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The first two authors contributed equally to this work.

Introduction
Suicidal behavior and stroke are both dramatic events that contribute to an increased risk of death and functional impairments. The World Health Organization has established that 15 million people suffer from stroke worldwide each year with 5 million of them dying and another 5 million becoming permanently disabled [1]. Stroke is considered one of the most devastating of all neurological disorders, often causing death or gross physical impairment and disability [2]. Although strokes can and do occur at any age, in the United States in 2001, 74.5% of all strokes occurred among people age 75 or older, while 88% occurred among individuals aged 65 or older: the risk of having a stroke more than doubles each decade after 55 years of age [3].

In the United States, approximately 32,000 individuals die by suicide each year [4] and 5000 (14%) of them are older than 65 years of age. In 2007, the rate of suicide in the elderly was 14.3 per 100,000 compared to 10.9 suicides per 100,000 in the general population [5]. Previous studies have shown that physical illnesses, especially neurological disorders, increase suicide risk [6–10]. Moreover, it has been well established that people who survive a stroke often develop poststroke depression which is consistently implicated as an important risk factor for suicide [11–13]. Given that stroke and suicide are both leading causes of death and contribute to significant societal costs, the purpose of this review is to investigate whether or not individuals who suffer a stroke are at an increased risk of having suicidal thoughts or dying by suicide.

Material and Methods
To provide a new and timely review examining the association between stroke and suicide, we performed a careful Medline, Ex-
All of the studies included are reported in Table 1. Authors (GS, PG). In addition, we also examined reference lists and contacted experts in the field. This search strategy identified 31 articles; of these 16 were eligible for the purpose of this review. All of the studies included are reported in Table 1.

Suicidal Ideation and Suicidal Plans in Stroke Patients

The original studies investigating the relation between stroke and suicidal plans were conducted by Kishi and colleagues in 1996 [14,15]. The researchers recruited 301 patients and evaluated their suicidal plans after suffering an acute stroke (i.e., baseline) and at 3, 6, 12, and 24 months follow-up. They identified stroke as a risk factor for suicide in both studies, demonstrating that 6.6% of patients reported acute-onset suicidal plans, whereas 11.3% of stroke victims reported delayed-suicidal plans within 2 years of their stroke. The development of both acute- and delayed-onset suicidal plans in stroke patients has been found to be related to the presence of depressive disorders, particularly major depression, as well as to a prior history of stroke. The authors also noted some differences between the two kinds of onset, suggesting that the etiology of these two types of suicidal plans may be different. Specifically, delayed-onset suicidal plans have been found to be related to greater physical impairment from the stroke, and these patients had more frequent posterior lesions; whereas, acute-onset plans were associated with alcohol abuse and younger age. Furthermore, they found that suicidal ideation during the acute medical treatment period was associated with the presence of a diagnosable depressive disorder and that the severity of the illness was not an independent risk factor for developing a suicidal plan. This finding suggests that suicidal plans were not simply psychological reactions to physical impairment after the acute event.

Five years later, Pohjasvaara et al. [16] conducted a case-control study that substantiated confirmed Kishi’s [14,15] previous results providing further support for stroke being a significant risk factor for developing suicidal ideation. The authors of this study examined the frequency and clinical determinants of suicidal ideas at 3 and 15 months after stroke. They noted that the patients with suicidal ideas were more depressed at 3 and 15 months after stroke as compared to patients without suicidal ideas. Moreover, patients with suicidal ideas more often had a history of stroke, right-sided stroke, were more disabled, and more dependent in living 15 months after stroke. The researchers also found that motivated aspects of depression (e.g., anxiety, hyperemotionalism) were more common in depressed stroke patients, whereas the unmotivated or biologically determined aspects (e.g., suicidal ideas, depressed mood, feelings of guilt) were more frequently reported in patients with an endogenous form of major depression. Unmotivated aspects, if present in stroke patients, were often attributed to the actual condition (stroke), but not to endogenous depression. This may explain why recurrent strokes have been found to be an independent correlate of suicidal ideas 15 months after stroke.

