0.001). STR+CHD patients more often than patients without CHD had: arterial hypertension (AH) - 97.7% and 88.4% (p<0.001); chronic heart failure (CHF) - 85.2% and 33.8% (p<0.001); atrial fibrillation (AF) - 33.3% and 4.6% (p<0.001); history of previous stroke - 19.7% and 12.7% (p=0.01). In STR+CHD group were also more often diagnosed: diabetes (22.5% and 14.1%; p=0.003); obesity (9.1% and 1.4%; p<0.001); respiratory diseases (26.5% and 19%; p=0.01); kidney diseases (24.9% and 18.3%, p=0.03). The proportion of patients with digestive diseases (36.2% and 30.6%, p=0.10) and anemia (5.0% and 5.6%, p=0.59) did not differ significantly. During 4-year follow-up in STR+CHD group compared with patients without CHD: all-cause mortality was higher (36.8% and 14.5%, p<0.001); there were no significant differences of the incidence of nonfatal recurrent STR in compared groups (14.2% and 4.6%, p=0.26).

**Conclusions.** Patients with history of stroke and concomitant CHD compared with group without CHD had higher incidence of AH, CHF, AF, recurrent stroke, diabetes, respiratory and kidney diseases, obesity. Patients of STR+CHD group had significantly higher proportion of ischemic stroke before enrollment in the registry and higher all-cause mortality during 4-year follow-up. So, the most multidisciplinary approach and a special attention for the treatment and prevention in these patients is necessary. Besides, there is a need for more research in this field, that probably answer whether early diagnosis of CHD and aggressive treatment can decrease the risk of fatal and nonfatal complications in patients with ischemic stroke.

## ASSESSMENT OF THE QUALITY OF CARDIOVASCULAR PHARMACOTHERAPY BEFORE AND AFTER STROKE IN OUTPATIENT SETTING: THE DATA OF REGISTRY REGION-M

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**Aim:** to estimate the quality of cardiovascular pharmacotherapy (QCP) with in outpatients before and after (within 2 years) an acute cerebrovascular accident - ACVA (stroke or transient ischemic attack).

**Methods.** This study was performed using the data of prospective registry REGION-M which included patients with acute CVA. Long-term follow-up included 684 patients discharged from the hospital from January 01, 2012 to April 30, 2017 assigned to the outpatient clinic in Moscow. QCP was assessed before hospitalization, 1-6 months and 6-22 months after hospitalization. Concomitant arterial hypertension was diagnosed in 92% of patients, coronary artery disease (CAD) - in 61.8%, atrial fibrillation (AF) – 16.4%.

**Results.** During one year period before hospitalization antiplatelets and statins were prescribed in 18% and 17% of patients with CAD, respectively, antihypertensive drugs - in 41.4% of patients with AH. Only 17% of patients with AF received oral anticoagulants. During 1-6 months after the ACVA in the group of patients with concomitant CAD the incidence of administration of antiplatelets increased to 65.0% ( $p<0.0001$ ) and of statins - to 40% ( $p<0.0001$ ). The proportion of hypertensives who received antihypertensive drugs increased up to 47.4% ( $p<0.0001$ ) and of patients with AF treated with oral anticoagulants increased to 36.0% ( $p=0.003$ ). During period 6-22 months after ACVA compared with period during 1-6 months after hospitalization these values decreased to 40.0 ( $p<0.0001$ ) for antiplatelets and to 28% ( $p<0.0001$ ) for statins in patients with CAD, to 41% ( $p=0.002$ ) for antihypertensive drugs in hypertension and to 33% ( $p=0.001$ ) for oral anticoagulants in patients with AF.

