



Post stroke dementia and Post stroke depression

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Abstract

Stroke is the rapid loss of brain function due to disturbance in the blood supply to the brain causing predominantly motor and sensory symptoms. However, stroke can cause some other symptoms. Post stroke dementia and depression are probably the most important non-motor consequences of stroke. Post stroke dementia and depression are important and often overlooked symptoms following stroke. Treatment options for Post stroke dementia and depression are still limited, therefore diagnosis of Post stroke dementia and depression is very important because it could lead to prevention of dementia and depression by appropriate control of vascular risk factors. Primary prevention depend on early identification and appropriate control of vascular risk factors, while secondary prevention must include energetic therapy to prevent stroke recurrence.

POST STROKE DEMENTIA

Introduction

Dementia is defined as a neurological syndrome consisting of impaired cognition that is severe enough to interfere with everyday activities of daily living (1). Post stroke dementia represents part of vascular dementia (VaD) which is the most common form of dementia in the elderly after Alzheimer's dementia (AD) (2). The term vascular dementia identifies patients with severe cognitive loss from cerebrovascular disease, either after large ischemic or hemorrhagic strokes, lacunar infarcts, microscopic cortical infarcts that do not cause clinical symptoms (silent strokes), or from cardiac and circulatory disorders causing incomplete white matter infarction (3). Recently a concept of vascular cognitive impairment (VCI) was introduced (4, 5, 6). The concept of VCI includes patients with classic vascular risk factors and some degree of cognitive loss, but not dementia. The term vascular cognitive impairment (VCI) has been used to refer to all forms of mild to severe cognitive impairment that are associated with a vascular insult, whether they meet criteria for vascular dementia or not (7-11). This form of impairment includes those who have cognitive dysfunction associated with stroke, multiple cortical infarcts, multiple subcortical infarcts, silent infarcts, strategic infarcts, multiple small vessel disease with white matter lesions, and lacunar infarcts. There is believe that appropriate prevention measures and treatment of the vascular risk factors could prevent the progression of VCI to vascular dementia (10-11), because it was recently demonstrated in the Canadian Study on Health and Aging (12) that some patients with VCI improved spontaneously after a 5-year follow-up, indicating that VCI does not always have to progress to vascular dementia.

In an attempt to approach the heterogeneity of the pathophysiology associated with VaD, a number of researchers have subclassified vascular dementia according to the pathophysiology of the lesion that causes the cognitive deficit. One simplified subclassification includes Post stroke dementia, subcortical VaD, and AD plus VaD (mixed dementia) (10). Post stroke dementia is defined as a cognitive impairment resulting from a thromboembolic or hemorrhagic event causing cognitive symptoms severe enough to impair everyday social and occupational functioning. Subcortical VaD is caused by lacunar infarcts and white matter lesions.

Epidemiology and Risk Factors

Population-based epidemiological studies and neuropathology data have confirmed that vascular dementia is responsible for about 20% of cases of dementia and that vascular lesions are commonly found in patients with AD. The role of vascular risk factors and strokes in AD is an area of intensive research (13-17), and decreased incidence of AD and vascular dementia was observed with control of hypertension (18), and with the use of statins (19).

Age is the most significant risk factor for any dementia; however, other factors associated with health status earlier in life may predispose older adults to developing VaD. Atherosclerotic risk factors such as smoking, hypertension, myocardial infarctions, hyperlipidemia, and diabetes mellitus predispose older adults to cerebrovascular disease causing VaD (20). Additionally, the presence of stroke-related factors as a consequence of hemorrhagic, ischemic, or embolic events in the brain may also cause VaD (21). The location and size of the stroke can also cause significant cerebral tissue loss and white matter disease, leading to VaD (20).

Based on projected figures for the growing proportion of elderly persons and increased incidence of ischemic heart disease and stroke, it has been postulated that vascular dementia may become the most common cause of dementia in the near future because it affects 30% of ischemic strokes and 26% of patients with congestive heart failure due to hypoperfusion (4, 22). On the other hand, Post stroke dementia (multi-infarct dementia) often remains underrecognized (23), and it is rare to diagnose vascular dementia after congestive heart failure, after major surgery in the elderly, or after coronary artery bypass graft.

