

# Five-year stroke rate in women with signs and symptoms of ischemia undergoing coronary angiography: a retrospective study from the NHLBI-sponsored Women's Ischemia Syndrome Evaluation (WISE)

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## Objective

Cardiovascular diseases including coronary artery disease and cerebrovascular disease remain major causes of morbidity, disability and death in most industrialised countries. Mortality from stroke is the fourth leading cause of death in the United States and a leading cause of long-term severe disability.<sup>1</sup> Stroke represents a disproportionate percentage of cardiovascular events in women compared to men and inclusion of stroke better predicts risk in women.<sup>2–4</sup> Prior Women's Ischemia Syndrome Evaluation (WISE) studies have determined elevated five-year major adverse cardiac event rates in women with signs and symptoms of ischemia and non-obstructive coronary artery disease, including a relatively high (2.5–5.2%) frequency of stroke. We explored the clinical setting and validation of these stroke events.<sup>5</sup> This study was approved by the site's internal review board and written informed consent was obtained for all subjects.

## Design

We conducted a retrospective chart review of self-reported stroke in a single Women's Ischemia Syndrome Evaluation centre of subjects enrolled 1998–2003.

## Setting

All women underwent clinically indicated coronary angiography, which was quantitatively and qualitatively evaluated for the presence and extent of coronary artery disease by the Women's Ischemia Syndrome Evaluation angiographic core laboratory

(obstructive coronary artery disease:  $\geq 50\%$  stenosis, non-obstructive coronary artery disease:  $\geq 20$  and  $< 50\%$ , and no coronary artery disease:  $< 20\%$  luminal stenosis in  $\geq 1$  epicardial coronary artery). All coronary segments with any visual abnormality (even luminal irregularities) were measured quantitatively with a computer-based edge detection algorithm or electronic calipers.<sup>5</sup>

## Participants

All participants in WISE are women with signs and symptoms of ischemia who underwent a baseline physical examination.<sup>4,5</sup> Demographic data, medical history and symptoms were collected. Cardiac risk was assessed using a self-report questionnaire inquiring for cardiac risk factors.

## Main outcome measures

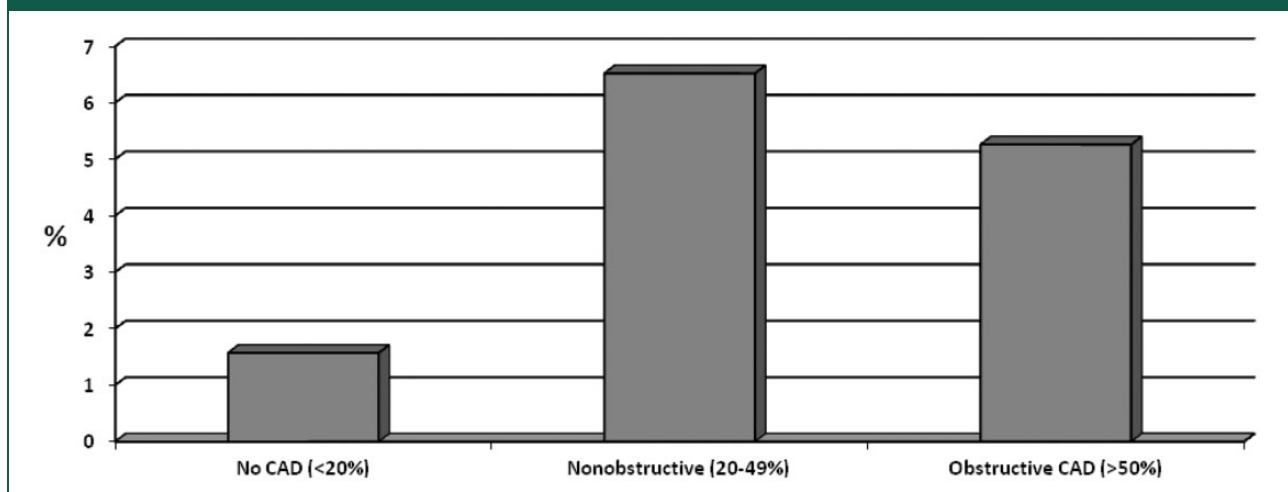
The definition of stroke used was a new onset neurological defect of central origin confirmed by brain imaging (CTA or MRI) evidence of cerebral infarction or intracerebral hemorrhage, as diagnosed by the treating physician and medical records. Three physicians separately reviewed medical charts in 2012 for the cases to confirm stroke/TIA history.

## Results

Among the 240 subjects enrolled, 61 dropped out or were lost to follow-up and 19 died, leaving 160 available with five-year follow-up. Demographic data of the subjects are shown in Table 1. Overall, 14 subjects reported stroke (9%). Among these 14 subjects, nine had available medical records to review (64%) and

**Table 1.** Demographics.

Baseline characteristics	No stroke (N = 153)	Confirmed stroke (N = 7)	p
Age (yrs ± SD)	57 ± 10	53 ± 11	0.35
Body mass index (±SD)	32 ± 8	30 ± 5	0.54
Systolic blood pressure (mmHg ± SD)	134.9 ± 20	148.6 ± 37	0.36
Diastolic blood pressure (mmHg ± SD)	75.9 ± 11	79.5 ± 11	0.38
Race (%)			1
African American	19	14	
Hispanic	2	0	
Caucasian	78	86	
Other	1	0	
Former smoker (%)	37	29	0.54
Current smoker (%)	22	43	0.54
History of HTN (%)	58	57	1
History of dyslipidemia (%)	56	100	0.08
History of diabetes (%)	29	57	0.24
Antihypertensive medication (%)	44	43	1
Aspirin (%)	57	43	0.53
Statin (%)	24	29	1

**Figure 1.** Confirmed stroke rates in women with and without obstructive CAD ( $p = 0.63$  across groups).

seven (78%) were confirmed to be strokes. For the two women with unconfirmed strokes, one had syncope with a negative stroke evaluation, while the second case had a negative stroke workup in the

setting of cirrhosis and liver transplant. Stroke rates were similar in women with and without obstructive coronary artery disease, although underpowered to detect group differences (Figure 1).

## Conclusions

Among women with signs and symptoms of ischemia undergoing coronary angiography for suspected ischemia, stroke was confirmed in the majority of cases. While stroke was most commonly associated with obstructive coronary artery disease, a relatively high rate was observed in subjects with non-obstructive coronary artery disease. While the current study results may not represent all women with suspected ischemic heart disease, future study should be directed at mechanistic studies and intervention trials aimed at improved understanding of stroke in this population.

## Declarations

**Competing interests:** None declared

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**Ethical approval:** All participants provided written informed consent, and all participating sites obtained Institutional Review Board approval.

**Guarantor:** NBM

**Contributorship:** AH coordinated the data analysis and wrote the first draft and finalized the manuscript; MZ participated in the analysis and writing and approved the final manuscript; PKM participated in the analysis and writing and approved the final manuscript; CS participated in the analysis and writing and approved the final manuscript; GL participated in the analysis and writing and approved the final manuscript; SD participated in the analysis and writing and approved the final manuscript; JP

participated in the analysis and writing and approved the final manuscript; EH participated in the analysis and writing and approved the final manuscript; BDJ participated in the analysis and writing and approved the final manuscript; CJP participated in the analysis and writing and approved the final manuscript and obtained the funding; DL participated in the analysis and writing and approved the final manuscript; SL participated in the analysis and writing and approved the final manuscript and CNBM participated in the analysis and writing and approved the final manuscript and obtained the funding.

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