Rao et al. [17] found that individuals with cerebrovascular disease were at an increased risk of suicide. Specifically, the researchers evaluated patients with stroke, transient ischemic attack (TIA), and with peripheral vascular disease (PVD) and concluded that the impairment of the frontal lobe increased both impulsivity and suicide risk. In accordance with these results, Santos et al. [18] examined 117 stroke patients and reported that 15% of acute stroke patients presented with suicidal thoughts. Additionally, the researchers demonstrated that stroke patients with suicidal idea- tion had a lower educational level and were more likely to have had a previous mood disorder or acute depression than those without suicidal thoughts. Similarly, Fuller-Thompson et al. [19] concluded that stroke survivors had twice the odds of depression and suicidal ideation as compared to those who had never suffered a stroke. Further, Caucasians and younger individuals had higher odds of poststroke depression and suicidal ideation.

Tang et al. [20] investigated the role of fatigue in stroke survivors and revealed that poststroke fatigue was a significant predictor of suicidal ideation independent of depression.

Finally, Chan et al. [21] found that high cerebrovascular risk factor (CVFR) scores (derived by the weighted sum of severities of specific factors such as systolic blood pressure, antihypertensive treatment, coronary vessel disease, diabetes mellitus, hypertension, atrial fibrillation, left-ventricular hypertrophy, and cigarette smoking) were associated with an increased risk for suicide in middle age and older adults after accounting for age, sex, depression diagnosis, the presence of stroke, and functional status.

