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# Brain and heart microvascular disease evaluated with cerebral MRI and myocardial perfusion entropy in SPECT, a neurovascular stroke patients' evaluation

Victor Mathieu

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Année : 2020

BRAIN AND HEART MICROVASCULAR DISEASE EVALUATED WITH CEREBRAL  
MRI AND MYOCARDIAL PERFUSION ENTROPY IN SCINTIGRAPHY:  
A NEUROVASCULAR STROKE PATIENTS' EVALUATION

THÈSE

PRÉSENTÉE POUR L'OBTENTION DU TITRE DE DOCTEUR EN MÉDECINE

DIPLÔME D'ÉTAT

Par : Victor MATHIEU

*[Données à caractère personnel]*

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## Summary

Remerciements .....	6
Summary .....	10
Abbreviations .....	11
Abstract .....	13
Résumé.....	14
Introduction.....	16
Methods .....	20
Study population .....	20
Stroke check up .....	20
Primary endpoint.....	21
Secondary endpoint .....	21
Assessment of myocardial microvascular statement.....	23
SPECT imaging protocol and analysis .....	23
Assessment of Myocardial Perfusion Entropy (MPE).....	24
Cerebral small vessels disease assessment .....	26
Statistical analysis.....	29
Results .....	30
Patient's characteristics .....	31
SPECT analysis .....	32
Neurological assessment and cerebral images analysis.....	33
Primary endpoint.....	34
Coronary disease screening .....	34
Discussion.....	35
The systemic microcirculatory disease hypothesis.....	35
Primary endpoint.....	38
Literature review .....	38
Coronary artery disease screening in patients with atherothrombotic stroke.....	41
Limits .....	44
Conclusion .....	46
Bibliography .....	48
Appendix .....	56

## Abbreviations

ARWMC: Age Related White Matter Changes

CABG: Coronary Artery Bypass Graft

CAD: Coronary Artery Disease

CFR: Coronary Flow Reserve

CHUGA: Centre Hospitalier Universitaire Grenoble Alpes

CMD: Coronary Microvascular Disease

CT: Computerized Tomography

IMR: Index of Myocardial Resistance

INOCA: Ischemia with Non-Obstructive Coronary Artery

LAD: Left Anterior Descending (artery)

LV: Left Ventricle

LVEDV: Left Ventricular End Diastolic Volume

LVEF: Left Ventricle Ejection Fraction

LVESV: Left Ventricular End Systolic Volume

MACE: Major Adverse Cardiovascular Event

MPE: Myocardial Perfusion Entropy

MRI: Magnetic Resonance Imaging

NO: Nitric Oxide

RCA: Right Coronary Artery

SPECT: Single Photon Emission Computed Tomography

TOE: Trans Oesophageal Echocardiography

TTE: Trans Thoracic Echocardiography

## Abstract

**Introduction-** Microvascular disease has been described in many organs, and is associated with poor outcome. The hypothesis of a diffuse organ damage is not answered, in particular the correlation of cerebral and myocardial microvascular dysfunction. This study is searching for a correlation between cerebral small vessels disease and coronary microvascular disease.

**Methods-** We included 38 patients who had a stroke from atherothrombotic origin hospitalized in the CHUGA stroke unit who were addressed to cardiology day hospital for a check-up including myocardial SPECT. All patients had a neurologic microvascular assessment using the Age-Related White Matter Changes scale on MRI or CT scan. SPECT images were analysed with a software attributing an entropy score, corresponding to the heterogeneity of pixels intensity of the myocardium. Coronary artery disease screening using SPECT was evaluated after a stroke in selected patients.

**Results-** We included 38 patients (mean age 64.2 years old +/- 10.9, 81% of men) who had a cerebral and myocardial microcirculation assessment after a stroke. No correlation has been found between ARWMC score and myocardial perfusion entropy, Spearman correlation -0,10  $p = 0,51$ .

Among all patients, 27.1% had abnormal SPECT and 20 % had a coronary angiogram, 9.1% had at least one severe coronary stenosis and 7.3% were revascularized, 80% of patients who underwent coronary angiogram had a treatment adaptation.

**Conclusion-** No association was found between cerebral microvascular disease and myocardial perfusion heterogeneity, using myocardial perfusion entropy. Coronary artery disease screening in selected patients who had a stroke is efficient, leading to coronary revascularisation and treatments modifications.

## Résumé

**Introduction-** L'atteinte microvasculaire est décrite dans de nombreux organes et est associée à un pronostic défavorable. Une atteinte microcirculatoire systémique est suspectée, plusieurs organes pouvant être atteints simultanément. L'association entre une atteinte microvasculaire cérébrale et myocardique n'a pas encore été prouvée, cette étude recherche une corrélation entre l'atteinte microcirculatoire de ces deux organes.

**Méthodes-** Nous avons inclus 38 patients qui ont été hospitalisés dans l'unité neurovasculaire du CHUGA, pour un AVC ischémique d'origine athérombotique présumée. Ces patients ont eu une évaluation de l'atteinte cérébrale microcirculatoire en utilisant le score ARWMC sur un scanner ou une IRM cérébrale. L'étude de l'atteinte myocardique a été réalisée en analysant l'hétérogénéité de perfusion myocardique en scintigraphie myocardique, appelée entropie de perfusion myocardique. Une corrélation entre ces deux scores a été recherchée, et la performance du dépistage de la coronaropathie a été évaluée chez cette population de patient ayant présenté un AVC ischémique athérombotique.

**Résultats-** Nous n'avons pas retrouvé de corrélation entre le score ARWMC et l'entropie de perfusion myocardique, corrélation de Spearman  $-0,10$ ,  $p=0,51$ . Parmi nos patients, 27.3% avaient une scintigraphie pathologique, 20 % des patients ont bénéficié d'une coronarographie, 9.1% avaient au moins une sténose significative et 7.3 % ont été revascularisés. Parmi les patients ayant eu une évaluation coronaire invasive, 80% ont bénéficié d'une adaptation thérapeutique personnalisée à l'issue de celle-ci.

**Conclusion-** Avec notre méthode d'évaluation, nous n'avons pas trouvé de corrélation entre les troubles de la microcirculation myocardique et cérébrale. Le dépistage de la coronaropathie par scintigraphie chez des patients à haut risque cardiovasculaire ayant présenté un AVC athérombotique semble efficace pour le diagnostic de sténoses coronaires sévères,



aboutissant à une revascularisation par angioplastie ou chirurgicale. Il permet aussi une adaptation thérapeutique personnalisée chez des patients présentant un athérome coronaire et un très haut risque cardiovasculaire.

## Introduction

Cardiovascular disease is the first cause of mortality worldwide responsible of 15.2 million of death (1) whether 31% of total mortality. It is the first cause of mortality in Europe too (2).

Macrovascular disease is now well known, whether it be cerebral, myocardial or peripheral arterial disease, sharing the same risk factors, each one having a different impact on the location of the organ damage. Major cardiovascular risk factors include the age depending on age, high blood pressure, diabetes mellitus, dyslipidaemia, smoking, family history of premature cardiovascular disease, and to a lesser extent, obesity, physical inactivity and metabolic syndrome (3–6).

Each risk factor has a different impact for developing either cerebrovascular, myocardial or peripheral artery damage (7,8). So, pathophysiological mechanisms are common, but also specific to develop one or another disease. The common mechanism of cardiovascular disease is the development of atherosclerosis. Macrovascular disease is well studied, but with the development of imagery, biology including molecular biology, nuclear medicine, some disease which were idiopathic, have now found a common explanation: the microvascular dysfunction.

Microvascular dysfunction is described in several organs including brain and heart.

The cerebral microvascular disease is highlighted by CT scan or MRI with parenchymatous damages of white matter, and deep grey nuclei. The lesions seen in sectional imaging is called leukoariosis, which means capillary rarefaction (9). These lesions correspond to a pathological point of view, to a loss of smooth muscle cells from the tunica media, deposits of fibrohyaline material, narrowing the lumen, and thickening of the vessel wall (10). These findings are secondary to chronic ischaemic lesions caused by small vessels disease. This ischaemia is extended to oligodendrocytes leading to their apoptosis, and the hypothesis that blood brain barrier is damage by small vessel disease is at study (11). These lesions are seen in many

pathologies like vascular dementia, Alzheimer disease, CADASIL (Cerebral autosomal dominant arteriopathy with subcortical ischaemic strokes and leukoencephalopathy) which is a model of microvascular cerebral disease (12). White matter intensities, are proved to be associated with ageing, diabetes and hypertension (13). The presence of cerebral small vessels disease is associated with a more than two-times increased risk of dementia at the age of 75. Leukoariosis is also associated with mood (14), cognitive (15,16), gait (17) and urinary dysfunction, affecting the quality of life of the patients, and having an impact on their autonomy, indirectly having a cost impact on the society (18). A correlation has been found between the progression of leukoariosis and the decline in cognitive performance (19), thus, discovering white matter intensities should have an incidence on the patient's care, and it could be a marker of progression of dementia when it is diagnosed and associated with leukoariosis.

Coronary microvascular disease has been described in many cardiopathies, resulting in a four grades classification made by Camici et al. (20) CMD in the absence of myocardial diseases and obstructive coronary artery disease, CMD in myocardial diseases without obstructive CAD, CMD in obstructive CAD, and finally iatrogenic CMD. CMD is an entity discovered in the last three decades, but is still a current issue, the first precise definition has been made recently by the COVADIS (Coronary Vasomotion Disorders International Study Group) in 2017 (21). With the development of functional pharmacological tests during a coronary angiography, we found out that this category of patients had a lower response to vasodilator molecules indicating a microcirculation dysfunction with a loss of flow auto regulation (22,23). Coronary microvascular disease is an underestimated disease, partly due to a lack of systematic procedures in patients addressed to the catheterization laboratory for a suspected cardiac ischemia, without finding any coronary stenosis. In trials studying patients with myocardial ischemia without significant coronary stenosis, more than 60 % of patients had abnormal response to acetylcholine test, 45% had inducible vasospasm and 55% had microvascular

impairment proved with Coronary Flow Reserve and/or Index of Microvascular Resistance (24). In another study, authors found out that 51% of men and 54% of women with suspected coronary artery disease had a coronary microvascular dysfunction, associated or not with coronary stenosis (25). CMD is associated with a poor prognosis, with cardiovascular outcomes including Myocardial Infarction, stroke, hospitalizations and death (26,27).

In 2000 Al Suwaidi & al showed that patients with severe endothelial dysfunction had 14% of major cardiac events after 28 months follow up against 0% in the mild and normal endothelial function (27). A meta-analysis published in 2017 by Brainin et al, including 26 prospective cohort studies, with a large panel of cardiopathies (angina, heart failure, hypertrophic cardiomyopathy, aortic stenosis, left atrial enlargement) proved that in all these groups, CMD was associated with significant more MACE than patients with normal microcirculation (28). Another study found out that patients with CMD had 30 % risk of developing CAD or an acute coronary event at 10 years. In 2018, a study proved that patients with persistent angina without obstructive CAD had a limited quality of life, but patients with a proved CMD had an improved quality of life under specific treatment (29).

