

ORIGINAL RESEARCH

Annual Trends in Risk Factor Control Status at the Time of Ischemic Stroke in South Korea

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BACKGROUND: This study aimed to evaluate secular trends in the control of major risk factors at the time of ischemic stroke to assess the real-world implementation of prevention guidelines and identify areas needing greater clinical attention for improved early stroke outcomes.

METHODS: We retrospectively analyzed data from a prospective, multicenter, nationwide registry of consecutive patients with acute ischemic stroke between 2011 and 2022. For risk factor controls of interest, hypertension, diabetes, dyslipidemia, and atrial fibrillation (AF) were considered. Well-controlled risk factors were defined as follows: “well-controlled hypertension”: hypertension with prior antihypertensive medication and systolic blood pressure <140 mmHg on admission; “well-controlled diabetes”: prior antidiabetic medication with glycated hemoglobin <7.0%; “well-controlled dyslipidemia”: prior statin therapy with low-density lipoprotein cholesterol <100 mg/dL; and “well-controlled AF”: presence of AF with prior oral anticoagulant use. Linear trends in control rates were tested via the Cochran–Armitage and linear contrast tests.

RESULTS: Among 76 962 patients (68.8±13.3 years; men, 59.0%), the adjusted rate of well-controlled hypertension decreased from 35.7% (95% CI, 34.0%–37.5%) in 2011 to 25.5% (95% CI, 24.4%–26.7%) in 2022, whereas well-controlled status improved for diabetes (26.4%–29.4%), dyslipidemia (22.2%–48.6%), and AF (26.0%–55.7%) from 2011 to 2022 ($P_{\text{trend}} < 0.001$). The rates of well-controlled risk factors were relatively higher in patients with a history of stroke than in those with no history of stroke, except for hypertension. The 3-month composite of stroke, myocardial infarction, and all-cause death significantly declined from 10.0% in 2011 to 8.6% in 2022 ($P_{\text{trend}} < 0.001$).

CONCLUSIONS: Our study confirmed a continuous increase in prestroke risk factor control, including diabetes, dyslipidemia, and AF, but the rate remained suboptimal at stroke onset. These findings may help inform strategies to improve risk factor management by identifying priority areas that warrant targeted intervention in clinical practice and population-level guidelines.

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Key Words: acute ischemic stroke ■ annual change ■ early outcome ■ risk factor ■ risk factor control

CLINICAL PERSPECTIVE

What Is New?

- This study examined how well common vascular risk factors are managed before stroke onset in South Korea over a 12-year period and how these trends may be related to early stroke outcomes.
- Over the past 12 years, the control of dyslipidemia, diabetes, and atrial fibrillation has improved among patients who experienced ischemic stroke; however, hypertension control declined during the same period, highlighting a gap in prevention efforts.

What Are the Clinical Implications?

- These longitudinal trends in risk factor control highlight both progress and persistent gaps in stroke prevention practices and these findings may help inform region-specific strategies and public health policies by identifying priority areas, such as hypertension control, that warrant targeted intervention in clinical practice and population-level guidelines.

Nonstandard Abbreviations and Acronyms

APC	annual percent change
CRCS-K-NIH	Clinical Research Collaborations for Stroke in Korea–National Institutes for Health
NOAC	non-vitamin K antagonist oral anticoagulant
TST	Treat Stroke to Target

Stroke is a significant cause of death and disability worldwide, particularly among older adults. Control of major vascular risk factors—hypertension, dyslipidemia, diabetes, and atrial fibrillation (AF)—is fundamental for reducing the stroke burden.^{1,2} Prestroke risk factor control, defined as appropriate medication use with guideline-recommended biomarker targets at stroke onset, has been linked to milder stroke severity and better outcomes.^{3–6}

Despite guideline recommendations,^{7,8} real-world control remains suboptimal: fewer than half of patients with hypertension achieve blood pressure (BP) goals,⁹

and statin use for dyslipidemia is especially low in primary prevention.^{10,11} These observations raise concerns about health care quality and emphasize the need to evaluate temporal changes in control status and outcomes. However, limited contemporary data exist on how well vascular risk factors are controlled at stroke onset and whether these rates have changed over time.

