AVC ischémique avec ou sans FA; CRYPTOGÉNIQUE ou « ESUS » (Embolic Stroke of Undetermines Source)

Ariane Mackey MD FRCP(C)
Neurologue
CHU de Québec / Hôpital de l'Enfant-Jésus
Professeure agrégée de clinique,
Faculté de médecine U. Laval, Québec

SSVQ 30 0ctobre 2015

Je ne connais pas de docteur qui a recu une lettre de remerciement pour un AVC qui n’est pas survenu

A. Mackey
Conflits d'intérêts potentiels
2 dernières années

CONFÉRENCES COMMANDITÉES

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RECHERCHE

- Astra Zeneca
- Covidien
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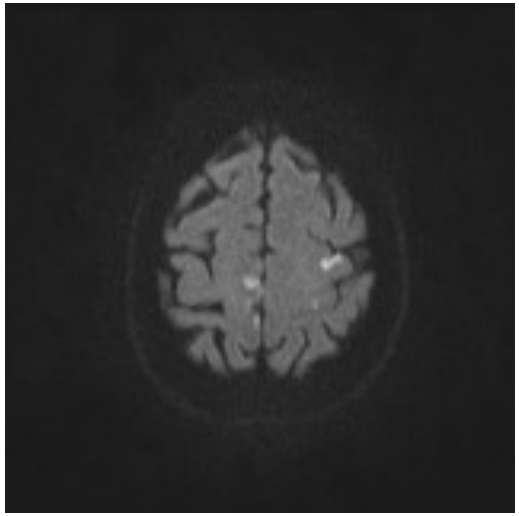
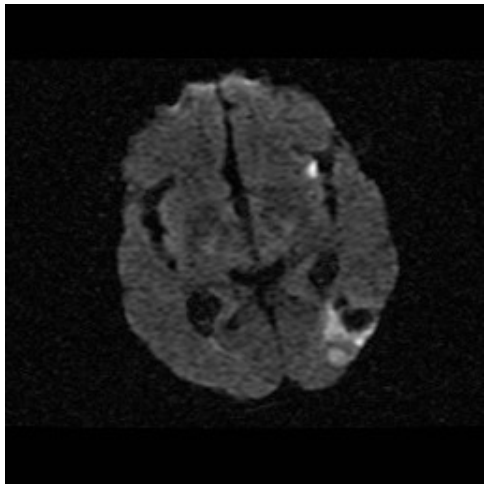
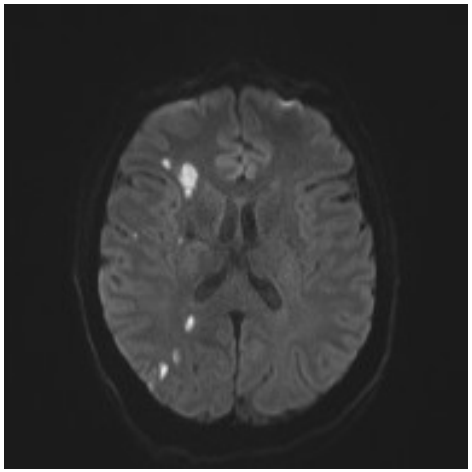
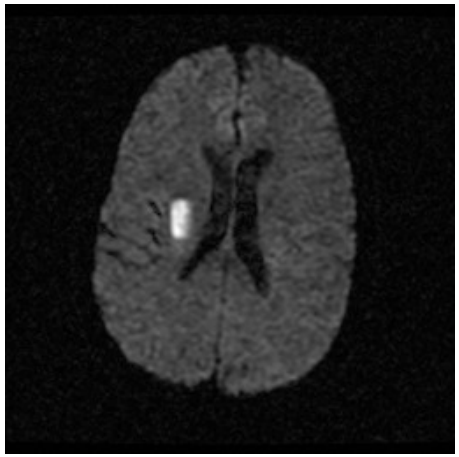
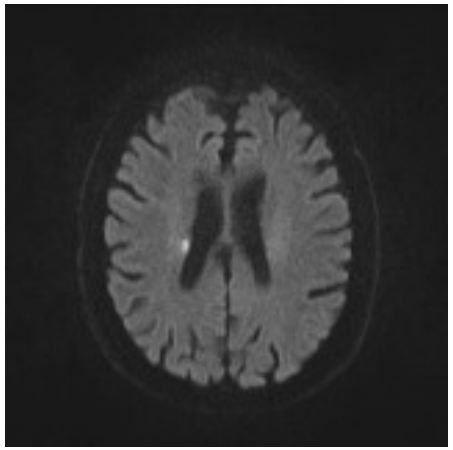
*** Aucun pour cette conférence**

Approximativement 20 à 40% des AVC ichémiques sont classifiés « cryptogéniques »

" Cryptogenic stroke is an apology for ignorance about the cause of ischaemic stroke"

Jonh Camm Sept 2014 J. Nat. Rev. Cardiol 11, 504-505

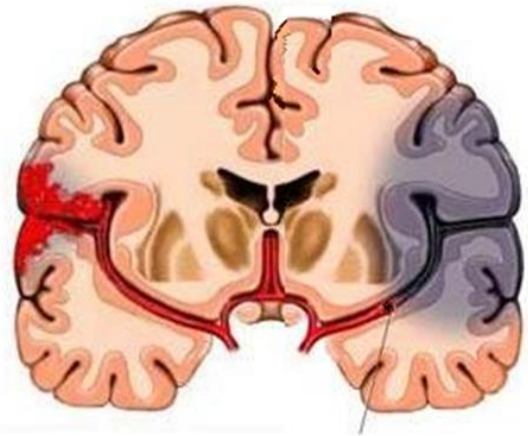
Questions

- Quand peut-on déclarer qu'un AVC est cryptogénique ?
- Est-ce que la plupart des AVC dit crypto seraient en fait de la FAP non diagnostiquée?
- Devrait-on les anticoaguler ?
- Chez qui doit-on faire un monitoring cardiaque prolongé ?
  - Dans quels délais minimum?
  - Pour combien de temps, quel gadget ?
  - Quelle durée et délais de FA vont justifier une Anticoagulothérapie

Stroke Etiologies

Vessel Rupture (15%)

Artery Occlusion (85%)



Etiology	%
Atherothrombotic Stenotic artery feeding area of infarction	25-30
Cardioembolic A thrombus or other material dislodges from the heart or aortic arch	20
Lacunar/Small Vessel Small; deep infarct	15-20
Other/Uncommon	5-10
Cryptogenic Unknown cause	25-30

Adams HP Jr, et al. *Stroke*. 1993;24;35-41.[33]
Foulkes MA, et al. *Stroke*. 1988;19:547-554.[34]

Sous types d'AVC ischémiques

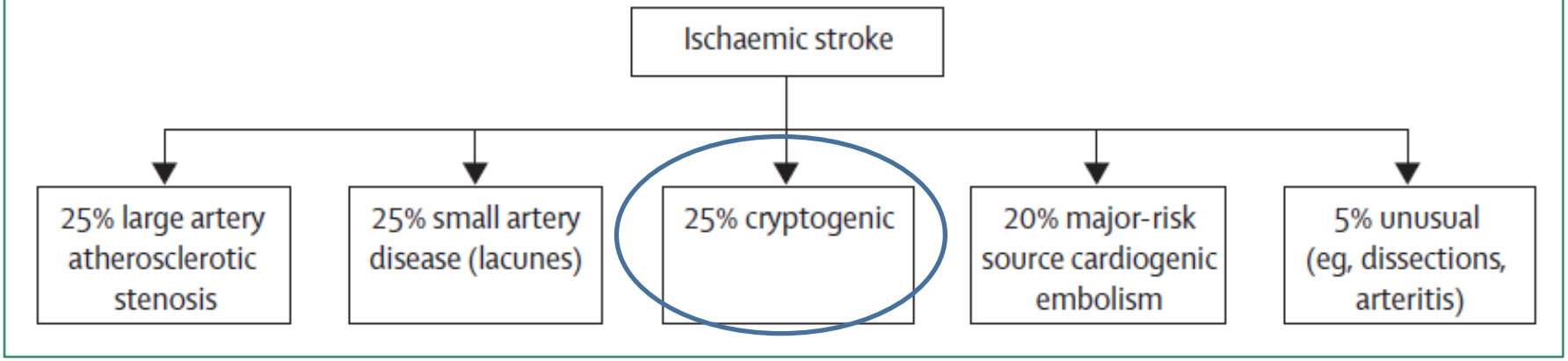


Figure 1: **Distribution of ischaemic stroke subtypes in North American and European studies**
The distribution in Asian and African populations differs from that in North American and European populations.

Robert G Hart, Hans-Christoph Diener, Shelagh B Coutts, J Donald Easton, Christopher B Granger, Martin J O'Donnell, Ralph L Sacco, Stuart J Connolly, for the Cryptogenic Stroke/ESUS International Working Group

Lancet Neurol **2014; 13: 429–38**

Prévalence des AVC crypto augmente chez jeunes (<40-50 ans) et diminue avec rigueur de l'investigation

AVC CRYPTOGÉNIQUE: pas définition officielle

- On a fait « investig de base »; CT et doppler et Holter… pas sténose de >50%, pas de FA
- On a tout fait (IRM, CTA tête et cou, Bilan thrombophilie, ETO):
  - Tout est normal
  - On a trouvé des causes +/-mineures potentielles; exemple : FOP, qq plaques Aorte
  - On a trouvé plusieurs causes: ex.: sténose carotidienne et FA

Pourquoi en parler

- Risque de récidive non négligeable
  - Ad 30% à un an (étude sud coréenne)
  - 1.2% récidive clinique à trois mois
  - 14% nouvelles lésion à l'imagerie à 3 mois

Bang OY, Lee PH, Joo SY, Lee JS, Joo IS, Huh K. Frequency and mechanisms of stroke recurrence after cryptogenic stroke. *Ann Neurol* 2003;54:227–234.

Bal S, Patel SK, Almekhlafi M, Modi J, Demchuk AM, Coutts SB. High rate of magnetic resonance imaging stroke recurrence in cryptogenic transient ischemic attack and minor stroke patients. *Stroke* 2012;43:3387–3388.

Lancet Neurol 2015; 14: 903–13

Incidence, outcome, risk factors, and long-term prognosis of cryptogenic transient ischaemic attack and ischaemic stroke: a population-based study

Linxin Li, Gabriel S Yiin, Olivia C Geraghty, Ursula G Schulz, Wilhelm Kuker, Ziyah Mehta, Peter M Rothwell, on behalf of the Oxford Vascular Study

Methods In a population-based study in Oxfordshire, UK, among patients with a first TIA or ischaemic stroke from April 1, 2002, to March 31, 2014, we compared cryptogenic events versus other causative subtypes according to the TOAST classification. We compared markers of atherosclerosis (ie, risk factors, coronary and peripheral arterial disease, asymptomatic carotid stenosis, and 10-year risk of acute coronary events) and of cardioembolism (ie, risk of cardioembolic stroke, systemic emboli, and new atrial fibrillation [AF] during follow-up, and minor-risk echocardiographic abnormalities and subclinical paroxysmal AF at baseline in patients with index events between 2010 and 2014).

Findings Among 2555 patients, 812 (32%) had cryptogenic events (incidence of cryptogenic stroke 0·36 per 1000 population per year, 95% CI 0·23–0·49). Death or dependency at 6 months was similar after cryptogenic stroke compared with non-cardioembolic stroke (23% *vs* 27% for large artery and small vessel subtypes combined; p=0·26) as was the 10-year risk of recurrence (32% *vs* 27%; p=0·91). However, the cryptogenic group had fewer atherosclerotic risk factors than the large artery disease (p<0·0001), small vessel disease (p=0·001), and cardioembolic (p=0·008) groups. Compared with patients with large artery events, those with cryptogenic events had less hypertension (adjusted odds ratio [OR] 0·41, 95% CI 0·30–0·56; p<0·0001), diabetes (0·62, 0·43–0·90; p=0·01), peripheral vascular disease (0·27, 0·17–0·45; p<0·0001), hypercholesterolaemia (0·53, 0·40–0·70; p<0·0001), and history of smoking (0·68, 0·51–0·92; p=0·01), and compared with small vessel and cardioembolic subtypes, they had no excess risk of asymptomatic carotid disease (adjusted OR 0·64, 95% CI 0·37–1·11; p=0·11) or acute coronary events (adjusted hazard ratio [HR] 0·76, 95% CI 0·49–1·18; p=0·22) during follow-up. Compared with large artery and small vessel subtypes combined, patients with cryptogenic events also had no excess of minor-risk echocardiographic abnormalities (cryptogenic 37% *vs* 45%; p=0·18) or paroxysmal AF (6% *vs* 10%; p=0·17) at baseline or of new AF (adjusted HR 1·23, 0·78–1·95; p=0·37) or presumed cardioembolic events (1·16, 0·62–2·17; p=0·64) during follow-up.

Interpretation The clinical burden of cryptogenic TIA and stroke is substantial. Although stroke recurrence rates are comparable with other subtypes, cryptogenic events have the fewest atherosclerotic markers and no excess of cardioembolic markers.

32% des 2555 patients avec 1er AVC/ ICT = crypto (420 ICT, 392 AVC)

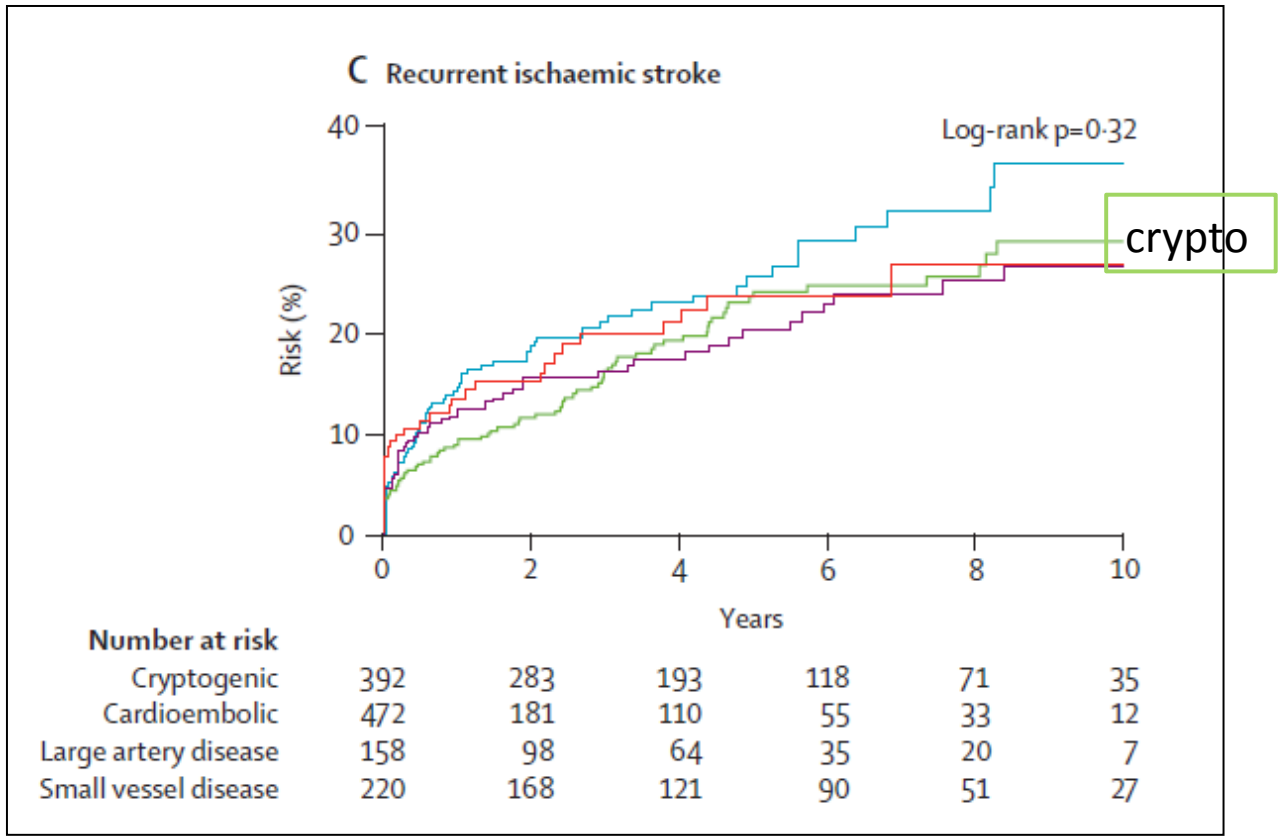
- Moins de marqueurs d'ASO
- Pas d'exès de marqueurs cardioemboliques