Microvascular dysfunction is a pathology identified in almost every organ (30–33), often sharing the same risk factors, but the question of a systemic disease is still not answered. Every single condition (ageing, diabetes, hypertension, smoking, obesity...) is not systematically associated with microvascular dysfunction. Some usual atherosclerosis risk factors like the sex condition, is inversed when studying microvascular dysfunction, with a higher proportion of female in CMD (34). Many studies tried to test if one organ damage is associated with other organs dysfunctions (35). Many correlations have been found, but discordant findings are also discovered (36), making this subject debated, in particular between cerebral and myocardial microvascular impairment.

In this context, we made a prospective study to search a correlation between cerebral small vessels disease, and coronary microvascular dysfunction. The purpose of this study is to search if the microvascular impairment is a systemic disease.

## Methods

We realized a prospective monocentric observational study at the CHUGA, using a cohort of patients include from 01/01/2016 to 01/02/2020.

### Study population

The study population is constituted of a very high cardiovascular risk in secondary prevention, who had an ischemic stroke from atherosclerotic aetiology presumed. We included every patient hospitalized in neurology unit for a stroke, who had the cardiac check up in the cardiology day hospital of the CHUGA. The stroke is confirmed by a sectional imaging (CT scan or MRI), excluding haemorrhagic strokes, with an atherosclerotic origin presumed. This presumption is based on the aetiology work-up after the stroke, finding atheroma on the supra aortic arteries, and at least one major cardiovascular risk factor, and the absence of an embolic origin (EKG, absence of embolic arrhythmia at the scope or the rhythm holter, no cardio embolic proof on the TTE and/or TOE, and no coagulation abnormality). The atheroma can be seen on the vascular doppler, on the CT scan or MRI.

Patients with a RANKIN score  $> 4$  were excluded from the study, their functional capacity and their dependence were not justifying a coronary disease screening.

### Stroke check up

A systematic check-up is recommended after a stroke (37). Complementary exams are done to search for a carotid or vertebral artery stenosis, and to search for a cardio embolic disease. This check-up contains a CT scan of supra aortic arteries with contrast product injection, electrocardiogram, doppler echography of cervical carotid arteries, a rhythm monitoring for 24 to 48 hours, a blood pressure holter, a transthoracic echocardiography. If there is a strong suspicion of cardioembolic stroke, a transoesophageal echocardiography is indicated that may

be completed with a bubble test. To precise the cardiovascular risks, a diabetes mellitus screening should be done with fasting plasma glucose, HbA1c or glucose tolerance test, a complete lipid blood sample is also indicated. A single photon emission computed tomography can be proposed for screening obstructive coronary disease, this screening is not recommended systematically but some statement paper consider it in specific categories of patients with a high cardiovascular risk. (38)

In our protocol, these complementary exams are done in two times, one part during the hospitalization in stroke unit, the second part in cardiology day hospital. SPECT are done in the cardiology day hospital unit from one to three months after the stroke, this delay respects a restricted time interval between the neurological et cardiological evaluation, et permit a stress test for the SPECT either with dipyridamole either with dobutamine.

#### Primary endpoint

The primary endpoint is the correlation score between the neurological score of leukoariosis, named Age-Related White Matter Changes, and a myocardial perfusion heterogeneity score evaluated with SPECT images. ARWMC is a quotation score of leukoariosis evaluated on cerebral MRI or CT scan (39). Myocardial perfusion heterogeneity is evaluated with short axis acquisitions SPECT images, evaluated by a program giving a Myocardial Perfusion Entropy score.

#### Secondary endpoint

The secondary endpoint of our study is to assess the screening of CAD with the use of SPECT, and assess the revascularisation rate in the cohort of neurological patients. To evaluate the efficiency of the cardiologic check-up in neurological patients, we included all patients addressed to cardiology day hospital with a SPECT programmed from 01/01/2016 to 01/02/2020. In this evaluation, patients with transient ischemic attack and patients with cardio

embolic stroke who had a high cardiovascular risk were included. We analyse the rate of pathologic SPECT, the rate and the results of coronary angiogram, the revascularisation rate and the treatment modifications.



## Assessment of myocardial microvascular statement

### SPECT imaging protocol and analysis

Stress tests and SPECT MPI were performed according to the recommendations of the European Association of Nuclear Medicine and European Society of Cardiology (40) and to the previously described routine protocols in use in our institution (41,42). Briefly, at the end of stress (exercise test or dipyridamole injection, 0.56mg/kg over 4 minutes), 74 - 92.5 MBq of Thallium-201 were injected intravenously, and initial gated-SPECT images were recorded 10 minutes later (DST-XLI, Sopha Medical, Paris, France). Three hours following stress, 37.5 MBq of Thallium-201 was injected at rest and gated-SPECT MPI was performed 15 minutes later (rest reinjection imaging). Images were acquired using a dual-head rotating digital gamma camera with a 180° circular orbit (32 projections, 30 sec each). A uniform imaging pre-treatment for the reconstruction of raw MPI data was applied, and images were reconstructed with a Butterworth filter (cut-off value, 0.3; roll-off value, 20) and reoriented to obtain transaxial sections of the left ventricle according to the three standard cardiac planes, resulting in sets of images for stress and rest sequences for each patient.

## Assessment of Myocardial Perfusion Entropy (MPE)

Dicom files corresponding to stress and rest short-axis images were extracted from the acquisition system and used for the determination of MPE using an algorithm developed in Matlab software (Mathworks, Natick, MA, USA), typically leading to 23-31 short axis slices extracted / patient. Briefly, short axis slices were selected starting from the slice containing the highest number of pixels with non-zero values. Starting from this slice and going either in the basal and apical directions, slices considered for analysis were included as long as they contained at least 1 pixel which intensity was >73% or >65% higher than the maximum pixel value observed over the whole LV reconstructed volume. Included slices were then interpolated to obtain a fixed total of 21 slices/patient. On each of these 21 slices, the position of the LV center was automatically estimated according to the methodology described by Sonesson et al (43). The LV center was used to convert the short-axis cartesian images into polar images using 64 interpolating angles to draw interpolation lines. The pixel of highest intensity along each of the 64 interpolation lines was selected and used to build a 64 x 21 pixels 2D map of myocardial perfusion (Figure 1). The 2D map of myocardial perfusion was then normalized from 0 to 1000 using the highest intensity pixel value in order to allow inter-patient comparisons and was further thresholded to 500 and 850 as previously described (44) MPE was finally computed from stress and rest 2D perfusion maps from each patient using the formula:

$$-\sum_{k=0}^{M-1} p_k \log_2(p_k)$$

where M was the number of intensity value and  $p_k$  was the probability associated with pixel intensity k.

Entropy quantifies the information contained in an image and can be viewed as a measure of disorder in the image. Entropy is also a lower bound of the average number of bits per pixel

required to encode an image without distortion. The entropy is therefore maximal for a uniform distribution, and equals zero for a constant image.

This method has not proved yet the correlation with IMR or CFR, but it has proved a poor prognosis in patients (45).

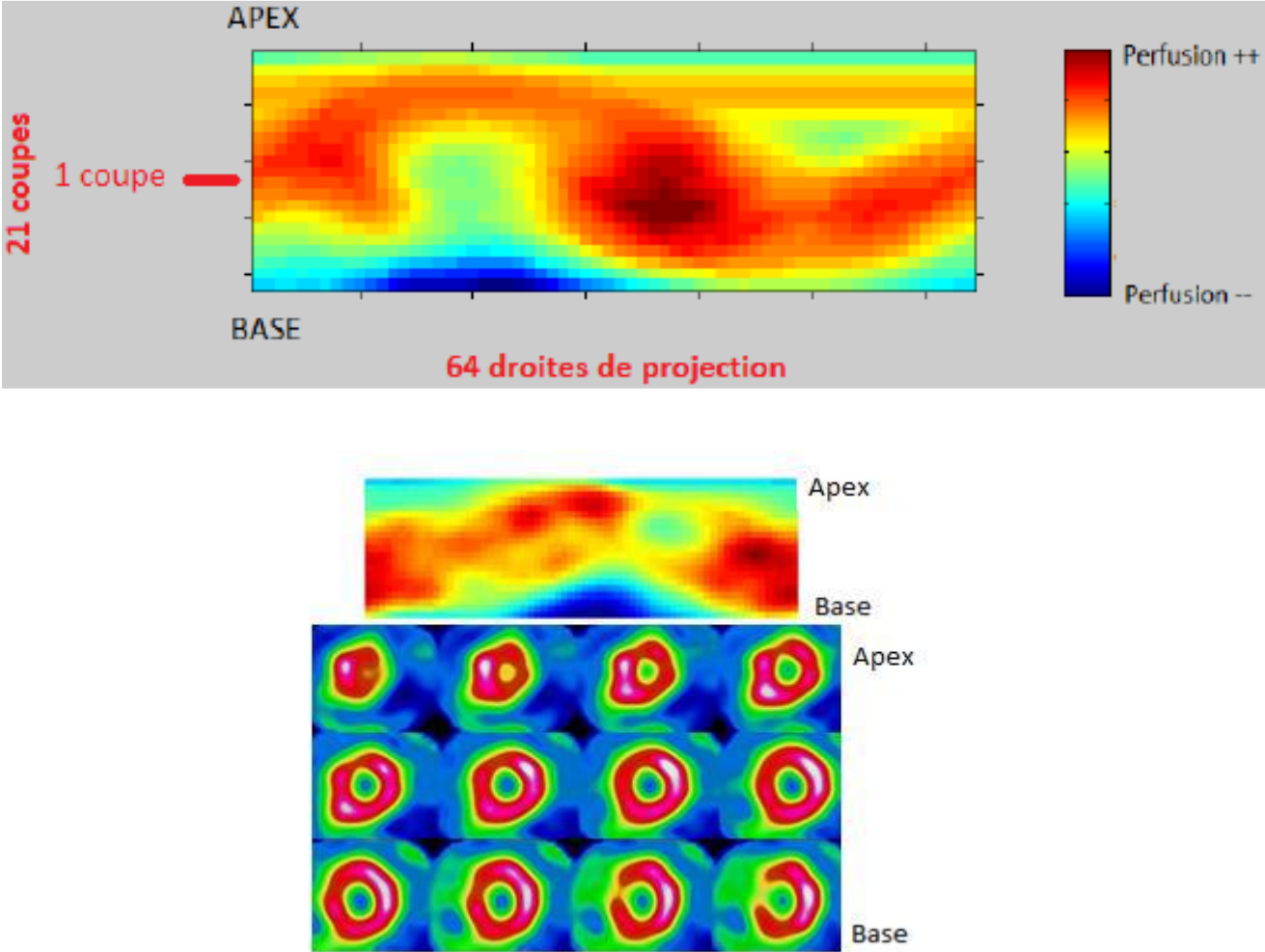


Figure 1: Short axis Thallium 201 MPI SPECT images and 2D myocardial perfusion map

## Cerebral small vessels disease assessment

Cerebral small vessels disease cannot be diagnosed directly on sectional imaging. The lesions seen correspond to the consequence of white matter ischemia due to microvascular dysfunction, also called leukoariosis. These lesions are located in the sub cortical white matter and in deep grey nuclei. These white matter changes can be observed either on CT scan and on cerebral MRI with T2 and FLAIR sequences. These sequences are systematically done when the exam is done to search for a stroke. In CT scan, the lesions are hypodensities, in MRI it corresponds to hypersignals. A few scores have been established to quantify the extent of leukoariosis, the mean one is called Age Related White Matter Changes (39,46,47). This score attributes a 0 to 3 score judging the severity of the leukoariosis, in 5 regions in both hemisphere giving un score out of 30. This score is validated on MRI and on CT scan. In our study, both MRI and CT scan are used because some patients only had a CT scan to confirm the stroke.