Therefore, using a large, prospective multicenter stroke registry, the aims of this study were to (1) examine annual trends in the proportion of patients with adequately controlled risk factors at the time of ischemic stroke between 2011 and 2022 and (2) examine whether changes in the proportion of patients with adequately controlled risk factors over time coincide with shifts in 3-month functional outcomes to infer a potential relationship.

METHODS

Subjects

This study was a retrospective analysis of a prospective, multicenter, nationwide registry of consecutive patients with acute stroke or transient ischemic attack admitted to 18 academic hospitals in South Korea, the CRCS-K-NIH (Clinical Research Collaborations for Stroke in Korea–National Institutes for Health) registry.^{12,13} Patients with acute ischemic stroke, confirmed by a positive ischemic lesion on diffusion-weighted imaging and apparent diffusion coefficient within 7 days of onset and admitted between January 2011 and December 2022 were included in the analysis for the study. Patients without information on glycated hemoglobin (HbA_{1c}), plasma glucose, and low-density lipoprotein cholesterol (LDL-C) levels at admission were excluded (Figure S1).

Data Collection

Demographic, clinical, imaging, and laboratory data were prospectively collected with standardized protocols. The monthly meetings of the steering committee monitored the completeness and consecutiveness of case registration throughout the study. For risk factor controls of interest, hypertension, diabetes, dyslipidemia, and AF were considered. In our registry, the presence of risk factors was determined via a combination of self-reported data, medical records, and laboratory measurements during the hospital stay. Hypertension was defined as (1) clinically diagnosed hypertension (history of hypertension) or (2) use of antihypertensive medication. Diabetes was defined as (1)

clinically diagnosed diabetes (history of diabetes), (2) use of insulin or antidiabetic agents, or (3) HbA_{1c} level $\geq 6.5\%$ at admission. Dyslipidemia was defined as (1) clinically diagnosed dyslipidemia (history of dyslipidemia), (2) use of lipid-lowering medication, or (3) LDL-C ≥ 130 – 160 mg/dL or total cholesterol ≥ 200 to 240 mg/dL at admission. AF (including paroxysmal or persistent) was defined as (1) a history of AF or (2) AF detected on the basis of in-hospital tests. Prior medication use was defined as the use of relevant drugs for at least 1 month before stroke onset, confirmed by self-reports, medical records, or prescription data.

Definition of Risk Factor Controls

For this study, prestroke risk factor control, specifically, “well-controlled” status at the time of the index stroke, was assessed via both medication history and admission biomarker levels: For example, although LDL-C < 100 mg/dL may suggest adequate lipid control, patients not receiving statin therapy were not classified as well controlled given the importance of statins in improving outcomes.^{14–17} “Well-controlled hypertension” was defined as prior antihypertensive use with an admission systolic blood pressure (SBP) < 140 mm Hg.^{18,19} To address the limitation that poststroke BP elevation is common and that defining control solely by admission SBP may be problematic, we also analyzed trends in patients with “hypertension and on antihypertensive,” regardless of admission SBP. “Well-controlled diabetes” was defined as prior use of antidiabetic medication with an admission HbA_{1c} $< 7.0\%$.²⁰ “Well-controlled dyslipidemia” was defined as prior statin use with an admission LDL-C < 100 mg/dL.²¹ “Well-controlled AF” was defined as prior use of oral anticoagulants before stroke. To complement this definition, we also examined annual trends in patients with AF treated with non-vitamin K antagonist oral anticoagulants (NOACs) or with warfarin within the therapeutic range (international normalized ratio, 1.7–3.0). Temporary discontinuation of NOACs before admission may have contributed to stroke occurrence, which we recognize as a limitation of the study. We additionally analyzed the proportion of patients who achieved target levels of SBP, LDL-C, and HbA_{1c} regardless of treatment status to examine trends in biomarker control independent of prior medication use.

For each risk factor, the rate of well-controlled status was defined as the proportion of patients with that risk factor who met the criteria for well-controlled status.

Patient Follow-Up and Additional Outcomes

Three months after initial ischemic stroke admission, patients were followed up by trained research coordinators via face-to-face or telephone interviews

via a standardized interview protocol.^{12,13} The outcomes analyzed were as follows: (1) a composite of stroke (either ischemic or hemorrhagic), myocardial infarction, and all-cause death; (2) recurrent stroke; and (3) all-cause death.

