Original Article

# Impact of Libido at 2 Weeks after Stroke on Risk of Stroke Recurrence at 1-Year in a Chinese Stroke Cohort Study

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## Abstract

**Background:** There were few studies on the relation between changes in libido and incidence of stroke recurrence. The aim of this study was to investigate the relationship between libido decrease at 2 weeks after stroke and recurrent stroke at 1-year.
**Methods:** It is a multi-centered, prospective cohort study. The 14th item of the Hamilton Depression Rating Scale-17 was used to evaluate changes of libido in poststroke patients at 2 weeks. Stroke recurrence was defined as an aggravation of former neurological functional deficit, new local or overall symptoms, or stroke diagnosed at re-admission.
**Results:** Among 2341 enrolled patients, 1757 patients had completed follow-up data, 533 (30.34%) patients had decreased libido at 2 weeks, and 166 (9.45%) patients had recurrent stroke at 1-year. Multivariate logistic regression analysis showed that, compared with patients with normal libido, the odds ratio (*OR*) of recurrent stroke in patients with decreased libido was reduced by 41% (*OR* = 0.59, 95% confidence interval [*CI*]: 0.40–0.87). The correlation was more prominent among male patients (*OR* = 0.52, 95% *CI*: 0.31–0.85) and patients of ≥60 years of age (*OR* = 0.57, 95% *CI*: 0.35–0.93).
**Conclusions:** One out of three stroke patients in mainland China has decreased libido at 2 weeks after stroke. Decreased libido is a protective factor for stroke recurrence at 1-year, which is more prominent among older male patients.

**Key words:** Libido; Prospective Study; Recurrence; Stroke

## Introduction

Decreased libido is a common sexual dysfunction among middle-aged and older people. Najman *et al*.'s group reported that, in the normal population, 16% of 50–59 years old male and 41% of 66–74 years old male had decreased libido.[1] Mitchell *et al*.[2] reported that nearly 40% of females aged between 66 and 74 years had decreased libido. The incidence of decreased libido was even higher than 50% in patients with stroke in Hong Kong.[3] Previous studies have shown that among population without stroke history, decreased libido was strongly associated with erectile dysfunction (odds ratio [*OR*] = 4.38, 95% confidence interval [*CI*]: 1.39–13.82).[4] Chung *et al*.[5] also reported that in similar population erectile dysfunction is associated with increased risk of first onset stroke. In a meta-analysis of prospective cohort studies, erectile dysfunction is associated with increased risk of newly onset and recurrent stroke by 35% (relative risk = 1.35, 95% *CI*: 1.19–1.54).[6] Based on these evidence, it is reasonable to anticipate a possible association between decreased libido and newly onset or recurrent stroke. Previous epidemiological studies have shown that stroke was the leading cause for disability in China as well as in the other countries.[7,8] Libido is important for human beings. However, the relation between the two conductions remains unclear, as there were few studies on the relation between changes in libido and incidence of stroke recurrence, and almost no study was about Chinese stroke population. This study was performed based on partial data of the prospective cohort study on incidence and outcome of patients with poststroke depression in China, which was

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the first large-scale national multi-center prospective cohort study on poststroke depression in mainland China.[9] The aim of this study was to investigate the relation between decreased libido and stroke recurrence among Chinese stroke population. We hypothesized that early stage decreased libido is related with risk of recurrent stroke at 1-year after stroke.

## Methods

The current study was a multi-centered prospective cohort study performed among 56 secondary or tertiary hospitals during April 2008 to April 2010 in mainland China. Study protocol and related information can be found in our previous published paper.[9] This study was a *post-hoc* subgroup analysis to investigate the impact of libido decrease at 2 weeks after stroke on the risk of stroke recurrence at 1-year. This study was approved by the Ethic Committee of Beijing Tiantan Hospital and was in compliance with the principal of *Declaration of Helsinki*. All patients or legal representatives signed the informed consent form.