The scale of ARWMC is given below:

White matter lesions:

- 0: no visible lesions
- 1: focal lesions (>5mm)
- 2: beginning confluence of lesions
- 3: Diffuse involvement of the entire region, with or without involvement of U fibers

Basal Ganglia lesions

- 0: No lesions
- 1: 1 focal lesion (>5mm)
- 2: >1 focal lesion
- 3: Confluent lesions

The different regions in both hemispheres evaluated are: frontal lobe, parieto occipital lobe, temporal lobe, infra tentorial region, basal ganglia (containing striatum, globus palidus, thalamus, internal and external capsula, insula).

Infarcted regions are excluded from the quotation. The final score is out of 30. The ARWMC score is evaluated for the five first patients in double reading with Pr Detante (Neurology Physician), then in single reading.

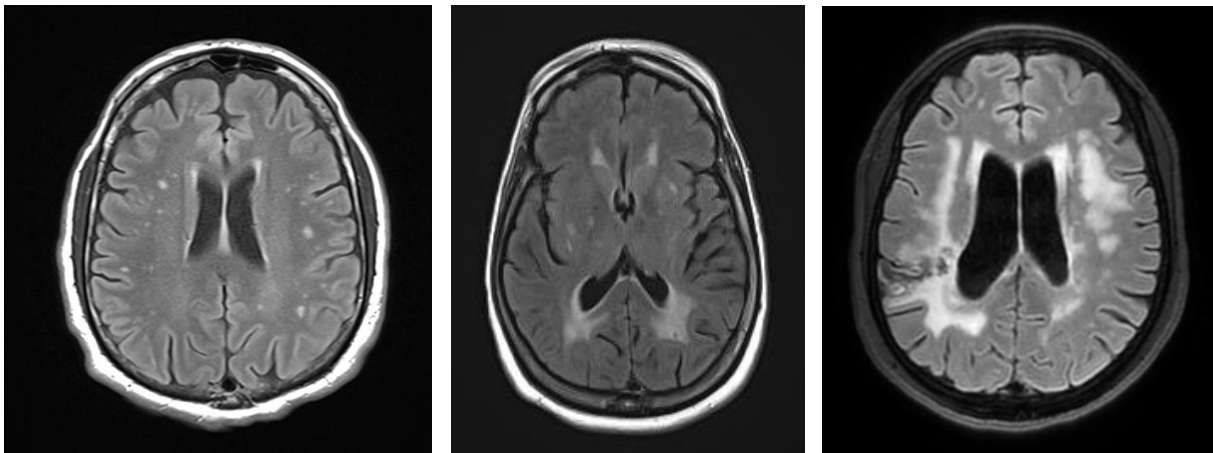


Figure 2: stage 1 (at the left) to stage 3 (at the right) of ARWMC scale, on FLAIR MRI acquisition.

Fazekas score was evaluated in all patients. Fazekas score is a simpler method to assess leukoariosis on one frame of a CT scan or a MRI. Fazekas score attributes from 0 to 3 depending on severity, the periventricular leukoariosis. (46,48) Fazekas score is attributed on one single sectional image containing lateral ventricles, frontal and parieto occipital lobes.

The Fazekas scale is detailed below:

- 0: no lesions
- 1: focal lesions
- 2: beginning confluence of lesions
- 3: multiples confluent lesions

## Statistical analysis

Analysis was performed using SPSS 21 software (SPSS Inc., Chicago, IL). Continuous variables are expressed as mean  $\pm$  SD or median (25th, 75th percentile) and discrete variables as percentage. Relationships between the variables were assessed using Pearson's correlation analysis. A p-value  $< 0.05$  was considered as statistically significant for all the analyses.

## Results

From the January 1<sup>st</sup> 2016 to February 1<sup>st</sup> 2020, 371 patients were addressed to cardiology day hospital for post stroke check-up. Among them, 64 had a check-up with a myocardial SPECT planned. In these 64 patients, 8 were excluded because of a transient ischemic attack, 7 patients had cardio embolic stroke, 5 patients didn't come to their convocation, 3 patients refused the SPECT, 2 patients had cerebral imaging in another hospital, one had migraine. Finally, we included 38 patients in our study.

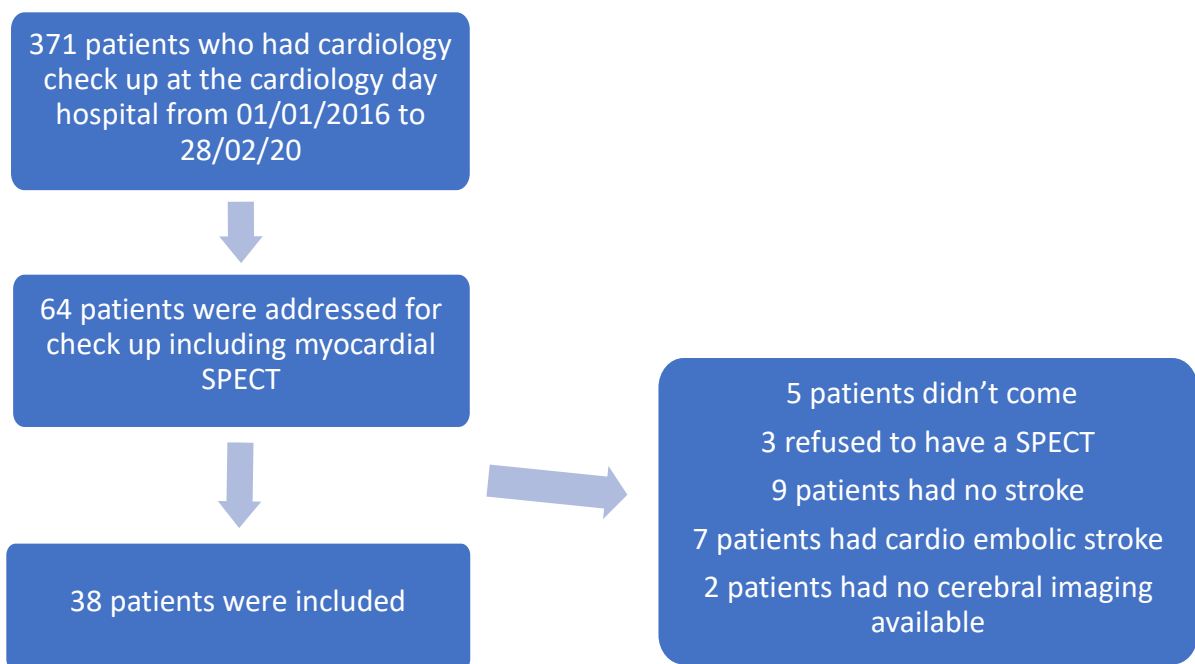


Figure 3: Flow chart



## Patient's characteristics

In our 38 patients, the mean age was 64.2 +/- 10.9 years old, 31 (81%) were men.

Patient characteristics are summarized in Table 1.

Patients characteristics			Total n=38
Age, year (SD)			64.2 (10.80)
Gender			
	Male, n (%)		32 (81)
	Female, n (%)		6 (19)
Weight, kg (SD)			80.2 (15.91)
Height, m (SD)			1.72 (0.09)
BMI, Kg/m <sup>2</sup> (SD)			27.1 (4.78)
Hypertension, n (%)			25 (64.1)
Diabetes mellitus, n (%)			9 (23.1)
Dyslipidemia, n (%)			9 (23.1)
Stroke, n (%)			0 (0)
Myocardial infarction, n (%)			2 (5.1)
Peripheral arteriopathy, n (%)			2 (5.1)
Family history, n (%)			3 (7.7)
Active smoking, n (%)			16 (41)

Table 1: Patients characteristics

## SPECT analysis

In SPECT, 13.2% of stress images quality was excellent, 84.2% was good and 2.6 % acceptable, 55.3% of images had no artefacts, 36.8% had mild artefacts and 7.9% had moderate artefacts. Patients had normal LVEF (61.3%), normal volumes (LVTDV 72.6 mL; LVTSV 28.8mL). SPECT and Myocardial Perfusion Entropy values are summarized in table 2

SPECT characteristics		Total n=38
Pathologic SPECT, n (%)		10 (26.3)
Ischemia %, m (SD)		10.3 (6.8)
Necrosis %, m (SD)		1.7 (2.7)
SRS m (SD)		3.4 (2)
SSS m (SD)		4.4 (3.1)
LVEF m (SD)	rest	stress
	61.3 (9.7)	59.5 (8.9)
LVEDV mL, m (SD)	rest	stress
	72.6 (27.3)	64.9 (17.5)
LVESV mL, m (SD)	rest	stress
	28.8 (16.1)	27.1 (12)
Entropy		
Decubitus non gated		4.4256 (0.3315)

Table 2: SPECT Characteristics

## Neurological assessment and cerebral images analysis

The average NIHSS score of the patients was 5.9 (+/- 5.3), the RANKIN score was 1.7 (+/- 1.5), and the average maximal diameter of the stroke was 23 mm (+/- 1.7). The mean ARWMC score was 5.2 (+/- 4.9), and the mean FAZEKAS score was 1.0 (+/- 0.96).

Cerebral imaging characteristics are summarized in table 3.