Ethics Statement

Clinical information was collected from the CRCS-K-NIH registry with approval from the local institutional review boards of all the participating centers. A waiver for informed consent was provided because of study subject anonymity and minimal risk to the participants.

Data Availability

The data used in this study are available upon reasonable request to the corresponding author. Access to the data requires the submission of a legitimate academic research proposal, which will be reviewed and approved by the steering committee.

Statistical Analysis

The general characteristics are presented as the means $\pm$ SDs or medians with interquartile ranges for continuous variables and numbers and percentages for categorical variables. To obtain the *P* values for linear trends in baseline characteristics according to the 3 time periods, the Cochran–Armitage trend test, Mantel–Haenszel χ^2 test, and linear contrast test for ANOVA were used for categorical variables and continuous variables. Missing values for continuous variables were imputed using the median value of each variable. For categorical variables, missing entries were replaced with a reference or absence category. The following parameters had missing data, and the proportions of missing values were as follows: height (2.0%), weight (1.2%), creatinine (0.1%), hemoglobin (0.5%), platelet count (0.1%), and white blood cell count (0.1%). Linear trends in risk factors and rates of well-controlled risk factors were tested with the Cochran–Armitage trend test and the linear contrast test in logistic regression. The linear contrast test in logistic regression was performed to evaluate the linear trend of the adjusted rates of well-controlled risk factors, where the adjusted variables were considered to be the clinical relevance of risk factor control before ischemic stroke: age, sex, body mass index, history of stroke, history of coronary artery disease, history of transient ischemic attack, and history of peripheral artery disease. Additionally, to identify changes in the trend of adjusted rates of well-controlled risk factors, joinpoint regression was estimated via the Joinpoint Regression Program.²² By fitting segmented linear regression models to the

data, joinpoint analysis can identify points at which the rate of change in the data significantly deviates. The average annual percentage change (APC) is then calculated on the basis of these identified joinpoints, providing a comprehensive understanding of the average annual percentage change.

The log-rank test for trend and a linear contrast test in Cox proportional hazards regression were used to evaluate the statistical significance of changes in survival outcomes according to the calendar year. To examine the associations between calendar year and outcomes, a marginal Cox model with a robust variance estimator was used to account for the center effect.²³ Adjusted variables were considered clinically relevant variables for outcome as follows: age, sex, National Institutes of Health Stroke Scale score, body mass index, history of stroke, history of coronary artery disease, hypertension (control status), diabetes (control status), dyslipidemia (control status), AF (control status), large-artery steno-occlusion, reperfusion therapy, stroke subtypes, glucose, SBP, creatinine, and calendar year.

All the statistical analyses were performed via SAS software version 9.4 (SAS Institute Inc., Cary, NC). For the joinpoint analysis, we used the Joinpoint Regression Program version 5.0.2 (Statistical Research and Applications Branch, National Cancer Institute).

RESULTS

General Characteristics

In total, 76 962 patients (aged 68.8±13.3 years; men, 59.0%) were ultimately analyzed. The general characteristics of the study population at 4-year intervals from 2011 to 2022 are shown in Table 1. After the initial period of 2011 to 2014, there was an increase in the proportion of men, early arrivals within 24 hours of stroke onset, and minor strokes with a National Institutes of Health Stroke Scale score of 0 to 4. The mean age, weight, height, and body mass index of the study patients increased over time. Risk factors such as hypertension, diabetes, and dyslipidemia decreased from 2015 to 2018 but rose again from 2019 to 2022. However, the rates of prior anticoagulant and statin use continued to increase over time.

