Leukoaraiosis: From an Ancient Term to an Actual Marker of Poor Prognosis

Leonardo Pantoni, MD, PhD

The term leukoaraiosis (from the Greek leuko, white, and araiosis, rarefaction) was introduced in 1986 by Hachinski, Potter and Merskey to designate bilateral and symmetrical areas in the periventricular and centrum semiovale white matter that appeared hypodense on CT scans and hyperintense on T2-weighted MRI.1,2 Leukoaraiosis was supposed to be “a neutral term, exact enough to define white-matter changes, sufficient as a description or label, and demanding no more than that available today.9

Over the last 10 years, evidence has been mounting on the prevalence, clinical significance, and prognostic value of white matter changes (Table). Nowadays, we know that minimal changes are almost invariably found in the general population.10,11 Data are sufficient to sustain that the mildest degree of leukoaraiosis is to be considered as an almost normal finding in the brain of elderly patients. However, evidence has also accumulated showing that moderate-to-severe white matter changes are not so benign. They are in fact correlated with motor and gait disturbances,12 depressive symptoms,13 urinary disturbances,14 and some cognitive deficits15; the extent of these latter, however, is likely also influenced by possibly associated lesions such as lacunar infarcts and coexisting degenerative diseases.16–19 Longitudinal studies have outlined also a predictive role of leukoaraiosis in terms of less favorable prognosis in the general population and in a number of clinical conditions (Table). It is therefore essential in studies on white matter changes to abandon the mere assessment of their presence, and it is crucial to recognize their most severe degrees because these are likely the ones bearing clinical consequences. Further studies are needed to determine whether mild-to-moderate changes progress over time to become severe. Most of the studies with a longitudinal assessment of leukoaraiosis, however, have found that the most powerful predictor of progression is indeed baseline leukoaraiosis severity.20,21 Perhaps, the most important result in recent years has been the demonstration that leukoaraiosis represents a marker of poor prognosis, particularly in terms of increased mortality and risk of dementia.22–24 In a multicenter study, the severity of white matter changes at baseline was an independent predictor of the transition from a normal functional status to disability already after 1 year.25 The same study showed that this transition was mainly explained by cognitive and motor performances decline. This is of relevance because it suggests that the clinical effect of white matter changes is likely a composite one where different clinical correlates interact to cause loss of independence.

The presence of leukoaraiosis has been identified as a marker of less favorable prognosis also in the acute stroke
settings. In particular, white matter changes have been associated with an increased risk of hemorrhagic transformation of the brain infarct in patients subjected to thrombolysis; this increased risk is probably partially influenced by the copresence of lacunar infarcts. In this issue of Stroke, the article by Ay and colleagues adds further evidence about the prognostic significance of leukoaraiosis in this setting. These authors have shown that leukoaraiosis volume at the time of acute ischemic stroke is a predictor of infarct size growth. In this study, leukoaraiosis severity was volumetrically assessed whereas ischemic lesions on admission and follow-up were identified with diffusion and perfusion images. Clearly, this protocol is applicable only in centers with high expertise in neuroimaging techniques and not on a routine basis. But the relevance of the study is to have shown that a neuroimaging correlate of an underlying disease, leukoaraiosis, needs to be carefully looked at, assessed, and quantified; further studies will tell us whether this can be done by using simple visual rating scales or if it requires volume assessment and more sophisticated MRI techniques.

Disclosures
None.

References

Table. Some of the Clinical Correlates and Prognostic Significance of White Matter Changes (Leukoaraiosis)

<table>
<thead>
<tr>
<th>Clinical correlates (cross-sectional studies)</th>
<th>Prognostic significance (follow-up studies)</th>
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<tbody>
<tr>
<td>Cognitive deficits (particularly in terms of speed of mental processing, attention, and executive functions)</td>
<td>Increased risk of small-vessel strokes</td>
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<tr>
<td>Impaired mobility and balance, disturbances of gait</td>
<td>Increased risk of vascular mortality</td>
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<tr>
<td>Mood disturbances and depressive symptoms</td>
<td>Increased risk of bleeding in patients on anticoagulation</td>
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<td>Urinary incontinence</td>
<td>Increased risk of bleeding in patients undergoing cerebral thrombolysis</td>
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<tr>
<td>Decreased activity of daily living functionality</td>
<td>Increased surgical risk in patients undergoing carotid artery surgery</td>
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<tr>
<td>Poorer clinical outcome in patients with infratentorial strokes</td>
<td>Increased risk of dementia (in the general population)</td>
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<tr>
<td>Increased risk of dementia (in stroke patients)</td>
<td>Increased risk of transition to disability</td>
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</tbody>
</table>

None.


**KEY WORDS:** leukoaraiosis ▪ white matter changes ▪ disability ▪ MRI ▪ prognosis ▪ stroke
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