Original Article

Relationship between hysterectomy and stroke in National Health and Nutrition Examination Survey (NHANES) 2007–2018: a cross-sectional study

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Background: Hysterectomy is the most common type of gynecological operation in the United States. However, complications can occur during or after the operation. Some studies suggest that hysterectomy may increase the risk of stroke. However, other studies have found different conclusions on this matter. This inconsistent conclusion may be due to small sample sizes or limited covariates. So, we sought to further investigate the correlation between hysterectomy and stroke.

Methods: Our analysis was based on the data from 2007–2018 National Health and Nutrition Examination Survey (NHANES). We excluded participants with missing hysterectomy data (Question "Have you had a hysterectomy, including a partial hysterectomy, that is, surgery to remove {your/her} uterus or womb?"), participants with missing stroke data (Question "Has a doctor or other health professional ever told you that you had a stroke?), a total of 15,241 participants were included in our analysis. To estimate the correlation between hysterectomy and stroke, logistic regression models were used after adjusting for sociodemographic and health-related factors, including age, race, education level, marital status, annual family income, body mass index (BMI), alcohol consumption in the past 12 months, having smoked at least 100 cigarettes in a lifetime, hypertension, hypercholesterolemia, and diabetes.

Results: The unadjusted model suggests that women who had undergone a hysterectomy were 3.15 [95% confidence interval (CI): 2.67–3.71] times more likely to have a stroke than women who had not undergone a hysterectomy. In the crude and fully-adjusted models, the correlation between hysterectomy and stroke was consistent [odds ratio (OR)$_{\text{crude-adjusted}}$ =1.55 (95% CI: 1.30–1.85), OR$_{\text{fully-adjusted}}$ =1.36 (95% CI: 1.14–1.63)]. In the subgroup analysis stratified by age, hysterectomy seemed to have more risk for stroke occurrence regardless of subgroup, even after adjusting sociodemographic and health-related factors. Interestingly, the women who were less than or equal to 50 years old had greater odds of stroke (OR$_{\text{fully-adjusted}}$ =1.96) compared with women who were aged older than 50 (OR$_{\text{fully-adjusted}}$ =1.42).

Conclusions: In our study, we concluded hysterectomy may increase the risk of stroke. However, as our study is a cross-sectional study and unmeasured covariates may still exist, more researches are required to confirm this conclusion.

Keywords: Hysterectomy; stroke; National Health and Nutrition Examination Survey (NHANES)

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Introduction

Hysterectomy is the most common type of gynecological operation in the United States. Transabdominal, transvaginal, laparoscopic, or a combination of these techniques are used to perform hysterectomies (1). However, complications can occur during or after the operation, such as intestinal or urinary injuries, and postoperative chronic pain (2). Further, some studies suggest that hysterectomy may increase the risk of hypertension (3), diabetes (4), stroke (5), thyroid cancer (6,7), renal cell carcinoma (8), and bipolar disorder (9). Findings of a correlation between hysterectomy and stroke are controversial.

Hypertension, diabetes, obesity, smoking, and endogenous steroid hormones deficiency are major risk factors for stroke (10). Some studies have shown the that the endogenous steroid hormones of women decrease following hysterectomy (11,12), which may increase the risk of stroke (13). In a nationwide study in Sweden, hysterectomy was associated with an increased risk of stroke in women under the age of 50 (14). However, other studies have reported conflicting results. A nested cohort study shows that hysterectomy didn't increase the risk of cardiovascular disease (15). The opposite conclusion may due to small sample size and different covariates included. Given the conflicting findings, it is necessary to re-confirm the correlation between hysterectomy and stroke. The National Health and Nutrition Examination Survey (NHANES) is a representative survey of the national population of the United States, providing multitudinous information about the nutrition and health of the general United States population using a complex, multistage, probability sampling design (16). So, we used this database to further analyze the relationship between hysterectomy and stroke. We present the following article in accordance with the STROBE reporting checklist (available at https://atm.amegroups.com/article/view/10.21037/atm-22-4681/rc).

Methods

Study population

The NHANES is a national survey designed to determine the health and nutritional status of people in the United States. The data of this cross-sectional survey has been released biennially since 1999. In our study, a total of 15,241 female participants were selected from 2007 to 2018. A flow diagram detailing the selection process for participants in this study is shown in *Figure 1*. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

Hysterectomy

Question RHD280 in the "Reproductive Health" section of the NHANES 2007–2018 asked, "Had a hysterectomy? [Have you had a hysterectomy, including a partial hysterectomy, that is, surgery to remove (your/her) uterus or womb?]". Based on an answer of "yes" or "no" to this self-report question, the participants were categorized into "hysterectomy" and "non-hysterectomy" groups, respectively.