Annual Changes in Risk Factor Controls

The detailed annual changes in the 4 risk factors and control status at the time of ischemic stroke are shown in Tables S1 and S2 and Figure 1. In terms of well-controlled risk factors, well-controlled hypertension gradually decreased annually, whereas well-controlled diabetes, dyslipidemia, and AF increased with time (Table 2). The rates of well-controlled hypertension at the time of ischemic stroke decreased from 35.5%

in 2011 to 26.3% in 2022 (adjusted rates, 35.7% [95% CI, 34.0–37.5] and 25.5% [95% CI, 24.4–26.7], respectively). The rates of well-controlled diabetes increased over time, increasing from 26.6% in 2011 to 31.2% in 2022 ($P_{\text{trend}} < 0.001$) (adjusted rates, 26.4% and 29.4%, respectively; $P_{\text{trend}} = 0.02$). Well-controlled dyslipidemia increased from 23.8% in 2011 to 49.6% in 2022 (adjusted rates, 22.0% and 48.6%, respectively) during these 12 year-year intervals ($P_{\text{trend}} < 0.001$ in both analyses). Additionally, well-controlled AF increased from 14.6% in 2011 to 34.3% in 2022 (adjusted rates, 26.0% and 55.7%, respectively) over the same period. Supportive analyses of “hypertension and on antihypertensives” and “AF and on oral anticoagulants” (within the therapeutic range for warfarin or NOAC) are shown in Table S2, and controlled risk factor status regardless of prior medication is shown in Table S3 and Figure S2.

The joinpoint analysis of the APC in adjusted rates of well-controlled risk factors is shown in Figure 2. With respect to the rates of well-controlled hypertension, the APC was significantly different from the 0 point (APC, −4.03 [95% CI, −10.9 to −2.5]), with decreasing trends since 2013. For rates of well-controlled dyslipidemia, the APC was significantly different from the 0 point, and 2 joinpoints were observed in 2013 and 2020. For well-controlled AF, 1 joinpoint was observed in 2014 with increasing trends. However, for well-controlled diabetes, although an increasing pattern was observed over the study period, the APC was not statistically significant.

Risk Factor Controls by Subgroup

Annual changes in the rates of well-controlled risk factors in a predefined subgroup of patients with a “history of stroke” are shown in Tables S4 and S5 and Figure S3. The rates of well-controlled risk factors were relatively higher in patients with a history of stroke than in those with no history of stroke, except for hypertension.

Annual Changes in Early Vascular Outcome

The annual event rates of 3-month vascular outcomes are presented in Figure 3 and indicate significant trends toward decreasing event rates for the 3-month composite of stroke, myocardial infarction, and all-cause death ($P_{\text{trend}} < 0.001$); stroke ($P_{\text{trend}} = 0.02$); and all-cause death ($P_{\text{trend}} < 0.001$) (Table S6). After adjusting for relevant variables, similar trends were observed in the 3-month composite of stroke, myocardial infarction, and all-cause death, stroke, and all-cause death (Table S7). Joinpoint regression analyses are shown in Figure S4. From approximately 2011 to 2017, the 3-month composite of stroke, myocardial infarction, and all-cause