**Conclusion.** The quality of cardiovascular pharmacotherapy and of stroke prevention in outpatient setting was insufficient in patients both before and after ACVA, but was significantly better during post-stroke period of monitoring in primary care medical system compare with period before hospitalization

## ANGIOTENSIN II RECEPTOR BLOCKER AMELIORATES NEUROTROPHIC SUPPORT AND NEURORESTORATION AGAINST ALZHEIMER'S DISEASE BY INHIBITING HIPPOCAMPAL APOPTOSIS AND INFLAMMATORY RESPONSES

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**Background.** Alzheimer's disease and other neurodegenerative diseases frequently leads to long-term cognitive problems and physical disability yet remains without effective therapeutics. Sartans (Angiotensin II AT(1) Receptor Blockers, ARBs), a hypertensive drug, has powerful neuroprotective agents in vivo and protect against IL-1 $\beta$  neurotoxicity.

**Objective.** To determine the effect of angiotensin II receptor blockers (ARBs) in protecting central neurons against nutrient deprivation-induced apoptosis in vitro and to elucidate the underlying mechanisms of Alzheimer's disease.

**Methods.** Comprehensive and structured search on Pubmed/Medline, Embase, EBSCO, and Cochrane Central Register of Controlled Trials was performed on March – May 2016. Concurrent cohort study and experimental trials (including randomized and non-randomized trials) designed to evaluate the effects of ARB in alzheimer's disease patients were included. After conducting article screening towards 24 articles according to the inclusion and exclusion criteria, there were 8 articles left, in which statistical analysis were performed with Chi-square and Fisher's exact test.

**Results.** Evidence suggests that ARBs effectively inhibit oxidative stress, amyloid beta protein (A $\beta$ ) metabolism, and tau phosphorylation invitro. Pretreatment with telmisartan, candesartan, losartan or valsartan (0.1 to 20  $\mu$ M) for 2 hours prior to glutamate exposure, with order of potency: telmisartan > candesartan > losartan > valsartan. Consistent with invitro studies, recent meta-analysis studies and 2 prospective, randomized, double-blind trial have shown the effectiveness of ARBs in preventing AD and/or slowing its progression, thus ARBs are considered to be a potential candidate for the treatment of Alzheimer's disease (AD).

**Conclusion.** This study suggests that ARBs may provide a novel, safe therapeutic approach to treat brain disorders associated with enhanced inflammation. Long-term clinical trials for cognitive assessment and brain imaging techniques are needed to clarify the effectiveness of ARBs in Alzheimer's disease and other dementia treatment.

**Keywords:** ARBs, Alzheimer's disease, Dementia, Hippocampal Apoptosis, Neurorestoration

# ISCHEMIC STROKE RISK MARKERS AFTER 1 YEAR OF ACUTE CORONARY SYNDROME FOLLOW-UP IN A PATIENT WITH SINUS RHYTHM

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## Background

The risk of ischemic stroke increases after acute coronary syndrome; it may be related to left ventricular thrombi, which tend to develop within the first two weeks or to brain hypoperfusion following decreased cardiac output in patients with cerebrovascular disease. The presence of heart damage can induce cardiac arrhythmias, which in turn can increase the risk of stroke in the long term. There is, however, limited evidence on the duration of the elevated risk of stroke in patients with ACS and its direct link to heart injury.

## Purpose

The objective of the study is to determine the clinical and echocardiographic markers of the risk of an ischemic stroke after one year of follow-up of the patient hospitalized for an acute coronary syndrome.

## Methods

By a prospective single-center study carried out in patients with acute coronary syndrome hospitalized in an intensive cardiological care unit and a follow-up for 1 year after discharge from the hospital, the prevalence and the clinical and echocardiographic risk factors for the occurrence of ischemic stroke are evaluated in patients with sinus rhythm.

## Results

304 consecutive patients are included and screened. In the general population, there is a clear predominance of men with a sex ratio of 2.4 and an average age of 63.2 years. The prevalence of ischemic strokes is 4.9%; 1,6 % ischemic strokes in hospital and 3.3% at the discharge, the clinical and echocardiographic risk markers of ischemic stroke after binary logistic regression are: STEMI (RR=3.8;95%CI=1.2-12,p=0.02), polyarterial vascular disease (RR=7.4;95%CI=2.6-21.2,p<0.01), female sex (RR=4.4;95%CI=1.5-13.2,p<0.01), Left ventricular ejection fraction < 40% (RR=3.7;95%CI=2.4-7.4,p=0.01), Extensibility index > 2 (RR=2.2;95%CI=1.4-5.3,p<0.01), Left atrial volume index > 34ml/m<sup>2</sup> (RR=2.5;95%CI=1.6-6.4,p=0.01).