Suicide and Suicide Attempt in Stroke Patients

To estimate the percentage of suicides in patients who suffered a stroke, Stenager et al. [22] conducted an epidemiological study in Denmark over a period of 25 years from 1973 to 1998. In a sample of almost 38,000 patients with stroke, the researchers reported that 140 (7.2%) patients had died by suicide and suicide risk was significantly higher after stroke, especially in women and in the age group up to 60 years. Similar findings were reported in another study conducted in Denmark during the same time period [23]. Specifically, Teasdale and Engberg [23] found that there was an increased risk of suicide after stroke with the greatest risk being among younger patients, in relatively less severe cases, and within the first 5 years after stroke. Interestingly, the authors also concluded that the risk for suicide decreased with the duration of hospitalization and suggested that patients who had suffered more severe strokes requiring longer hospitalization could have more functional impairments reducing their capacity to carry out a suicidal act. In a recent population-based study examining the prevalence of stroke in suicide victims in Northern Finland [24], results indicated that 70% of stroke patients who died by suicide suffered from prestroke depression, with the highest risk for suicide being within 2 years after stroke. As previously noted, Teasdale and En-
<table>
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<tr>
<th>Study</th>
<th>Study design</th>
<th>Eventual follow-up</th>
<th>Participants</th>
<th>Main findings</th>
<th>Limitations</th>
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<tbody>
<tr>
<td>Kishi et al. [14]</td>
<td>Case-control study</td>
<td>No</td>
<td>301 patients (cases n = 20 controls n = 281) evaluated for suicidal plans after acute stroke</td>
<td>19 patients had suicidal plans and 1 attempted suicide (6.6%). Of those patients, 15 (75%) had major depressive disorder (MDD), 3 had minor depression (15%), and 1 (10%) was not depressed compared to 281 (93.4%) who did not have suicidal plans. Those who had suicidal plans were more likely to have greater frequency of alcohol abuse, psychiatric disorders especially major depression, a previous personal history of cerebrovascular accidents, and sensory deficits compared to those who had not. Suicidal patients were younger, had poorer social functioning, and greater cognitive impairment than nonsuicidal patients. 57 patients were diagnosed with MDD, of which 15 (26.3%) reported suicidal plans and 42 did not have a plan. Depressed patients who reported suicidal plans had greater social withdrawal and brooding than depressed patients without suicidal plans.</td>
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<td>Authors evaluated only suicidal thoughts without investigating suicidal behavior so they were unable to know whether these patients attempted or died by suicide. Patients with deficits in comprehension were excluded; therefore, findings may be not applicable to all patients with stroke. Participants were predominantly of low socioeconomic status; so, the findings may not be generalizable to other socioeconomic classes.</td>
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<td>Kishi et al. [15]</td>
<td>Longitudinal case-control study</td>
<td>24 months</td>
<td>301 patients (cases with acute-onset n = 20, delayed-onset n = 16, controls n = 117) evaluated for suicidal plans after acute stroke</td>
<td>16 (11.3%) who did not have suicidal plans at the initial evaluation developed suicidal plans later, including 2 who attempted suicide, 7 after 6 months, 3 after 12 months, and 6 after 24 months. 10 of them had an initial diagnosis of MDD, 2 minor depression and 4 are not depressed vs. 117 who never developed suicidal plans over 24 months. Greater frequency of alcohol abuse in acute-onset suicidal patients than in delayed-onset or nonsuicidal groups. Higher frequency of previous cerebrovascular accidents in both acute- and delayed-onset suicidal groups than in nonsuicidal group. Acute-onset suicidal patients were younger, had poorer social functioning, and greater cognitive impairment than nonsuicidal patients. 57 patients were diagnosed with MDD, of which 15 (26.3%) reported suicidal plans and 42 did not have a plan. Depressed patients who reported suicidal plans had greater social withdrawal and brooding than depressed patients without suicidal plans.</td>
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<td>Katayama et al. [25]</td>
<td>Case reports of suicides</td>
<td>No</td>
<td>6 (n = 5 men, n = 1 woman) patients who died unexpectedly by suicide within 6 months after stroke</td>
<td>4 patients attempted suicide, 2 survived None were diagnosed with MDD prior to stroke</td>
<td>Small sample size that did not allow findings to be generalized No data from any statistical analysis The study was retrospective in nature; therefore, it may be subject to recall bias</td>
</tr>
<tr>
<td>Scott et al. [27]</td>
<td>Retrospective study, data from</td>
<td>No</td>
<td>37,915</td>
<td>Those who had a heart attack and stroke were more likely (OR 1.9; 1.1–3.5) to have lifetime attempts in the total sample as well as among ideators with a plan (OR 2.7; 0.9–8.0) and to have lifetime ideation in the total sample (OR 1.9; 1.3–2.8)</td>
<td>The study did not directly investigate the association between stroke and suicide but rather the association between suicide and several physical conditions Retrospective self-reports of the occurrence and timing of suicidal behavior, mental disorders, and covariates such as childhood adversity Possible bias in terms of sample selection: mixed results about stroke and heart attack were reported Physical conditions that were assessed via self-report</td>
</tr>
<tr>
<td>Tang et al. [20]</td>
<td>Cross-sectional survey</td>
<td>No</td>
<td>595 patients with acute ischemic stroke admitted in Hong Kong from 2005 to 2008</td>
<td>76 patients (12.8%) reported suicidality Subjects who reported suicidality scored higher on the Fatigue Severity Scale (FSS) than those without suicidality Association between fatigue and suicidality is independent of depression</td>
<td>Having recruited an hospital-based sample may preclude generalizability of findings to patients treated in other settings</td>
</tr>
<tr>
<td>Voaklander et al. [28]</td>
<td>Case–control study</td>
<td>No</td>
<td>3601 (cases n = 602, controls n = 2999) evaluated between 1993 and 2002</td>
<td>55 (10%) patients with stroke died by suicide compared to 2865 who did not</td>
<td>The study did not directly investigate the association between stroke and suicide</td>
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<td>Placido et al. [29]</td>
<td>Time series of 27 years between 1979 and 2005</td>
<td>No</td>
<td>3,364,908 deaths from suicide, ischemic heart disease or stroke</td>
<td>Incidence of death from suicide was positively correlated with ischemic heart disease and stroke ($r = 0.92; P &lt; 0.0001$)</td>
<td>Potential underestimation of comorbidities. The study was retrospective in nature. Authors did not include several variables (e.g., social isolation, loss of spouse, family history of suicide) known to be risk factors for suicide in the elderly. The study did not directly investigate the association between stroke and suicide. Time-series analysis may suffer from several limitations, especially the association between life events in different subjects. Cardiovascular risk related to highly lethal events was underestimated. Cardiovascular risk in suicide is underestimated because of early death.</td>
</tr>
<tr>
<td>Forsstrom et al. [24]</td>
<td>Retrospective population-based study of suicide victims in northern Finland from 1988 to 2007</td>
<td>No</td>
<td>2,283 suicide victims</td>
<td>75 (3.4%) patients suffered from stroke. 80% were not under the influence of alcohol. Compared to other victims, suicide victims were about 20 years older and more often women. Approximately 70% of suicide victims with a previous stroke suffered from pre-stroke depression compared to 30% who never suffered from depression</td>
<td>Data derived from only patients who needed hospitalization. The study did not include a control group. The severity of stroke in suicide victims was not evaluated.</td>
</tr>
<tr>
<td>Teasdale et al. [23]</td>
<td>Retrospective study</td>
<td>No</td>
<td>114,098 patients discharged from hospital during 1979 and 1993</td>
<td>359 suicides occurred in the study. Standardized mortality ratio (SMR) was greater in men than in women. SMR greatest in patients under 50 and lowest for patients 80 or older and relatively severe cases. Suicides were negatively related to duration of hospitalization, suicidal risk was lowest for those hospitalized for more than 3 months and highest for those hospitalized for less than 2 weeks.</td>
<td>Over 50% of the diagnoses of stroke were of the undefined subtype. Recording of suicide as cause of death may be unreliable and under-reported. There are no data on laterality of stroke.</td>
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<tr>
<td>Stenager et al.</td>
<td>Retrospective study</td>
<td>No</td>
<td>37,869</td>
<td>Risk factors for suicide is greatest up to about 5 years after stroke. 140 (7.2%) died by suicide. Stroke increases suicidal risk especially in the age group up to age 60 and in women.</td>
<td>The study did not include a control group. The study was retrospective in nature.</td>
</tr>
<tr>
<td>Rao [17]</td>
<td>Case–control study</td>
<td>No</td>
<td>100 subjects of which 75 were cases (25 patients with TIA, 25 patients with PVD, 25 patients with stroke), 25 controls aged 65 years or older.</td>
<td>Peripheral vascular disease (PVD) patients did not perform significantly worse than control subjects on any of the neuropsychological tests. The PVD group differed significantly from the stroke group on all neuropsychological tests except on aspects of frontal lobe function (verbal fluency F and BDCS) and memory; the TIA group only differed from the stroke group on the Trail-Making Test and verbal fluency S. The general pattern of neuropsychological impairment appears similar in patients with TIA and in those with PVD, suggesting some similarity in etiopathological mechanisms. TIA may result in more prolonged cognitive impairment, particularly in frontal lobe function. This group may be at increased risk of vascular dementia as well as impulsivity and suicide.</td>
<td>Small sample size. Patients included in this study may have cognitive impairment potentially influencing neuropsychological performance.</td>
</tr>
<tr>
<td>Pohjasvaara [16]</td>
<td>Longitudinal follow-up study</td>
<td>15 months</td>
<td>286 patients</td>
<td>The frequency of suicidal ideas was found to be high at both 3 and 15 months of follow-up after stroke. Patients with suicidal ideas were not more cognitively disabled in comparison with patients without suicidal ideas. Patients with stroke have been shown to have an increased risk of suicide. The frequency of suicidal ideas increased with the time elapsed from stroke.</td>
<td>Authors assessed only suicidal ideas instead of suicidal behavior, so they did not know whether someone attempted suicide or died by suicide.</td>
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Table 1 (Continued)