Pour les AVC crypto: Même taux de récurrence d'AVC à 90 jours et durant F/U ad 10 ans que ceux avec cause déterminée

Lancet Neurol 2015; 14: 903–13

Cryptogenic
Cardioembolic
Large artery disease
Small vessel disease

AVC seulement



Aucune donnée probante ou recommandations dans les guidelines pour guider la prévention secondaire

Pourquoi le « concept » ESUS (avril 2014)

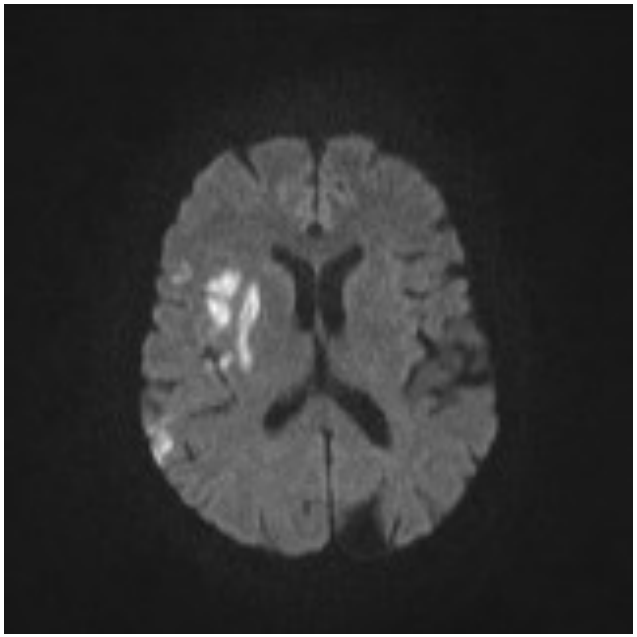
(Embolic Stroke of Undetermines Source)

Pourquoi le « concept » ESUS (avril 2014)

- Parce que la plupart de ces AVC sont probablement d'origine thromboembolique
- L'origine du thrombus est probablement
  - Carotide <50% ou vertébrale
  - « minor » or « covert » cardiac source
  - Aorte
  - Veines via FOP
  - Ou.. FAP non découverte
  - Ou état hypercoagulable
- Donc possiblement mieux traitée avec ANTICOAGULANTS que antiplaquettaires
- Venue des NOACS devenus DOACS (moins d'HIP): occasion de faire essais cliniques… établir lignes de conduite

Christiane 65 ans

- sous ASA, ..
- parésie facio brachiale droite,
- doppler ; plaque 40% visuellement , pas d'aug. vélocités
- télémétrie 48h : pas de FA, ETT: N



- Classifié Crypto /ESUS ?
- Doit –on faire
  - CTA tête ? (*pas aigu*)
  - CTA cou
  - ETO
  - Bilan thrombophilie
  - Monito prolongé ?
- On ajoute Plavix ?
- On donne statine à haute dose ?

ESUS : C'EST QUOI ?

Embolic strokes of undetermined source: the case for a new clinical construct

Robert G Hart, Hans-Christoph Diener, Shelagh B Coutts, J Donald Easton, Christopher B Granger, Martin J O'Donnell, Ralph L Sacc
Stuart J Connolly, for the Cryptogenic Stroke/ESUS International Working Group

Lancet Neurol 2014; 13: 429–38

Panel 2: Criteria for diagnosis of embolic stroke of undetermined source*

- Stroke detected by CT or MRI that is not lacunar†
- Absence of extracranial or intracranial atherosclerosis causing ≥50% luminal stenosis in arteries supplying the area of ischaemia
- No major-risk cardioembolic source of embolism‡
- No other specific cause of stroke identified (eg, arteritis, dissection, migraine/vasospasm, drug misuse)

*Requires minimum diagnostic assessment (panel 3). †Lacunar defined as a subcortical infarct smaller than or equal to 1·5 cm (≤2·0 cm on MRI diffusion images) in largest dimension, including on MRI diffusion-weighted images, and in the distribution of the small, penetrating cerebral arteries; visualisation by CT usually needs delayed imaging greater than 24–48 h after stroke onset. ‡Permanent or paroxysmal atrial fibrillation, sustained atrial flutter, intracardiac thrombus, prosthetic cardiac valve, atrial myxoma or other cardiac tumours, mitral stenosis, recent (<4 weeks) myocardial infarction, left ventricular ejection fraction less than 30%, valvular vegetations, or infective endocarditis.

- Non lacunaire…
- Pas de sténose >50%...
- Pas de source majeure de cardio-embol *
- Pas d'autre cause spécifique identifiée..
  - Dissection,
  - migraine…
  - drogues

Imparfait, beaucoup de critiques possibles , possiblement peu utile en dehors de la recherche
Mais guidelines = essais cliniques requis…

Panel 4: Comparison of cryptogenic stroke versus embolic stroke of undetermined source

Diagnostic criteria

*Cryptogenic ischaemic stroke**

- No arterial stenosis (>50%) or occlusion coupled with non-lacunar infarct on imaging
- No clinical lacunar syndrome if imaging shows no infarct or small (<1·5 cm) subcortical infarct
- No major-risk or medium-risk cardioembolic sources

Embolic stroke of undetermined source (ESUS)

- Non-lacunar brain infarct on imaging
- Open arteries (<50% stenosis) proximal to the infarct
- No major-risk cardioembolic source

Necessary diagnostic assessment

*Cryptogenic ischaemic stroke**

Not specified†

Embolic stroke of undetermined source (ESUS)

- Brain CT or MRI showing non-lacunar infarct
- Precordial echocardiography
- ECG and cardiac monitoring for ≥24 h
- Imaging of the extracranial and intracranial arteries supplying the area of the brain infarct

Limitations

*Cryptogenic ischaemic stroke**

- Inclusion of variable fraction of lacunar infarcts and intracranial arterial stenosis dependent on extent of diagnostic assessment (varies from study to study, and usually not described in detail)

Embolic stroke of undetermined source (ESUS)

- Transoesphageal echocardiography not recommended, and hence aortic arch atherosclerosis not characterised

ECG=electrocardiogram. *Criteria for cryptogenic stroke are not standardised; TOAST criteria for stroke of undetermined cause are considered here, excluding those with two or more potential causes.[115] †Some patients will have no likely cause established despite an extensive assessment. In others, no cause is found but the assessment was cursory.[115] In most studies of cryptogenic stroke, the extent of diagnostic imaging is not reported.

CRYPTO vs ESUS

- Classifié Crypto / ESUS ?
- Minimum d'investigation requis pour ESUS
- ETO non requis (donc ASO Ao ascendante NE)

Investigation proposée pour « étampe « ESUS »

Panel 3: Proposed diagnostic assessment for embolic stroke of undetermined source*

- Brain CT or MRI
- 12-lead ECG
- Precordial echocardiography
- Cardiac monitoring for ≥24 h with automated rhythm detection†
- Imaging of both the extracranial and intracranial arteries supplying the area of brain ischaemia (catheter, MR, or CT angiography, or cervical duplex plus transcranial doppler ultrasonography)

*Imaging of the proximal aortic arch is not needed; special blood tests for prothrombotic states only if the patient has a personal or family history of unusual thrombosis or associated systematic signs or disorder. †Cardiac telemetry is not sufficient.

- La tête: IRM > CT
- Le cœur:
  - ECG
  - Holter 24 h
  - ETT
- Les vaisseaux
  - Extracraniens et intracraniens

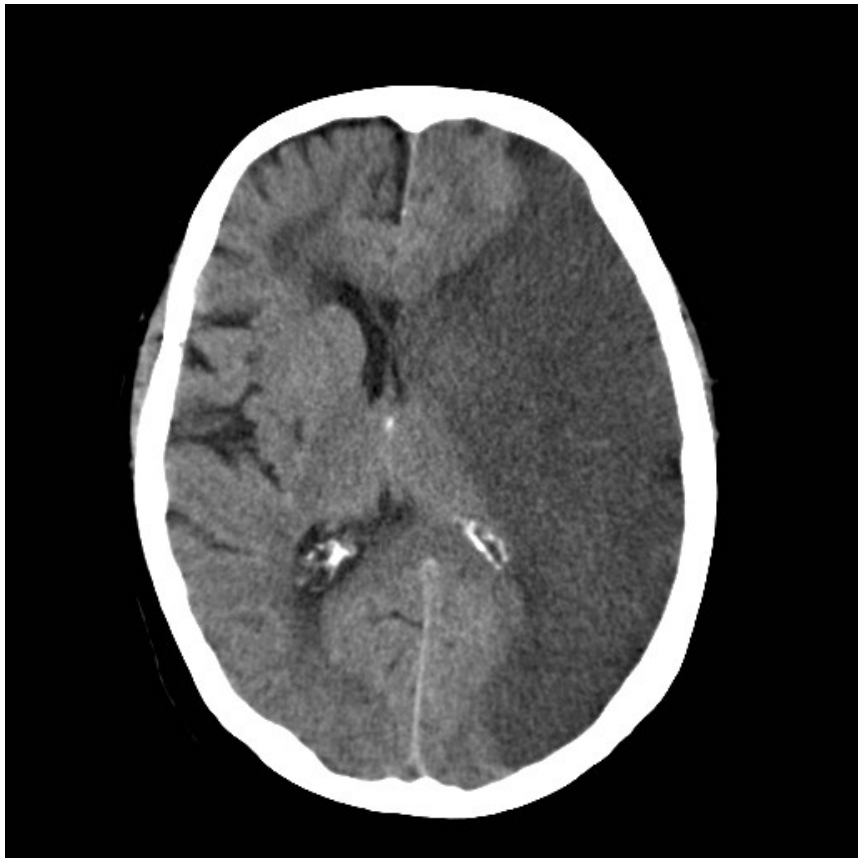
*ETO, bilan thrombophilie: Non requis

Au quotidien
Comment choisir l'investigation

- Balance entre coût et « yield » potentiel
- Considérer charactéristiques du patient
- Considérer l'effet potentiel sur une décision thérapeutique (ex AVC majeur.. Pauvre prognostic, Patient dément, cancer actif..)

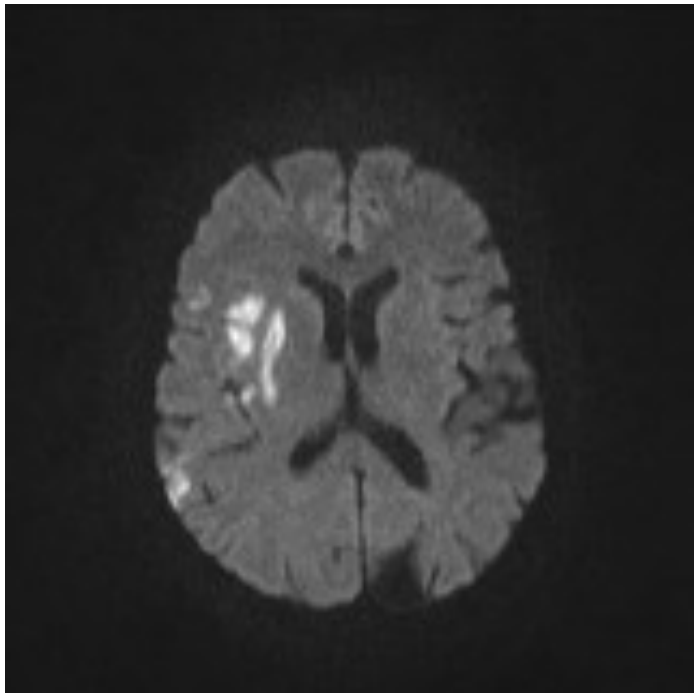
  – BREF le GBS et souvent plusieurs options acceptables

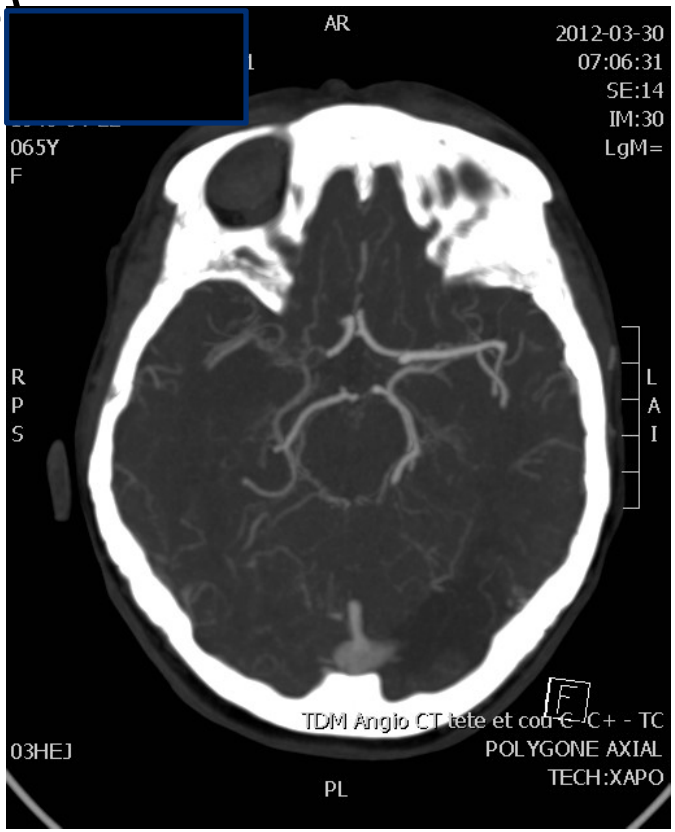
Choisir l'investigation
GBS….>> Guidelines… Soins pall



De retour à Christiane

- Angio scan de la <u>tête</u>: occlusion M1
- … ICT franc <u>même territoire</u> per hospit sous ASA et Plavix
- Etiol: crypto ou ESUS (éligible)





Sous types d'AVC ischémiques

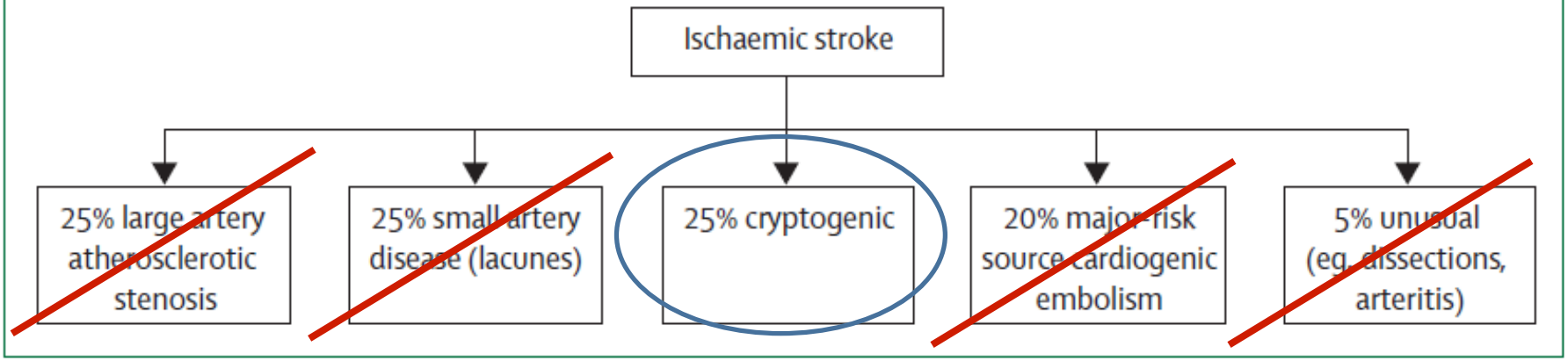


Figure 1: **Distribution of ischaemic stroke subtypes in North American and European studies**
The distribution in Asian and African populations differs from that in North American and European populations.