Subcortical ischemic vascular dementia results from small-vessel disease, and produces lacunar strokes and incomplete white matter infarction (24) having relatively poor prognosis of lacunes in terms of cognitive outcome (25). Furthermore, silent lacunar strokes appear to double the risk of dementia (26). It has been postulated that chronic brain edema from damage of the blood-brain barrier could explain their poor outcome (27). Lacunes are markers of small-vessel disease and should prompt a search for diagnosis and treatment of relevant risk factors.

Pathophysiology

Vascular dementia results from brain injury caused by stroke and cerebral ischemia or haemorrhage. Single ischemic or thromboembolic infarcts occurring in strategic areas of the dominant hemisphere (eg, angular gyri, mediodorsal thalamus, anterior thalamus) may cause a dementia-like syndrome without the involvement of large volumes of cerebral matter. In general, volume of tissue loss is a poor predictor of the severity of the cognitive impairment. More commonly, progressive cognitive deficits and dementia can result from multiple temporally placed small cerebral infarcts. Frontal subcortical regions supplied by small penetrating arterioles may be especially prone to degenerative changes in patients with poorly controlled hypertension, diabetes mellitus, or both. A less common cause of vascular dementia is global hypoxic-ischemic injury (eg, following cardiac arrest). Irreversible cognitive impairment is frequently observed following coronary bypass surgery (28).

Less understood form of vascular dementia is Binswanger encephalopathy, causing mostly subcortical dementia features. Postmortem, myelin loss is observed and is most prominent in the hemispheric deep white matter. Axonal drop out is also observed with little or no signs of inflammation. Neuroimaging shows decreased white matter density on computer tomography (CT) scanning and decreased white matter intensity on magnetic resonance imaging (MRI). However, frequently on these neuroimaging scans lacunar strokes are observed.

Dementia associated with cerebrovascular disease is also observed in a rare genetic condition, ie, cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy – CADASIL (29). Affected patients often present with migraines with aura. Recurrent strokes start when the patients are aged 30-50 years. Multiple lacunar infarcts, mainly in the frontal white matter and basal ganglia, lead to progressive cognitive decline and finally dementia. However, cognitive decline is thought to begin even before strokes occur, suggesting that chronic cerebral hypoperfusion in the absence of overt stroke might be sufficient to cause significant neuronal circuit disruption.

Diagnosis

A diagnosis of VaD would be appropriate for an individual who presents with an acute onset and stepwise progression of cognitive impairment (30). Three specific elements are required for a clinician to diagnose an individual with VaD: the first is demonstration of cognitive impairment, the second is existence of cerebrovascular disease, and the third is the relationship between two disorders (30, 31, 32). Many individuals with VaD have a generalized cognitive deficit with less striking memory loss (6, 9). In fact, a more common form of cognitive impairment associated with VaD is compromised executive functioning, which involves goal-directed behaviour, initiation of sequences, and problem-solving abilities (6, 33). Cerebrovascular subcortical lesions in the prefrontal

cortex resulting in subcortical VaD can often cause cognitive impairments associated with executive functioning. To determine if executive impairments exist in individuals with VaD, specific neuropsychological tests of executive functioning such as the Trail-Making Test, the Executive Interview, and the Clock Drawing Test may be used (6). There are several nonspecific clinical symptoms associated with vascular dementia. Individuals with typical subcortical lesions may display extrapyramidal symptoms and instability leading to falls. Urinary frequency and incontinence, as well as dysarthria and dysphagia, are common symptoms (10). The Hachinski Ischemic Scale accounts for factors associated with vascular development of dementia such as the onset of the cognitive impairment, the risk factors related to stroke, behavioural abnormalities such as depression and emotional incontinence, and focal neurological symptoms (21). A score lower than 4 renders a diagnosis of AD, whereas a score of greater than 7 is classified as multi-infarct dementia (9, 34), while score of five to six may suggest the so called mixed dementia – Alzheimer's dementia and vascular dementia. The patient must demonstrate some form of cerebrovascular pathology as displayed by brain imaging studies (CT or MRI). Neuroimaging studies demonstrate vascular lesions that may differ in size depending on the degree of vascular pathology. These lesions range from a single lacunar stroke to multiple cortico-subcortical strokes and periventricular white matter ischemia (6, 9). A final factor required for the diagnosis of VaD is the fact that cognitive impairment occurred some time after the cerebrovascular event, usually within three months, but this three months criterion is being disputed in some discussions (6, 8).