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<tr>
<td>Chan et al. [21]</td>
<td>Case-control study</td>
<td>No</td>
<td>172 patients (cases were 84, controls were 74)</td>
<td>Depression was the main correlate of suicidal ideas at 3 months after stroke, but at 15 months after stroke, suicidal ideas were also correlated with more disabling and right-sided stroke, especially in patients with a history of previous strokes. A higher CVRF score (derived by the weighted sum of severities of specific factors) was reported in cases (8.01 ± 6.46) than in controls (4.97 ± 3.81) Risk factors for cerebrovascular diseases confer higher risk for suicide in middle aged and older adults</td>
<td>Prevalence of affective disorders in the community controls was higher than the medium value previously reported, which was probably due to sampling bias Systematic misclassification of suicide because of different criteria adopted by judicial systems across different socio-cultural settings</td>
</tr>
<tr>
<td>Fuller-Thomson et al. [19]</td>
<td>Case-control study</td>
<td>No</td>
<td>132,221 patients</td>
<td>7.4% of patients with stroke were depressed, whereas only 5.2% were depressed without stroke Suicidal ideation: 15.2% in cases; 9.4% in controls After adjusting for socio-demographic factors, stroke survivors had twice the odds of depression (OR: 2.21) and suicidal ideation (OR: 2.07) After a reduction in functional limitation and activities in daily living limitations, both ORs (OR depression: 1.29; OR suicidal ideation: 1.37) decreased Functional limitations confer a higher risk of developing suicidal ideation Higher frequency of both depression and suicidal ideation in Caucasian and younger individuals</td>
<td>The cross-sectional nature of the sample precluded the causal interpretation of study variables. The authors did not know the information regarding treatment received or stroke’s severity or when it occurred Sample was biased toward healthier individuals with stroke because of its exclusion of institutionalized individuals</td>
</tr>
<tr>
<td>Santos et al. [18]</td>
<td>Cross-sectional study</td>
<td>No</td>
<td>177 (104 men, 73 women) acute stroke patients</td>
<td>27 patients (15%) developed suicidal thoughts and 6 (22%) had a plan to die by suicide, but none completed the act. Among these, 23 (85%) were depressed, 13 (48%) had a previous mood disorder, and 5 (19%) had a recurrent stroke. 63</td>
<td>Lack of long-term follow-up data Small part of sample was probably not reliable because of cognitive impairment Young age of the sample limits the external validity of the results</td>
</tr>
<tr>
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<tr>
<td>Garden et al. [26]</td>
<td>Case report study</td>
<td>No</td>
<td>2</td>
<td>Neither patient expressed suicidal thoughts, but both developed poststroke depression</td>
<td>Small sample size that did not allow findings to be generalized</td>
</tr>
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Table 1 (Continued)