Outcomes (stroke)

Question MCQ160F in the "Medical Conditions" section of the NHANES 2007–2018 asked, "Have you ever been told you had a stroke? (Has a doctor or other health professional ever told you that you had a stroke?)". Based on an answer of "yes" or "no" to this self-report question, the participants were categorized into the "stroke" and "non-stroke" groups, respectively.

Covariates

Based on previous studies (13,14), a number of covariates may have affected the relationship between hysterectomy and stroke in our study, including age, race, education level, marital status, annual family income, body mass index (BMI), alcohol consumption in the past 12 months, having smoked at least 100 cigarettes in a lifetime, hypertension, hypercholesterolemia, and diabetes.

Statistical analysis

The statistical analyses were conducted using EmpowerStats software. Descriptive analyses were conducted to assess the distribution of participants' demographic and other characteristics between females who had and who had not undergone a hysterectomy. The continuous variables are described as the mean ± standard deviation. The categorical variables are described as the number (percentage). P values less than 0.05 were considered significant. Logistic regression models were used to explore the correlation between hysterectomy and stroke. Odds ratios (ORs) and 95% confidence intervals (95% CIs) were obtained. We used a crude-adjusted model controlling for age and race, and a fully-adjusted model controlling for all of the

covariates mentioned above.

Results

Females who had suffered a stroke differed to those who had not suffered a stroke in relation to a number of demographic and health-related characteristics (see *Table 1*).

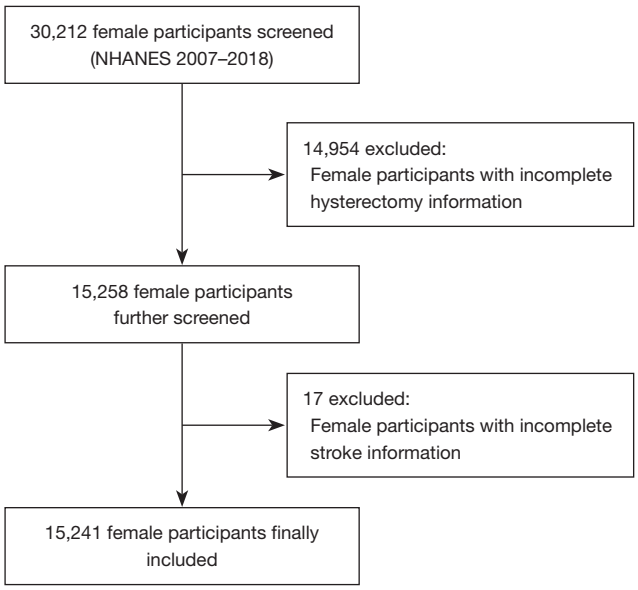

Figure 1 Flow diagram of the selection of eligible participants from the NHANES 2007–2018. NHANES, National Health and Nutrition Examination Survey.

Compared to those who had not suffered a stroke, the participants who had suffered a stroke were older, and most were aged ≥40 years (aged 40–49: 19.41% *vs.* 17.40%, aged 50–59: 16.30% *vs.* 16.18%, aged 60–69: 24.54% *vs.* 17.23%, aged ≥70: 44.54% *vs.* 15.91%). Additionally, compared to the non-stroke group, there were more non-Hispanic White participants (49.08% *vs.* 40.60%), non-Hispanic Black participants (28.07% *vs.* 21.32%), participants with an education level less than high school (57.98% *vs.* 44.48%), married participants (90.59% *vs.* 81.97%), and participants with an annual family income below $20,000 (37.31% *vs.* 22.73%) in the stroke group. Our study also showed that hypercholesterolemia (57.65% *vs.* 32.48%), hypertension (78.15% *vs.* 36.03%), diabetes (31.76% *vs.* 12.17%) and having smoked at least 100 cigarettes in a lifetime (51.26% *vs.* 34.86%) all differed significantly between the 2 groups (P<0.05 for each).

We found a positive correlation between hysterectomy and stroke in all 3 models [non-adjusted model: OR =3.15 (95% CI: 2.67–3.71); crude-adjusted model: OR =1.55 (95% CI: 1.30–1.85); fully-adjusted model: OR =1.36 (95% CI: 1.14–1.63)]. These results are presented in *Table 2*.

There was a significant association between hysterectomy and stroke in the participants aged ≥20 years. In the subgroup analysis, which was stratified by age, we found the positive correlation between hysterectomy and stroke in all models (aged ≤50: $OR_{\text{non-adjusted model}}$ =4.06, $OR_{\text{crude-adjusted model}}$ =3.83, $OR_{\text{fully-adjusted model}}$ =1.96; aged >50: $OR_{\text{non-adjusted model}}$ =1.75, $OR_{\text{crude-adjusted model}}$ =1.66, $OR_{\text{fully-adjusted model}}$ =1.42).