## Discussion

Acute coronary syndrome is a bed that promotes ischemic strokes even more extensive associated with severe left ventricular systolic dysfunction and left ventricular remodeling thus promoting the formation of thrombi responsible for stroke of embolic origin and a low cerebral flow aggravated by underlying cerebrovascular disease.

## Conclusion

Stroke after an acute coronary syndrome remains a serious complication involving the life-threatening prognosis, the integration of risk markers in a prognostic model allows to guide the therapeutic attitude.

Keywords: Acute coronary syndrome, ischemic stroke, risk markers, polyarterial vascular disease, embolic stroke

## Disclosure of interest

The authors declare that they have no competing interest.

## AUGMENTING RISK PREDICTION TOOLS TO COMPARE UTILITIES OF CHA<sub>2</sub>DS<sub>2</sub>-VASC AND HAS-BLED

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**Purpose:** To investigate the utility of augmenting AF risk prediction tools by incorporating additional item level information.

**Methods:** We created a development cohort by linking individual-level hospital and prescribing datasets including all adult patients in Scotland with incident AF between 2009 -2017. We created augmented scores for CHA<sub>2</sub>DS<sub>2</sub>-VASC and HAS-BLED prediction tools, adding one additional level of detail to each component item. We performed logistic regressions to assess prognostic ability of original and augmented risk prediction tools against outcomes of stroke, bleeding, mortality, and care home admission. We compared model performance using discrimination and calibration plots.

**Results:** From 117,749 patients, using original and augmented CHA<sub>2</sub>DS<sub>2</sub>-VASC tools, 23.76% and 23.46% were classified at low, 56.22% and 54.54% at moderate, 20.02% and 22.00% at high risk of stroke, respectively. With original and augmented HAS-BLED tools, 52.46% and 24.48% were classified at low, 43.21% and 52.98% at moderate, 4.33% and 22.54% at high risk of bleeding, respectively. With the augmented tool, we observed a statistically significant shift in those proportions. Original and augmented tools performed similarly (AUC > 0.6). Our augmented HAS-BLED tool (unadjusted) appeared to perform slightly better than the original tool in predicting mortality (AUC 0.615) and care-home admission (AUC 0.615).

**Conclusions:** We have shown that it is possible to use routinely recorded clinical data to augment AF risk prediction tools. However, the improvements in prognostic utility were negligible. Future augmentation strategies should consider novel risk factors such as polygenomic risk scores, and timing of risk factor acquisition that could be added to traditional cardiovascular factors.



# CARDIAC RISK FACTORS FOR STROKE: A COMPREHENSIVE MENDELIAN RANDOMIZATION STUDY

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**Background:** Observational evidence suggests an association of stroke with various cardiac traits beyond atrial fibrillation (AF), the leading source of cardioembolism. However, controversy remains regarding a true causality of these findings. Confounding effects of AF, atherosclerosis, and hypertension are of particular interest, as these risk factors are shared by stroke and heart disease.

**Purpose:** We leveraged genetic data to systematically assess causal associations between cardiac traits and the risk of stroke. Compared to observational studies, Mendelian Randomization (MR) is less susceptible to confounding and may thus help to elucidate cardiac risk factors for stroke beyond AF.

**Methods:** We applied two-sample MR to explore the associations between genetic predisposition to 66 cardiac traits and risk of stroke in 40,585 cases and 406,111 controls from the MEGASTROKE consortium. We included all cardiac phenotypes with sufficient genetic data, including cardiovascular diseases, cardiac imaging traits, electrocardiographic (ECG) traits, and blood biomarkers. Outcomes included stroke and stroke subtypes (any stroke, any ischemic stroke, large-artery stroke, cardioembolic stroke, small vessel stroke, undetermined stroke aetiologies). To disentangle the effects of individual cardiac traits from established risk factors, we performed multivariable MR analyses adjusting for AF, coronary artery disease (CAD) and systolic blood pressure (SBP). The majority of analyses were well-powered.