Cerebral MRI or CT scan Characteristics			Total n=38
Maximal stroke size, mm (SD)			23.7 (13.9)
Fazekas score, m (SD)			1.0 (0.96)
ARWMC score, m (SD)			5.2 (4.9)
		Right	Left
	Frontal lobe, m (SD)	0.97 (1.0)	1.08 (0.94)
	Parieto occipital lobe, m (SD)	1.0 (1.04)	1.03 (0.97)
	Temporal lobe, m (SD)	0.21 (0.47)	0.32 (0.62)
	Infratentorial area, m (SD)	0.18 (0.46)	0.16 (0.44)
	Basal ganglia, m(SD)	0.16 (0.44)	0.08 (0.27)
RANKIN score, m (SD)			1.7 (1.5)
NIHSS, m (SD)			5.9 (5.3)

Table 3: Cerebral images characteristics

### Primary endpoint

There was no correlation between ARWMC and MPE scores, spearman correlation was -0.10,  $p = 0.52$ .

In all risk factors studied, no association neither with ARWMC, neither with Myocardial perfusion entropy was found.

### Coronary disease screening

Among the 64 patients who were addressed to the cardiology day hospital for a check-up containing a myocardial SPECT, 55 patients (85.9%) benefited from the exam. Among them, 16 patients had an abnormal SPECT (29.1%), 11 went to coronary angiogram (20%). After proofreading, 5 patients who had abnormal SPECT were considered of false positive because of artefacts, or had not enough ischemia to undergo an invasive coronary exploration. For patients who had a coronary angiogram, 2 had multi vessels disease, one was managed with medical treatment, one with CABG. Two patients had bitroncular stenosis and were both revascularized with two stents, one patient had a single vessel stenosis and had one stent. Five patients had diffuse atheroma without significant stenosis. None of the patients benefited from a microvascular assessment by invasive method (CFR or IMR).

Eight of the ten patients who had a coronary angiogram had a treatment modification. Three went from a single to a dual anti platelet therapy. The five others had an intensification of their cardiovascular lowering risk treatment, including an introduction of beta blocker, angiotensin conversion enzyme inhibitor, thiazide inhibitor, and modification of the anti-diabetic treatment with introduction of glucagon like peptide 1 analogue. Four of the six patients who were not revascularized benefited from a treatment modification to lower cardiovascular risk.

Patients modification treatments are available in appendix 2.

## Discussion

### The systemic microcirculatory disease hypothesis

Microcirculation is defined by a vessel diameter  $< 200 \mu\text{m}$ , containing three compartments, arterioles, capillaries and venules (32). These three components are in a constant regulation to assess its role, to adapt blood flow and vascular permeability for tissue metabolism. It uses autocrine, paracrine, endocrine system to communicate, and is under the influence of autonomic nervous system. Microcirculation is the major determinant for vascular resistance, so it is the principle place for blood pressure regulation (49). Macro and microcirculation are sharing similar mechanisms and risk factors such as hypertension, diabetes and glucose intolerance, dyslipidaemia (50) but microvascular disease can reach patients without macrovascular damage. Functioning of microcirculation involves blood flow regulation by vasodilation or constriction, vascular permeability, cellular proliferation and angiogenesis.

The concomitant impairment between macro et microcirculation is not systematic but has been demonstrated in few circumstances, for example, patients presenting hypertension (51), diabetes (52) or chronic renal failure (53), had a capillary rarefaction on tissue biopsies. Patients without proven hypertension but in the upper limit of blood pressure have also been shown to have less capillaries than people with a lower blood pressure (54).

A corner stone of microvascular disease is endothelial dysfunction. Endothelium can be considered as a single organ responsible for maintaining homeostasis in each organ (55). It is the main component of capillaries, and its polymorphism permit son adapt itself to each organ demand. It can be continuous, discontinuous, fenestrated, sinusoidal, associated with a basement membrane or subendothelial cells to assure its functions. Endothelium role is to procure enough nutriments to the cell and to evacuate cellular waste. To permit sufficient exchanges, endothelium can modulate vascular permeability to fluids and molecules, and also

regulate leucocytes migration by dint of LEUCOCYTES Adhesion Molecules (LEUCAM), which contain integrins, selectins, and immunoglobulins (56).

Endothelium has a major place in regulating hemostasia in both ways. The secretion of NO and prostacyclin will have anti thrombotic and vasodilation action. Tissue plasminogen activator, secreted by endothelium, produces activated plasmin which degrades fibrin then having an antithrombotic action. Thrombomodulin which is an endothelial transmembrane protein, with its co-factor thrombin is able to activate protein C, and then inactivate factors V and VIII implicate in the coagulation cascade. In the other way, endothelial cells can secrete Willebrand factor, tissue factor and plasminogen activator inhibitor and will lead to the clot formation and coagulation activation. In physiological condition, the two systems are in balance to avoid spontaneous thrombosis, but able to activate coagulation systems if the capillary is damaged (57).

Microcirculation, by the action of endothelium, is the most important determinant of vascular resistance and blood flow auto regulation (49). The NO and prostacyclin produced by endothelial cells will have a vasodilation action on smooth muscle, at contrary, the production of endothelin or thromboxane A<sub>2</sub> will promote vasoconstriction. This blood flow regulation is mediated by tissue metabolism, shear stress, autonomic nervous system, and by circulating hormones like angiotensin II and endothelin.

The systemic microvascular disease hypothesis is based on endothelial dysfunction which will lead to a loss of blood flow auto regulation and an inadequacy between the needs and contributions of the cell. With the impairment of endothelial function, we understand that this trouble will impact every organ. Endothelial dysfunction will unbalance all the mechanisms in favour of vasoconstriction, thrombosis, inflammation, cellular proliferation and fibrosis.

A model of systemic microvascular disease is obesity (58,59). It is recognised as a risk factor for developing endothelial dysfunction. The role of white adipose tissue is to stock mobilizable energy in opposition to brown adipose tissue which regulate thermogenesis. In obesity, the accumulation of adipocytes in white adipose tissue will cause an increase in cellular size from 50 to 150-200  $\mu\text{m}$ . This will lead to a diminution of oxygen diffusion, and associated with vascular rarefaction, will cause chronic hypoxia (60,61). The consequence will be a change of adipocyte secretion, a diminution of adiponectin secretion, which is an insulin sensibiliser cytokine reducing diabetes risk, lower atherogenesis, and having an anti-inflammatory role (62). Adipocytes will also secrete more leptin, a satiety hormone, which have lower effects in obese patients. Leptin stimulates sympathetic tonus favouring vasoconstriction and endothelial dysfunction. Other cytokines are overproduced in obese patients like resistin, TNF alpha, interleukine 6 and 18, having a pro inflammatory role (60).

Insulin resistance is also implicated in endothelial dysfunction. Insulin is implicated in many signalisation routes. In one hand, insulin activates eNOS (endothelial Nitric Oxyde Synthase) through a PI 3 kinase protein, and will product NO (60). In the other hand, insulin activates ERK  $\frac{1}{2}$  way, resulting in endothelin production, which the most powerful vasoconstrictor agent known. Endothelin has also an inflammatory role, stimulating cellular proliferation and fibrosis. For healthy people, insulin effects are in favour of PI 3 kinase and NO synthesis, but for obese patients, the balance is in favour in the other signalising way, causing inflammation, fibrosis and vasoconstriction.

As proved before for obese patients, microvascular impairment is the endpoint of many cellular pathways and cannot be considered as single factor issue. Obesity is one of the risk factors, but few others have been identified (36,51,63), and as many of them a secondary to modifiable risk factors, prevention of the major cardiovascular risk factors should be intensified.

## Primary endpoint

In our study, we didn't find any correlation between ARWMC score and Myocardial Perfusion Entropy in a population of patients who suffered from an ischemic stroke.

## Literature review

The studies interesting coronary microvascular disease and cerebral small vessels disease are few.

Weidmann et al proposed to study cerebral perfusion with a technetium 99 HMPAO brain SPECT in patients presenting cardiac syndrome X (64). Their definition for Syndrome X was symptoms of myocardial ischemia on exercise test without any significant coronary stenosis, and presenting a slow flow at the contrast product injection during coronary angiogram. No microvascular measurement was done at the coronary angiogram. Many exclusion criteria were applied, among them any type of cardiopathy (valvular, hypertrophic, dilated or restrictive), hypertension, diabetes and patients with neurologic symptoms, or with a history of cerebral ischemia, cerebral disorder, and pathologic findings on carotid artery sonography. They included 90 patients with syndrome X, 76% had brain perfusion abnormalities, that were predominant in men (81% vs 69.8%). Their findings are interesting because of the high prevalence of perfusion abnormalities.

PAI et al made a similar study using a technetium 99 ethyl cysteinate dimer to assess cerebral perfusion (65). They made a study including 30 patients with syndrome X (typical anginal chest pain with a positive stress ECG test finding and normal coronary arteries on angiography, without CFR or MRI performed). They had a dipyridol stress and resting thallium 201 myocardial perfusion SPECT and were divided in two groups, normal vs abnormal SPECT. Patients with altered left ventricle ejection fraction, dyslipidaemia, overweight, neurological symptoms and neurological disorders were excluded. Ninety-five percent of patients with



pathological myocardial perfusion SPECT had hypoperfusion lesions on brain SPECT vs 20% in patients with normal myocardial SPECT (p value < 0.001).

The last study we found on the brain and myocardial perfusion was made by Sun et al. (66). Their study is very close to Weidmann's, they included 40 patients with typical anginal chest pain with positive exercise test and normal coronary arteries on angiography. Patients with altered LVEF < 50%, regional wall motion abnormalities, hypertension, diabetes, systemic vascular disease, patients who smoked and patients with any cerebral disorder or symptom were excluded. Patients were divided into two groups, one with abnormal Thallium 201 myocardial perfusion SPECT, and the other one with normal SPECT. 92 % of patients with abnormal myocardial SPECT had multiple hypoperfusion lesions on Technecium 99m HMPAO brain SPECT vs 12 % in the normal myocardial SPECT group (p<0.001). The design of this study is very close to Weidmann's, but they used a more performant gamma camera for the brain SPECT, with a better resolution.

In these three studies, only Weidmann's study was fulfilling the CMD definition. These studies are suggesting a correlation between cerebral and myocardial perfusion abnormalities, but their choice to exclude patients with diabetes, hypertension and overweight is objectionable since they are risk factors identified for microvascular impairment. When excluding the more important and more frequent risk factors of small vessels disease (hypertension, diabetes, smoking), the conclusions cannot be extended to the patients we often face, presenting an advanced age, diabetes, hypertension and smoking. Another thing to underline, is the young population they included: in Sun's study, the mean age was 45 YO, in Pai's study they were from 37 to 50 YO (no mean communicated) and in Weidmann's study the mean age was 55 YO. Choosing young patients without the principle risk factors identified for small vessels disease, may select a disease with microvascular disorder, but not representing the disease we face daily.

Finally, their brain perfusion method is debatable, the European Association of Nuclear Medicine Neuro-imaging Committee (ENC) published guidelines in 2009 for the use of brain SPECT (67). HMPAO and ECD SPECT can be used to assess brain perfusion in patients presenting mild cognitive impairment or dementia, but they precise that these methods do not provide absolute quantitative flow values but rather estimate relative regional flow differences based on the comparison of count density ratios between various regions. Johnson et al found out in a study with 5 years of follow up, that brain SPECT at baseline evaluation was more pathological in patients with Alzheimer disease and in patients who will develop Alzheimer disease, than in control group (68). In the same study, no brain SPECT pattern could differentiate patients who will develop cognitive impairment without Alzheimer disease, from the control group without cognitive decline.