Table 1 Characteristics of the study sample with and without stroke

Characteristics	Total (n=15,241)	Non-stroke (n=14,646)	Stroke (n=595)	P value*
Hysterectomy or not				<0.001
Hysterectomy	3,470 (22.77)	3,192 (21.79)	278 (46.72)	
Non-hysterectomy	11,771 (77.23)	11,454 (78.21)	317 (53.28)	
Age group (years)				<0.001
20–29	2,462 (16.15)	2,452 (16.74)	10 (1.68)	
30–39	2,444 (16.04)	2,423 (16.54)	21 (3.53)	
40–49	2,604 (17.09)	2,548 (17.40)	56 (19.41)	
50–59	2,466 (16.18)	2,369 (16.18)	97 (16.30)	
60–69	2,670 (17.52)	2,524 (17.23)	146 (24.54)	
≥70	2,595 (17.03)	2,330 (15.91)	265 (44.54)	
BMI (kg/m^2)	29.146±7.927	29.553±8.104	29.038±9.239	0.439

Table 1 *(continued)*

Table 1 *(continued)*

Characteristics	Total (n=15,241)	Non-stroke (n=14,646)	Stroke (n=595)	P value*
Race				<0.001
Mexican American	2,296 (15.06)	2,250 (15.36)	46 (7.73)	
Other Hispanic	1,709 (11.21)	1,667 (11.38)	42 (7.06)	
Non-Hispanic White	6,238 (40.93)	5,946 (40.60)	292 (49.08)	
Non-Hispanic Black	3,290 (21.59)	3,123 (21.32)	167 (28.07)	
Other	1,708 (11.21)	1,660 (11.33)	48 (8.07)	
Education level				<0.001
Less than high school	6,859 (45.00)	6,514 (44.48)	345 (57.98)	
Above high school	8,362 (54.87)	8,113 (55.39)	249 (41.85)	
Missing	20 (0.13)	19 (0.13)	1 (0.17)	
Marital status				<0.001
Married	12,545 (82.31)	12,006 (81.97)	539 (90.59)	
Unmarried	2,687 (17.63)	2,631 (17.96)	56 (9.41)	
Missing	9 (0.06)	9 (0.06)	0 (0.00)	
Annual family income				<0.001
Below $20,000	3,551 (23.30)	3,329 (22.73)	222 (37.31)	
Above $20,000	11,459 (75.19)	11,094 (75.75)	365 (61.34)	
Missing	231 (1.52)	223 (1.52)	8 (1.34)	
Hypercholesterolemia				<0.001
Yes	5,100 (33.46)	4,757 (32.48)	343 (57.65)	
No	9,483 (62.22)	8,458 (57.75)	223 (37.48)	
Missing	1,460 (9.58)	1,431 (9.77)	29 (4.87)	
Hypertension				<0.001
Yes	5,742 (37.67)	5,277 (36.03)	465 (78.15)	
No	9,483 (62.22)	9,354 (63.87)	129 (21.68)	
Missing	16 (0.10)	15 (0.10)	1 (0.17)	
Diabetes				<0.001
Yes	1,971 (12.93)	1,782 (12.17)	189 (31.76)	
No	12,889 (84.57)	12,505 (85.38)	384 (64.54)	
Missing	381 (2.50)	359 (2.45)	22 (3.70)	
Smoked at least 100 cigarettes in a lifetime				<0.001
Yes	5,411 (35.50)	5,106 (34.86)	305 (51.26)	
No	9,822 (64.44)	9,532 (65.08)	290 (48.74)	
Missing	8 (0.05)	8 (0.05)	0 (0.00)	
Alcohol consumption in the past 12 months	2.376±1.490	2.472±1.474	2.551±1.085	0.195

Mean ± standard deviation for the continuous variables. N (percentage) for the categorical variables. *, the Kruskal-Wallis rank-sum test was used for the continuous variables. If the frequency of the categorical variables was <10, Fisher's exact probability analysis was used. BMI, body mass index.

Table 2 Association between hysterectomy and stroke

Groups	Non-adjusted model, OR (95% CI)	Crude-adjusted model, OR (95% CI)	Fully-adjusted model, OR (95% CI)
Non-hysterectomy	Reference	Reference	Reference
Hysterectomy	3.15 (2.67, 3.71)	1.55 (1.30, 1.85)	1.36 (1.14, 1.63)

The non-adjusted model was adjusted for nothing. The crude-adjusted model was adjusted for age and race. The fully-adjusted model was adjusted for age, race, education level, marital status, annual family income, BMI, alcohol consumption in the past 12 months, having smoked at least 100 cigarettes in a lifetime, hypertension, hypercholesterolemia, and diabetes. BMI, body mass index; OR, odds ratio; CI, confidence interval.

