



Paolo Scacciatella SC Cardiologia - Cardiologie Ospedale Regionale - Hôpital Régional U. Parini Aosta - Aoste WE DON'T HAVE ENOUGH EVIDENCE, WE TRUST OUR EXPERIENCE

TURIN

October 24<sup>th</sup>-26<sup>th</sup>

2019

A patient with migraine, positive MR and PFO: what to do?

Let's close the PFO



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Global, regional, and national burden of migraine and tension-type headache, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016

Lancet Neurol 2018; 17: 954-76

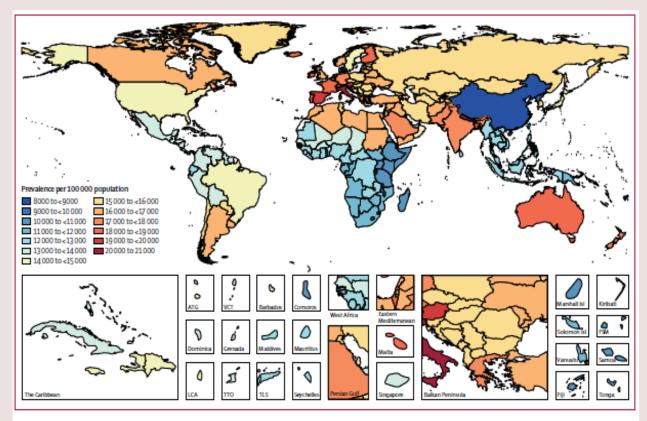


Figure 1: Age-standardised prevalence of migraine per 100 000 population by location for both sexes, 2016



#### MIGRAINE

"...a condition marked by recurring moderate to severe headache with throbbing pain that usually lasts from four hours to three days, typically begins on one side of the head but may spread to both sides, is often accompanied by nausea, vomiting, and sensitivity to light or sound, and is sometimes preceded by an aura and is often followed by fatigue..."



A meta-analysis of case-control studies of the association of migraine and patent foramen ovale

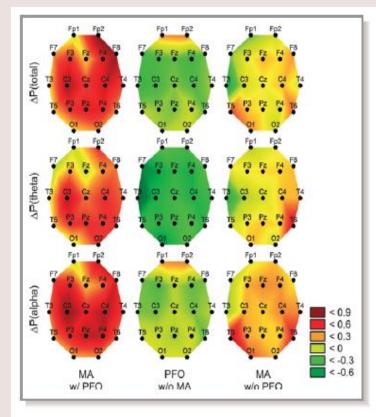
Hisato Takagi (MD, PhD)\*, Takuya Umemoto (MD, PhD), for the ALICE (All-Literature Investigation of Cardiovascular Evidence) Group

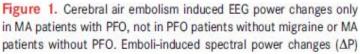
Journal of Cardiology 67 (2016) 493-503

On the basis of the first meta-analysis of 21 case-control studies enrolling >5500 participants, we confirmed that PFO is associated with 3.4-fold migraine-with-aura and 2.5-fold migraine-with/ without-aura prevalence but <u>unassociated with migraine-without-aura prevalence</u>. The association of migraine with (and with/ without) aura and PFO was robust, even pooling not only unadjusted but also adjusted (although small number of) relative risk estimates.



Paradoxical Air Microembolism Induces Cerebral Bioelectrical Abnormalities and Occasionally Headache in Patent Foramen Ovale Patients With Migraine





Changes in cerebral bioelectrical activity (i.e. cortical spreading depressions, CSDs) may be triggered by:

