

risk stratification factors are being incorporated into clinical practice and affecting the incidence of PML.

P-RH, NC, and IC are employees of and hold stock or stock options, or both, in Biogen.

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Optimal stroke prevention in patients with PFO

We read with interest Bernhard Meier's Comment¹ on the Article by Scott E Kasner and colleagues,² suggesting that current recommendations on the treatment of patients with stroke patients and patent foramen ovale (PFO) should be reconsidered. Meier states that "in patients with a stroke and PFO as the presumed cause, PFO closure with a device should be considered first, oral anticoagulation (eg, with rivaroxaban) second (due to the accumulating bleeding risk), and aspirin should not be considered at all".¹

As members of the editorial committee of the Italian National Guidelines on Stroke, in December 2018, we summarised the available evidence for PFO closure compared with medical treatment, that shows the very low risk of events in the medical group that included patients treated with anticoagulation or antiplatelet therapy (1% per year), and published our rapid recommendations.³ We recommend

percutaneous closure of PFO in highly selected patients with cryptogenic ischaemic stroke or transient ischaemic attack, defined after accurate diagnostic screening. That is, when uncontrolled vascular risk factors are absent, in patients aged younger than 61 years, and in patients with particular anatomical features of PFO (large size or association with aneurysm of the interatrial septum), also taking into account patient preferences. We also published a comment in the same report, to document the risk of atrial fibrillation and draw attention to the need to inform patients of this risk. Atrial fibrillation or flutter after PFO closure occurred in 4.4% of patients in the RESPECT trial, 4.6% of patients in the CLOSE trial, and 6% in the GORE-REDUCE trial.⁴

When considering the strengths and limitations of existing clinical trials to inform the selection of patients for PFO closure, the importance of actively involving patients in the treatment decision and of informing them of the potential risks and benefits of treatment should not be overlooked.

Based on current evidence, we disagree with Meier's statement that aspirin should not be considered.¹ In agreement with the 2018 European consensus paper on the management of patients with PFO,⁵ we believe that, when a medical therapy is chosen, the individual risk of bleeding should be weighed against the risk of PFO-related stroke recurrence, in close collaboration with the patient. When the patient has a high haemorrhagic risk, is poorly compliant, or when proper anticoagulant monitoring cannot be guaranteed, or the risk of stroke recurrence is deemed to be low, an antiplatelet therapy should be prescribed.

We declare no competing interests.

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Primum non nocere: a call for balance when reporting on CTE

As clinicians and researchers in traumatic brain injury and neurodegeneration, we are concerned by the tone of reporting on chronic traumatic encephalopathy (CTE) that has developed over the past decade, highlighted in an article in *The New York Times*.¹ Misleading reporting can have unintended, negative consequences and we call for balance from the medical and scientific communities and the media when communicating on issues related to CTE.

Contrary to common perception, the clinical syndrome of CTE has not yet been fully defined,² its prevalence is unknown, and the neuropathological diagnostic criteria are no more than preliminary.³ We have an incomplete understanding of the extent or distribution of pathology required to

produce neurological dysfunction or to distinguish diseased from healthy tissue, with the neuropathological changes of CTE reported in apparently asymptomatic individuals.^{4,5} Although commonly quoted, no consensus agreement has been reached on staging the severity of CTE pathology. A single focus of the pathology implicated in CTE is not yet sufficient evidence to define disease.

Recognising limitations of the diagnostic process in human pathology, pathologists are careful to note that they are merely providing an opinion, thereby acknowledging that another pathologist might reasonably reach a different conclusion on the same case.⁶ In diagnoses where the criteria for assessment and reporting are established by broad consensus, the expectation is that variance in opinion is minimised. However, at this time, while CTE diagnostic criteria are far from established, discordance in opinions on individual cases is to be expected.¹

Unfortunately, the uncertainties around the clinical syndrome and the pathological definition of CTE are not acknowledged adequately in much of the current research literature or related media reporting, which at times has resembled science by press conference.⁷ Too often an inaccurate impression is portrayed that CTE is clinically defined, its prevalence is high, and pathology evaluation is a simple positive or negative decision. This distorted reporting on CTE might have dire consequences. Specifically, individuals with potentially treatable conditions, such as depression or post-traumatic stress disorder, might make decisions on their future on the basis of a misplaced belief that their symptoms inevitably herald an untreatable, degenerative brain disease culminating in dementia.

We propose that the principle of, first, to do no harm, is used when communicating on CTE, whatever the platform. In particular, the many remaining uncertainties should always

be acknowledged. Otherwise, the risk of doing harm is very real.

Declarations of interest are listed in the appendix.

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The Madwoman: a portrait of a choreic woman?

The Madwoman is part of a series of four canvases known as the *Cycle of the living*, painted by the Italian futurist artist Giacomo Balla, best known for capturing light, movement, and speed in his works. *The Madwoman*, painted in 1905, depicts an unsteady, ambiguously gesturing, clumsy woman standing at the threshold of a doorway. Looking at this shocking portrait of a woman who seems to have lost her balance, brings to mind the words of Huntington in his report,¹ published in 1871: "The eyelids are kept winking, the brows are corrugated, and then elevated... the mouth is drawn in various directions, giving the patient the most ludicrous appearance imaginable... The hands are kept rolling, first the palms upward, and then the back. The shoulders are shrugged, and the feet and legs kept in perpetual motion, the toes are turned in, and then everted; one foot is thrown across the other, and then suddenly withdrawn, and, in short, every conceivable attitude and expression is assumed, and so varied and irregular are the motions gone through with, that a complete description of them would be impossible."

The woman in the painting was Matilde Garbini. She was one of Balla's most studied subjects, depicted in almost 100 of his drawings. In particular, Balla made several sketches to study Garbini, trying to capture her awkward movements. Garbini, often found begging and drunk, lived in the slums of Rome, Italy.² She lived close to thieves and this could easily get her into trouble. Balla's daughter noted that Garbini wrote a letter to the artist

from jail, some years later, and Balla eventually arranged for her release.²

In 1910, Balla was one of the co-signatories of the *Manifesto of futurist painters*. The Futurist movement depicted modern life as a dynamically unfolding forcefield of bodies in motion.

The Madwoman shows how much he spent during his career studying the dynamics of movement. *The Madwoman* not only demonstrates Balla's ability to capture movement, creating a vivid visualisation of chorea, even in the present era of video demonstrations of movement disorders, but also reflects his great empathy for the social outcasts of the time.

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The Madwoman by Giacomo Balla, 1905, oil on canvas, 175x115 cm: Galleria Nazionale d'Arte Moderna (GNAM), Rome, Italy