Table 1. General Characteristics of the Subjects According to the Time Period

	Total	2011–2014	2015–2018	2019–2022	<i>P</i> _{trend} value*
No.	76962	17964	26860	32138	
Age, y, mean±SD	68.8±13.0	67.8±12.8	68.5±12.9	69.6±13.2	<0.001
Male, n (%)	45415 (59.0)	10442 (58.1)	15673 (58.4)	19300 (60.1)	<0.001
Arrival within 24 h, n (%)	54394 (70.7)	12513 (69.7)	19033 (70.9)	22848 (71.1)	0.001
Height, cm, mean±SD	162.5±9.0	162.2±8.9	162.5±9.0	162.8±9.1	<0.001
Weight, kg, mean±SD	63.1±12.1	62.3±11.5	62.9±12.0	63.7±12.4	<0.001
Body mass index, mean±SD	23.8±3.6	23.6±3.5	23.7±3.5	23.9±3.7	<0.001
NIHSS, median (IQR)	3 (1–7)	4 (1–8)	4 (1–8)	3 (1–7)	<0.001
NIHSS score 0–4	45923 (59.7)	10395 (57.9)	15706 (58.5)	19822 (61.7)	<0.001
Prestroke modified Rankin Scale score 0–1, n (%)	67136 (87.2)	15295 (85.1)	23720 (88.3)	28121 (87.5)	<0.001
TOAST, n (%)					0.012
Large-artery atherosclerosis	26591 (34.6)	6451 (35.9)	8903 (33.1)	11237 (35.0)	
Small-vessel occlusion	13751 (17.9)	3094 (17.2)	4980 (18.5)	5677 (17.7)	
Cardioembolism	15856 (20.6)	3873 (21.6)	5675 (21.1)	6308 (19.6)	
Other pathogenesis	2619 (3.4)	399 (2.2)	922 (3.4)	1298 (4.0)	
Undetermined	18145 (23.6)	4147 (23.1)	6380 (23.8)	7618 (23.7)	
History of transient ischemic attack, n (%)	1334 (1.7)	380 (2.1)	437 (1.6)	517 (1.6)	<0.001
History of stroke, n (%)	15813 (20.5)	3710 (20.7)	5345 (19.9)	6758 (21.0)	0.123
History of coronary artery disease, n (%)	7150 (9.3)	1605 (8.9)	2353 (8.8)	3192 (9.9)	<0.001
History of peripheral artery disease, n (%)	642 (0.8)	100 (0.6)	165 (0.6)	377 (1.2)	<0.001
Hypertension, n (%)	51256 (66.6)	12314 (68.5)	17495 (65.1)	21447 (66.7)	0.003
Diabetes, n (%)	29312 (38.1)	7496 (41.7)	9740 (36.3)	12076 (37.6)	<0.001
Dyslipidemia, n (%)	24034 (31.2)	5612 (31.2)	7351 (27.4)	11071 (34.4)	<0.001
Current smoker, n (%)	17713 (23.0)	4570 (25.4)	6067 (22.6)	7076 (22.0)	<0.001
AF, n (%)	16032 (20.8)	3761 (20.9)	5703 (21.2)	6568 (20.4)	0.1
Prior antiplatelet, n (%)	21634 (28.1)	5377 (29.9)	7228 (26.9)	9029 (28.1)	<0.001
Prior anticoagulant, n (%)	4817 (6.3)	817 (4.5)	1606 (6.0)	2394 (7.4)	<0.001
Prior statin, n (%)	16906 (22.0)	3061 (17.0)	5328 (19.8)	8517 (26.5)	<0.001
Prior antihypertension, n (%)	39363 (51.1)	9691 (53.9)	13213 (49.2)	16459 (51.2)	<0.001
Prior antidiabetes, n (%)	19293 (25.1)	5013 (27.9)	6281 (23.4)	7999 (24.9)	<0.001
Large artery steno-occlusion, n (%)					<0.001
No	37317 (48.5)	8200 (45.6)	13095 (48.8)	16022 (49.9)	
Mild (<50%)	6796 (8.8)	1706 (9.5)	2295 (8.5)	2795 (8.7)	
Significant (>50%)	13327 (17.3)	3215 (17.9)	4497 (16.7)	5615 (17.5)	
Occlusion	19522 (25.4)	4843 (27.0)	6973 (26.0)	7706 (24.0)	
Reperfusion therapy, n (%)					<0.001
No	63662 (82.7)	15037 (83.7)	22075 (82.2)	26550 (82.6)	
Intravenous thrombolysis only	6518 (8.5)	1802 (10.0)	2360 (8.8)	2356 (7.3)	
Endovascular thrombectomy only	3750 (4.9)	426 (2.4)	1294 (4.8)	2030 (6.3)	
Combined intravenous thrombolysis+endovascular thrombectomy	3032 (3.9)	699 (3.9)	1131 (4.2)	1202 (3.7)	
White blood cell count, mean±SD	8.2±3.6	8.4±3.6	8.2±3.2	8.2±4.0	<0.001
Blood urea nitrogen, mg/dL, mean±SD	17.6±9.1	17.4±9.0	17.4±8.9	17.9±9.2	<0.001
Creatinine, mg/dL, mean±SD	1.01±0.90	1.01±0.90	1.01±0.90	1.02±0.90	0.131
Hemoglobin, mg/dL, mean±SD	13.6±2.1	13.6±2.0	13.6±2.0	13.6±2.1	0.157
Low-density lipoprotein, mg/dL, mean±SD	106.0±38.2	109.8±37.8	105.8±37.5	104.1±38.9	<0.001
Platelet count, mean±SD	229.9±74.9	229.8±78.6	230.5±73.6	229.4±73.8	0.575
Glycated hemoglobin, %, mean±SD	6.3±1.4	6.4±1.4	6.3±1.4	6.3±1.4	<0.001

(Continued)