**Results:** We found strong independent associations between AF and cardioembolism and between CAD and large-artery stroke, as anticipated. Furthermore, our data-driven analyses indicated associations between genetic predisposition to both heart failure (HF) and lower resting heart rate (HR) with stroke risk. However, these associations were fully explained by AF, CAD and SBP in multivariate analyses. We further found genetically proxied P-wave terminal force in V1, an ECG marker of atrial cardiopathy, to be inversely associated with the risk of large-artery stroke.

**Conclusion:** Available genetic data do not support substantial effects of cardiac traits on the risk of stroke, beyond known risk factors. This suggests that confounding is indeed an issue in previous observational findings, and that additional studies are needed to validate independent cardiac effects on stroke risk.

## PROTEIN CONVERTASE SUBTILISIN-KEXIN TYPE 9 INHIBITORS AND STROKE PREVENTION: SYSTEMATIC REVIEW AND META-ANALYSIS

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**Background and Purpose:** Proprotein Convertase Subtilisin-Kexin Type 9 (PCSK9) inhibitors are associated with reduction of major cardiovascular events in patients with established atherosclerotic disease. We aimed to investigate the effect of PCSK9 inhibitors in patients with and without previous stroke and according to baseline low density lipoprotein cholesterol (LDL-C) levels.

**Methods:** We searched PubMed and Scopus until 20/05/2020 for randomized controlled trials on cardiovascular outcomes, comparing a PCSK9 inhibitor to placebo. We employed Bayesian models with a prior that assumed small between-study variance and inverse variance random-effects models with the Paule-Mandel (PM) heterogeneity estimator.

**Results:** Two randomized controlled trials with 46,488 patients met the selection criteria (111,571 patient-years). Stroke occurred at a rate of 0.59 per 100 patient-years in patients treated with PCSK9 inhibitor and 0.78 in the placebo group (HR:0.76, 95%CI:0.66-0.88, for the PM estimator; I<sup>2</sup>=0%). The effect of PCSK9 inhibitors on stroke remained consistent independently of the presence of previous stroke (P for interaction=0.097). The effect of PCSK9 inhibitors on stroke was similar between patients with baseline LDL-C ≥ 80mg/dl and patients with LDL-C < 80mg/d (P for interaction: 0.528). PCSK9 inhibitors did not increase the risk of hemorrhagic stroke in patients with previous cardiovascular event (HR:1.02, 95%CI:0.67-1.56, for the PM estimator, I<sup>2</sup>=0%).

**Conclusions:** Among patients with previous cardiovascular events, the risk of stroke was significantly reduced in both patients with and without previous stroke treated with PCSK9 inhibitors irrespective of the baseline LDL-C levels. The risk of hemorrhagic stroke was not increased in patients treated with PCSK9 inhibitors.

## SEX DIFFERENCES IN BASELINE PROFILES AND SHORT-TERM OUTCOMES IN PATIENTS UNDERGOING CLOSURE OF PATENT FORAMEN OVALE

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**Introduction/Purpose:** Although sex differences have been emphasized in stroke and congenital heart disease, there has been limited investigation on their role in patent foramen ovale (PFO). In fact, key guidelines on the management of PFO do not comment on sex or gender specific considerations in characteristics or outcomes of patients. We aimed to explore differences by sex in baseline profiles, procedural characteristics, and short-term outcomes of patients undergoing transcatheter PFO closure.

**Methods:** Data of adult patients undergoing transcatheter PFO closure at the Toronto General Hospital from 1997 to 2017 was retrospectively analyzed. Baseline information included demographic characteristics, medical history, diagnostic and procedural information, and periprocedural complications. Post-closure outcomes were captured at index hospitalization and during the first follow-up.