Christiane

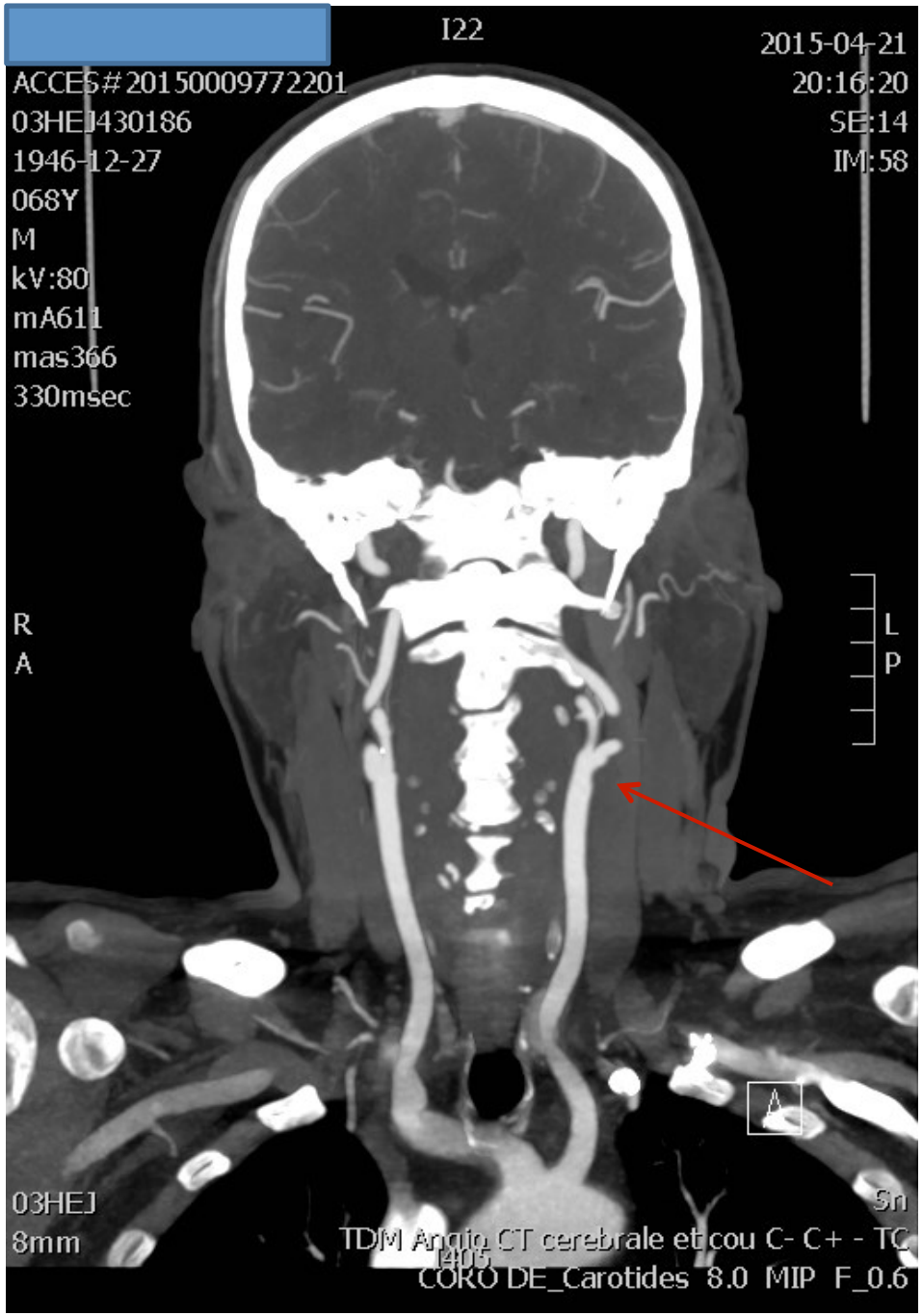
- Angio scan du cou : plaque d'allure ulcérée 40-45% CIG
- Sypmto sous ASA et Clopi
- Finalement opérée

- « Premier pitfall »:Une sténose de < 50 % peut être symptomatique….
- Conduite +/-empirique: héparine vs chx vs double AP

Monsieur Thériault 21 avril 2015

- 67 HTA pas d'antithrombotique
- 2 « ICT » francs même pattern : trouble de la parole et faiblesse de la main droite 15-30 minutes

- CT : rien
- IRM; petit AVC cortical gauche (pas lacune)
- CTA tête ; normal
- CT cou: protusion d'une plaque vs thrombus dans CIG non sténosante
- CRYPTO ?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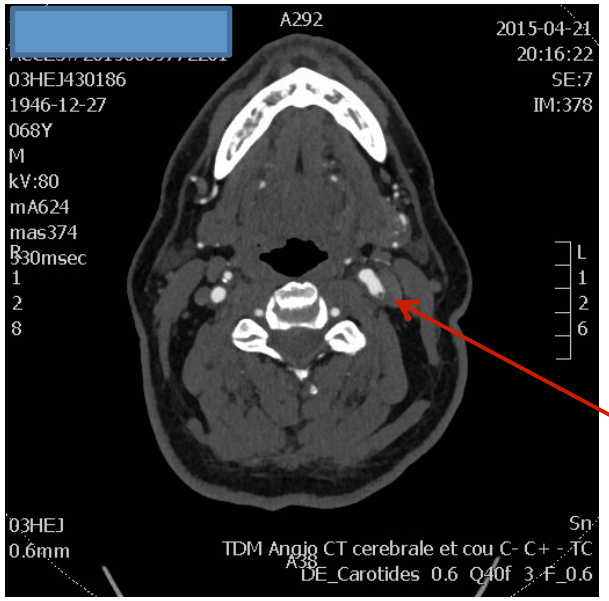
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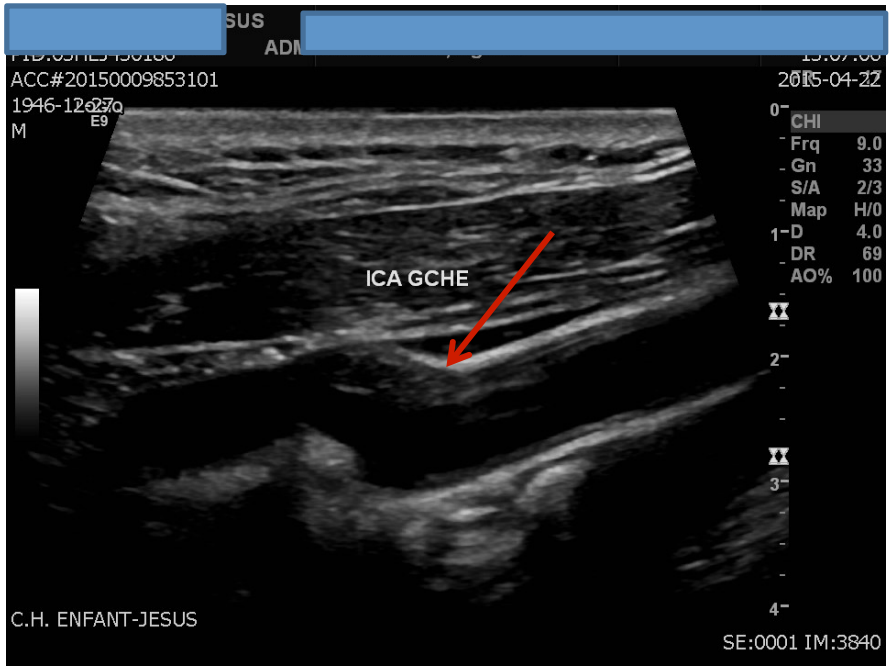
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Imagerie de PLAQUE…

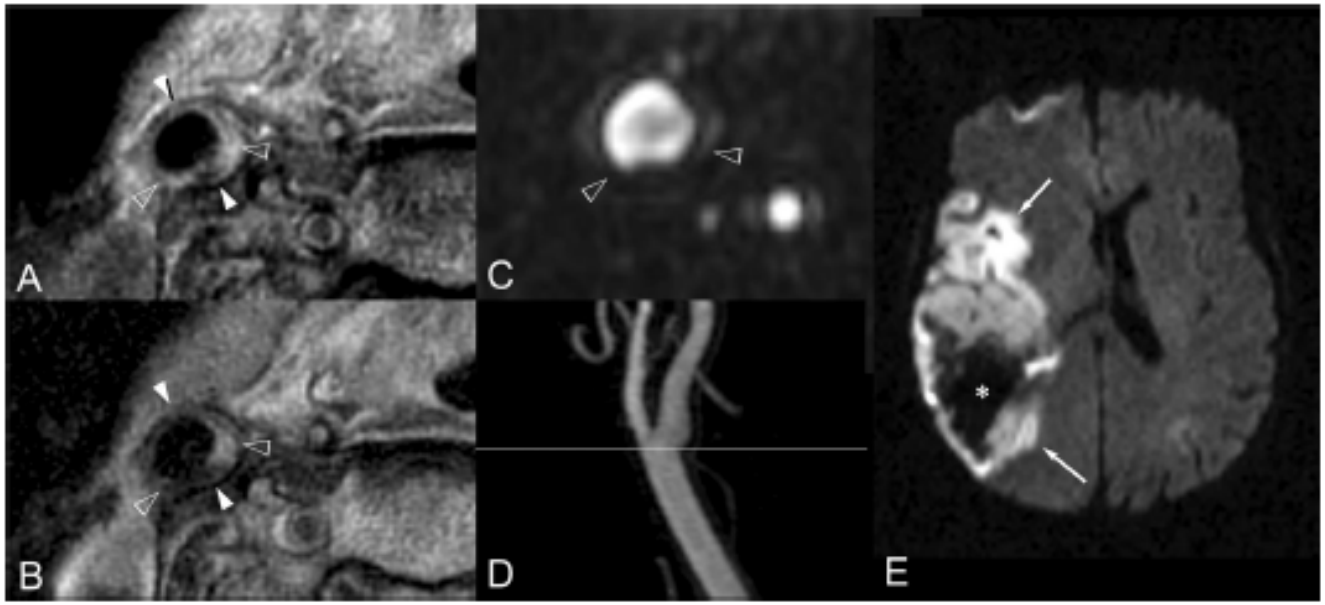
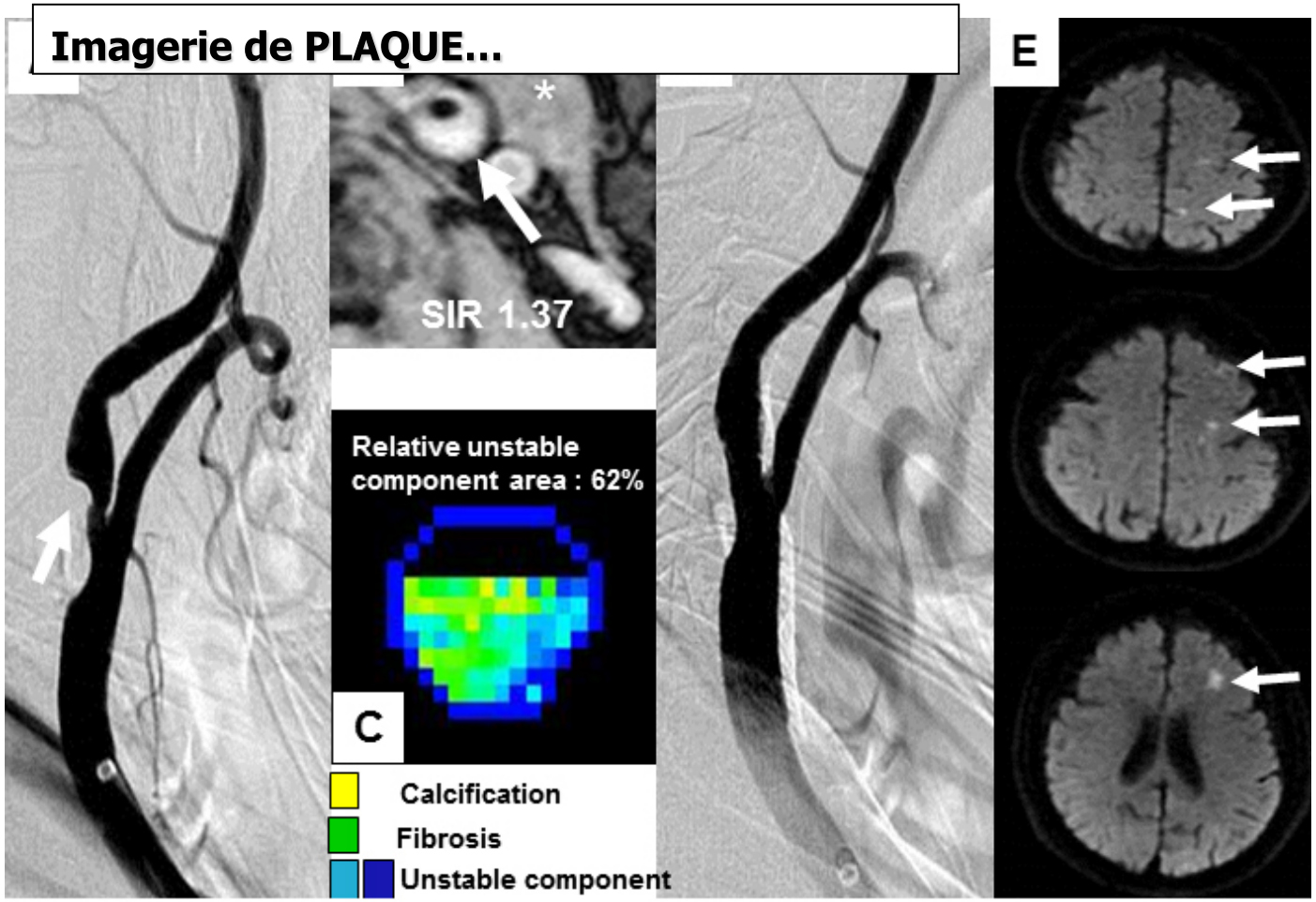


Figure 3. A through E, Nonstenotic hemorrhagic, thrombotic type VI atherosclerotic plaque, and acute middle cerebral artery territory hemorrhagic stroke. A 77-year-old woman with hypertension, untreated hyperlipidemia, and a current cigarette smoking habit presented with left-sided weakness and mental status changes and was imaged 8 hours from onset. A and B, T1- and T2-weighted axial blood-suppressed MR images demonstrate an abnormal eccentrically thickened right common carotid artery wall as indicated ranging between hollow arrowheads. Radial signal inhomogeneity in this region suggests type VI atherosclerotic plaque. C is axially reformatted 3D MRA data. D is a maximum intensity projection of those data simulating a projectional arteriogram demonstrating no significant luminal stenosis. A reference line indicating the level of A, B, and C is demonstrated. The region of greatest plaque volume as identified on A and B and demarcated between hollow arrowheads on A, B, and C shows heterogeneous intrinsic signal intensity compatible with intramural hemorrhage with a geographically associated focal region of endoluminal irregular contour on C indicating overlying thrombosis in situ and securing the overall classification of type VI. Image E is the clinical cerebral diffusion-weighted image that demonstrates a large acute right hemisphere middle cerebral artery territory hemorrhagic infarction (*).