The National Institute for Neurological Disorders and Stroke-Association Internationale pour la Recherche et l'Enseignement en Neurosciences (NINDS-AIREN) defined criteria for VaD (31). However, these criteria, published in 1993, i.e. almost 20 years ago, are considered outdated. Therefore recently the American Heart Association and the American Stroke Association supported by the American Academy of Neurology and the Alzheimer's Association published criteria for vascular cognitive impairment and they introduced the term: vascular mild cognitive impairment (VaMCI) similar to mild cognitive impairment and present diagnostic criteria for it (36). These criteria define VaD as probable VaD and possible VaD, and VaMCI as probable, possible and unstable VaMCI (Table 1).

TABLE 1.

Vascular Cognitive Impairment

1. The term VCI characterizes all forms of cognitive deficits from VaD to MCI of vascular origin.
2. These criteria cannot be used for subjects who have an active diagnosis of drug or alcohol abuse/dependence. Subjects must be free of any type of substance for at least 3 months.
3. These criteria cannot be used for subjects with delirium.

Dementia

1. The diagnosis of dementia should be based on a decline in cognitive function from a prior baseline and a deficit in performance in ³ 2 cognitive domains that are of sufficient severity to affect the subject's activities of daily living.
2. The diagnosis of dementia must be based on cognitive testing, and a minimum of 4 cognitive domains should be assessed: executive/attention, memory, language, and visuospatial functions.
3. The deficits in activities of daily living are independent of the motor/sensory sequelae of the vascular event.

Probable VaD

1. There is cognitive impairment and imaging evidence of cerebrovascular disease and:
 - a. There is a clear temporal relationship between a vascular event (eg, clinical stroke) and onset of cognitive deficits, or
 - b. There is a clear relationship in the severity and pattern of cognitive impairment and the presence of diffuse, subcortical cerebrovascular disease pathology (eg, as in CADASIL).
2. There is no history of gradually progressive cognitive deficits before or after the stroke that suggests the presence of a nonvascular neurodegenerative disorder.

Possible VaD

There is cognitive impairment and imaging evidence of cerebrovascular disease but

1. There is no clear relationship (temporal, severity, or cognitive pattern) between the vascular disease (eg, silent infarcts, subcortical small-vessel disease) and the cognitive impairment.
2. There is insufficient information for the diagnosis of VaD (eg, clinical symptoms suggest the presence of vascular disease, but no CT/MRI studies are available).
3. Severity of aphasia precludes proper cognitive assessment. However, patients with documented evidence of normal cognitive function (eg, annual cognitive evaluations) before the clinical event that caused aphasia could be classified as having probable VaD.
4. There is evidence of other neurodegenerative diseases or conditions in addition to cerebrovascular disease that may affect cognition, such as:
 - a. A history of other neurodegenerative disorders (eg, Parkinson disease, progressive supranuclear palsy, dementia with Lewy bodies);
 - b. The presence of Alzheimer disease biology is confirmed by biomarkers (eg, PET, CSF, amyloid ligands) or genetic studies (eg, PS1 mutation); or
 - c. A history of active cancer or psychiatric or metabolic disorders that may affect cognitive function.

VaMCI

1. VaMCI includes the 4 subtypes proposed for the classification of MCI: amnesic, amnesic plus other domains,

nonamnesic single domain, and nonamnesic multiple domain.

2. The classification of VaMCI must be based on cognitive testing, and a minimum of 4 cognitive domains should be assessed: executive/attention, memory, language, and visuospatial functions. The classification should be based on an assumption of decline in cognitive function from a prior baseline and impairment in at least 1 cognitive domain.
3. Instrumental activities of daily living could be normal or mildly impaired, independent of the presence of motor/sensory symptoms.