### Key inclusion and exclusion criteria

Patients who were admitted into hospital consecutively and met the following inclusion criteria were recruited: (1) Age ≥18 years old; (2) acute stroke, which was defined as sudden onset of focal or overall nerve function deficit, lasting more than 24 h, with no apparent disturbance caused by other than that of vascular origin (primary and metastatic neoplasm, dural hematoma, postseizure paralysis, head trauma, etc.), based on the World Health Organization criteria.[10] Acute stroke included cerebral infarction, intracerebral hemorrhage, and subarachnoid hemorrhage (SAH), which were affirmed by computerized tomography or magnetic resonance imaging;[10] (3) onset of stroke was within 14 days. Exclusion criteria includes: (1) Unable to finish a psychiatric examination due to reduced level of consciousness, unable to understand the questionnaires, hearing impairment, aphasia, or dysarthria, etc.; (2) unwilling or unable to be followed-up.

### Baseline variables at admission

The recorded baseline data included: (1) Demographic features; (2) risk factors for stroke recurrence: Hypertension (defined as a history of hypertension or administration of antihypertensive drugs), mellitus diabetes (defined as a history of diabetes or administration of lower glucose drugs), hyperlipidemia (defined as a history of hyperlipidemia or administration of lower lipid drugs), a history of stroke, cardiovascular disease, smoking (defined as a current smoker or smoked within 1 month), or excess drinking alcohol (defined as ≥5 standard alcohol per day); (3) clinical features: National Institutes of Health Stroke Scale (NIHSS) score at admission,[11] systolic pressure, diastolic pressure (the auscultatory method of blood pressure [BP]) measurement with mercury was used within 24 h after admission. The operators were trained with standardized technique, and the patient must be properly prepared and positioned. At least two measurements were made and the average of the measurement was recorded),[12] stroke types; (4) interventions: Use of thrombolytic drugs, anti-platelet or, anticoagulation drugs, antidepressants, lipid lowering drugs, glucose lowering drugs, and whether a patient received stroke education. Detailed contents and methods can be found in our previous paper.[9]

### Libido evaluation at 2 weeks after stroke

Neurologists who had been trained to administer the Hamilton Depression Rating Scale interviewed patients at 2 weeks after the onset of stroke.[13] The 14$^{th}$ item is a questionnaire of "Do you have libido decrease?" The response choices include "no," "mild decrease", or "severe decrease" representing a score of 0, 1, or 2 respectively. In our study, normal libido was defined as "no" libido decrease (0 score); libido decrease was defined as "mild" (1 score) or "severe" (2 scores). Depression status of patients was also evaluated by the Diagnostic and Statistical Manual of Mental Disorders-IV.[14]

### Follow-up at 1-year after stroke

Stroke recurrence was defined as an aggravation of former neurological functional deficit, new local or overall symptoms (such as sudden aphasia, facial paralysis, limb weakness, or disturbance of consciousness, etc.), or stroke diagnosed at re-admission (including ischemic stroke, or cerebral hemorrhage or SAH).[15] Investigators who made follow-up were blind to patients' baseline status. Details of follow-up methods and contents are referred to our previous paper.[9]

### Statistical analysis

Logistic regression was used to explore the relationship between libido decrease and stroke recurrence. Model 1 was adjusted for age and gender. Model 2 was adjusted for age, gender, and other variables of significant difference at baseline between patients with or without recurrent stroke (including diabetes, personal stroke history, use of anti-hypertension medications), plus other risk factors for recurrent stroke (including hypertenion, hyperlipidemia, a history of cardiovascular disease, smoking, excess drinking alcohol), and the NIHSS score at admission. A $P < 0.05$ was considered statistically significant. SPSS 17.0 software was used for all data analysis (SPSS Inc., Chicago, IL, USA).

## Results

### Baseline variables

Among 2828 patients recruited in our study, 43 patients missed libido data at 2 weeks, 423 patients missed important data at baseline, 21 patients were lost to follow-up, 2341 patients were finally enrolled [Figure 1]. The 1757 patients (75.05%) had complete data on stroke recurrence at 1-year poststroke onset. Among these patients, 1139 (64.83%) were male with a mean age of 60.46 ± 11.73 years, and 618 (35.17%) were female with mean age of 63.62 ± 11.41 years. There were 1478 (84.12%) cases of ischemic stroke and 279 (15.88%) cases of hemorrhagic stroke at the baseline including 249 (14.17%) cases of cerebral hemorrhage and 30 (1.71%) cases of SAH.

Compared with patients without complete data, fewer patients with complete data had a history of smoking (41.89% vs. 48.80%, $P$ = 0.004) and stroke education (84.63% vs. 88.36%, $P$ = 0.027), but more patients had history of ischemic stroke (84.12% vs. 77.57%, $P$ = 0.000) and anti-platelet drug usage (81.56% vs. 74.49%, $P$ = 0.000). There were no statistical differences in other variables between the two groups.