Table 3 Association between hysterectomy and stroke in different age ranges

Groups	Non-adjusted model, OR (95% CI)	Crude-adjusted model, OR (95% CI)	Fully-adjusted model, OR (95% CI)
Age ≤50 years			
Non-hysterectomy	Reference	Reference	Reference
Hysterectomy	4.06 (2.44, 6.74)	3.83 (2.30, 6.38)	1.96 (1.13, 3.42)
Age >50 years			
Non-hysterectomy	Reference	Reference	Reference
Hysterectomy	1.75 (1.46, 2.09)	1.66 (1.38, 1.99)	1.42 (1.18, 1.72)

No covariates were adjusted in the non-adjusted model. The crude-adjusted model was adjusted for race. The fully-adjusted model was adjusted for race, education level, marital status, annual family income, BMI, alcohol consumption in the past 12 months, having smoked at least 100 cigarettes in a lifetime, hypertension, hypercholesterolemia, and diabetes. BMI, body mass index; OR, odds ratio; CI, confidence interval.

Interestingly, the women who were less than or equal to 50 years old had greater odds of stroke ($OR_{fully\text{-}adjusted}$ =1.96) compared with women who were aged older than 50 ($OR_{fully\text{-}adjusted}$ =1.42). These results are presented in *Table 3*.

Discussion

We used the data of NHANES 2007–2018 in this multi-model observation study. The results of the 3 models in this study are consistent, and indicate that hysterectomy may be associated with an increased risk of stroke. In China, the mean age for natural menopause is 48–52 years (17). For patients in this age range, doctors always suggest that patients undergo a hysterectomy rather than a lesion resection due to uterine fibroids or adenomyoma of the uterus. Thus, we divided the participants into 2 groups according to the age of 50 years. In the subgroup analysis, which was stratified by age, the women who were less than or equal to 50 years old had greater odds of stroke compared with women who were aged older than 50 in the 3 models.

Our findings are in line with those of previous studies. For example, in a Swedish national study (14), hysterectomy was associated with an increased risk of stroke [hazard ratio (HR) 2.22 (95% CI: 1.01–4.83)], especially in females aged <50 years. In another cohort study in Taiwan, similar results were reported even after adjusting for covariates related to cardiovascular disease (18). Poorthuis *et al.* found that women who had hysterectomy had 6% higher risks of ischemic stroke. This relative risk (RR) was more extreme at younger age of surgery (19). However, contradictory results have been reported in other studies. For example, a prospective cohort study with a follow-up period >6 years in Korea concluded that hysterectomy is not associated with an increased risk of either ischemic or hemorrhagic stroke at any age (20). However, this study did not consider possible confounders, such as smoking, obesity and other medical diseases involving the risk factors of stroke. In a systematic review and meta-analysis, hysterectomy was considered a protective factor against stroke (RR =0.88 (95% CI: 0.85–0.90) in women who underwent hysterectomy *vs.* no hysterectomy]. However, this study did not explain why hysterectomy is the protective factor for stroke (21).

There is some evidence explaining the risk of stroke in females who have undergone a hysterectomy. Notably,

there is some evidence that there is a biological basis for the increased risk of stroke in females who have undergone a hysterectomy. Specifically, research has shown that a hysterectomy interferes with the ovarian blood flow supply, which leads to a decrease in ovarian function and estrogen levels (22,23). Several studies have concluded that compared to pre-menopausal females, follicle stimulating hormone levels are elevated and estrogen levels are low in patients after a hysterectomy without an oophorectomy (11,12,24,25). Low estrogen levels leave blood vessels unprotected (26). In our study, females aged <50 years had higher OR values. This may be related to the reasons above.

Our study had a number of strengths. First, we used a population-based data set comprising millions of subjects. After screening, 15,241 participants were included in our study. Second, the large sample of females in the United States who completed the NHANES guarantee less spurious findings. Third, our rigorous methodology, including 3 distinct models, led to consistent results, and we also took the influence of age into account.

However, it should be noted that this study had some limitations. First, because of the cross-sectional design of the study, we were unable to ascertain whether the strokes occurred before or after the hysterectomies were performed. Second, unmeasured confounding factors may have existed in this study.

Conclusions

Hysterectomy may increase the risk of stroke. It is not yet clear whether the surgery itself leads to stroke; however, doctors and patients should take this possibility into account when considering options for treating benign diseases of the uterus.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://atm.amegroups.com/article/view/10.21037/atm-22-4681/rc

Conflicts of Interest: Both authors have completed the ICMJE uniform disclosure form (available at https://atm.amegroups.com/article/view/10.21037/atm-22-4681/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

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