Probable VaMCI

1. There is cognitive impairment and imaging evidence of cerebrovascular disease and:
 - a. There is a clear temporal relationship between a vascular event (eg, clinical stroke) and onset of cognitive deficits, or
 - b. There is a clear relationship in the severity and pattern of cognitive impairment and the presence of diffuse, subcortical cerebrovascular disease pathology (eg, as in CADASIL).
2. There is no history of gradually progressive cognitive deficits before or after the stroke that suggests the presence of a nonvascular neurodegenerative disorder.

Possible VaMCI

There is cognitive impairment and imaging evidence of cerebrovascular disease but:

1. There is no clear relationship (temporal, severity, or cognitive pattern) between the vascular disease (eg, silent infarcts, subcortical small-vessel disease) and onset of cognitive deficits.
2. There is insufficient information for the diagnosis of VaMCI (eg, clinical symptoms suggest the presence of vascular disease, but no CT/MRI studies are available).
3. Severity of aphasia precludes proper cognitive assessment. However, patients with documented evidence of normal cognitive function (eg, annual cognitive evaluations) before the clinical event that caused aphasia could be classified as having probable VaMCI.
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 - c. A history of active cancer or psychiatric or metabolic disorders that may affect cognitive function.

Unstable VaMCI

Subjects with the diagnosis of probable or possible VaMCI whose symptoms revert to normal should be classified as having „unstable VaMCI”

Clinical manifestation

Patients with VaD are cognitively impaired in executive functioning activities such as organizing, planning, and initiating sequential events. Patients with VaD have relatively mild memory loss but usually have early executive dysfunction, and loss of executive control function is characterized by lack of planning, disorganized thought, behavior, or emotion (37-40). Therefore, it is very similar to subcortical neurodegenerative dementias, sometimes called dysexecutive cognitive impairment. Complex activities such as cooking, dressing, and housekeeping are predominantly affected in patients with (40, 41). However, most of the current tests for assessment of dementia are relatively insensitive to executive function, leading to underdiagnosis of vascular dementia. Executive dysfunction is relatively common among elderly people living in the community, affecting one in six non-demented individuals (41-45). Loss of executive function is an important cause of disability in non-demented community-dwelling individuals (42-45), as well as in patients with vascular dementia (46-50), and Alzheimer's dementia (51). Other cognitive domains such as memory, language, visuospatial skills and motor speed, or demographic features such as age, education and health status, have minimal contribution to activities of daily living (ADL). Similar conclusions were reached using two tests of executive function, the EXIT25 and a simple clock-drawing task (52, 53). Mini-mental state examination made no contribution to the regression model, while depression and physical illness contributed little additional variance to the model.

Apathy and depression frequently occur as a consequence of disruption of prefrontal circuits in patients after stroke and these symptoms are an important component in the development of VaD. Vascular depression is currently recognized as an independent condition (54, 55). A study of Post stroke patients in Finland (56) confirmed that executive dysfunction was the main determinant of abnormalities in both basic and instrumental ADL suggesting that executive function including instrumental ADL may be more sensitive for the diagnosis of vascular dementia and could accurately measure the effects of potential therapies. Instrumental ADL appear to be an appropriate examination for executive function in patients with post stroke cognitive decline (57-60), apathy and depression, although there is no total agreement with this concept (61). Other typical clinical features of vascular dementia include cases with sudden onset and slow or stepwise progression, often increasing in severity with each ischemic event: fluctuations are common and memory is only mildly affected. In VaD gait is typically disturbed, shuffling and with short steps, and often resembles that of patients with Parkinson's disease (62, 63).

Treatment

A number of medications have been used for the symptomatic treatment of VaD, including vasodilators such as niacin, calcium channel blockers, pentoxifylline,

antiplatelet agents, and nootropic agents such as memantine. More recently, the cholinesterase inhibitors donepezil, galantamine, and rivastigmine have been studied in controlled clinical trials in vascular dementia. Cholinergic deficits in the condition may result from ischemia of the nucleus basalis of Meynert or from interruption of cholinergic pathways by vascular lesions.

