Differential effects of hypertension in the aetiology of major intracerebral haemorrhage subtypes

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Hypertension, is more common in deep than in lobar ICH

Knowledge of the pathophysiology and management of primary intracerebral haemorrhage (ICH) has increased substantially over recent years, and the article by Jackson and Sudlow in this issue (*see p 1244*)¹ makes a further important contribution to our understanding of this serious illness. In a meticulously conducted meta-analysis of observational studies with defined localisation of the ICH, they have shown that overall a history of hypertension was about twice as common in deep ICH as in lobar ICH. However, there was considerable heterogeneity across studies, and sensitivity analyses restricted to higher quality studies markedly attenuated the differential effect of this exposure (or outcome). Thus, apart from highlighting the need for more methodologically robust studies in the area, the article challenges the long-held belief that chronic raised blood pressure, or what has traditionally been considered hypertension, is more relevant to deep basal ganglionic ICH, and that this exposure may also play a more important role in the pathogenesis of lobar ICH.

ICH has a higher mortality and morbidity than ischaemic stroke, but its lower incidence and greater complexity of diagnosis has restricted epidemiological data of risk factors. In particular, there continues to be uncertainty about how the importance of risk factors may

vary across different populations and ICH subtypes.² Meta-analysis, a systematic approach to identifying, appraising, synthesising and (if appropriate) combining the results of relevant studies to derive conclusions about a body of research, can yield the highest level of evidence about the effectiveness of interventions. This approach can also be applied to examine differences in associations of exposures (or outcomes) in non-randomised studies, although special attention is required to deal with important limitations.³ In addition to exposures not being randomly allocated, many studies have methodological problems, including both ascertainment and information biases, and there is inadequate control for potential confounding variables, as highlighted by Jackson and Sudlow as they pertain to ICH.¹ Moreover, methodological issues specifically related to meta-analysis, such as publication bias, can have a major effect on the combined results from observational studies.

Of course, the importance of raised blood pressure levels with regard to the risk of ICH in such a meta-analysis is likely to be substantially underestimated. Only a limited number of people with a history of hypertension are effectively identified in the population, particularly among the elderly, and single casual blood pressure

measurements are notoriously unreliable. Moreover, no account can be made of risk modification associated with treatment, although few people with hypertension are effectively treated to guideline-based targets. Furthermore, as discussed in the paper,¹ no account has been made of fluctuations in blood pressure levels, particularly with regard to nocturnal blood pressure decline and morning pressure surge, which have been associated with ICH.⁴ Given that amyloid angiopathy occurs commonly in the brains of older people and may lead to brittle walls and poor contractile capability of cerebral arterioles, the ultimate trigger of ICH may be the effects of intermittent high pulse pressure on blood flow. Taking stock of what is known in any field requires reviewing the existing literature, summarising it in an appropriate manner and exploring the implications of any heterogeneity in the results. Jackson and Sudlow have done a fine job, challenged contemporary thinking, and provided a platform for future investigation of ICH, a major cause of global disease burden.

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