Table 1. Continued

	Total	2011–2014	2015–2018	2019–2022	<i>P</i> _{trend} value*
Glucose, mg/dL, mean±SD	145.6±63.4	146.4±65.8	145.6±63.2	145.2±62.3	0.037
SBP, mmHg, mean±SD	149.0±27.9	146.7±27.1	147.5±27.5	151.5±28.6	<0.001
DBP, mmHg, mean±SD	85.0±16.5	85.2±15.9	84.1±16.0	85.5±17.1	0.038

AF indicates atrial fibrillation; DBP, diastolic blood pressure; NIHSS, National Institutes of Health Stroke Scale; SBP, systolic blood pressure; and TOAST, Trial of Org 10172 in Acute Stroke Treatment.

**P* value by the Cochran–Armitage trend test, the Cochran–Mantel–Haenszel test, and the linear contrasts test in ANOVA.

death significantly decreased, but there was no significant change from 2017 to 2022.

DISCUSSION

Our study, a prospective nationwide stroke registry in South Korea that analyzed 12 years of data from the CRCS-K-NIH registry and included >75 000 patients

with acute ischemic stroke, observed a rising annual trend in the proportion of patients with well-controlled prestroke risk factors, particularly dyslipidemia and AF. However, the overall rate of risk factor control at the time of stroke remained suboptimal. Although we were not able to directly analyze the causal relationship between improved risk factor control and outcomes, we noted a decreasing trend in the risk of early vascular events within 3 months over time. These findings