Compared with placebo, donepezil treatment groups showed statistically significant improvement in cognition, global function, and both basic and instrumental ADL (64, 65, 66).

Study of galantamine in vascular dementia showed a significant improvement in the behavioral symptoms in the treated group versus placebo (67).

The change from baseline on the neuropsychiatric inventory score at 22 months showed that the rivastigmine group improved while the aspirin group deteriorated. Also, the rivastigmine group showed significant improvements in executive function, behavioral symptoms, and caregivers' relative stress score relative to the aspirin group (68, 69).

Two trials of memantine in patients with mild to moderate vascular dementia the mean ADAS-cog and the mini-mental state examination scores improved significantly with memantine compared with deterioration with placebo and the nurses' observation scale for geriatric patients' disturbed behavior also showed differences in favor of memantine. Memantine therapy resulted in stabilization of patients with vascular dementia, compared with placebo controls (70, 71).

Primary and Secondary Prevention

The classic modifiable risk factors for vascular dementia include hypertension, cardiac abnormalities such as atrial fibrillation, smoking, lipid abnormalities, diabetes, and elevated homocysteine levels. Modifying and treating vascular risk factors leads to stroke prevention and lower the risk of Alzheimer's dementia and VaD.

In the extension of the Systolic Hypertension in Europe Study (SYST-EUR) long-term antihypertensive therapy reduced the risk of both Alzheimer's dementia and Post stroke vascular dementia by 55% with the treatment with the calcium-channel blocker nitrendipine (18). Antihypertensive treatment reduced the odds of incident cognitive impairment by 38% in a 946-participant cohort of African Americans and it was associated with a 28% reduction in the risk of recurrent stroke and a 38-55% reduction in the risk of dementia (72).

In the Perindopril Protection Against Recurrent Stroke Study (PROGRESS) blood pressure lowering in patients with previous stroke or transient ischemic attack significant reduction of cognitive decline and dementia was documented in the active treatment group, compared with the placebo (73, 74).

The Mediterranean diet, with its high content of fish, seafood, grains, vegetables, citrus fruits and olive oil, appears to be protective against vascular disease, as well

as moderate physical activity (75, 76). Finally, effortful mental activities appear to be protective against dementia, both Alzheimer's and vascular (77 – 85).

Conclusion

Vascular dementia is an important and often overlooked form of dementia. Projections indicate that it may become the most common form of dementia in the elderly affected by ischemic heart disease and stroke. Most cases of vascular dementia present with a subcortical form of dementia with prominent executive dysfunction that is usually not recognized as dementia by relatives or caregivers. Cholinergic treatment may improve the prognosis of the condition. Primary prevention of vascular dementia appears to depend on early identification and appropriate control of vascular risk factors. Secondary prevention, after clinical stroke or silent lacunes, must include energetic therapy to prevent stroke recurrence.

POST STROKE DEPRESSION

Introduction

Depression is a common mental disorder that presents with depressed mood, loss of interest or pleasure, feelings of guilt or low self-worth, disturbed sleep or appetite, low energy, and poor concentration (86). Post-stroke depression (PSD) is considered as the most frequent and important neuropsychiatric consequence of stroke since approximately one-third of stroke survivors experience depression. PSD has significant negative consequences on the recovery of motor and cognitive deficits, functional recovery and survival after stroke (87). The Diagnostic and Statistical Manual (DSM) IV categorizes post-stroke depression as »mood disorder due to a general medical condition (i.e. stroke)« with the specifiers of depressive features, major depressive-like episodes, manic features, or mixed features (88). Major depression and minor depression are the most frequently recognized expressions of PSD.

Epidemiology and risk factors

Pooled data on prevalence of all types of PSD in various populations differs significantly: data from four community-based studies show mean prevalence of 31,8% (range 30-44%), data from studies carried out in acute hospitals show prevalence between 25-47%, and studies done in rehabilitation centers show prevalence between 35-47% (89 – 93).