In 2018, a Japanese study found out that patients with mild to moderate white matter changes on MRI had regional perfusion abnormalities in brain SPECT, and hypertension was strongly associated with WMC (69).

In contrary to our study, Weidman, Pai and Shung included patients with a diagnostic of syndrome X, then find an association is easier than in our study, because the study population is not the same. In our study, we included patients who presented a stroke, without knowing if a cerebral or a myocardial microvascular impairment is present. Then our findings are depending on the prevalence of both organ damage.

To our knowledge, no studies have been using cerebral MRI to assess cerebral microvascular disease consequences, and test the correlation with CMD.

Vuorinen et al. followed 69 patients with macrovascular coronary heart disease for a mean time of 20.6 years (70). Cerebral MRI evaluation during follow up found a diminution of grey matter

volume compared to control group, whereas no difference was found in the evaluation of white matter.

Ikram et al. used the Rotterdam study cohort and evaluated dementia and white matter lesions between patients with unrecognized myocardial infarction and patients without MI. Dementia and white matter lesions were more important in patients who had a silent myocardial infarction (71).

Brunelli et al. published a case control study, including 16 patients with syndrome X and 16 controls (72). The syndrome X diagnostic was made on a positive exercise test in patients suffering from typical angina chest pain, with normal coronary arteries on angiography, and excluding spasm with ergonovine test. They studied cerebral blood flow reserve using Xenon 133 inhalation and its measurement with 32 epicranial probes, before and after acetazolamide intravenous administration. They found strictly the same cerebral blood flow reserve in the two groups (increase of 29.0 % +/- 14% vs 29.5 % +/- 11% in the control group).

#### Coronary artery disease screening in patients with atherothrombotic stroke.

In our study, we found out that 15 SPECTs had abnormal patterns (27.3%), but after proofreading by our nuclear physicians, only 11 exams were considered as pathological so the prevalence of pathological SPECT in our cohort is 20%. Nine percent of the patients had severe coronary stenosis, the other patients had intermediate stenosis or diffuse atheroma. Finally, 4 patients were revascularized.

Nigoghossian et al. (73) found a similar prevalence (15%) of abnormal dobutamine stress echography in a similar cohort of patients who had an ischemic stroke attributed to atherosclerosis. As in his study, all of our patients with pathologic stress test imaging didn't have a significant stenosis at the coronary angiogram. Maybe these patients may benefit from a microvascular assessment.

In another study, Arenillas et al. (74) included 65 patients with a stroke or a TIA associated with an intra cranial significant stenosis, and searched for silent myocardial ischemia. They found out that 52 % of their patients had an abnormal myocardial SPECT, which is higher than our rate. They published their study without knowing if patients with abnormal SPECT benefited of a coronary angiogram, then the false positive rate of the SPECT is unknown, but during exercise test, only 5% were positive because of clinical angina pectoris, and 20% with ST segment depression. The authors didn't mention the proportion of abnormal SPECTs due to artefacts.

In 2009, Ovbiagele et al. (75) made a feasibility study of screening CAD in patients after an ischemic stroke, with a Framingham score  $> 20$  %. The main result is that they proved the difficulty to organise a systematic screening in this category of patients, because only 44% of patients who had a good indication for non-invasive ischemic test, benefited of a stress dobutamine echography. The two reasons for this lack of performance were first the patient's noncompliance, and the second one was the physician's refusal. Forty-two percent of patients didn't come to their convocation, a few of them because of insurance issues, but most of them didn't come because of a lack of motivation and/or a lack of information of the goal of this exam. In our cohort, we suffered from the same problem, since 11 of 60 patients didn't come to their convocation. In Ovbiagele's study, 33 % of dobutamine echography didn't carry out because of the physician's refusal, then the problem that can be pointed out is the lack of information of the physicians about CAD in patients after a stroke.

The American Heart Association with the American Stroke Association published a statement paper in 2003 regarding CAD screening in patients with TIA or stroke (76). Ischemic tests should not be systematic after a stroke but some population may benefit of it. There are few reasons for a CAD screening in this population. First, the prevalence of CAD, symptomatic or silent ischemia, is high in patients who presented a TIA or a stroke. Studies found out that 20

to 40 % of these patients had silent ischemia (77,78). More recently in a meta-analysis published in 2016 including more than 50 000 patients who presented a first TIA or a first stroke, significant coronary stenosis was found in 30 % of the patients, and the risk of myocardial infarction the first year after a stroke was 3% (79).

Second, after a stroke, cardiac mortality is significant, after analysing studies including 30 000 patients, cardiac mortality is from 2 to 5% at 90 days after stroke (but authors precise that these deaths concern mainly patients with known CAD) (80,81).

In longer follow up studies, the incidence of myocardial event (myocardial infarction, cardiac death) is around 2 to 3 % per year during the three years after a stroke or TIA (82,83).

The long-term prognosis of patients is also strongly influenced by CAD. In the Rochester study, the cumulative incidence of myocardial infarction or sudden death after a stroke was 10.6% at 5 years, and even up to 17.4% at 5 years in the northern Manhattan study (84,85).

Few studies showed a high mortality in the three first months after a stroke due to the actual stroke or complications linked to it and to the hospitalization, but the mortality after this period is significantly linked to cardiac death. Between 1 and 5 years after a first stroke, the first cause of mortality was cardiac deaths (41%), after 5 years non vascular deaths become first but cardiac deaths are still more important than death because of recurrent stroke (33% versus 23 %) (86).

The conclusion of the ASA AHA statement is that a systematic coronary risk evaluation should be done after a stroke. It is based on the same guidelines as people in primary prevention, by calculating a coronary risk score at 10 years, using Framingham algorithm or SCORE score (87). A reduction of the number of cardiovascular risk factors should be done. Systematic non-invasive ischemic test is not recommended, but patients with a high risk at 10 years and patients with a significant carotid stenosis should be considered for either exercise ECG, SPECT, exercise or dobutamine echography. This statement paper is a little outdated and an update should help clinicians to better manage patients with stroke. Calvet et al. created a score named

PRECORDIS score, associating Framingham score and cervicocephalic significant atherosclerosis which was associated with an occult > 50 coronary stenosis on CTA, and the value of the score was associated with the severity of CAD (88). This PRECORDIS Score may be an easy tool accessible in every stroke unit to identify the patients who would benefit from a CAD screening.

More recent studies interested on cardiac computed tomography angiography or coronary artery calcium score to diagnose asymptomatic CAD, and predict poor prognosis in patients after a stroke. A Korean prospective cohort with 1893 patients with ischemic stroke found out that MACE was associated with asymptomatic coronary stenosis diagnosed on cardiac CTA (89). Cardiac CTA may be a tool to diagnose obstructive CAD, but this exam fails to recognise INOCA since it is an anatomic evaluation only.

### Limits

Our study has few limits. First, the assessment of cerebral small vessels disease is validated and correlates with poor outcome (10,16,19,90,91) but our myocardial perfusion technic hasn't proved a correlation with IMR during coronary angiogram yet with its gold standard. Myocardial perfusion entropy is associated with poor outcome in patients with diabetes but correlation between heterogeneity and IMR is poor (Non published data, EVACORY study, NCT0199595).

The second limit is the lack of statistical power because of our too small sample size to find an association between cerebral and myocardial microvascular dysfunction. Despite an inclusion period of 4 years, only 64 patients were addressed to cardiology day hospital for stroke check up with a coronary disease screening with SPECT. Among these patients, some of them didn't come to their convocation, and some were excluded from the study, because even if the coronary disease screening was justified, the origin of the stroke was cardio embolic. Since our cohort was including patients with a cerebral macrovascular damage, some of our patients could have

none of the two microvascular disease. Then to prove an association between the two organs damage was even more difficult.

Another limit could have been the single reading of the majority of the cerebral MRI, but the rating scale of ARWMC is easy to apply, and the strong correlation found between the two methods of evaluation (FAZEKAS and ARWMC) is in favour of consistency of our assessment.

## Conclusion

In this study, we didn't find any association between cerebral leukoariosis and perfusion heterogeneity on myocardial SPECT in patients who suffered from a stroke. Further study may be done using another type of myocardial SPECT analysis, the coronary reserve, to search for a common disease between the brain and the heart microvasculature. The neurology – cardiology branch seems to be interesting in selected patients with an acceptable rentability of SPECT to detect CAD, which is similar to other studies.



Thèse soutenue par : **Victor MATHIEU**

**TITRE : ETUDE D'UNE COHORTE DE PATIENTS AYANT PRESENTE UN AVC ISCHEMIQUE D'ORIGINE ATHEROTHROMBOTIQUE : EVALUATION DE LA MICROCIRCULATION CEREBRALE ET MYOCARDIQUE, ANALYSE DU DEPISTAGE DE CORONAROPATHIE PAR SCINTIGRAPHIE MYOCARDIQUE.**

CONCLUSION :

Les anomalies de la microcirculation sont décrites dans tous les organes, et partagent des facteurs de risques communs. L'association entre une atteinte cérébrale et myocardique est peu étudiée, et les techniques d'évaluation sont nombreuses.

Notre étude évalue la leucoariose cérébrale par le score Age Related White Matter Changes (ARWMC) en IRM, et l'entropie de perfusion myocardique (MPE) en scintigraphie (SPECT) chez des patients à très haut risque cardiovasculaire ayant présenté un AVC ischémique d'origine athérotrombotique.

Nous avons inclus 38 patients (âge moyen  $64.2 \pm 10.9$  ans, 81% d'hommes) qui ont bénéficié d'une cotation du score ARWMC en IRM cérébrale (score moyen  $5.2 \pm 4.9$ ) et d'une mesure de l'entropie de perfusion myocardique en SPECT.

Nous n'avons pas mis en évidence de corrélation entre l'atteinte microcirculatoire cérébrale et myocardique (corrélation de Spearman  $-0.10$   $p=0.52$ ). L'utilisation de la SPECT pour le dépistage de la coronaropathie chez les patients ayant présenté un AVC avec un profil athéromateux marqué, a mis en évidence 29.1% d'anomalies de perfusion, 18.2% des patients ayant une ischémie significative et ont bénéficié d'une coronarographie diagnostique. Parmi l'ensemble des patients, 9.1% avait une coronaropathie sévère et 7.3% ont été revascularisés. L'évaluation invasive du statut coronaire a abouti à une modification personnalisée de traitement pour 80% des patients.