**Results:** From 1,032 patients in the cohort sample, 80.7% underwent closure for cryptogenic stroke and 44.8% (n=462) were females. We observed significant sex-related differences at baseline; females were younger, less likely to have a history of smoking, and less likely to have cardiovascular risk factors such as dyslipidemia and coronary artery disease ( $p<0.05$ ). No differences were observed in procedural and in-hospital outcomes between sexes. At the first follow-up, recurrent cerebrovascular events were reported in 1.5% and 1.9% of patients in the 'cryptogenic stroke/TIA indications' and 'other indications' groups respectively, with no significant differences by sex. There were significant sex differences between some symptom presentation both pre- and post-closure, with females more likely to present with migraine symptoms at both timepoints ( $p<0.05$ ).

**Conclusions:** Although no differences in procedural and short-term outcomes between males and females undergoing transcatheter PFO closure were observed, significant baseline differences in characteristics may justify the need for sex-specific risk assessment and PFO closure criteria. There is a critical need for long-term, systematic studies to understand sex and gender differences in the PFO population.

# HEART AND BRAIN INTERACTION - ANTIPHOSPHOLIPID ANTIBODIES: AN IMPORTANT LINK

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## Background:

Antiphospholipid syndrome is associated with recurrent arterial and venous thrombosis. Cardiac and cerebral vessels are frequently involved in this autoimmune disease. Antiphospholipid Screening (APS) should be sought in young ischemic stroke as well as in many cardiac conditions.

## Purpose:

We conducted a retrospective study of APS cases presented to our stroke unit. The purpose was to review our practice and EULAR recommendations to improve future practice.

## Methods:

Case 1- A 37 years old Caucasian male presented with progressive headaches and visual disturbance for two months, diagnosed with papilledema and malignant hypertension. A new neurological deficit was assessed with CT Head, which showed left basal ganglia bleed. He was diagnosed with hypertension and hyperlipidemia at age 32 but the secondary hypertensive cause was not investigated had evidence of hypertensive-induced end-organ damage. His electrocardiogram showed left ventricular hypertrophy, renal function showed stage 3 chronic kidney disease. He had a watershed ischemic infarct while blood pressure was lowered down. APS screen was persistently triple positive. Renal biopsy showed chronic thrombotic angiopathy, suggestive of APS-induced renal damage and hypertension. Combined blood pressure pills and intensive lipid-lowering management were commenced to improve adherence, in addition to hydroxychloroquine and Warfarin. The prevalence of hypertension in primary APS or aPL-positive patients was significantly high (44%).

## Case 2-

A 27-years Asian female was diagnosed with symptomatic mitral valve prolapse at age of 25 and had a metallic mitral valve replacement. She was on long-term Warfarin with a target INR of 3 to 4. A year later she was diagnosed with Immune Thrombotic Thrombocytopenia, SLE, and triple positive APS screen, suggestive of secondary APS. She came to our unit with acute memory loss and an episode of confusion. Her CT Head showed thalamic infarct. Her Time in the Therapeutic Range (TTR) was >75%, admission INR was sub-therapeutic. Reduced INR and a flare-up of APS were the etiology in her case. APS test was not conducted when she initially attended cardiology service with mitral valve prolapse, which is a common cardiac manifestation of APS.

## Case 3:

A 55-years Caucasian male with medical illnesses of hypertension, and hyperlipidemia, presented to the stroke unit with a right middle cerebral artery stroke. CT Angiogram of cerebral vessels showed M2 thrombus and initial 72- hour Holter showed sinus rhythm. He had APS screening done due to persistently prolonged APTT on routine testing. He was diagnosed with primary APS. Old medical notes showed that he was previously investigated in a chest pain clinic but declined coronary angiogram and lost to follow up. An electrocardiogram showed old ischemic changes. Echocardiogram showed inferolateral hypokinesia, aortic regurgitation, and aortic root dilatation. Myocardial infarction is another manifestation of APS, including myocardial infarction with normal coronaries. . He was given dual antiplatelets based on a case series published in 2019.

## Conclusion:

Antiphospholipid antibodies predispose to arterial thrombosis and are an important link between cardiac and coronary pathologies. Our case series highlights a need to consider this condition while assessing young patients with ischemic stroke and cardiac conditions.