Patients were depressed without suicidal ideation. After conducting a logistic regression analysis, suicidal thoughts were more frequent in patients with a lower educational level (OR: 5.13), previous mood disorder (OR: 4.22), diabetes and acute depression (OR: 7.82). Acute depression, previous mood disorder, low educational level are independent risk factors for suicidal thoughts in stroke patients.
berg [23] concluded that the high risk period for suicide was 5 years after stroke; however, the authors did not consider the accelerated effect that depression has on suicidal behaviors. Conversely, Forsstrom et al. [24] recommend that suicide risk should be assessed and monitored not only in the long-term follow-up, but also during the 2 years immediately following stroke.

Moreover, two case reports [25,26] have investigated the association between stroke and suicide providing further support for this relation. Katayama et al. [25] evaluated 6 patients who attempted suicide within 6 months after stroke and hypothesized that these cases might have similar underlying organic processes contributing to both stroke and suicide attempts. The results revealed that four out of the six patients suffered from depression and five of the six patients evidenced a moderate disability following stroke. In a second case study, retrospective analysis of medical records was examined from two patients who developed mood disorders in the acute poststroke period and eventually went on to die by suicide, be suicide. The researchers found that although neither patient openly expressed suicidal thoughts, both developed poststroke depression, highlighting the importance of assessing for depressive symptoms and suicidality during the rehabilitation period following stroke [26]. In Table 1, we reported the findings from two additional studies [27–29] that are of particular interest, although they included mixed samples. Those studies did not directly investigate the role of stroke in suicidality but substantially confirmed the role of stroke as a risk factor for both attempted and completed suicide.

### Discussion

The findings from the current review suggest that patients who have suffered a stroke are at an increased risk of suicide. Stroke patients commonly develop depression following their stroke, which significantly contributes to suicidal ideation, attempts, and completed suicide. Further, the existing literature suggests that patients should be closely monitored for depression and suicide during the 5 years following stroke. Regarding age and gender, suicide rates among stroke victims seemed to have increased in the younger population and decreased among the elderly as well as occurred more frequently in women [30,31]. However, given that stroke usually affects people age 65 and older, suicide victims who had suffered from a stroke were about 20 years older than suicide victims who had never suffered a stroke [3].

Although there were only two studies that indicated having a diagnosis of a previous mood disorder in general and prestroke depression in particular could be a clinical determinant for suicide, several studies considered in this review demonstrated that most patients who developed suicidal ideation and plans or died by suicide after a stroke were depressed. This finding suggests that assessing for a diagnosis of depression and/or depressive symptomatology is critical for preventing suicide in patients who have suffered a stroke as a result of disease. Also, these findings are in line with the study conducted by Arciniegas and Anderson [10] who reported that a suicide attempt and completed suicide were significantly associated with depression, feelings of hopelessness or helplessness, and social isolation in patients with neurological disorders.