Among 1757 patients with complete data at 1-year poststroke, there were 166 (9.45%) cases of recurrent stroke. Compared with patients without recurrent stroke, the patients with recurrent stroke were older (65.11 years vs. 61.20 years, $P$ = 0.000) and more patients had history of diabetes (29.52% vs. 22.75%, $P$ = 0.050), history of stroke (34.94% vs. 22.19%, $P$ = 0.000), and anti-hypertension drug usage (64.46% vs. 56.69%, $P$ = 0.054). There was no statistical difference in depression between patients with or without recurrent stroke [Table 1].

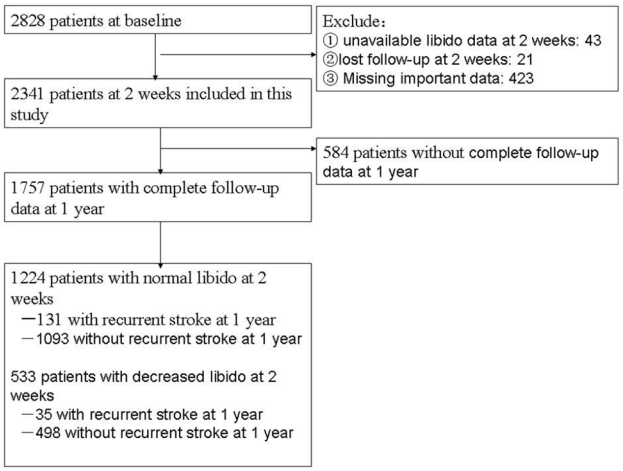


**Figure 1:** Patient inclusion chart.

## Relation between libido decrease at 2 weeks after stroke and stroke recurrence at 1-year

Among 1757 patients with complete data at 1-year, 1224 (69.66%) patients had normal libido and 131 (7.46%) patients had recurrent stroke; In contrast, among 533 (30.34%) patients who had reported libido decrease, only 35 (1.99%) patients had recurrent stroke. Multivariates regression analysis revealed that in Model 1, after adjusting for age and gender, the risk of stroke recurrence at 1-year in patients with libido decrease at 2 weeks poststroke was reduced by 42% ($OR$ = 0.58, 95% $CI$: 0.39–0.85); Similarly, in Model 2 after adjustment for further potential confounder variables, the risk of stroke recurrence at 1-year in patients with libido decrease at 2 weeks after stroke was reduced by 41% ($OR$ = 0.59, 95% $CI$: 0.40–0.87) [Figure 2].

We further analyzed the different impacts of libido decrease in female and male patients on the risk of stroke recurrence at 1-year. In 1139 male patients, 353 (30.99%) patients had reported libido decrease, in which 21 (1.84%) patients had recurrent stroke at 1-year. The risk of stroke recurrence at 1-year was markedly decreased by 48% ($OR$ = 0.52, 95% $CI$: 0.31–0.85) when comparing to male patients without decreased libido [Figure 2]. In 618 female patients, 180 (29.13%) patients had reported libido decrease, in which 14 (2.27%) patients had recurrent stroke at 1-year. Interestingly, unlike