The occurrence of PSD peaks three to six months after stroke and subsequent decline in prevalence at one-year reaches about to 50% of initial rates. In a study done on 100 stroke patients followed for 18 months, 46% of the patients had symptoms of PSD in the first two months after stroke, while only 12% of patients experienced first symptoms 12 months after stroke. The course of PSD can be rather lengthy, for example, symptoms of major depression identified in 27% of stroke patients persisted for approximately one year, while symptoms of minor

depression in 20% of stroke patients lasted for more than two years. Major depression occurs in up to 25% of patients; and minor depression, which has been defined as a depressed mood or loss of interest occurs in up to 30% of patients following stroke (92, 93). Minor depression appeared to be more variable, with both short term and long term depression occurring in these patients. Prevalence of major depression from four community-based studies ranged from 11-15%; from studies carried out in acute hospitals ranged from 10-27%; in studies done in rehabilitation centers ranged from 10- 40%. Prevalence of minor depression from four community-based studies ranged from 8-12%, from studies carried out in acute hospitals ranged from 11-20%, in studies done in rehabilitation centers ranged from 21-44% (91 – 96).

The various risk factors associated with PSD have included location and size of the stroke, temporal relation between PSD and stroke, and the size of the ventricles. Clinical studies have shown that longer duration of PSD have patients with stroke in the territory of the middle cerebral artery, compared with patients with posterior circulation strokes. Robinson et al have shown that there is so called anterior to posterior gradient which is different according to the hemisphere involved, being posterior to anterior for the left hemisphere and anterior to posterior for the right hemisphere (97). Bogousslavsky et al have shown that PSD is in strong correlation with lesions in the subcortical white matter, thalamus, basal ganglia, and brain stem, rather than cortical lesions with specific cortical disturbance (23). Starkestein *et al.* compared the magnitude of subcortical atrophy in brain CT studies obtained immediately after stroke. Patients who develop PSD had a significantly greater degree of atrophy at this stage than those who did not (98).

There is a higher frequency of left than right strokes in PSD patients if the symptoms develop in first 10 days, the relationship disappears if the onset of symptoms was 3 months after stroke. If the symptoms appear ≥ 1 year after stroke, right sided lesions are more frequent. Overt sadness is more frequently associated with left (86%) than right lesions (61%). Crying is also more frequent in left versus right lesions (50% vs. 20%). With right-side lesions anosognosia is clearly associated with neglect (95% vs. 34% for neglect vs no neglect). Regional cerebral blood flow values can also be valuable in PSD prediction. Lower cerebral blood flow (CBF) values in mesial temporal cortex may reflect dysfunction of limbic system and may be critical for the occurrence of depressive symptoms in patients with subcortical strokes. Patients with lower CBF in the left frontal or right parietooccipital regions were more depressed in comparison with those with other brain lesions (23, 97 – 103).

Diagnosis

The most frequently used scale for evaluating depression in stroke patients is the Hamilton Depression Rating Scale (HDRS). However, General Health Questionnaire (GHQ), Hospital Anxiety and Depression Scale (HADS), Aphasic Depression Rating Scale (ADRS), Beck Depres-

sion Inventory (BDI) or some modified scales such as the Lausanne Emotion in Acute Stroke Study (LEASS) can also be used in diagnosis of PSD (98). PSD has a negative impact on cognitive functioning, and for evaluation of cognitive functions most frequently used are Mini Mental State Exam (MMSE) and Montreal Cognitive Assessment (MoCA) (82, 83, 88).