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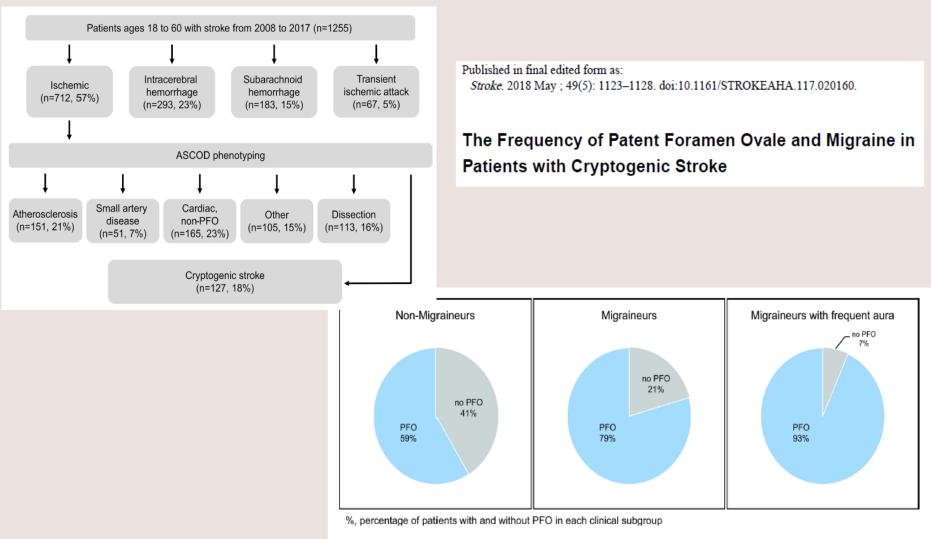
October 24<sup>th</sup>-26<sup>th</sup>

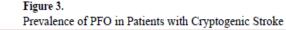
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- paradoxical cerebral thromboemboli
- and/or the direct passage of metabolites into the systemic circulation

resulting in irritation of the trigeminal nerve and brain's vascular network









Epidemiological Physiopatological Clinical TURIN

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PLAUSIBILITY



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Migraine and structural changes in the brain Neurology® 20

A systematic review and meta-analysis

Conclusions and future perspectives. The present review suggests that migraine may be a risk factor for structural changes in the brain. In comparison with nonmigraine controls, migraineurs have more WMAs ILLs and volumetric changes in GM and WM regions. The evidence on relationship to attack frequency and disease duration is equivocal. At present, the clinical and functional significance of these brain lesions is uncertain. Guidelines

Neurology® 2013;81:1260-1268

MRI. Only patients with atypical headache, a recent change in headache pattern, other symptoms (such as seizures), or focal neurologic symptoms or signs are recommended for MRI of the brain.

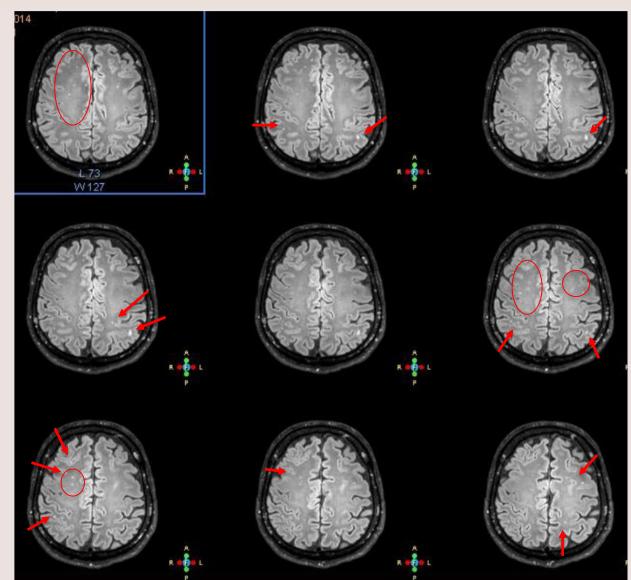
Patients with WMAs can be reassured. Patients with ILLs should be evaluated for stroke risk factors.