Imagerie de PLAQUE…



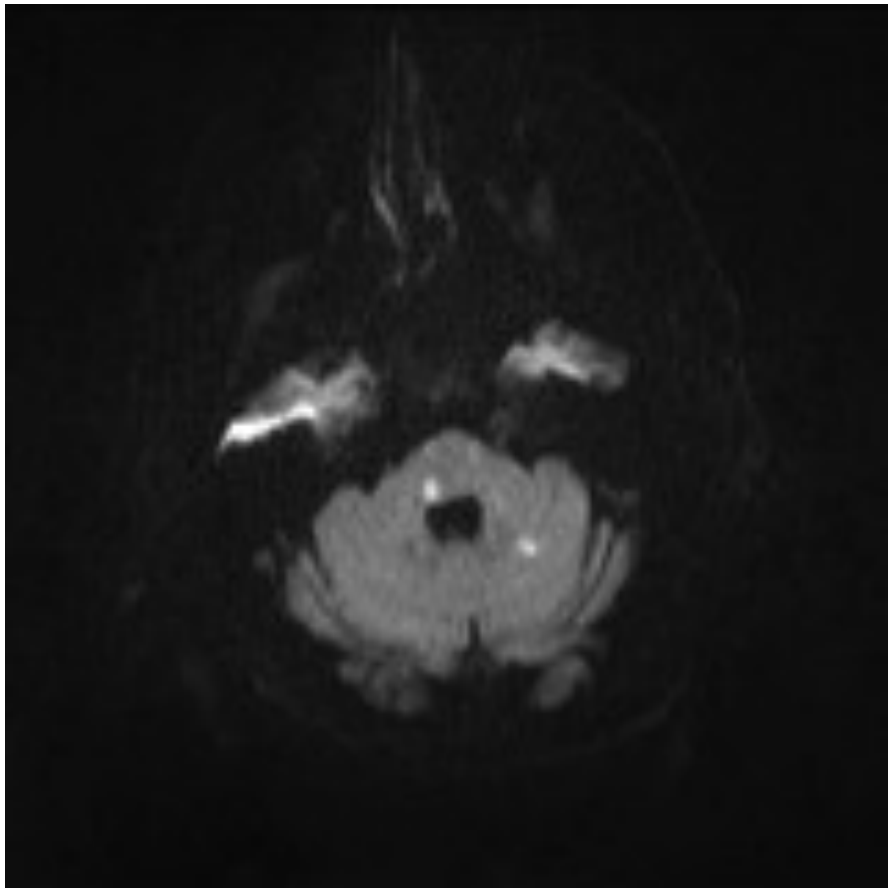
Plaque non sténosante peu être instable
Management: AC ? Double AP ,
statine :oui

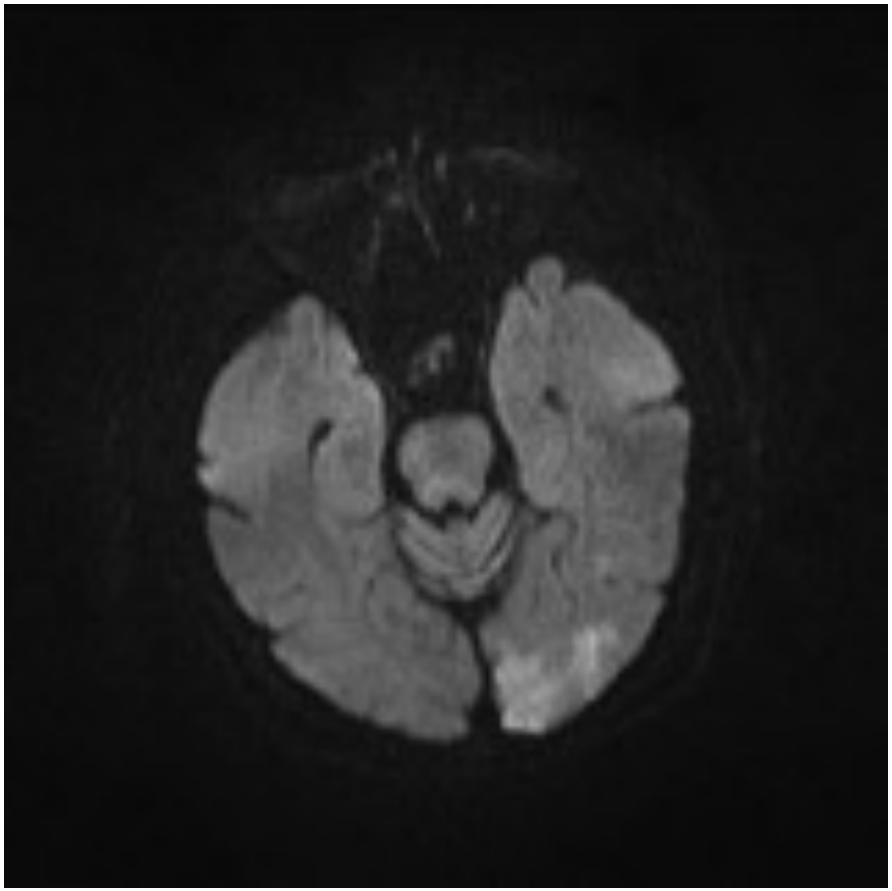
Madame P. Tremblay, 3 novembre 2014

- 69 ans, diabétique , hypertendue, obèse
- Facial périphérique droit
- Paralysie du regard conjugé vers la droite
- Hémianopsie gauche
- Pas de dysphagie pas de troubles moteurs

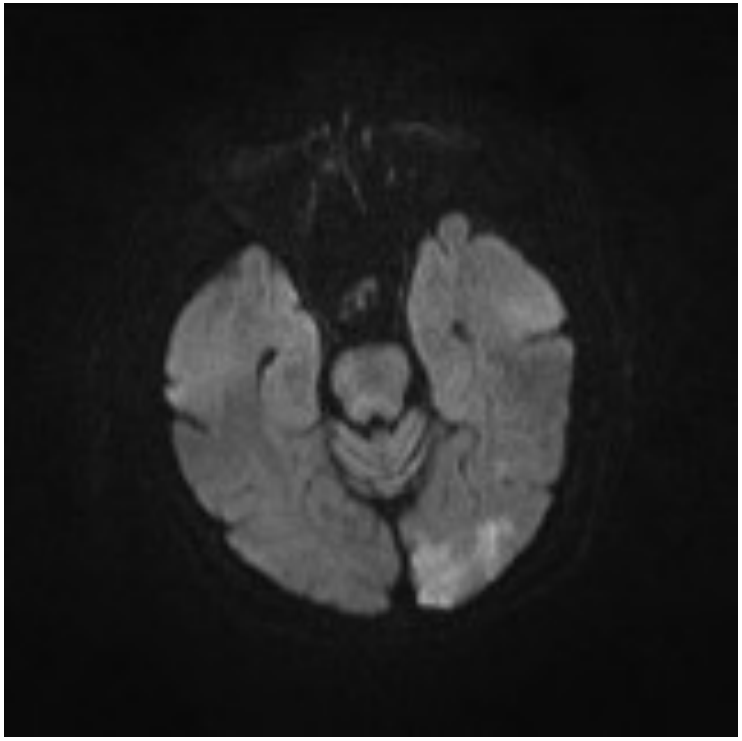
Ou est la Lésion ?

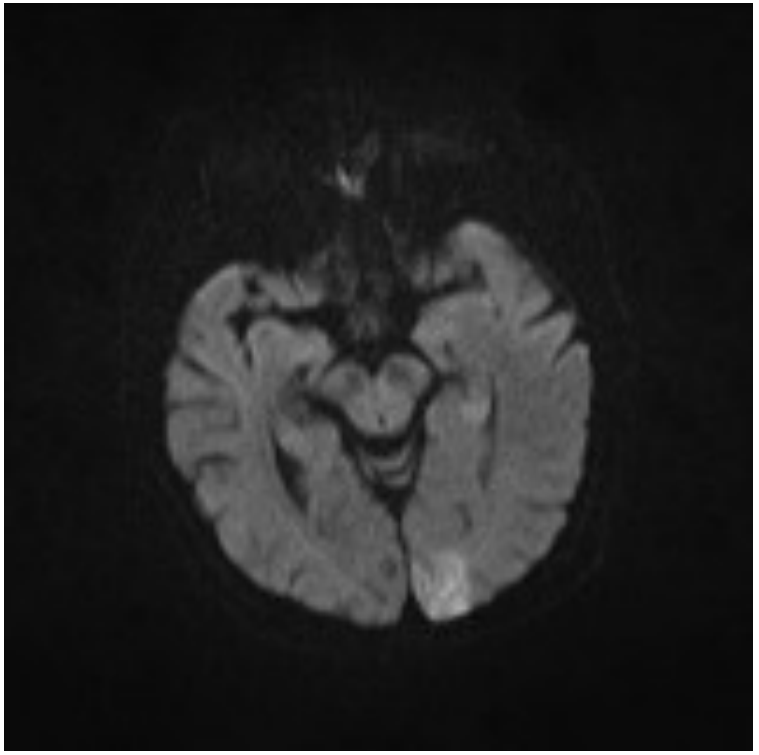
P. Tremblay nov 2014



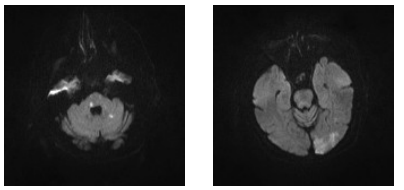


P. Tremblay nov 2014





P. Tremblay nov 2014



AVC ischémiques fosse post

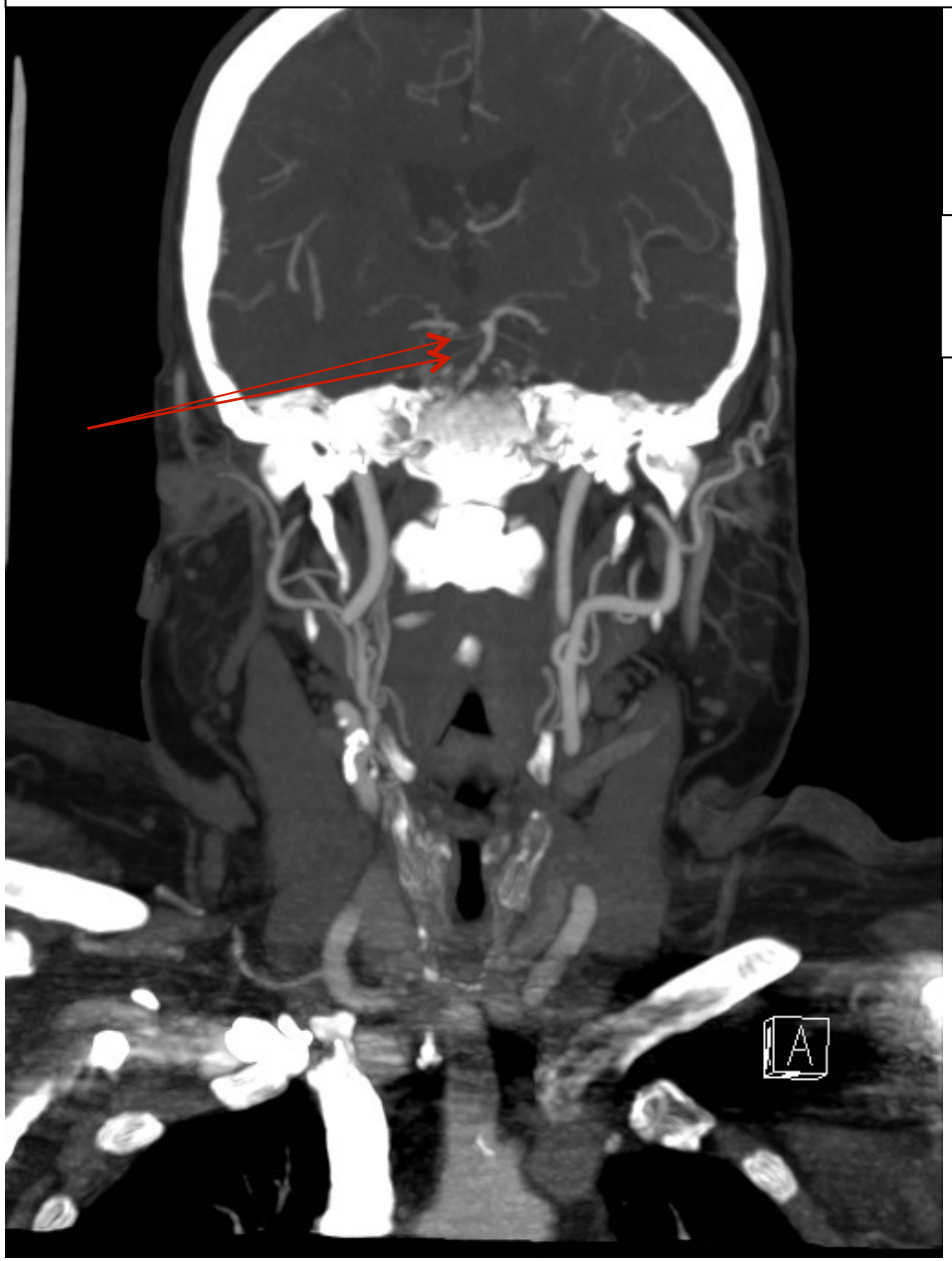
protubérance droite
cervelet gauche
lobe occipital gauche

- Doppler cervical
  - Pas de sténose carotidienne
  - Flux antérograde normal dans les deux vertébrales
- ETT: N , Holter 48 h : normal

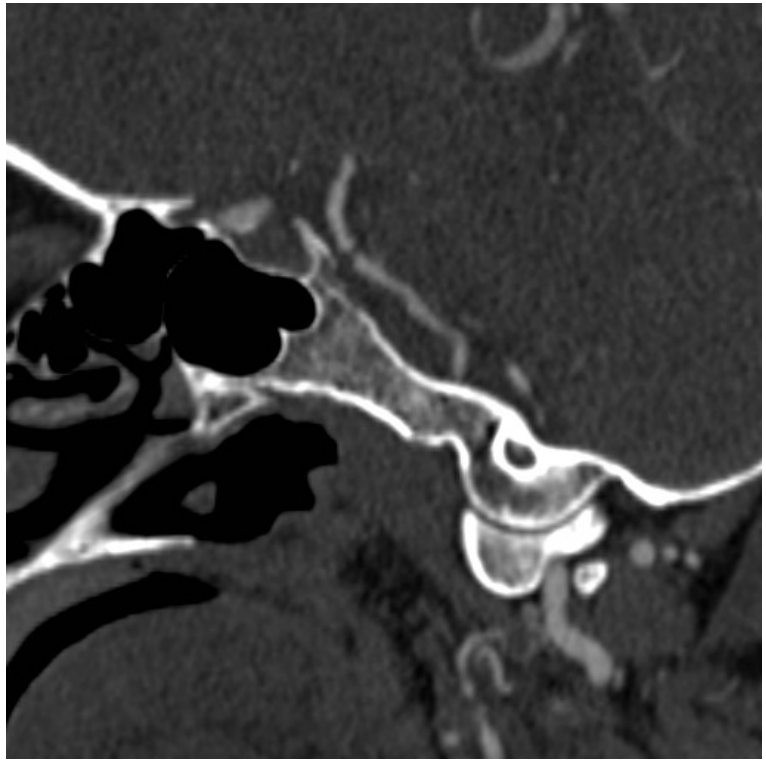
.....CRYPTO ?