L'évaluation de la microcirculation par l'entropie de perfusion myocardique n'a pas montré de corrélation avec la leucoariose cérébrale en IRM. Le dépistage de la coronaropathie par SPECT chez des patients neurovasculaires sélectionnés est efficace et permet une personnalisation de la prise en charge.

VU ET PERMIS D'IMPRIMER

Grenoble, le : 19/11/20

LE DOYEN

Pour le Président  
et par délégation  
Le Doyen de Médecine  
Pr. Patrice MORAND

Pr Patrice MORAND

LE PRESIDENT DE LA THESE



Pr Gérald VANZETTO

## Bibliography

1. Les 10 principales causes de mortalité. Disponible sur : <https://www.who.int/fr/news-room/fact-sheets/detail/the-top-10-causes-of-death>
2. Townsend N, Wilson L, Bhatnagar P, Wickramasinghe K, Rayner M, Nichols M. Cardiovascular disease in Europe: epidemiological update 2016. *Eur Heart J*. 7 nov 2016;37(42):3232-45.
3. EUROASPIRE Study Group. EUROASPIRE: A European Society of Cardiology survey of secondary prevention of coronary heart disease: Principal results. *Eur Heart J*. 2 oct 1997;18(10):1569-82.
4. Lifestyle and risk factor management and use of drug therapies in coronary patients from 15 countries. Principal results from EUROASPIRE II Euro Heart Survey Programme. *Eur Heart J*. 1 avr 2001;22(7):554-72.
5. Kotseva K, Wood D, Backer GD, Bacquer DD, Pyörälä K, Keil U, et al. EUROASPIRE III: a survey on the lifestyle, risk factors and use of cardioprotective drug therapies in coronary patients from 22 European countries. *Eur J Cardiovasc Prev Rehabil*. avr 2009;16(2):121-37.
6. Kotseva K, De Backer G, De Bacquer D, Rydén L, Hoes A, Grobbee D, et al. Lifestyle and impact on cardiovascular risk factor control in coronary patients across 27 countries: Results from the European Society of Cardiology ESC-EORP EUROASPIRE V registry. *Eur J Prev Cardiol*. mai 2019;26(8):824-35.
7. Amouyel P. Une action sur un nombre limité de facteurs de risque permettrait de réduire au moins de moitié les taux de survenue de maladies cardiovasculaires. *Rev Prat*. 2005;9.
8. Motreff DP. Facteurs de risque cardio-vasculaire. 2005;7.
9. Longstreth WT, Manolio TA, Arnold A, Burke GL, Bryan N, Jungreis CA, et al. Clinical Correlates of White Matter Findings on Cranial Magnetic Resonance Imaging of 3301 Elderly People: The Cardiovascular Health Study. *Stroke*. août 1996;27(8):1274-82.
10. Pantoni L. Cerebral small vessel disease: from pathogenesis and clinical characteristics to therapeutic challenges. *Lancet Neurol*. juill 2010;9(7):689-701.
11. Wardlaw JM, Sandercock PAG, Dennis MS, Starr J. Is Breakdown of the Blood-Brain Barrier Responsible for Lacunar Stroke, Leukoaraiosis, and Dementia? *Stroke*. mars 2003;34(3):806-12.
12. Chabriat H, Joutel A, Dichgans M, Tournier-Lasserre E, Bousser M-G. Cadasil. *Lancet Neurol*. juill 2009;8(7):643-53.

13. Chamorro A. Periventricular White Matter Lucencies in Patients With Lacunar Stroke: A Marker of Too High or Too Low Blood Pressure? *Arch Neurol.* 1 oct 1997;54(10):1284.
14. Teodorczuk A, O'Brien JT, Firbank MJ, Pantoni L, Poggesi A, Erkinjuntti T, et al. White matter changes and late-life depressive symptoms: Longitudinal study. *Br J Psychiatry.* sept 2007;191(3):212-7.
15. Pantoni L, Poggesi A, Inzitari D. The relation between white-matter lesions and cognition: *Curr Opin Neurol.* août 2007;20(4):390-7.
16. Frisoni GB, Galluzzi S, Pantoni L, Filippi M. The effect of white matter lesions on cognition in the elderly—small but detectable. *Nat Clin Pract Neurol.* nov 2007;3(11):620-7.
17. Guttmann CRG, Benson R, Warfield SK, Wei X, Anderson MC, Hall CB, et al. White matter abnormalities in mobility-impaired older persons. *Neurology.* 28 mars 2000;54(6):1277-83.
18. Sado M, Ninomiya A, Shikimoto R, Ikeda B, Baba T, Yoshimura K, et al. The estimated cost of dementia in Japan, the most aged society in the world. *PLoS One.* 2018;13(11):e0206508.
19. Schmidt R, Petrovic K, Ropele S, Enzinger C, Fazekas F. Progression of Leukoaraiosis and Cognition. *Stroke.* sept 2007;38(9):2619-25.
20. Crea F, Camici PG, Bairey Merz CN. Coronary microvascular dysfunction: an update. *Eur Heart J.* 1 mai 2014;35(17):1101-11.
21. Kunadian V, Chieffo A, Camici PG, Berry C, Escaned J, Maas AHEM, et al. An EAPCI Expert Consensus Document on Ischaemia with Non-Obstructive Coronary Arteries in Collaboration with European Society of Cardiology Working Group on Coronary Pathophysiology & Microcirculation Endorsed by Coronary Vasomotor Disorders International Study Group. *Eur Heart J.* 6 juill 2020;ehaa503.
22. Ong P, Camici PG, Beltrame JF, Crea F, Shimokawa H, Sechtem U, et al. International standardization of diagnostic criteria for microvascular angina. *Int J Cardiol.* janv 2018;250:16-20.
23. Fearon WF, Kobayashi Y. Invasive Assessment of the Coronary Microvasculature: The Index of Microcirculatory Resistance. *Circ Cardiovasc Interv.* déc 2017;10(12). doi/10.1161/CIRCINTERVENTIONS.117.005361
24. Ong P, Athanasiadis A, Borgulya G, Mahrholdt H, Kaski JC, Sechtem U. High Prevalence of a Pathological Response to Acetylcholine Testing in Patients With Stable Angina Pectoris and Unobstructed Coronary Arteries. *J Am Coll Cardiol.* févr 2012;59(7):655-62.
25. Murthy VL, Naya M, Taqueti VR, Foster CR, Gaber M, Hainer J, et al. Effects of Sex on Coronary Microvascular Dysfunction and Cardiac Outcomes. *Circulation.* 17 juin 2014;129(24):2518-27.

26. Jespersen L, Hvelplund A, Abildstrom SZ, Pedersen F, Galatius S, Madsen JK, et al. Stable angina pectoris with no obstructive coronary artery disease is associated with increased risks of major adverse cardiovascular events. *Eur Heart J*. 2 mars 2012;33(6):734-44.
27. Suwaidi JA, Hamasaki S, Higano ST, Nishimura RA, Holmes DR, Lerman A. Long-Term Follow-Up of Patients With Mild Coronary Artery Disease and Endothelial Dysfunction. *Circulation*. 7 mars 2000;101(9):948-54.
28. Brainin P, Frestad D, Prescott E. The prognostic value of coronary endothelial and microvascular dysfunction in subjects with normal or non-obstructive coronary artery disease: A systematic review and meta-analysis. *Int J Cardiol*. mars 2018;254:1-9.
29. Reriani M, Flammer AJ, Duhé J, Li J, Gulati R, Rihal CS, et al. Coronary endothelial function testing may improve long-term quality of life in subjects with microvascular coronary endothelial dysfunction. *Open Heart*. févr 2019;6(1):e000870.
30. Ford TJ, Rocchiccioli P, Good R, McEntegart M, Eteiba H, Watkins S, et al. Systemic microvascular dysfunction in microvascular and vasospastic angina. *Eur Heart J*. 7 déc 2018;39(46):4086-97.
31. Thompson CS, Hakim AM. Living Beyond Our Physiological Means: Small Vessel Disease of the Brain Is an Expression of a Systemic Failure in Arteriolar Function: A Unifying Hypothesis. *Stroke*. mai 2009;40(5). doi/10.1161/STROKEAHA.108.542266
32. Houben AJHM, Martens RJH, Stehouwer CDA. Assessing Microvascular Function in Humans from a Chronic Disease Perspective. *J Am Soc Nephrol*. déc 2017;28(12):3461-72.
33. Bosetti F, Galis ZS, Bynoe MS, Charette M, Cipolla MJ, del Zoppo GJ, et al. "Small Blood Vessels: Big Health Problems?": Scientific Recommendations of the National Institutes of Health Workshop. *J Am Heart Assoc*. 26 oct 2016;5(11). doi/10.1161/JAHA.116.004389
34. Anderson RD, Petersen JW, Mehta PK, Wei J, Johnson BD, Handberg EM, et al. Prevalence of Coronary Endothelial and Microvascular Dysfunction in Women with Symptoms of Ischemia and No Obstructive Coronary Artery Disease Is Confirmed by a New Cohort: The NHLBI-Sponsored Women's Ischemia Syndrome Evaluation—Coronary Vascular Dysfunction (WISE-CVD). *J Intervent Cardiol*. 11 mars 2019;2019:1-8.
35. Berry C, Sidik N, Pereira AC, Ford TJ, Touyz RM, Kaski J, et al. Small-Vessel Disease in the Heart and Brain: Current Knowledge, Unmet Therapeutic Need, and Future Directions. *J Am Heart Assoc*. 5 févr 2019 ;8(3). doi/10.1161/JAHA.118.011104