## **CLINICAL APPROACH**



*Pt 40 years old Migraine WA No neurol disord Incidental MR* +

...a odds matter ... - SIZE - SITE



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The clinical importance of white matter hyperintensities on brain magnetic resonance imaging: systematic review and meta-analysis

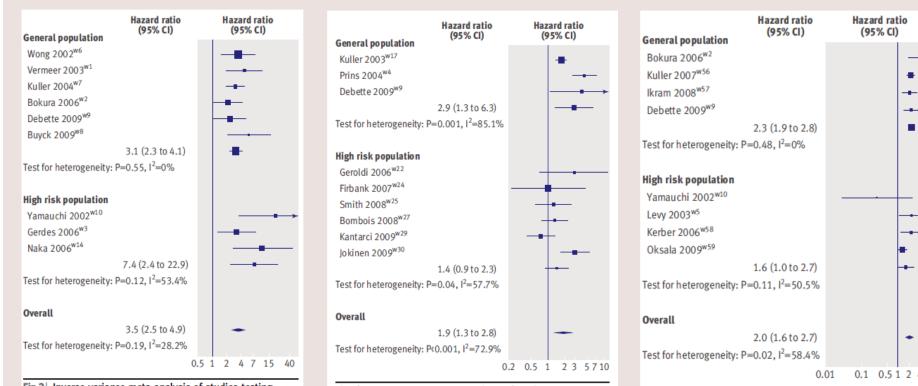


Fig 2 Inverse variance meta-analysis of studies testing association of white matter hyperintensities with incident stroke

Fig 3 Inverse variance meta-analysis of studies testing association of white matter hyperintensities with incident dementia

BMJ 2010;341;c3666

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		0.1	0.512410							
Fig 4   Inverse variance meta-analysis of studies testing association of white matter hyperintensities with mortality										



**EXPERT REVIEW** 

#### **European position paper on the** management of patients with patent foramen ovale. General approach and left circulation thromboembolism

Christian Pristipino<sup>1</sup>\*, Horst Sievert<sup>2,3</sup>, Fabrizio D'Ascenzo<sup>4</sup>, Jean Louis Mas<sup>5</sup>, Bernhard Meier<sup>6</sup>, Paolo Scacciatella<sup>4</sup>, David Hildick-Smith<sup>7</sup>, Fiorenzo Gaita<sup>4</sup>, Danilo Toni<sup>8</sup>, Paul Kyrle<sup>9</sup>, John Thomson<sup>10</sup>, Genevieve Derumeaux<sup>11</sup>, Eustaquio Onorato<sup>12</sup>, Dirk Sibbing<sup>13</sup>, Peter Germonpré<sup>14</sup>, Sergio Berti<sup>15</sup>, Massimo Chessa<sup>16</sup>, Francesco Bedogni<sup>16</sup>, Dariusz Dudek<sup>17</sup>, Marius Hornung<sup>2</sup>, and Jose Zamorano<sup>18</sup>, joint task force of European Association of Percutaneous Cardiovascular Interventions (EAPCI), European Stroke Organisation (ESO), European Heart Rhythm Association (EHRA), European Association for Cardiovascular Imaging (EACVI), Association for European Paediatric and Congenital Cardiology (AEPC), ESC Working group on GUCH, ESC Working group on Thrombosis, European Haematological Society (EHA), European Underwater and Baromedical Society (EUBS)

#### **Definitions of PFO-related left circulation** thromboembolism

PFO has been associated with left circulation thromboembolism to several organs;<sup>30</sup> therefore we promote the use of standardised definitions.

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Cryptogenic ischaemic left circulation embolisms are defined as any definite ischaemia (symptomatic or asymptomatic) occurring in an arterial bed which lacks a known cause despite investigation. Patients presenting with this clinical picture should be screened for the presence or absence of a PFO. However, when a PFO is thought likely to be implicated in a cryptogenic embolism, the event should be classified as PFO-related instead of cryptogenic.<sup>31</sup> Current classifications do not yet generally include this aspect. 32-35

#### TYPE OF STATEMENT Strong statement for the intervention

POSITION STATEMENTS

The position of our societies is to perform percutaneous closure of a PFO in carefully selected patients aged from 18 to 65 years with a confirmed cryptogenic stroke, TIA, or systemic embolism and an estimated high probability of a causal role of the PFO as assessed by clinical, anatomical and imaging features.