- Investiguez-vous d'avantage ? (monito?, angioscan ?)
- Vs AC ?

P. Tremblay nov 2014



Stenose 80% artère basilaire
Occlusion P1



Sous types d'AVC ischémiques

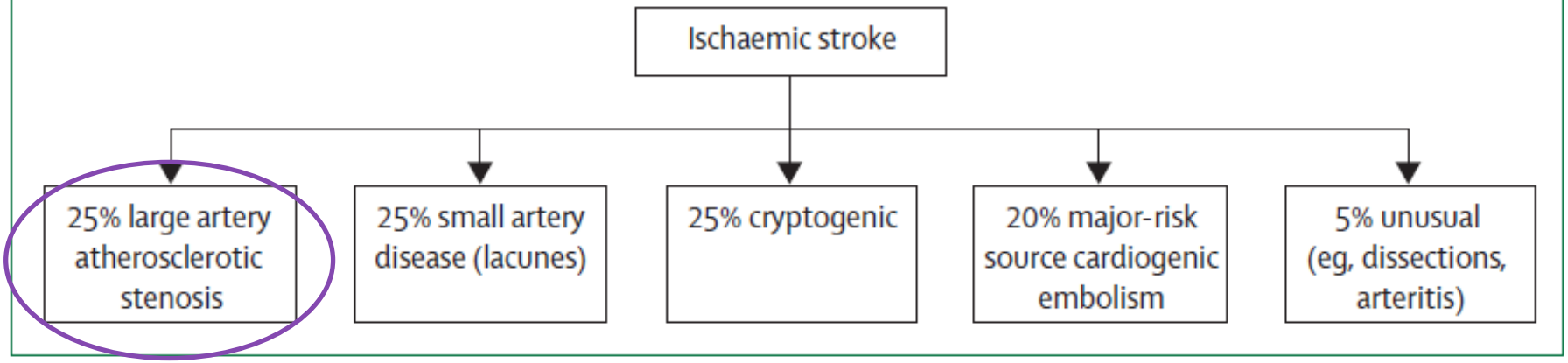


Figure 1: **Distribution of ischaemic stroke subtypes in North American and European studies**
The distribution in Asian and African populations differs from that in North American and European populations.

Robert G Hart, Hans-Christoph Diener, Shelagh B Coutts, J Donald Easton, Christopher B Granger, Martin J O'Donnell, Ralph L Sacco, Stuart J Connolly, for the Cryptogenic Stroke/ESUS International Working Group

Lancet Neurol 2014; 13: 429–38

Conclusions :ASO gros vx vs Crypto

- Peu être sympto si < 50%
  - Imagerie de plaque à l'IRM…
  - DTC: HITS…
- Ne devrait probablement pas être classé crypto
- Préciser imagerie vasculaire au besoin
- Traitement médical « agressif »
  - Double antiplaquettaire, statine
- Considérer revasculariser même si < 50% (CHX ou Stent) si symptomatique malgré TX médical

CAS de Rock le 21 avril 2015
Crypto vs ……..

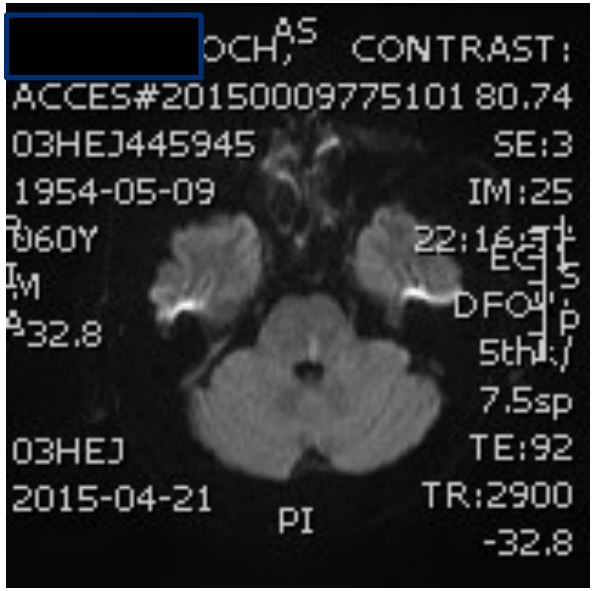
Rock Simard 60 ans ,pas de RX No 445945
21 avril 2015 ambul: diplopie brève mais franche et vertige de 3-4 heures référé de Ste Anne
Examen : Normal TA 157/80, TDM tête normal
Dx: ICT VB prob ASA stat ..clinique ICT demain

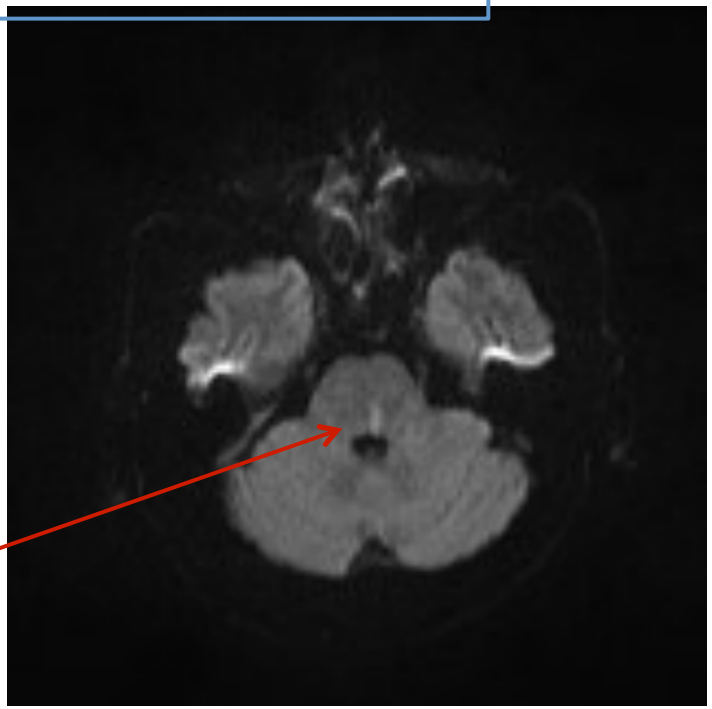
Revient le soir même à l'URGENCE: diplopie, OIN ?, ataxie +++, dysmétrie bilatérale
TDM: normal, **Angiocan tête et cou: N (pas** d'ASO significative, pas de dissection)
Monito 24 : N
Déficits encore présent après 36h
Crypto /ESUS ? Non:« stroke pas détecté à l'imagerie »

On fait IRM ?

Crypto vs

Rock Simard 445945 20 avril ambul: diplopie brève et vertige de 3-4 heures
TDM tête normal
Revient le soir même: diplopie OIN ataxie dysmétrie bilat
TDM normal, Angiocan tête et cou: N(pas de dissection)
ECG ; pas de FA Monito : N
Déficits encore présent après 36h
Crypto /ESUS ?
On fait IRM ?





Lacunes

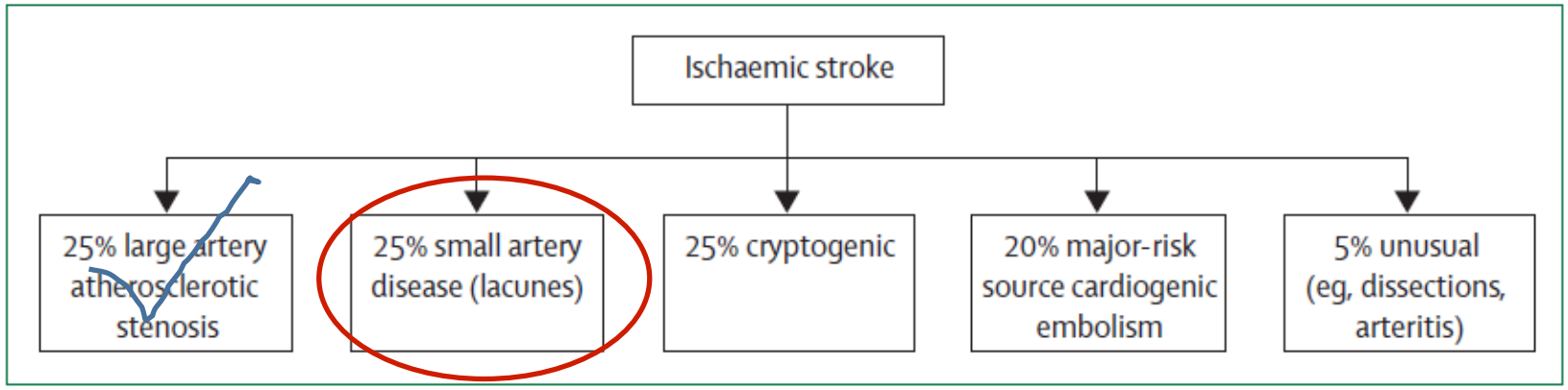
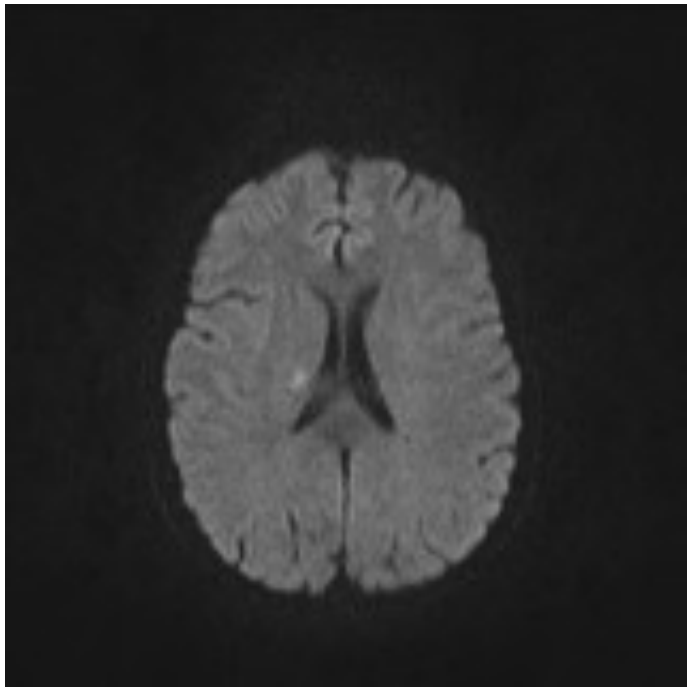


Figure 1: **Distribution of ischaemic stroke subtypes in North American and European studies**
The distribution in Asian and African populations differs from that in North American and European populations.



Très fréq
non vue
à la TDM

Lacunes

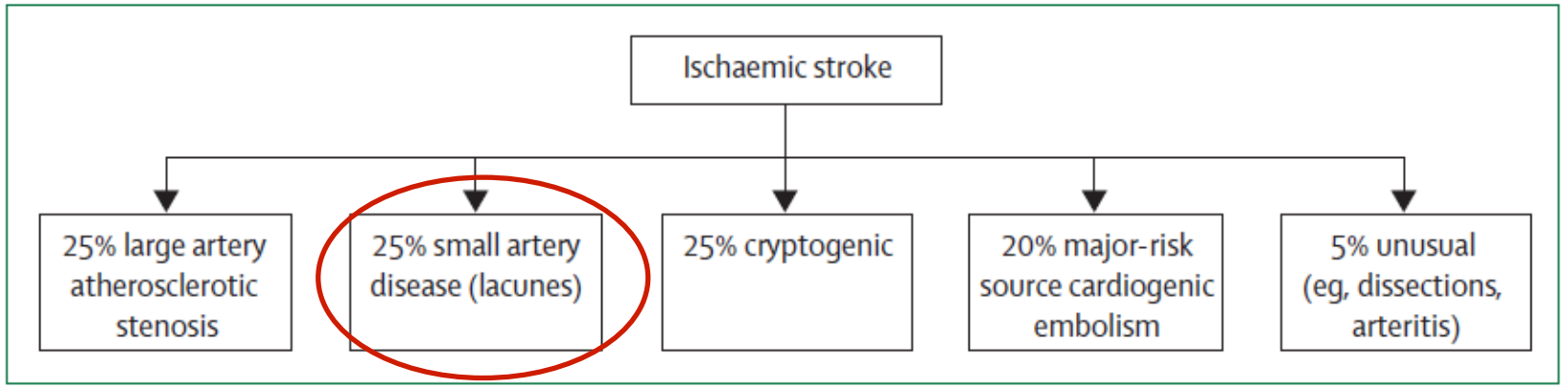


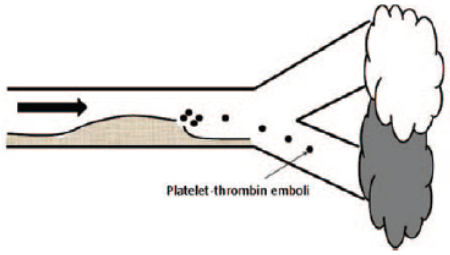
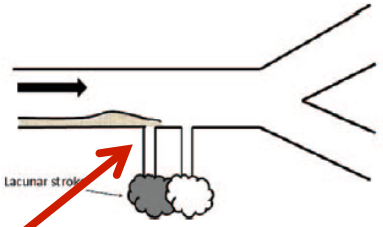
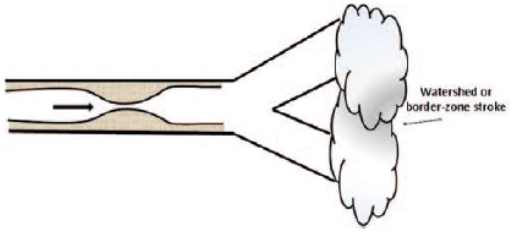
Figure 1: **Distribution of ischaemic stroke subtypes in North American and European studies**
The distribution in Asian and African populations differs from that in North American and European populations.