36. Edwards MS, Wilson DB, Craven TE, Stafford J, Fried LF, Wong TY, et al. Associations Between Retinal Microvascular Abnormalities and Declining Renal Function in the Elderly Population: The Cardiovascular Health Study. *Am J Kidney Dis.* août 2005;46(2):214-24.
37. Powers WJ, Rabinstein AA, Ackerson T, Adeoye OM, Bambakidis NC, Becker K, et al. Guidelines for the Early Management of Patients With Acute Ischemic Stroke: 2019 Update to the 2018 Guidelines for the Early Management of Acute Ischemic Stroke: A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association. *Stroke.* déc 2019 ;50(12). doi/10.1161/STR.000000000000211
38. Ronan G. ACCF/AHA/ASE/ASNC/HFSA/HRS/SCAI/SCCT/SCMR/STS 2013 Multimodality Appropriate Use Criteria for the Detection and Risk Assessment of Stable Ischemic Heart Disease: A Report of the American College of Cardiology Foundation Appropriate Use Criteria Task Force, American Heart Association, American Society of Echocardiography, American Society of Nuclear Cardiology, Heart Failure Society of America, Heart Rhythm Society, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Computed Tomography, Society for Cardiovascular Magnetic Resonance, and Society of Thoracic Surgeons. *J Nucl Cardiol.* févr 2014;21(1):192-220.
39. Wahlund LO, Barkhof F, Fazekas F, Bronge L, Augustin M, Sjögren M, et al. A New Rating Scale for Age-Related White Matter Changes Applicable to MRI and CT. *Stroke.* juin 2001;32(6):1318-22.
40. Hesse B, Tägil K, Cuocolo A, Anagnostopoulos C, Bardiés M, Bax J, et al. EANM/ESC procedural guidelines for myocardial perfusion imaging in nuclear cardiology. *Eur J Nucl Med Mol Imaging.* juill 2005;32(7):855-97.
41. Vanzetto G, Ormezzano O, Fagret D, Comet M, Denis B, Machecourt J. Long-Term Additive Prognostic Value of Thallium-201 Myocardial Perfusion Imaging Over Clinical and Exercise Stress Test in Low to Intermediate Risk Patients: Study in 1137 Patients With 6-Year Follow-Up. *Circulation.* 5 oct 1999;100(14):1521-7.
42. Vanzetto G, Boizel R, Halimi S, Ormezzano O, Belle L, Fagret D, et al. Effects of a myocardial ischaemia-guided therapeutic program on survival and incidence of coronary events in asymptomatic patients with diabetes: the ARCADIA study. *Diabetes Metab.* déc 2007;33(6):459-65.
43. Soneson H, Ubachs JFA, Ugander M, Arheden H, Heiberg E. An Improved Method for Automatic Segmentation of the Left Ventricle in Myocardial Perfusion SPECT. *J Nucl Med.* 1 févr 2009;50(2):205-13.
44. Johnson NP, Gould KL. Clinical Evaluation of a New Concept: Resting Myocardial Perfusion Heterogeneity Quantified by Markovian Analysis of PET Identifies Coronary Microvascular Dysfunction and Early Atherosclerosis in 1,034 Subjects. :12

45. Djaileb L, Seiller A, Fraguas-Rubio A, Leenhardt J, A. Martin A, Poujol J, Broisat A, Miranda J, Vanzetto G, Fagret D, Desvignes M, Ghezzi C, Riou L, Barone-Rochette G. Prognostic value of myocardial perfusion entropy quantified from SPECT myocardial perfusion images. NEJM submitted
46. Scheltens P, Erkinjuntti T, Leys D, Wahlund L-O, Inzitari D, del Ser T, et al. White Matter Changes on CT and MRI: An Overview of Visual Rating Scales. *Eur Neurol.* 1998;39(2):80-9.
47. Fazekas F, Chawluk J, Alavi A, Hurtig H, Zimmerman R. MR signal abnormalities at 1.5 T in Alzheimer's dementia and normal aging. *Am J Roentgenol.* août 1987;149(2):351-6.
48. Rudilosso S, San Román L, Blasco J, Hernández-Pérez M, Urra X, Chamorro Á. Evaluation of white matter hypodensities on computed tomography in stroke patients using the Fazekas score. *Clinical Imaging.* nov 2017;46:24-7.
49. Pries AR, Secomb TW, Gaehtgens P. Structural autoregulation of terminal vascular beds: vascular adaptation and development of hypertension. *Hypertens Dallas Tex* 1979. janv 1999;33(1):153-61.
50. Johnson PC. Overview of the Microcirculation. In: *Microcirculation.* Elsevier; 2008 . p. xi-xxiv.
51. Feihl F, Liaudet L, Waeber B. The macrocirculation and microcirculation of hypertension. *Curr Hypertens Rep.* juin 2009;11(3):182-9.
52. Hadi HA, Suwaidi JA. Endothelial dysfunction in diabetes mellitus. *Vasc Health Risk Manag.* :24.
53. Thang OHD, Serné EH, Grooteman MPC, Smulders YM, ter Wee PM, Tangelder G-J, et al. Capillary rarefaction in advanced chronic kidney disease is associated with high phosphorus and bicarbonate levels. *Nephrol Dial Transplant Off Publ Eur Dial Transpl Assoc - Eur Ren Assoc.* nov 2011;26(11):3529-36.
54. Antonios TF, Singer DR, Markandu ND, Mortimer PS, MacGregor GA. Rarefaction of skin capillaries in borderline essential hypertension suggests an early structural abnormality. *Hypertens Dallas Tex* 1979. oct 1999;34(4 Pt 1):655-8.
55. Hadi HA, Carr CS, Al Suwaidi J. Endothelial Dysfunction: Cardiovascular Risk Factors, Therapy, and Outcome. *Vasc Health Risk Manag.* sept 2005;1(3):183-98.
56. Wautier JL, Setiadi H, Vilette D, Weill D, Wautier MP. Leukocyte adhesion to endothelial cells. *Biorheology.* 1990;27(3-4):425-32.
57. Gross PL, Aird WC. The endothelium and thrombosis. *Semin Thromb Hemost.* 2000;26(5):463-78.
58. Fuster JJ, Ouchi N, Gokce N, Walsh K. Obesity-induced Changes in Adipose Tissue Microenvironment and Their Impact on Cardiovascular Disease. *Circ Res.* 27 mai 2016;118(11):1786-807.

59. Sorop O, Olver TD, van de Wouw J, Heinonen I, van Duin RW, Duncker DJ, et al. The microcirculation: a key player in obesity-associated cardiovascular disease. *Cardiovasc Res.* juill 2017;113(9):1035-45.
60. Muris DMJ, Houben AJHM, Schram MT, Stehouwer CDA. Microvascular dysfunction: an emerging pathway in the pathogenesis of obesity-related insulin resistance. *Rev Endocr Metab Disord.* mars 2013;14(1):29-38.
61. Trayhurn P. Hypoxia and Adipose Tissue Function and Dysfunction in Obesity. *Physiol Rev.* janv 2013;93(1):1-21.
62. Fuster JJ, Ouchi N, Gokce N, Walsh K. Obesity-Induced Changes in Adipose Tissue Microenvironment and Their Impact on Cardiovascular Disease. *Circ Res.* 27 mai 2016;118(11):1786-807.
63. Sörensen BM, Houben AJHM, Berendschot TTJM, Schouten JSAG, Kroon AA, van der Kallen CJH, et al. Prediabetes and Type 2 Diabetes Are Associated With Generalized Microvascular Dysfunction: The Maastricht Study. *Circulation.* nov 2016;134(18):1339-52.
64. Weidmann B, Jansen WC, Bock A, Assheuer J, Tauchert MO. Technetium-99m-HMPAO Brain SPECT in Patients With Syndrome X. *Am J Cardiol.* avr 1997;79(7):959-61.
65. Pai P-Y, Liu F-Y, Kao A, Lin C-C, Lee C-C. A Higher Prevalence of Abnormal Regional Cerebral Blood Flow in Patients With Syndrome X and Abnormal Myocardial Perfusion. *Jpn Heart J.* 2003;44(2):145-52.
66. Sun S-S, Shiao Y-C, Tsai S-C, Ho Y-J, Wang J-J, Kao C-H. Cerebral Perfusion in Patients With Syndrome X: A Single Photon Emission Computed Tomography Study. *J Neuroimaging.* avr 2001;11(2):148-52.
67. Johnson KA, Moran EK, Becker JA, Blacker D, Fischman AJ, Albert MS. Single photon emission computed tomography perfusion differences in mild cognitive impairment. *J Neurol Neurosurg Psychiatry.* 20 oct 2006;78(3):240-7.
68. Kapucu ÖL, Nobili F, Varrone A, Booi J, Vander Borght T, Någren K, et al. EANM procedure guideline for brain perfusion SPECT using 99mTc-labelled radiopharmaceuticals, version 2. *Eur J Nucl Med Mol Imaging.* déc 2009;36(12):2093-102.
69. Ishibashi M, Kimura N, Aso Y, Matsubara E. Effects of white matter lesions on brain perfusion in patients with mild cognitive impairment. *Clin Neurol Neurosurg.* mai 2018;168:7-11.
70. Vuorinen M, Damangir S, Niskanen E, Miralbell J, Rusanen M, Spulber G, et al. Coronary Heart Disease and Cortical Thickness, Gray Matter and White Matter Lesion Volumes on MRI. *Obukhov AG, éditeur. PLoS ONE.* 10 oct 2014;9(10):e109250.

71. Ikram MA, van Oijen M, de Jong FJ, Kors JA, Koudstaal PJ, Hofman A, et al. Unrecognized Myocardial Infarction in Relation to Risk of Dementia and Cerebral Small Vessel Disease. *Stroke*. mai 2008;39(5):1421-6.
72. Brunelli C, Nobili F, Spallarossa P, Olivotti L, Rossettin P, Rodriguez G, et al. Cerebral blood flow reserve in patients with syndrome X. *Coron Artery Dis*. août 1996;7(8):587-90.
73. Nighoghossian N, Cakmak S, Derex L, Barthelet M, Thibault H, Finet G, et al. Silent Coronaropathy: Usefulness of Dobutamine Stress Echocardiography in Ischemic Stroke. *Eur Neurol*. 2006;56(4):211-6.
74. Arenillas JF, Candell-Riera J, Romero-Farina G, Molina CA, Chacón P, Aguadé-Bruix S, et al. Silent Myocardial Ischemia in Patients With Symptomatic Intracranial Atherosclerosis: Associated Factors. *Stroke*. juin 2005;36(6):1201-6.
75. Ovbiagele B, Liebeskind DS, Kim D, Ali LK, Pineda S, Saver JL. Optimizing Screening and Management of Asymptomatic Coronary Artery Disease in Patients With Stroke and Patients With Transient Ischemic Attack. *Stroke*. oct 2009;40(10):3407-9.
76. Adams RJ, Chimowitz MI, Alpert JS, Awad IA, Cerqueria MD, Fayad P, et al. Coronary Risk Evaluation in Patients With Transient Ischemic Attack and Ischemic Stroke. :13.
77. Di Pasquale G, Andreoli A, Pinelli G, Grazi P, Manini G, Tognetti F, et al. Cerebral ischemia and asymptomatic coronary artery disease: a prospective study of 83 patients. *Stroke*. nov 1986;17(6):1098-101.
78. Rokey R, Rolak LA, Harati Y, Kutka N, Verani MS. Coronary artery disease in patients with cerebrovascular disease: A prospective study. *Ann Neurol*. juill 1984;16(1):50-3.
79. Gunnoo T, Hasan N, Khan MS, Slark J, Bentley P, Sharma P. Quantifying the risk of heart disease following acute ischaemic stroke: a meta-analysis of over 50 000 participants. *BMJ Open*. janv 2016;6(1):e009535.
80. The International Stroke Trial (IST): a randomised trial of aspirin, subcutaneous heparin, both, or neither among 19 435 patients with acute ischaemic stroke. *The Lancet*. mai 1997;349(9065):1569-81.
81. Sandercock PA, Leong TS. Low-molecular-weight heparins or heparinoids versus standard unfractionated heparin for acute ischaemic stroke. Cochrane Stroke Group, éditeur. *Cochrane Database Syst Rev*. 4 avr 2017; doi.10.1002/14651858.CD000119.pub4
82. Boling B, Keinath K. Acute Ischemic Stroke. *AACN Adv Crit Care*. 15 juin 2018;29(2):152-62.
83. Bjerkreim AT, Khanevski AN, Thomassen L, Selvik HA, Waje-Andreassen U, Naess H, et al. Five-year readmission and mortality differ by ischemic stroke subtype. *J Neurol Sci*. août 2019;403:31-7.