**Table 1: Comparison of baseline variates between patients with and without recurrent stroke**

| Characteristics* | Without recurrent stroke ($n$ = 1591) | With recurrent stroke ($n$ = 166) | $P$ |
|---|---|---|---|
| Age, years, mean (SD) | 61.20 (11.68) | 65.11 (11.44) | <0.000 |
| Female | 556 (34.95) | 62 (37.35) | 0.537 |
| Diabetes | 362 (22.75) | 49 (29.52) | 0.050 |
| Hyperlipidemia | 339 (21.31) | 35 (21.08) | 0.947 |
| Hypertension | 1053 (66.18) | 121 (72.89) | 0.081 |
| Smoking | 666 (41.86) | 70 (42.17) | 0.939 |
| Excess drinking alcohol | 63 (3.96) | 4 (2.41) | 0.320 |
| Cardiovascular disease history | 364 (22.88) | 42 (25.30) | 0.481 |
| Previous stroke history | 353 (22.19) | 58 (34.94) | <0.000 |
| SBP at admission, mmHg, mean (SD) | 151.55 (24.01) | 151.17 (23.05) | 0.843 |
| DBP at admission, mmHg, mean (SD) | 89.17 (14.44) | 88.78 (13.73) | 0.735 |
| NIHSS score at admission, median (IQR) | 4 (2–7) | 4 (2–7) | 0.183 |
| Ischemic stroke | 1330 (83.60) | 148 (89.16) | 0.062 |
| Intravenous thrombolysis | 31 (1.95) | 3 (1.81) | 0.900 |
| Anticoagulation drugs | 226 (14.20) | 30 (18.07) | 0.179 |
| Antihypertension drugs | 902 (56.69) | 107 (64.46) | 0.054 |
| Antiplatelet drugs | 1292 (81.21) | 141 (84.94) | 0.238 |
| Lowering lipid drugs | 924 (58.08) | 91 (54.82) | 0.419 |
| Lowering blood glucose drugs | 393 (24.70) | 52 (31.33) | 0.062 |
| Stroke education | 1347 (84.66) | 140 (84.34) | 0.912 |
| Depression | 454 (28.54) | 56 (33.73) | 0.160 |

Data are shown as $n$ (%) except where otherwise indicated. *SD: Standard deviation; IQR: Interquartile range; NIHSS: National Institutes of Health Stroke Scale; SBP: Systolic blood pressure; DBP: Diastolic blood pressure.

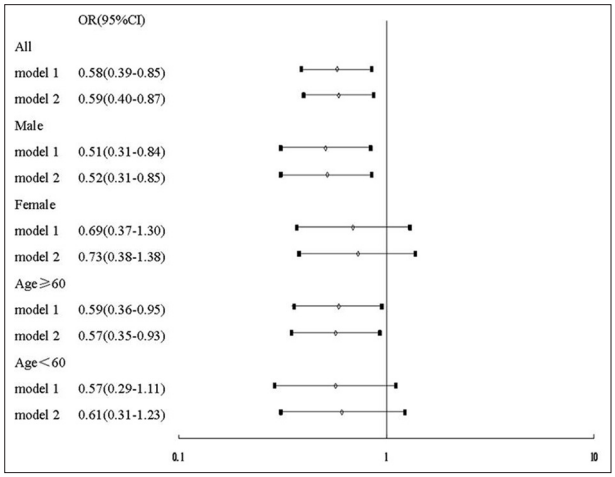


**Figure 2:** Adjusted odds ratios (95% confidence interval) of recurrent stroke at 1-year in patients with decreased libido versus those with normal libido. Model 1: Adjusted for age and gender. Model 2: Adjusted for age, gender, and other variates of significant difference at baseline between patients without and with recurrent stroke (including diabetes, personal stroke history, antihypertension drugs), plus other risk factors for recurrent stroke (including hypertenion, hyperlipidemia, a history of cardiovascular disease, and smoking, excess drinking alcohol) and National Institutes of Health Stroke Scale at admission.

to what's observed in male patients, the risk of recurrent stroke was not significantly reduced in female patients with decreased libido compared to female patients without libido decrease (*OR* = 0.73, 95% *CI*: 0.38–1.38) [Figure 2].

We performed the statistical analysis on differential impacts of the libido decrease on the risk of stroke recurrence at 1-year poststroke in patients of ≥60 years of age and patients of <60 years of age. Among 970 patients aged ≥60 years, there were 308 (31.75%) patients exhibited decreased libido 2 weeks after the stroke, among which 24 (2.47%) patients had reported recurrent stroke at 1-year. Compared with patients with normal libido, the risk of recurrent stroke at 1-year was significantly reduced by 43% in patients with decreased libido (*OR* = 0.57, 95% *CI*: 0.35–0.93) [Figure 2]. For patients of <60 years of age, 225 out of 787 (28.59%) patients reported decreased libido and 11 (1.40%) patients had recurrent stroke at 1-year; The risk of developing recurrent stroke was not significantly different when comparing to patients without decreased libido at 2 weeks after the stroke (*OR* = 0.61, 95% *CI*: 0.31–1.23) [Figure 2].