- Définition surtout radiologique
- Existe clinique « classique »,
- patients alertes svt HTA ou DM
- Lésion ischémique sous corticale dans le territoire d'une artériole perforante (lipohyalinose..)
  - Aigue à la diffusion: < 20mm
  - Chronique; < 15mm

**Cependant….peut être due à ASO ou embole

Lacunes; *branch occlusive disease*

Table 1. Use of HRMRI to Determine Mechanism of Ischemia in ICAD

Mechanism of Ischemia	HRMRI Identification of Mechanism	Impact on Stroke Care
Plaque rupture with local occlusion or artery-to-artery embolization 	-Identification of characteristics consistent with plaque rupture (eg, contrast enhancement of plaque or intraplaque hemorrhage)	-Consider more aggressive antiplatelet use to prevent clot propagation and statins to stabilize plaque
Plaque overgrowth of perforator artery ostia 	-Identification of plaque location within arteries, whether or not conventional imaging identifies stenosis	-Determine that a lacunar stroke is due to ICAD and that a cryptogenic stroke is due to ICAD
Hypoperfusion through stenotic artery 	-Identification of relative lumen size by direct measurement of vessel area compared to lumen area (ie, account for external remodeling)	-More accurately determine severity of stenosis and components of plaque that may result in selection of alternative treatments (eg, angioplasty)

HRMRI indicates high-resolution magnetic resonance imaging; ICAD, intracranial atherosclerotic disease.

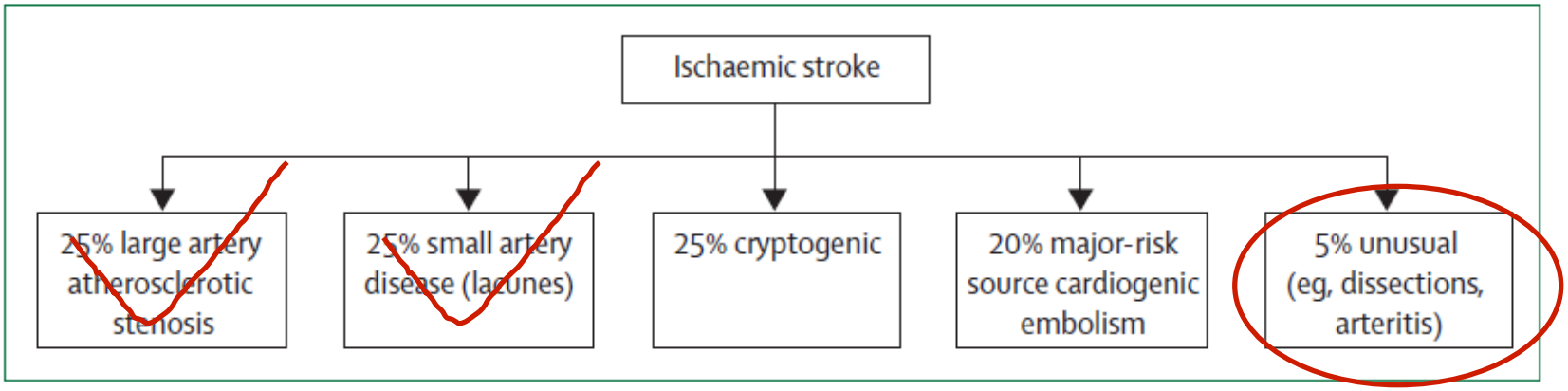


Figure 1: **Distribution of ischaemic stroke subtypes in North American and European studies**
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Annie 30 ans

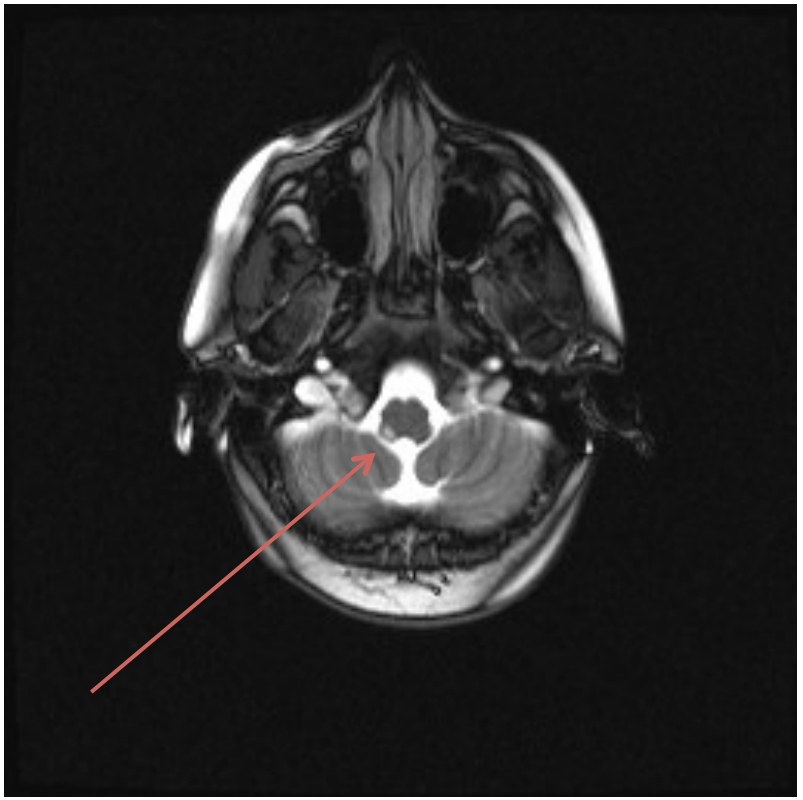
- Apparition aigue d'ataxie vertiges , diplopie dysphagie il y 3 jours …en voyage
- Chiro la veille des S/S avec manipulation cervivale
- IRM: AVC bulbaire lat. post
- Investig étiol: négative , angio CT du cou fait 6 jours post événement

*On fait une monito prolongé ?

Cryto/ESUS ?

Lacune ??

- IRM



Guidelines : pas utile

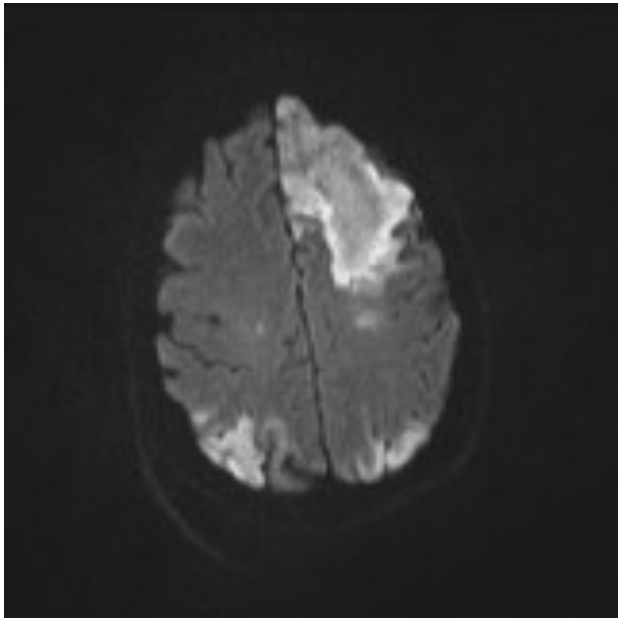
GBS: utile

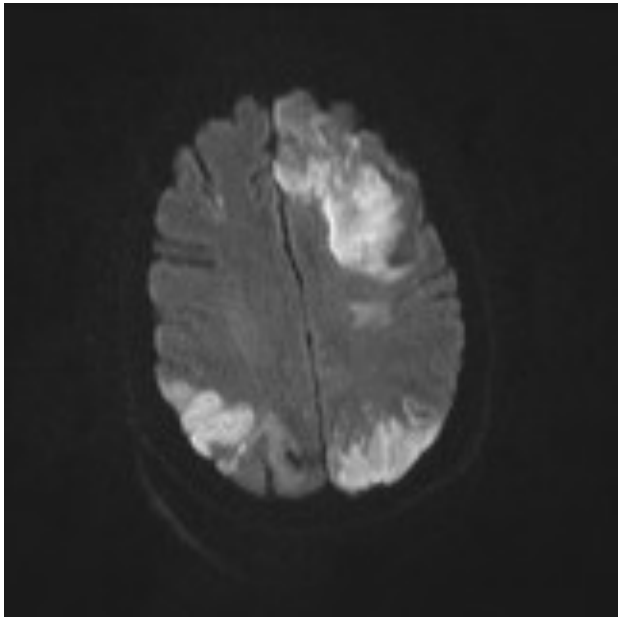
Les « Pitfalls »

- La dissection manquée car imagerie du cou faite trop tard ou qualité sous optimale
- Le thrombus mobile qui a « disparu « au moment du test diagnostique
- Les risques transitoires causant potentiellement états hypercoagulables: infections, stress , trauma
- Les néoplasies connues ou leurs traitements
- Les néoplasies occultes

Sarah H 78 ans

- 4 AVC en un mois
- Territoires différents
- Investigation étiologique : négative
- Source cardio-embol et FA cherchée ++++: rien



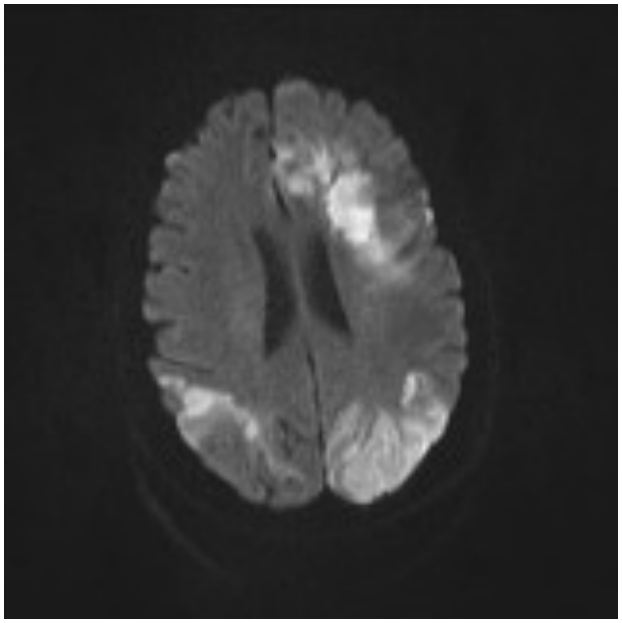


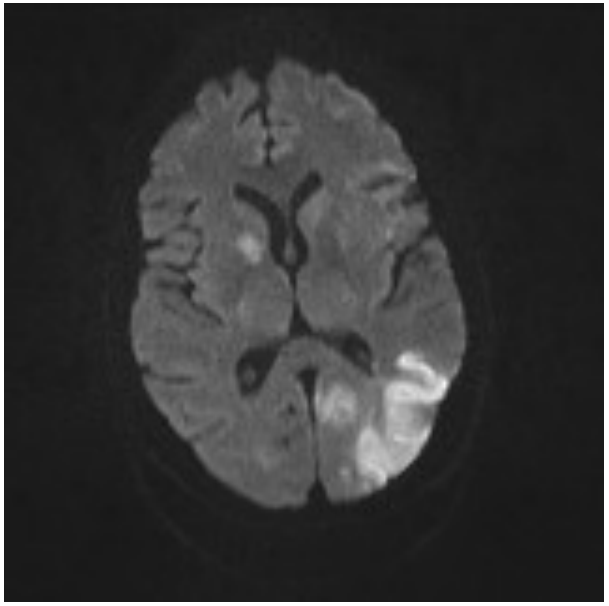
Sarah H 78 ans

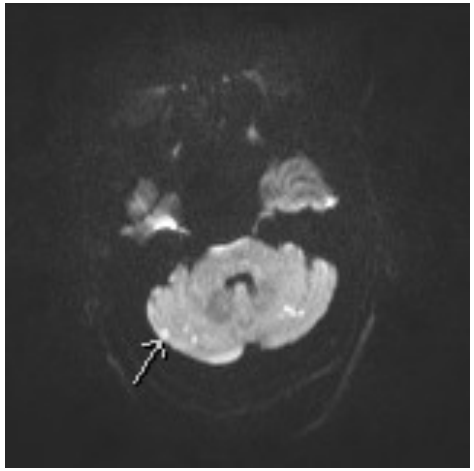
Son dernier IRM

TDM TAP: suspicion de néo de la vessie

D-Dimères







Stroke and Cancer

The Importance of Cancer-Associated Hypercoagulation as a Possible Stroke Etiology

Christopher J. Schwarzbach, MD; Anke Schaefer, PhD; Anne Ebert, PhD; Valentin Held, MD; Manuel Bolognese, MD; Micha Kablau, MD; Michael G. Hennerici, MD; Marc Fatar, MD

Background and Purpose—The importance of cancer-associated hypercoagulability as a possible stroke etiology in patients with cancer has received relatively little attention to date. A recent study has suggested that cancer-associated hypercoagulation may be of special importance in the absence of conventional stroke mechanisms.

Methods—We identified patients with ischemic stroke sequentially admitted to our stroke center with the additional diagnosis of active and malignant cancer from 2002 to 2011. By using our prospectively collected stroke, MRI, and laboratory data banks, the etiology and risk factors of stroke, types of cancer, deep vein thrombosis/pulmonary embolism, D-dimer levels, and diffusion-weighted imaging lesion patterns were compared to an age- and sex-matched control group. Patients with cancer with a conventional stroke etiology and patients with an unidentified and/or cancer-associated stroke etiology were analyzed separately.

Results—One hundred forty patients with cancer and 140 control subjects were included. Unidentified stroke ($P<0.001$) and infarction in multiple vascular territories ($P<0.001$) were significantly more frequent and D-dimer levels significantly higher ($P<0.05$) in patients with cancer. Vice versa, risk factors such as hypertension ($P<0.05$) and hyperlipidemia ($P<0.01$) were more prevalent in control subjects. Deep vein thrombosis and pulmonary embolism were more frequent ($P<0.01$) and D-dimer levels higher ($P<0.01$) in the patients with unidentified and/or cancer-associated stroke etiology compared to the patients with cancer with a conventional stroke etiology. Lung and pancreatic cancer were significantly overrepresented and D-dimer levels higher in these patients compared with other patients with cancer ($P<0.01$).

Conclusions—Our data confirm the concept of cancer-associated hypercoagulation as a widely underestimated important stroke risk factor in patients with cancer, especially in those with severely elevated D-dimer levels and in the absence of conventional risk factors. **(*Stroke*. 2012;43:3029-3034.)**

Causes incertaines..mineures..management pas clair …….ESUS

Panel 1: Causes of embolic strokes of undetermined source

Minor-risk potential cardioembolic sources*

Mitral valve

- Myxomatous valvulopathy with prolapse
- Mitral annular calcification

Aortic valve

- Aortic valve stenosis
- Calcific aortic valve

Non-atrial fibrillation atrial dysrhythmias and stasis

- Atrial asystole and sick-sinus syndrome
- Atrial high-rate episodes
- Atrial appendage stasis with reduced flow velocities or spontaneous echodensities

Atrial structural abnormalities

- Atrial septal aneurysm
- Chiari network

Left ventricle

- Moderate systolic or diastolic dysfunction (global or regional)
- Ventricular non-compaction
- Endomyocardial fibrosis

Covert paroxysmal atrial fibrillation

Cancer-associated

- Covert non-bacterial thrombotic endocarditis
- Tumour emboli from occult cancer

Arteriogenic emboli

- Aortic arch atherosclerotic plaques
- Cerebral artery non-stenotic plaques with ulceration

Paradoxical embolism

- Patent foramen ovale
- Atrial septal defect
- Pulmonary arteriovenous fistula

*Minor-risk sources are more often incidentally present than is the stroke cause when identified in an individual stroke patient, are associated with a low or uncertain rate of initial stroke, and consequently cause-effect relation and management implications are usually unclear.