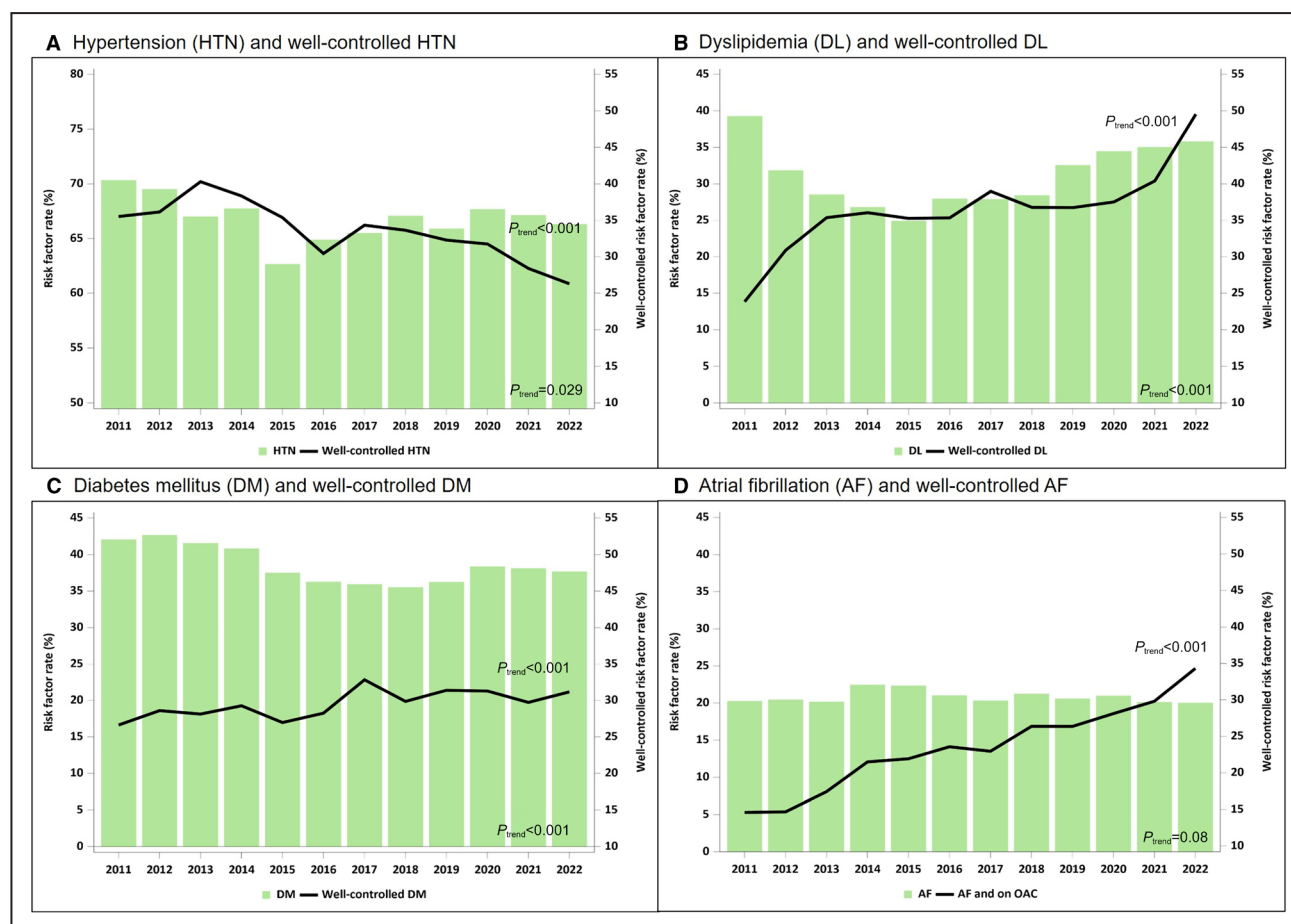


Figure 1. Annual proportions of risk factors and well-controlled risk factors.

A, Hypertension, **(B)** dyslipidemia, **(C)** diabetes, and **(D)** AF. The definitions of well-controlled risk factors were as follows: (1) well-controlled hypertension: prior antihypertensive therapy and admission SBP <140 mm Hg; (2) well-controlled diabetes: prior antidiabetic medication and admission HbA_{1c} <7.0%; (3) well-controlled dyslipidemia: prior statin medication and admission LDL-C <100 mg/dL; and (4) well-controlled AF: prior oral anticoagulant medication before stroke. AF indicates atrial fibrillation; DL, dyslipidemia; DM, diabetes; HbA_{1c}, glycated hemoglobin; HTN, hypertension; LDL-C, low-density lipoprotein cholesterol; OAC, oral anticoagulant; and SBP, systolic blood pressure.

Table 2. Annual Changes in Well-Controlled Risk Factors at the Time of Index Stroke, Unadjusted and Adjusted

	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	P _{trend} value*
No.	4123	3996	4608	5237	6326	6314	6724	7496	8488	7572	7932	8146	
Hypertension, n/N (%)	1030/2900 (35.5)	1004/2778 (36.1)	1244/3088 (40.3)	1360/3548 (38.3)	1402/3964 (35.4)	1247/4098 (30.4)	1512/4405 (34.3)	1691/5028 (33.6)	1806/5594 (32.3)	1627/5125 (31.7)	1512/5326 (28.4)	1420/5402 (26.3)	<0.001
Adjusted, % (95% CI)	35.7 (34.6–37.5)	36.4 (34.6–38.2)	40.6 (38.8–42.3)	38.5 (36.9–40.1)	35.3 (33.9–36.9)	30.4 (29.0–31.8)	34.2 (32.8–35.6)	33.4 (32.1–34.8)	31.9 (30.7–33.2)	31.1 (29.8–32.4)	27.9 (26.7–29.1)	25.5 (24.4–26.7)	<0.001
Dyslipidemia, n/N (%)	386/1620 (23.8)	393/1273 (30.9)	465/1315 (35.4)	506/1404 (36.0)	556/1577 (35.3)	624/1766 (35.3)	731/1876 (39.0)	784/2132 (36.8)	1015/2763 (36.7)	979/2610 (37.5)	1123/2780 (40.4)	1446/2918 (49.6)	<0.001
Adjusted, % (95% CI)	22.0 (19.9–24.1)	29.5 (26.9–32.1)	33.8 (31.1–36.5)	35.7 (33.1–38.4)	34.5 (32.0–37.0)	35.4 (33.1–37.8)	38.0 (35.7–40.4)	36.2 (34.1–38.4)	35.8 (34.0–37.8)	35.4 (33.5–37.3)	39.6 (37.7–41.5)	48.6 (46.7–50.5)	<0.001
Diabetes, n/N (%)	462/1735 (26.6)	488/1706 (28.6)	539/1916 (28.1)	626/2139 (29.3)	640/2373 (27.0)	647/2290 (28.3)	793/2415 (32.8)	795/2662 (29.9)	966/3077 (31.4)	909/2905 (31.3)	899/3024 (29.7)	957/3070 (31.2)	<0.001
Adjusted, % (95% CI)	26.4 (24.4–28.6)	28.4 (26.2–30.6)	28.6 (26.5–30.7)	29.2 (27.3–31.2)	26.6 (24.8–28.4)	28.2 (26.3–30.1)	32.2 (30.4–34.1)	29.1 (27.4–30.8)	30.1 (28.5–31.8)	29.6 (27.9–31.3)	28.2 (26.6–29.8)	29.4 (27.8–31.1)	0.018
AF, n/N (%)	122/836 (14.6)	120/818 (14.7)	162/930 (17.4)	253/1177 (21.5)	310/1414 (21.9)	313/1328 (23.6)	314/1368 (23.0)	420/1593 (26.4)	461/1749 (26.4)	447/1590 (28.1)	476/1597 (29.8)	560/1632 (34.3)	<0.001
Adjusted, % (95% CI)	26.0 (20.8–32.1)	26.6 (21.3–32.8)	32.1 (26.3–38.5)	38.4 (32.3–44.7)	39.7 (33.7–46.0)	41.0 (35.0–47.4)	40.8 (34.8–47.1)	44.7 (38.8–50.9)	45.6 (39.6–51.6)	48.5 (42.4–54.5)	51.0 (44.9–57.1)	55.7 (49.6–61.6)	<0.001