Clinical manifestation

In acute phase of stroke there are some conditions that should be distinguished from PSD such as: anosognosia or poor recognition of the neurological deficit, and fatigue classified as pseudodepressive syndrome after stroke. Also, modified mental processing can affect up to one third of stroke patients who have no, or only poor, memory of what actually happened during the acute phase of stroke. This usually occurs without specific damage to the anatomical structures involved in memory processing. Emotional lability, sometimes also referred to as post stroke emotionalism or catastrophic reactions, is reported in about 10% of stroke patients. It is an abnormal lability of mood during which the patient laughs or cries for no evident reason, suffers anxiety, apathy and loss of psychic self-activation (athymhormia). Typically the patient does not feel the expected emotion associated with the outward reaction, and patient can with no apparent reason change from laughter to crying (60, 92, 93, 96, 97). The clinical manifestations of PSD are similar to those of late onset depression, but it is identified in patients that may have clinically apparent or silent strokes or subcortical bilateral white matter ischemic disease. Mostly affected are patients after the age of 65 years. The symptoms of PSD consist of mood abnormalities, neuropsychological disturbances with impairment of executive functions and a greater tendency to psychomotor retardation, poor insight and impaired activities of daily living. Vegetative symptoms consist of disturbances of sleep, libido and low level of energy, were significantly more frequent among depressed than non-depressed stroke patients at initial evaluation, and after 3, 6, 12 and 24 months (91, 92).

There is a bidirectional relationship between stroke and depression: there is a high prevalence of depression between stroke patients and there is a higher risk for stroke in depressed people even when other conventional stroke risk factors are under control (60). In one study it have been shown that previous stroke is a risk factor for PSD (92). In another studies authors shown that patients with major PSD had significantly more cognitive deficits than non depressed patients who experienced a similar location and size of the left hemisphere stroke, this was not the case for strokes in the right hemisphere (98, 99), while Lausanne Emotion in stroke study had shown no statistical significance (100).

When symptoms of depression appear more than one year after stroke right sided lesions were more frequent. Stroke severity and disability may cause a reactive depressive process in early stages after stroke, but probably does not mediate the development of PSD in the long

term. There was a significantly higher prevalence of PSD among patients with non-fluent aphasia, but not among patients with fluent aphasia. The presence of PSD has been found to have negative impact on recovery of cognitive function, recovery of ability to perform activities of daily living (ADL), mortality risks (101 – 103).

DESTRO study has shown higher frequency of women with PSD (35.39% without and 48.56% with PSD) (90, 104, 105). FINNSTROKE study has shown that older age as independent predictor of PSD (93), Erriks-son M et al has shown younger age as predictor of PSD (106), DESTRO study has shown no statistical significance, therefore results are still controversial. Meta-analyses has shown no statistical significance between the age and PSD (107). There were 20% of stroke patients who made no recovery, 60% made complete recovery, however, in evaluating recurrent stroke there must be informations about previous disability. Also, there were more ADL dependent (11,6% vs 7%), and living alone (54,8% vs 45,3%) patients without PSD (92, 101, 108).

Treatment and prevention

PSD treatment has the aim to achieve complete symptom remission of the depressive episode that may have a positive impact on recovery of neurological deficits (109, 110). The efficacy of pharmacotherapy of PSD has been investigated in several studies with tricyclic antidepressants and selective serotonin reuptake inhibitors. In one study it was shown that responders to treatment with antidepressant medication had higher MMSE scores compared with placebo (109). In another study authors compared recovery of motor deficit and disability in PSD patients treated with antidepressant medications versus placebo finding that treated patients were significantly more likely to achieve symptom remission (111). Prevention with sertraline in the doses from 50-150 mg/day has shown during one year in a double blind study that among treated patients 8,3% developed a PSD, compared to 22,8% patients on placebo (112). One study shown that patients treated with nortryptiline had an increased survival probability at six years (61% vs placebo 34%) (107). Another study found that nortryptiline (100 mg/day) compared with fluoxetine (40 mg/day) and placebo had shown significant improvement (113). Double blind placebo controlled study of fluoxetine (20 mg/day) versus placebo showed that patients on active treatment experienced comparable improvement during first 4 weeks, by 12 weeks patients on fluoxetine continued to improve while those on placebo had experienced recurrence of symptoms (114). Citalopram and nortryptiline double blind studies failed to show improvement of cognitive deficits even in the presence of depression improvement (115, 116).

Conclusion

It is important to recognize and diagnose post stroke depression. This is not only because of the increased suffering depression causes to patients who already have

much to cope with, but because depression after stroke is associated with worse prognosis and there are evidences that pharmacological treatment could substantially improves this outlook.

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