Lancet Neurol 2014; 13: 429–38

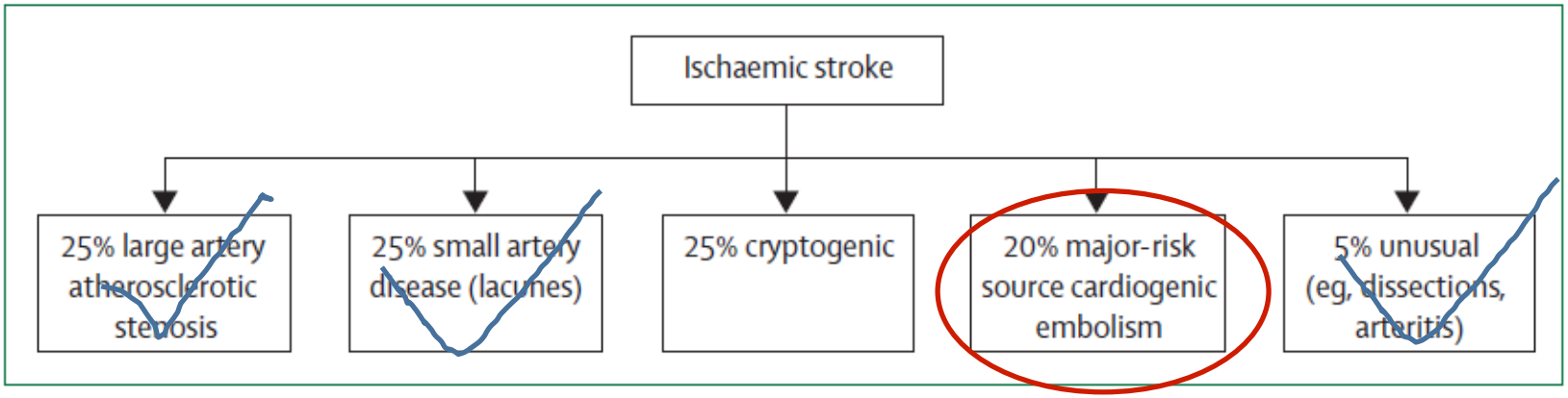


Figure 1: **Distribution of ischaemic stroke subtypes in North American and European studies**
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Panel 2: **Criteria for diagnosis of embolic stroke of undetermined source***

- Stroke detected by CT or MRI that is not lacunar†
- Absence of extracranial or intracranial atherosclerosis causing ≥50% luminal stenosis in arteries supplying the area of ischaemia
- No major-risk cardioembolic source of embolism‡
- No other specific cause of stroke identified (eg, arteritis, dissection, migraine/vasospasm, drug misuse)

*Requires minimum diagnostic assessment (panel 3). †Lacunar defined as a subcortical infarct smaller than or equal to 1·5 cm (≤2·0 cm on MRI diffusion images) in largest dimension, including on MRI diffusion-weighted images, and in the distribution of the small, penetrating cerebral arteries; visualisation by CT usually needs delayed imaging greater than 24–48 h after stroke onset. ‡Permanent or paroxysmal atrial fibrillation, sustained atrial flutter, intracardiac thrombus, prosthetic cardiac valve, atrial myxoma or other cardiac tumours, mitral stenosis, recent (<4 weeks) myocardial infarction, left ventricular ejection fraction less than 30%, valvular vegetations, or infective endocarditis.

- FA ou FAP
- Thrombus intracardiac
- Valve prosthétique
- Myxome de l'oreillette
- Sténose mitrale
- IM récent <4 semaines
- FE<30%
- Végétations valvulaires
- Endocardite

Questions

- Quand peut-on déclarer qu'un AVC est cryptogénique ?
- Est-ce que la plupart des AVC dit crypto seraient en fait de la FAP non diagnostiquée?
- Chez qui doit-on faire un monitoring cardiaque prolongé ?
  - Dans quels délais minimum?
  - Pour combien de temps, quel gadget ?
  - Quelle durée et délais de FA vont justifier une Anticoagulothérapie ?
  - Trouvaille de FA = cause de l'AVC ?

Crypto: plus on cherche plus on trouve

..Trouvaille n'égale pas certitude étiologique ni modification thérapeutique sauf FA

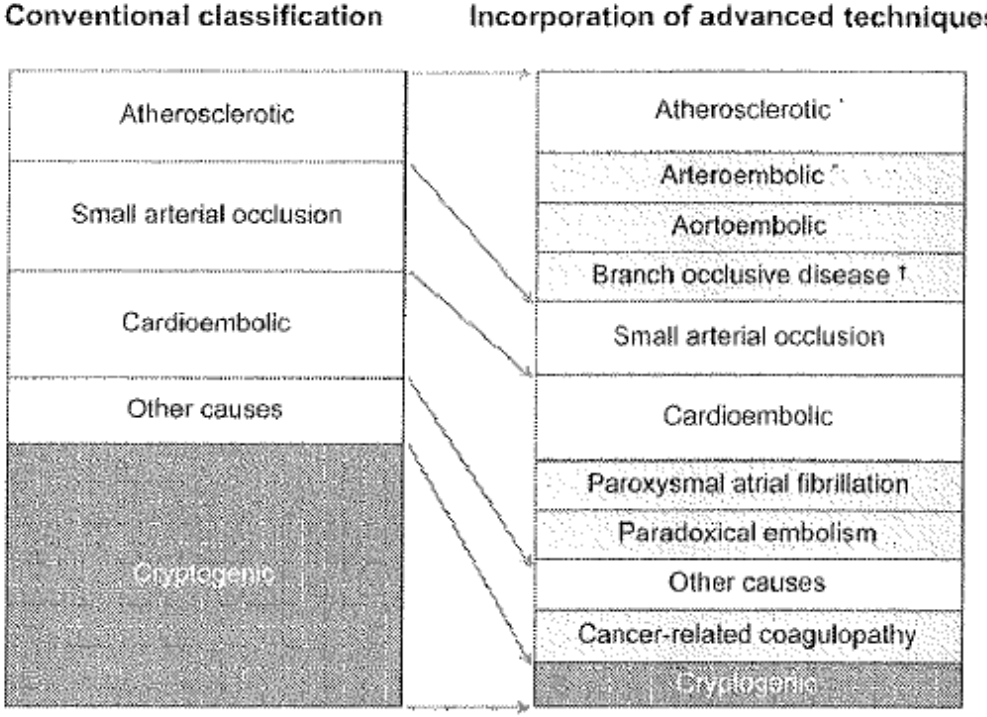
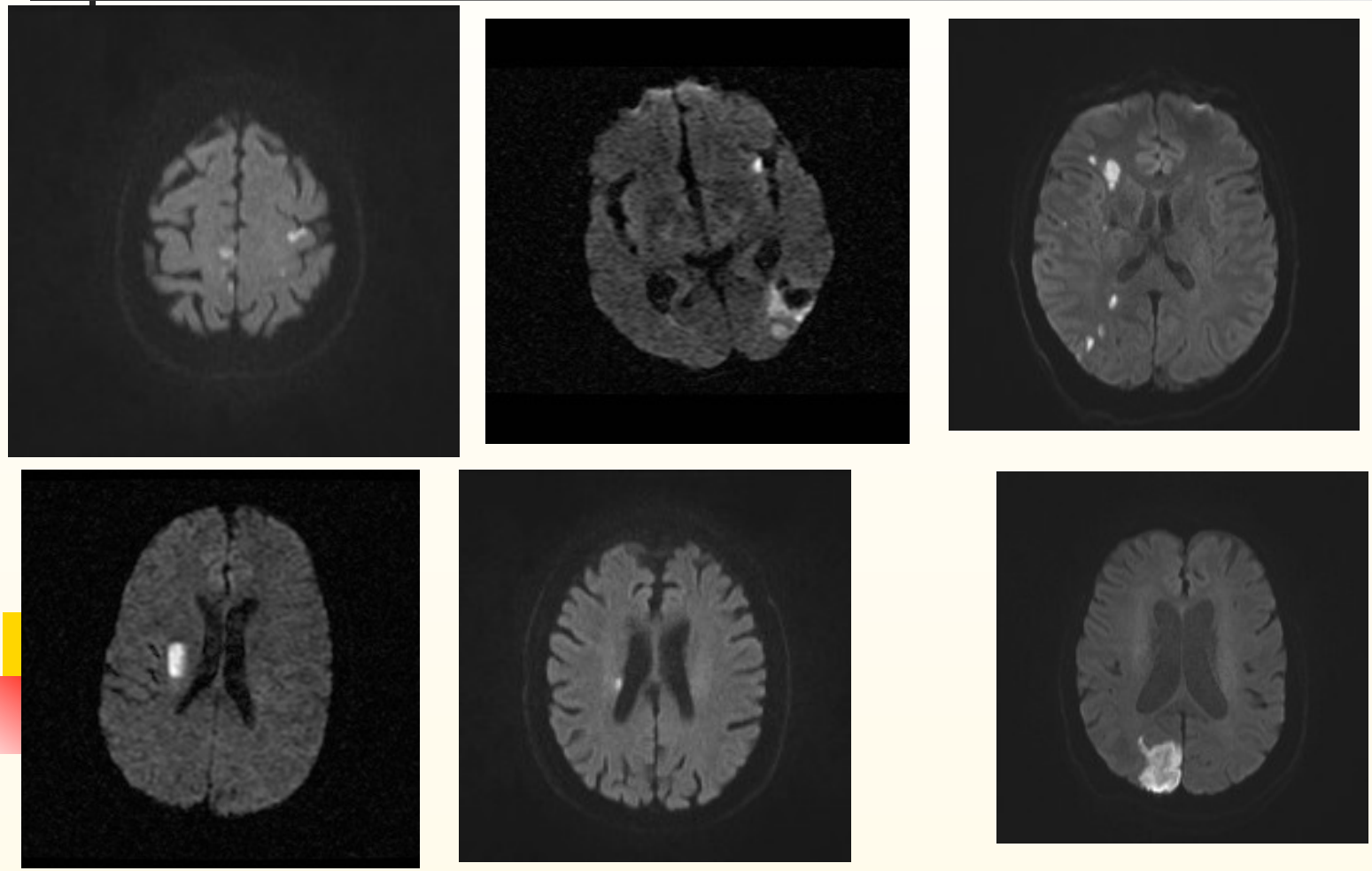


Figure 6. Changes in stroke subtypes with application of advanced diagnostic techniques. *Either intracranial or extracranial vessels. †Intracranial vessels.

(*Stroke*. 2014;45:1186-1194.)

L'Étiquette n'a pas tant d'importance

AVC CRYPTO vs découverte de FAP



CRYSTAL AF

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Cryptogenic Stroke and Underlying Atrial Fibrillation

Tommaso Sanna, M.D., Hans-Christoph Diener, M.D., Ph.D., Rod S. Passman, M.D., M.S.C.E., Vincenzo Di Lazzaro, M.D., Richard A. Bernstein, M.D., Ph.D., Carlos A. Morillo, M.D., Marilyn Mollman Rymer, M.D., Vincent Thijs, M.D., Ph.D., Tyson Rogers, M.S., Frank Beckers, Ph.D., Kate Lindborg, Ph.D., and Johannes Brachmann, M.D., for the CRYSTAL AF Investigators*

EMBRACE

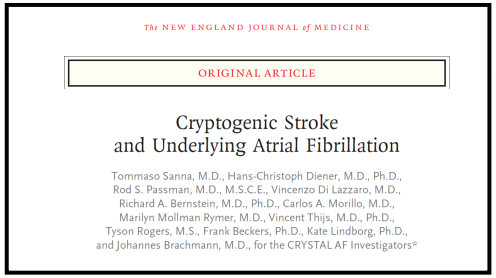
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JUNE 26, 2014 VOL. 370 NO. 26

Atrial Fibrillation in Patients with Cryptogenic Stroke

David J. Gladstone, M.D., Ph.D., Melanie Spring, M.D., Paul Dorian, M.D., Val Panzov, M.D., Kevin E. Thorpe, M.Math., Judith Hall, M.Sc., Haris Vaid, B.Sc., Martin O'Donnell, M.B., Ph.D., Andreas Laupacis, M.D., Robert Côté, M.D., Mukul Sharma, M.D., John A. Blakely, M.D., Ashfaq Shuaib, M.D., Vladimir Hachinski, M.D., D.Sc., Shelagh B. Coutts, M.B., Ch.B., M.D., Demetrios J. Sahlas, M.D., Phil Teal, M.D., Samuel Yip, M.D., J. David Spence, M.D., Brian Buck, M.D., Steve Verreault, M.D., Leanne K. Casaubon, M.D., Andrew Penn, M.D., Daniel Selchen, M.D., Albert Jin, M.D., David Howse, M.D., Manu Mehdiratta, M.D., Karl Boyle, M.B., B.Ch., Richard Aviv, M.B., Ch.B., Moira K. Kapral, M.D., and Muhammad Mamdani, Pharm.D., M.P.H., for the EMBRACE Investigators and Coordinators*

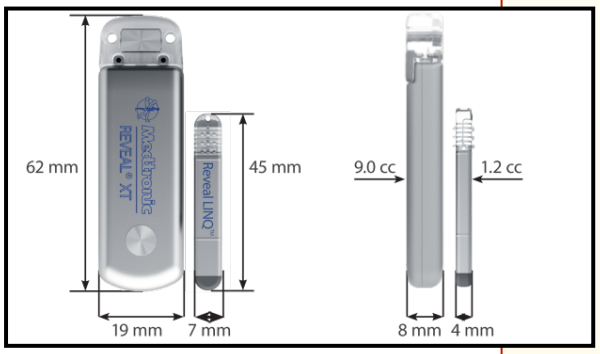
Background



- **Selon les « guidelines » La documentation d'une FA est requise pour initier une anticoagulothérapie**
- La FA est svt non détectée car paroxystique et asymtomatique
- Methodes de détection: Monitoring intra hospitalier, ECG sériés, Holter 24h-96h, Monitoring long terme: externe ou ICM(Insertable Cardiac Monitoring)…
- Etudes diffèrent en terme de critères, durée, endpoint ect donc pas de recommandations cliniques fermes
- Guidelines suggèrent monitoring 24h en réalisant que la durée optimale est incertaine
- Dans AVC crypto : durée et la méthode de monitoning est à la discrétion du MD

Objectifs de CRYSTAL AF

- Étude prospective randomisée, ouverte, multicentrique, post marketing
- Déterminer si monitoring cardiaque long terme avec ICM (REVEAL XT, Medtronic) est supérieur au monitoring standard pour détecter une FA chez les patients avec AVC cryptogénique
- End point primaire: Détection de FA* à 6 mois
- Secondaire:
  - Détection de FA à 12 mois
  - Durée de la FA
  - Corrélation avec symptômes d'AVC / ICT
  - Introduction d'AC



* Épisode de RC irrégulier sans ondes P, de > 30 sec

Principales inclusions / exclusions

Inclusions

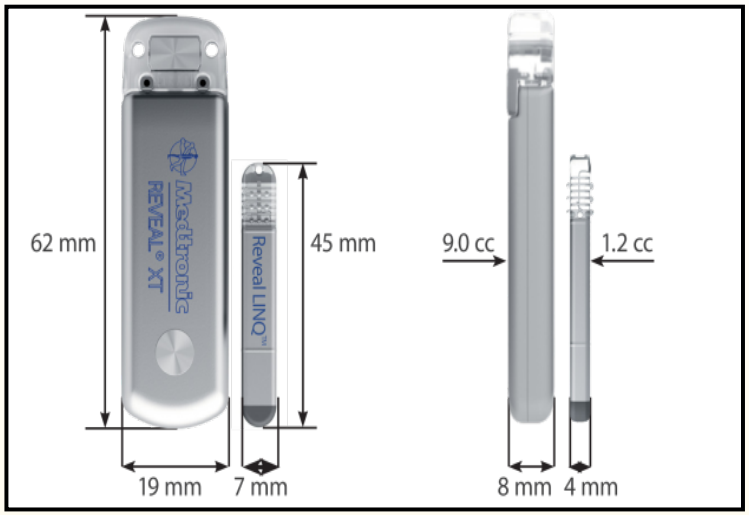
- 40 ans ou plus
- AVC/ICT crypto confirmé à l'imagerie (IRM ou CT)
- < 90 jours, sans mécanisme déterminé;
  - ECG, monito ou Holter 24 h
  - ETO **
  - Imagerie vaisseaux tête et cou
  - Recherche état hypercoagulable si <55ans

Exclusions

- Hx de FA
- Indic ferme ou Contre-indication à l'AC
- Indication de pacemaker ou pace-défib.