The role of depression in suicide after stroke is an important issue given that the depression is the most common psychiatric complication after stroke and is highly associated with suicidality. Kouwenhoven et al. [32], in fact, argued that poststroke depression (PSD) is one of the most prevalent affective disorders after stroke and occurs in at least one quarter of all stroke survivors during the first year. In this longitudinal study, the researchers described the lived experience as it develops over time among stroke survivors suffering from early depressive symptoms. Depressive following stroke is a complex phenomenon and is not fully understood. The onset of depressive symptoms following stroke may be the result of a brain injury or a psychological reaction, which may complicate and delay stroke rehabilitation, contributing to poorer outcomes and increased functional dependence as compared to nondepressed stroke survivors. Furthermore, PSD may also become chronic in nature or even lead to death [28,30].

Generally, having an affective disorder is considered a major health problem and is often a burden impeding effective medical care [33]. Major depression has been identified as an independent stroke risk factor [34]. Also, subjects with major depression and bipolar disorder have a greater prevalence of established risk factors for vascular disease, including diabetes mellitus [35–38], obesity, [39–45], and less consistently hypertension [46–51].

Another major issue concerns adherence to treatment. Untreated depression (and particularly untreated bipolar disorder) is a significant predictor of negative outcome in patients having affective disorders. Medication nonadherence is a relevant obstacle to translating treatment efficacy from research settings into effectiveness in clinical practice [52]. Estimates of medication nonadherence for unipolar and bipolar disorders range from 10 to 60%; reduced adherence is associated with increased suicide risk. Extended courses of medication may be critical in improving the long-term outcome of patients with affective disorders [52]. Although effective treatment strategies exist, they are frequently misused in clinical practice; therefore, more efforts should be directed to improve treatment adherence among patients with major affective disorders to decrease patient symptoms burden, stroke risk, mortality and suicidal risk as well as to enhance poststroke healthcare utilization [52,53]. Early identification and treatment for depressive symptoms may significantly reduce suicidal risk in stroke patients [20].

Overall, the nature of the relationship between depression and stroke mortality is not well understood and many questions remain regarding prevention and treatment. Although depression after stroke has been associated with greater mortality, it is not entirely clear whether depression is a contributor to poststroke mortality as an individual risk factor or as an independent factor negatively influencing other stroke risk factors [54].

Other additional factors such as affective temperaments and personality dimensions may play a relevant role in determining the link between stroke and depression and contributing to suicide risk [55–58]. Personality disorders may have a marked impact on patients’ interpersonal relationships, and social and occupational functioning leading to problematic interactions in the medical setting. The treatment for medical and psychiatric disorders is
more complicated in patients with comorbid personality disorders [55]. Moreover, affective temperaments may be useful tools in screening and identifying those affective disorder patients, particularly bipolar patients who are at higher risk of suicidal behavior [56,57]. An increase in behavioral and emotional disorders has also been observed after stroke in childhood. Daseking et al. [58] investigated 111 children aged 3–18 years who suffered a stroke and found that children may be at higher risk of behavioral (social and attention) and school-based problems related to stroke. Subjects with perinatal stroke and stroke in childhood had more behavioral and temperamental problems when compared to children with stroke in infancy. Further research in this area is warranted to elucidate the relationship between depression and suicide in stroke victims.

This review has a number of limitations. First, no meta-analytic technique has been used to evaluate the results. Secondly, the authors chose to report those studies available in the literature that could support a broad analysis of the topic so as to offer a tutorial study. Despite a careful and systematic search, we extrapolated those studies that presented original data; however, a number of additional articles could have been added as useful sources of information.

Conclusion

Stroke confers substantial risk for suicide, particularly in young adults and in women. The factors most frequently implicated in suicide among stroke victims are poststroke depression, previous mood disorder, prior history of stroke, and cognitive impairment. Given the frequency of stroke and poststroke depression, clinicians should assess and monitor depression in stroke patients, particularly during the rehabilitation period, to reduce suicide risk.

Conflict of Interest

The authors declare no conflict of interest.

References