#### Improvement of Migraine After Patent Foramen Ovale Percutaneous Closure in Patients With Subclinical Brain Lesions

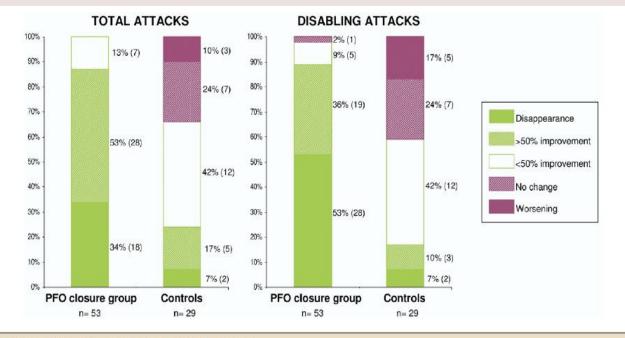
#### A Case-Control Study

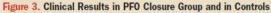
JACC: CARDIOVASCULAR INTERVENTIONS

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PUBLISHED BY ELSEVIER INC.

Carlo Vigna, MD, FESC,\* Nicola Marchese, MD,\* Vincenzo Inchingolo, MD,†





Clinical results at 6-month follow-up compared with the 6-month evaluation period according to treatment allocation. Values next to bars refer to the percentage and the absolute number of patients in every clinical subgroup. PFO = patent foramen ovale.



Catheterization and Cardiovascular Interventions 75:494-504 (2010)

#### Systematic Review and Meta-Analysis of Currently Available Clinical Evidence on Migraine and Patent Foramen Ovale Percutaneous Closure: Much Ado About Nothing?

Gianfranco Butera,<sup>1\*</sup> MD, PhD, Giuseppe G. L. Biondi-Zoccai,<sup>2</sup> MD, Mario Carminati,<sup>1</sup> MD,

Outcome:	03 Rate of cure or improvement							
Study			% (rendom)		Weight		% (rando	m)
or sub-category		% (SE)	95% CI		*		95% C	1
Jesurum	79.0000	(4.6000)		+	13.93	79.00	169.98,	88.021
Slevin	85.0000	(5.2000)			12.28	85.00	174.81,	95.191
dubiel	87.0000	(4.9000)		-	13.08	87.00	177.40,	96.601
Morandi	88.2000	(7.8000)		+	7.31	88.20	172.91,	103.491
Post	65.3000	(9.3000)			5.59	65.30	147.07,	83.531
Schwerzmenn	81.8000	(5.8000)			10.84	81.80	170.43,	93.171
Reisman	70.0000	(6. 5000)			9.40	70.00	157.26,	82.741
Anzola	88.0000	(4. 6000)		-	13.93	88.00	178.98,	97.021
Giardini	91.4000	(4. 7000)			13.64	91.40	182.19,	100.611
Total (95% CI)				٠	100.00	83.09	178.25,	87.931
Test for heteroge	mety: Chi? = 13.91, df = 8 (P	= 0.08), P = 42.5%		•				
	flect: Z = 33.65 (P < 0.0000							

Fig. 3. Forest plot of the rate of cure or improvement among patients with patent foramen ovale being treated with percutaneous closure.

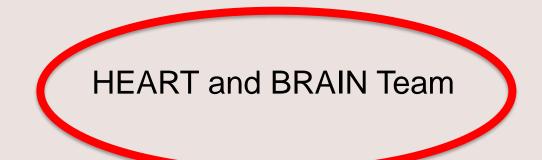




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«The Migraine Policy of my Center»

Outside of specific trials, percutaneous closure of a PFO is proposed on a case-by-case basis, after an in-depth multidisciplinary evaluation, in carefully-selected patients suffering from migraines with aura and MR signs suggesting clinical or silent cerebrovascular disease







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#### A patient with migraine, positive MR (suggestive for embolic lesions) and PFO: what to do?

After a Heart and Brain Team full evaluation Let's close the PFO





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