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COMMENTARY: Dementia after Three Months and One Year from Stroke: New Onset or Previous Cognitive Impairment?

Salvatore Caratozzolo, Andrea Scalvini, Francesco Lanfranchi, Silvia Pelizzari, Marina Zanetti, Luca Rozzini, Alessandro Padovani

Department of Clinical and Experimental Science, University of Brescia, Brescia, Italy, 25123, Italy

Article Info

***Correspondence:**
Dr. Salvatore Caratozzolo, MD
Department of Clinical and Experimental Science, University of Brescia, Brescia, Italy, 25123, Italy
Piazzale Spedali Civili, 1
25100, Brescia, Italy
E-Mail: salvatore.caratozzolo@hotmail.com
Telephone: 0039 030 3995632
Fax: 0039 030 3849205

Stroke and dementia are common pathological conditions in Western countries[1,2]. Although historically considered two distinct nosological entities, given the frequency with which stroke and cognitive impairment are compresent in the same patient[3,4], recent years have seen a growing interest about the opportunity to demonstrate specific interrelationships between stroke and dementia.

In a non-negligible percentage of cases, ranging from 20% to 80%, stroke was associated with the occurrence of a variable degree of cognitive impairment[5-8], from mild cognitive deficit to frank dementia. This wide range of prevalence rates could be attributed to differences in care setting, inclusion/exclusion criteria (presence of pre-stroke dementia, primary vs recurrent stroke), criteria adopted for the diagnosis of cognitive impairment, and the interval time after stroke.

A recent study including pathologic evaluation shows that stroke survivors who subsequently develop dementia (post-stroke dementia) in most cases (75%) meet the criteria for the diagnosis of vascular dementia, while the remaining exhibit a mixed pathological picture, with both vascular and neurodegenerative features[9-11]. Autopsy series have indeed shown that the prevalence of pure vascular dementia accounted for only 8-15% of cases, while the great majority of cases referred to a mix of vascular and degenerative pathology[12].

The term post-stroke dementia (PSD) was coined to define any dementia occurring after stroke, despite the fact its origin is attributable to vascular or degenerative causative factors alone, or to a mixture of the two. Therefore, it's evident that PSD can be due to a complex etiology, with various combinations of vascular disease (great and/or small vessels disease) and neurodegenerative non-vascular disease. Vascular lesions in "strategic" areas for cognitive function (e.g. angular gyrus, medial frontal lobes, the inferior-medial portion of temporal lobes, hippocampal or thalamic regions)[11] can be responsible for those cases of PSD for which a pure vascular pathogenesis may explain the occurrence of dementia. In contrast, other cases of PSD seem to be attributable to a neurodegenerative pathogenic mechanism of damage, triggered or, more likely, promoted by stroke. Regarding to this point, stroke could encourage beta-amyloid deposition, promoting the sequence of pathological events typical of AD which finally leads to neuronal death[13]. It's

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even possible that the disruption of blood-brain barrier related to stroke permits a leakage of plasma components (e.g. proteases or exogenous noxious agents) into the brain parenchyma, thus causing further brain damage and neuronal loss[14].

Considering the high proportion of stroke survivors developing PSD, as well as its prognostic implications, the individuation of clinical, instrumental and biological factors related to a higher risk for developing PSD has become of increasing interest. We can expect that thorough these acquisitions it will be possible to shed light on the nature of the causative relationship between stroke and dementia.

Among demographic factors, age and educational level are those found to be more strictly related to the risk of PSD. Age is a risk factor for both stroke and cognitive impairment. A recent study shows that the risk of PSD increases exponentially after 65 years of age[15]. A higher cognitive reserve can increase the tolerance to cognitive decline, thus patients with a lower educational level may have a greater chance of developing PSD, as well as earlier after stroke[16]. Sex seems to be a not relevant demographic factor regarding the occurrence of PSD, with data more frequently in favor of an equivalent prevalence in men and women[15,16].

The presence of cognitive impairment before stroke, although often undiagnosed, is a well-defined risk factor for PSD, as demonstrated in a recent meta-analysis[17] [17].

With regard to cardiovascular risk factors, it has long been recognized their significant role in both stroke and cognitive impairment[18].

Regarding imaging findings, different studies have identified global cortical atrophy, medial temporal lobe atrophy (MTLA), cerebral silent infarcts and subcortical white matter lesions (WMLs) as possible predictors of PSD[18,19]. Adherence to guidelines for the identification and definition of the abnormalities documented through MRI sequences has allowed to demonstrate the significant effect of WMLs and MTLA in the development of PSD[20,21]. In addition to the size and location of vascular lesion itself[22], the involvement of fiber tracts connecting cognitive centers might be essential for the development of PSD, hence the emerging interest in diffusion tensor imaging (DTI) techniques[23].