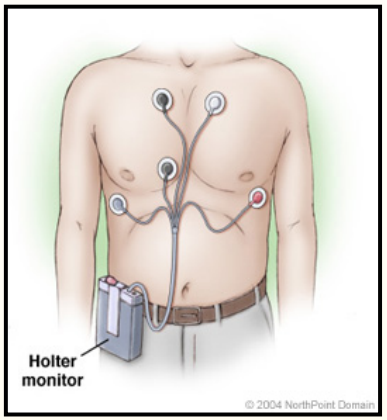
Comparaison des méthodes de monitoring

Monitoring continu REVEAL XT (IRM compatible)



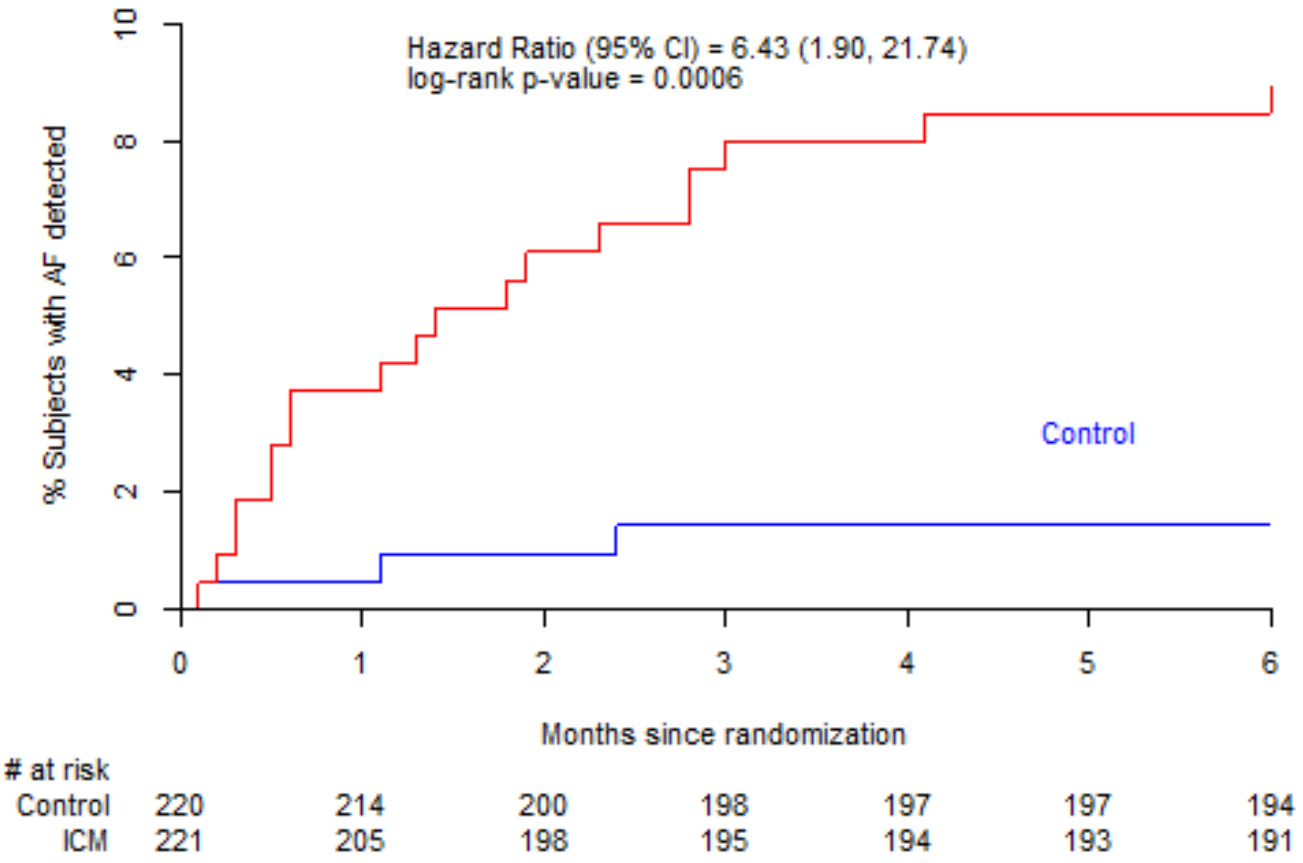
- Données transmises à distance via le Medtronic Carelink Network

Monitoring standard



- Les deux:
- Visites à 1 mois et au 6 mois par la suite
- Episodes de FA idendifiées: adjudiqués par comité inépendant

Primary Endpoint: Detection of AF at 6 months
ICM finds 6x more patients with AF



Conclusions:

- Le Moniteur Cardiaque Implanté est supérieur au monitoring standard pour la détection de la FA chez patients avec AVC cryptogénique
  - 6 mo : 8.9% (HR: 6.43) , « NNT »* = 14
  - 12 mo: 12.4% (HR:7.2), « NNT »* = 10
  - 36 mo: 30% (HR 8.7), « NNT »* = 4
- 92.3 % des patients avec FA dans CRYSTAL AF ont eu au moins une journée de > 6 minutes de FA
- Détection de FA a changé le management vers l'anticoagulothérapie dans 97%

* Number Needed to be Implanted to detect a first episode of AF

Discussion / questions:

- Dans CRYSTAL-AF Taux de détection plus bas de FA (8-12%) que dans études comparables (ad 25%)
  - Investigation plus rigoureuse pré-rando
  - Adjudication indépendante des épisodes de FA
  - Caractérisiques de base différentes: plus jeunes , moins d'HTA
- La FA découverte post AVC est –elle responsable de l'événement initial ??

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David J. Gladstone, M.D., Ph.D., Melanie Spring, M.D., Paul Dorian, M.D., Val Panzov, M.D., Kevin E. Thorpe, M.Math., Judith Hall, M.Sc., Haris Vaid, B.Sc., Martin O'Donnell, M.B., Ph.D., Andreas Laupacis, M.D., Robert Côté, M.D., Mukul Sharma, M.D., John A. Blakely, M.D., Ashfaq Shuaib, M.D., Vladimir Hachinski, M.D., D.Sc., Shelagh B. Coutts, M.B., Ch.B., M.D., Demetrios J. Sahlas, M.D., Phil Teal, M.D., Samuel Yip, M.D., J. David Spence, M.D., Brian Buck, M.D., Steve Verreault, M.D., Leanne K. Casaubon, M.D., Andrew Penn, M.D., Daniel Selchen, M.D., Albert Jin, M.D., David Howse, M.D., Manu Mehdiratta, M.D., Karl Boyle, M.B., B.Ch., Richard Aviv, M.B., Ch.B., Moira K. Kapral, M.D., and Muhammad Mamdani, Pharm.D., M.P.H., for the EMBRACE Investigators and Coordinators*

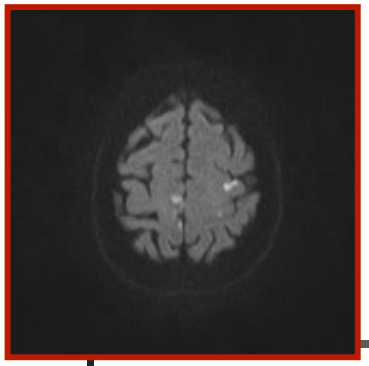
AF Detection	Detection Rate, %
30-day monitor	16.1
Control – 24-h monitor	3.2

Gladstone DJ, et al. *N Engl J Med*. 2014;370:2467-2477.[42]

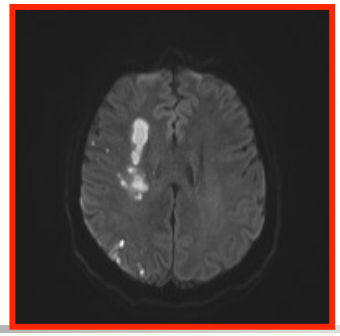
Table 1 AF detected by outpatient cardiac monitoring in patients with cryptogenic stroke

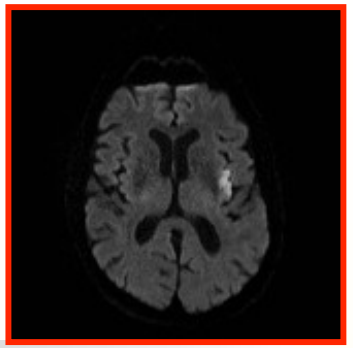
Study (year)	No. of patients	AF definition	Monitoring type and duration	AF detection yield	Notes
Tayal et al[18] (2008)	56	Any duration	MCOT: 21 days	Overall: 23% AF <30 seconds: 18% AF >30 seconds: 5%	Median time to AF detection: 7 days (2-19)
Elijovich et al[19] (2009)	20	Not defined	Event monitor: 30 days	20%	
Gaillard et al[20] (2010)	98	32 seconds	Transtelephonic monitoring: 30 days	9%	
Bhatt et al[21] (2011)	62	30 seconds	MCOT: 28 days	Overall: 24% AF ≥ 5 minutes: 9%	93% of AF was detected within first 21 days Median duration of monitoring: 21 days (range 2–28 days)
Flint et al[22] (2012)	236	5 seconds	MCOT: 30 days	Overall: 11% AF ≤30 seconds: 4% AF >30 seconds: 7%	
Kamel et al[23] (2013)	20	30 seconds	MCOT: 21 days	0%	Only 64% completed 21 days
Miller et al[24] (2013)	156	30 seconds	MCOT: 30 days	Overall: 17% AF <30 seconds: 12% AF ≥30 seconds: 5%	Only 62% completed 21 days
EMBRACE; Gladstone et al[12] (2014)	572	30 seconds	Event monitor: 30 days vs 24-hour Holter	16.1% (45/280) event monitor 3.2% (9/277) 24-hour Holter	
		2.5 minutes		9.9% (28/284) event monitor 2.5% (7/277) 24-hour Holter	

AF = atrial fibrillation; MCOT = mobile cardiac outpatient telemetry.



Est-ce de la FAP ??





- Infarctus territoires multiples ou cortical
- Hx de palpitations…
- Dilatation oreillette gauche
- ESV multiples
- Imagerie vasculaire normale
- Age avancé

More likely

- Infarctus une seul territoire ou lacune
- Pas d'histoire de palpitations…
- Pas de dilatations de l'oreillette
- Pas/peu de ESV
- ASO à l'imagerie des vaisseaux

Less likely

Questions

- Quand peut-on déclarer qu'un AVC est cryptogénique ?
- Est-ce que la plupart des AVC dit crypto seraient en fait de la FAP non diagnostiquée? non
- Chez qui doit-on faire un monitoring cardiaque prolongé ? Si FA « likely »
  - Dans quels délais minimum? On ne sais pas
  - Pour combien de temps, quel gadget ? On ne sais pas
  - Quelle durée et délais de FA vont justifier une Anticoagulothérapie ? Pas clair
  - Trouvaille de FA = cause de l'AVC ?

Canadian Stroke Best Practice Recommendations: secondary prevention of stroke guidelines, update 2014

Shelagh B. Coutts[1], Theodore H. Wein[2], M. Patrice Lindsay[3]*, Brian Buck[4], Robert Cote[5], Paul Ellis[6], Norine Foley[7], Michael D. Hill[1], Sharon Jaspers[8], Albert Y. Jin[9], Brenda Kwiatkowski[10], Carolyn MacPhail[11], Dana McNamara-Morse[12], Michael S. McMurtry[13], Tania Mysak[14], Andrew Pipe[15], Karen Silver[16], Eric E. Smith[1], Gord Gubitz[17], and on behalf of the Heart, and Stroke Foundation Canada Canadian Stroke Best Practices Advisory Committee

ii. In cases where the ECG or initial cardiac rhythm monitoring (e.g. 24 or 48 h ECG monitoring) does not show atrial fibrillation but a cardioembolic mechanism is suspected, prolonged ECG monitoring is recommended in selected patients for detection of paroxysmal atrial fibrillation (Evidence Level B) (17).

Questions

- Quand peut-on déclarer qu'un AVC est cryptogénique ?
- Est-ce que la plupart des AVC dit crypto seraient en fait de la FAP non diagnostiquée? NON
- Chez qui doit-on faire un monitoring cardiaque prolongé?

- MONITO prolongé :
  - Dans quels délais minimum/ maximiun? On ne sais pas
  - Pour combien de temps, quel gadget ? Incertain
  - Quelle durée (30 sec ? 6 minutes? 30 minutes ?) et délais post AVC de découverte FA (30 jours 180 jours) vont justifier une Anticoagulothérapie ? Pas clair
  - Trouvaille de FA =
    - cause de l'AVC , inflammation, état hypercoagulable, importance de la forme de l'auricule (chicken wing, cauliflower, cactus…)?
    - Conséquence de l'AVC ?
    - Découverte fortuite ?

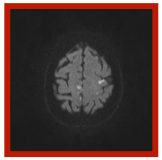
ESSAIS CLINIQUES RANDOMISÉS
ESUS: rando DOAC vs ASA

RE-SPECT ESUS

- DABIGATRAN (150 bid ou 110 bid) vs ASA 100 mg die
- ESUS <3 mois
- >50 ans
- Si <60 ans: HTA ou DM ou IC
- 6,000 patients
- Primary end point: récidive d'AVC

NAVIGATE ESUS

- RIVAROXABAN 15 mg vs ASA 100 mg die
- ESUS <6 mois
- >18 ans
- Si <60 ans: HTA ou DM ou IC
- 7,000 patients
- Primary end point: récidive d'AVC et embolies systémiques



CONCLUSIONS

- **Le pattern de l'ischémie à l'IRM est un bon outil pour nous orienter vers une piste étiologique**
- **Une plaque d'ASO de < 50% peut être la cause de l'AVC (imagerie de plaque)**
- **Soyez conscient des « pitfalls »**
  - **Dissection ratée car imagerie tardive ou sous optimale**
  - **Thrombus mobile disparu**
  - **Etats hypercoagulables transitoires ou néo occulte (D-Dimères)**
  - **Causes mineures dont le rôle étiologique est incertain (ESUS: rando si possible ds étude)**
- **Considérer monito prolongé si FA suspectée: multiples territoires, plusieurs ES, age avancé**
- **A l'heure actuelle pas d'indication d'anticoaguler si pas de FA ou autre source de cardio-embolie démontrée**

FIN