84. Sacco RL, Wolf PA, Kannel WB, McNamara PM. Survival and recurrence following stroke. The Framingham study. *Stroke*. mai 1982;13(3):290-5.
85. Hartmann A, Rundek T, Mast H, Paik MC, Boden-Albala B, Mohr JP, et al. Mortality and causes of death after first ischemic stroke: The Northern Manhattan Stroke Study. *Neurology*. 11 déc 2001;57(11):2000-5.
86. Hardie K, Hankey GJ, Jamrozik K, Broadhurst RJ, Anderson C. Ten-Year Survival After First-Ever Stroke in the Perth Community Stroke Study. *Stroke*. août 2003;34(8):1842-6.
87. Conroy R. Estimation of ten-year risk of fatal cardiovascular disease in Europe: the SCORE project. *Eur Heart J*. juin 2003;24(11):987-1003.
88. Calvet D, Song D, Yoo J, Turc G, Sablayrolles J-L, Choi BW, et al. Predicting Asymptomatic Coronary Artery Disease in Patients With Ischemic Stroke and Transient Ischemic Attack: The PRECORIS Score. *Stroke*. janv 2014;45(1):82-6.
89. Yoo J, Song D, Baek J-H, Kim K, Kim J, Song T-J, et al. Poor long-term outcomes in stroke patients with asymptomatic coronary artery disease in heart CT. *Atherosclerosis*. oct 2017;265:7-13.
90. Savva GM, Forster G, Matthews FE. Age, Neuropathology, and Dementia. *N Engl J Med*. 2009;8.
91. Pantoni L. Leukoaraiosis: From an Ancient Term to an Actual Marker of Poor Prognosis. *Stroke*. mai 2008;39(5):1401-3.
92. Furuta A, Ishii N, Nishihara Y, Horie A. Medullary arteries in aging and dementia. *Stroke*. avr 1991;22(4):442-6.

## Appendix

### BILAN CARDIOLOGIQUE POST-AVC

Mail : [secretariatdjcvt@chu-grenoble.fr](mailto:secretariatdjcvt@chu-grenoble.fr) ET [secretariatneurovasculaire@chu-grenoble.fr](mailto:secretariatneurovasculaire@chu-grenoble.fr)  
Tel : 67 670 Fax : 67 136 (secrétariat) Tel : 69 388 / 65 789 / 66 942 (secrétariat UNV)

ET demande scintigraphie (si « profil athérome ») au Fax Médecine Nucléaire : 65 138

Nom :	Prénom :	Date de naissance :
Tel. patient :		

Poids : kg Taille : BPCO :  Oui  Non Asthme :  Oui  Non

✓ Type d'AVC

Infarctus cérébral Présence d'athérome au doppler TSA ou angioscan  Oui  Non  
 Infarctus cérébral  
 Hématome cérébral  
Étendu  Oui  Non  
Localisation :

✓ Date de l'AVC :

Patient :  valide  fauteuil  lit

✓ Antécédents et facteurs de risque cardio-neuro-vasculaire :

Infarctus myocarde  Ant.  Inf.  Autre Date :  
 Sténose coronaire  IVA/Dg  Cx/Mg  CD Date :  
 Angioplastie  IVA/Dg  Cx/Mg  CD Date :  
 Pontage  IVA/Dg  Cx/Mg  CD Date :  
Actuellement :  Angor effort  Angor repos  Asymptomatique

Tabac  Diabète  Dyslipidémie  HTA  
 Micro-albuminurie  Artériopathie  
 Antécédent familial  
Autre :

Rétrécissement aortique serré  Insuffisance rénale  Insuffisance hépatique  Allergies :

Autre :

Risque de grossesse :  Oui  Non

✓ Traitements en cours :

✓ Localisation du patient :

Domicile  Neurologie vasculaire  MPR Sud  MPR Tullins  SSR Les Granges

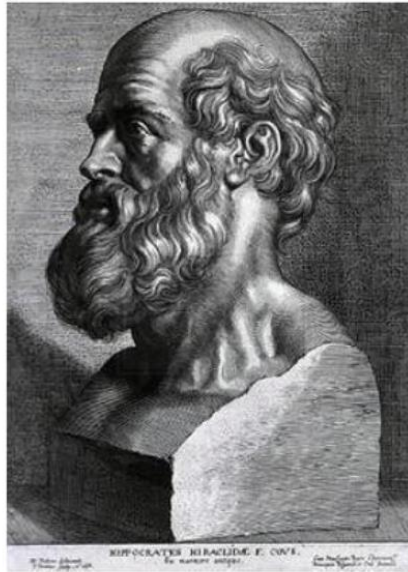
✓ Examens demandés :

Profil « cardio-embolique » (FA ? / FOP ? / Cardiopathie emboligène ?)  
 Holter ECG 24 h (uniquement si absence de scope fiable enregistré durant 48h)  
 R-Test 2 semaines (Holter implantable si R-Test négatif)  
 ETT  
 ETO (< 60 ans)

Profil « athéromateux » (bilan vasculaire ?) : bilan à 1,5-2 mois de l'AVC  
 ETT  
 Mesure ambulatoire de PA  
 Dépistage coronaropathie asymptomatique si âge < 80 ans : scintigraphie myocardique Persantine (ou Dobutamine si BPCO ou Asthme) : !!! Fax en scintigraphie  
Réfèrent cardio : Pr Barone-Rochette pour « Cohorte AVC-athérome »  
Bi anti-agrégation possible :  oui  non  oui avec délai préciser : ....

Patients	Aspirine	Plavix	IEC/ARA2	Beta Bloquant	Anti HTA	Statine	Anti diabétique	Modification de traitement
1	1		1	1		1		1
2	1	1	1	1	1	1		1
3	1	1	1			1		1
4	1							
5	1	1				1		1
6	1	1						1
7	1		1			1	3	1
8	1							
9	1	1	1			1		
10	1		1			1		
11	1		1	1				1
12		1	1		1	1	4	1
13	1		1	1		1		1
14	1					1		
15	1		1		2			
16	1		1		1			1
Total	15	6	11	4	4	10	2	10

Appendix 2: Abnormal SPECT patients treatments



## **SERMENT D'HIPPOCRATE**

*En présence des Maîtres de cette Faculté, de mes chers condisciples et devant l'effigie d'HIPPOCRATE,*

*Je promets et je jure d'être fidèle aux lois de l'honneur et de la probité dans l'exercice de la Médecine.*

*Je donnerai mes soins gratuitement à l'indigent et n'exigerai jamais un salaire au dessus de mon travail. Je ne participerai à aucun partage clandestin d'honoraires.*

*Admis dans l'intimité des maisons, mes yeux n'y verront pas ce qui s'y passe ; ma langue taira les secrets qui me seront confiés et mon état ne servira pas à corrompre les mœurs, ni à favoriser le crime.*

*Je ne permettrai pas que des considérations de religion, de nation, de race, de parti ou de classe sociale viennent s'interposer entre mon devoir et mon patient.*

*Je garderai le respect absolu de la vie humaine.*

*Même sous la menace, je n'admettrai pas de faire usage de mes connaissances médicales contre les lois de l'humanité.*

*Respectueux et reconnaissant envers mes Maîtres, je rendrai à leurs enfants l'instruction que j'ai reçue de leurs pères.*

*Que les hommes m'accordent leur estime si je suis fidèle à mes promesses.*

*Que je sois couvert d'opprobre et méprisé de mes confrères si j'y manque.*

**ETUDE D'UNE COHORTE DE PATIENTS AYANT PRESENTE UN AVC ISCHEMIQUE D'ORIGINE ATHEROTHROMBOTIQUE : EVALUATION DE LA MICROCIRCULATION CEREBRALE ET MYOCARDIQUE, ANALYSE DU DEPISTAGE DE LA CORONAROPATHIE PAR SCINTIGRAPHIE MYOCARDIQUE.**

**Résumé :**

**Introduction-** L'atteinte microvasculaire est décrite dans de nombreux organes et est associée à un pronostic défavorable. Une atteinte microcirculatoire systémique est suspectée, plusieurs organes pouvant être atteints simultanément. L'association entre une atteinte microvasculaire cérébrale et myocardique n'a pas encore été prouvée, cette étude recherche une corrélation entre l'atteinte microcirculatoire de ces deux organes.

**Méthodes-** Nous avons inclus 38 patients qui ont été hospitalisés dans l'unité neurovasculaire du CHUGA, pour un AVC ischémique d'origine athérombotique présumée. Ces patients ont eu une évaluation de l'atteinte cérébrale microcirculatoire en utilisant le score ARWMC sur un scanner ou une IRM cérébrale. L'étude de l'atteinte myocardique a été réalisée en analysant l'hétérogénéité de perfusion myocardique en scintigraphie myocardique, appelée entropie de perfusion myocardique. Une corrélation entre ces deux scores a été recherchée, et la performance du dépistage de la coronaropathie a été évaluée chez cette population de patient ayant présenté un AVC ischémique athérombotique.

**Résultats-** Nous n'avons pas retrouvé de corrélation entre le score ARWMC et l'entropie de perfusion myocardique, corrélation de Spearman -0,10,  $p=0,51$ . Parmi nos patients, 27.3% avaient une scintigraphie pathologique, 20 % des patients ont bénéficié d'une coronarographie, 9.1% avaient au moins une sténose significative et 7.3 % ont été revascularisés. Parmi les patients ayant eu une évaluation coronaire invasive, 80% ont bénéficié d'une adaptation thérapeutique personnalisée.

**Conclusion-** Avec notre méthode d'évaluation, nous n'avons pas trouvé de corrélation entre les troubles de la microcirculation myocardique et cérébrale. Le dépistage de la coronaropathie par scintigraphie chez des patients à haut risque cardiovasculaire ayant présenté un AVC athérombotique semble efficace pour le diagnostic de sténoses coronaires sévères, aboutissant à une revascularisation par angioplastie ou chirurgicale. Il permet aussi une adaptation thérapeutique personnalisée chez des patients présentant un athérome coronaire et un très haut risque cardiovasculaire.

**MOTS CLÉS :** Microcirculation, leucoarirose, hétérogénéité de perfusion myocardique, entropie de perfusion myocardique

**FILIÈRE :** Médecine - DES cardiologie et maladies vasculaires

**SOUTENUE :** le 1<sup>er</sup> Décembre 2020

**ADRESSE DE L'AUTEUR :** [Données à caractère personnel]

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