In our study we have progressively recruited patients admitted to our clinic between March and November 2011 for suspected stroke.

Data registered on initial assessment included the following: age; gender; education; living condition; and risk factors for stroke including smoking, alcoholism, hypertension, diabetes mellitus, atrial fibrillation, and ischemic heart disease (history of angina pectoris or myocardial infarction). During hospitalization, all patients underwent standard blood laboratory test, urinalysis, and a neurological assessment to evaluate initial stroke severity. Brain CT was performed without contrast, within 24 hours, by means of 5-mm contiguous slices. We analyzed the measure of MTLA by using the criteria of Jobs et al.[25] The minimum width of each medial temporal lobe (combined hippocampal formation and parahippocampal gyrus) was measured in millimeters at the narrowest point (irrespective of side), after image was angled with the brain stem (between the anterior and posterior limits of the brain stem)[25].

The major limitation of this study is the use of CT scans precluding a precise anatomical description of atrophy. We hypothesized that cortical atrophy was due to neurodegenerative damage. Despite CT scan is largely superseded by the use of magnetic resonance imaging (MRI) scans for MTLA evaluation, we propose the CT measurement method for its speed and low cost.

At 3 months (n = 114) and 1 year (n = 105) follow-up, a multidimensional assessment was performed with the aim to detect patients affected by PSD (Mini Mental State Examination, MMSE; Instrumental Activities of Daily Living, IADL).

Post-stroke patients was diagnosed as affected by dementia if MMSE <24 and IADL> 1 function loss, according with the criteria definition of cognitive impairment that influenced the ability of daily living in patients affected[26,27].

Therefore, we tried to define what factors at baseline (time of stroke onset) were able to predict the presence of PSD at 3 months and 1 year.

We have found a prevalence of PSD of 24.6% and 35.2% at 3 months and 1 year respectively, in agreement with data already existing in the literature.

Advanced age (OR 1.11, 95% CI 1.0-1.2), educational level (OR .6, 95% CI .4-.8), IQCODE score (Informant Questionnaire on Cognitive Decline in the Elderly; OR .78, 95% CI .1-5.9), apathy (OR 2.3, 95% CI 1.1-3.7), and MTLA (OR 6.14, 95% CI 1.4-26.2) were found to be independently associated with the presence of PSD at 3 months (p< .05). Advanced age (OR 1.1, 95% CI 1.0-1.2), IQCODE score (OR .05, 95% CI .0-.9), MTLA (OR 1.3, 95% CI 1.0 -1.6), and APACHE II (Acute Physiology and Chronic Health Evaluation; OR 0.6, 95% CI .4-.9) were found to be independently associated with the presence of PSD at 1 year (p< .05).

Our study shows that older age, lower education level, previous cognitive impairment and MTLA are factors independently related to PSD, a finding consistent with data already existing in the literature, as discussed above. The fact that low educational level, previous cognitive

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impairment and MTLA are well-known risk factors for AD[24] [24], but not for stroke, is coherent with the hypothesis that PSD origins as a primary neurodegenerative disease, successively promoted by vascular pathology, which could sustain a secondary degenerative process finally leading to the clinical expression of dementia. In support of this hypothesis concerning the primary degenerative nature of PSD, no significant association between cardiovascular risk factors or previous stroke and PSD was found in our study. In contrast, however, a large number of studies are in favor of this association, which we haven't confirmed probably because of the reduced sample size. The use of advanced imaging techniques, more expensive and less easily available than those used in our study (CT), such as MRI (including DTI sequences) or PET (using markers for beta amyloid or tau protein or microglial activation), can represent a key element for clarifying the real nature of PSD and the underlying pathogenesis.

Another finding emerged in our study was the demonstration of a significant association between the presence of apathy after stroke and PSD at 3 months. Few data regarding the role of neuropsychiatric and behavioral changes as predictors of PSD exist in the literature. Considering that apathy is a common condition in early stages of AD, we can consider our finding as a further element in support of the primarily degenerative nature of PSD.

Finally, APACHE seems to be an independent predictor of PSD after 1 year from the cerebrovascular event. It will be important in following studies to understand the real influence of the APACHE II score in predicting PSD and to compare it with the stroke variables themselves.

Our hope is that all these acquirements will lead to the identification of viable and useful strategies to prevent PSD, or, at least, reduce its severity and/or progressivity.

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