## Discussion

In our study, nearly 1 out of 3 patients had reported decreased libido at 2 weeks after stroke, and the risk of stroke recurrence at 1-year in patients with decreased libido was reduced more than 40%. In order to exclude the impact of common risk factors and common psychological factors (including depression) on stroke recurrence,[16] these variables were adjusted in the multivariates regression models. The outcomes from adjusted multivariates regression models consistently indicated the protective effects of libido decrease at 2 weeks poststroke on stroke recurrence at 1-year. However, as other factors such as socialeconomical factors, urinary system diseases, hormone levels, or reproductive system diseases, may also influence libido or risk of stroke recurrence, there might be a strong relation but not causal association between libido decrease and lack of stroke recurrence. In addition, although there were no significant difference in risk factors (including hypertension, hyperlipedemia, diabetes, a history of stroke, and a history of cardiovascular disease, etc.), between patients with or without complete data of stroke recurrence, there was higher rate in smoking status in patients without complete 1-year data at follow-up. As this population accounts for 24.95% of our study, our conclusion should not be extrapolated to all general populations simply.

To our knowledge, there were few literatures about the association between libido decrease in poststroke patients and the risk of stroke recurrence. Studies from both Möller *et al*. and Muller reported that the risk of myocardial ischemia at 2 h after sexual intercourse in patients with coronary heart disease was increased 1.7 times (*OR* = 2.70, 95% *CI*: 1.30–6.50).[17,18] Similar to coronary heart disease, sexual intercourses can increase the risk of stroke recurrence possibly due to elevation of BP during sexual intercourse, which may lead to atheromatous plaque fracture,[19] consequently causing formation of arterial embolism or acute thrombosis. Meanwhile, increased BP is known to be a common risk factor for hemorrhagic cerebral stroke. Additionally, elevation of chest pressure during sexual intercourse may result in thrombus entering into left heart from right atrium and vena cava system in a few patients with patent foramen ovale, which further induces cerebral artery embolism.[20] A third possible reason is that during sexual intercourse, cerebral oxygen demand can increase, which may induce the deterioration of poorly perfused brain tissue and turn it into infracted tissue. Lastly, elevation of sympathetic nerve activity during sexual intercourse may be accompanied with cerebral arteriospasm, which further aggravates cerebral ischemia.[21,22] Hence, we speculated that libido decrease may reduce the risk of stroke recurrence via decreasing sexual activities as a result of decreased libido. This may explain the protective effect of libido decrease on stroke recurrence. More evidence in depth from prospective studies need to be done in order to confirm the hypothesis.

We found that libido decrease played a more distinct role in stroke recurrence in male patients compared to female patients. Previous studies reported that sexual dysfunction was associated with atherosclerosis in arterial bed of supplying pelvic cavity.[23] Additionally, morbidity rate of atherosclerosis was higher in male than that in female,[24] which may contribute to the differential effect of decreased libido on stroke recurrence in male patients in our study. Previous studies showed that mechanisms of sexual dysfunction in female and male patients were different.[25] However, whether this is a key reason for the differential impacts of libido decrease on stroke recurrence is not clear. In our study, libido decrease had a more prominent role in reducing the risk of stroke recurrence in patients aged ≥60 years, which may be due to the fact that age is a risk factor for stroke recurrence.[26] The relationship between

libido and the risk of stroke recurrence by different age and gender still requires further in-depth study.

Some limitations in our study still need to be taken into consideration. First, libido decrease was not measured by special scale, which would influence its reliability, although there was certain degree of comparability as the questionnaire for libido decrease in our study were similar to that of formal scale.[27] Second, patients with critical conditions were not enrolled into our study. The study results should be extrapolate with caution when applying to general stroke populations. Third, survival analysis was not performed because of great loss of data at 1-year after stroke (24.95%) that would consequently affect statistical power. Lastly, as this study was a *post-hoc* subgroup analysis, some confounding factors like sex hormone and variables that may affect on stroke recurrence such as body mass index were not available. Nevertheless, results from multivariates regression analysis models were in consistency, which strengthened reliability of our conclusions. Although the study has some limitations, it's the first nationwide multi-centered large-scale correlation study on the association between libido changes and stroke recurrence of stroke patients in mainland China. It provides critical evidence for clinical physicians and stroke patients in China under the context of relatively conservative sex culture and rare related studies.

In conclusion, nearly one out of three patients with acute stroke in mainland China had libido decrease at 2 weeks. Libido decrease could reduce the risk of stroke recurrence at 1-year. This protective effect was more prominent in senior male patients.

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