Adjusted variables: age, sex, body mass index, history of stroke, history of coronary artery disease, history of transient ischemic attack, and history of peripheral artery disease. N, number of patients with corresponding risk factors; n, number of patients with good control status. AF indicates atrial fibrillation.

*P value from the Cochran–Armitage trend test.

suggest that efforts to improve prestroke risk factor management have been partially successful, yet substantial gaps remain.

Controlling risk factors is crucial, particularly in primary and secondary prevention, where lifestyle modifications and appropriate pharmacotherapy are recommended for effective management.^{2,24–26} Our study revealed a progressive increase in the well-controlled status of prestroke risk factors over time. To address the possibility that improvements in risk factor control were merely due to an increased number of treated patients, we analyzed the proportion of patients who achieved target levels of LDL-C, HbA_{1c}, and SBP regardless of treatment status. As shown in Figure S2, target achievement trends closely mirrored those in the treated population, with minimal differences between the ever-treated and target-achieved groups. These findings suggest that improvements in prestroke risk factor management reflect both broader treatment coverage and more effective achievement of guideline-recommended targets.

Among the evaluated risk factors, dyslipidemia was associated with the most pronounced improvement in control status. The adjusted proportion of patients with well-controlled dyslipidemia increased by ≈26.6% during the study period, from 22.0% (95% CI, 19.9–24.1) in 2011 to 48.6% (95% CI, 46.7–50.5) in 2022. Joinpoint regression identified notable inflection points in approximately 2013 and 2020. The sharp increase after 2020 likely coincides with the publication of the TST (Treat Stroke to Target) study in 2019,²⁷ highlighting the importance of LDL-C lowering in stroke and suggesting a coincidental correlation. Additionally, the increasing trend before 2013 seems to correlate with previous findings indicating that lower LDL-C levels were associated with a lower risk of vascular outcomes.^{28,29} Over time, dyslipidemia guidelines have increasingly recommended lower LDL-C targets and emphasized the importance of intensive lipid-lowering treatment.¹⁷ Our study suggests a growing inclination in real-world practice among patients with stroke to use statins for LDL-C control.

The use of oral anticoagulants for the treatment of AF before stroke occurrence has significantly increased; it rose from ≈26.0% (95% CI, 20.8–32.1) in 2011 to 55.7% (95% CI, 49.6–61.6) in 2022, an absolute increase of nearly 30%. Significant changes in the rates of well-controlled AF were observed from 2014 to 2015. In Korea, since the introduction of NOAC insurance coverage in 2015, the use rate of oral anticoagulants has increased. Recent evidence has demonstrated that the use of NOAC serves as a mediator for improved annual outcomes in patients with stroke.³⁰ However, between 2011 and 2015, before the widespread availability of NOACs in Korea, the proportion of patients admitted with an international normalized ratio of 1.7 to

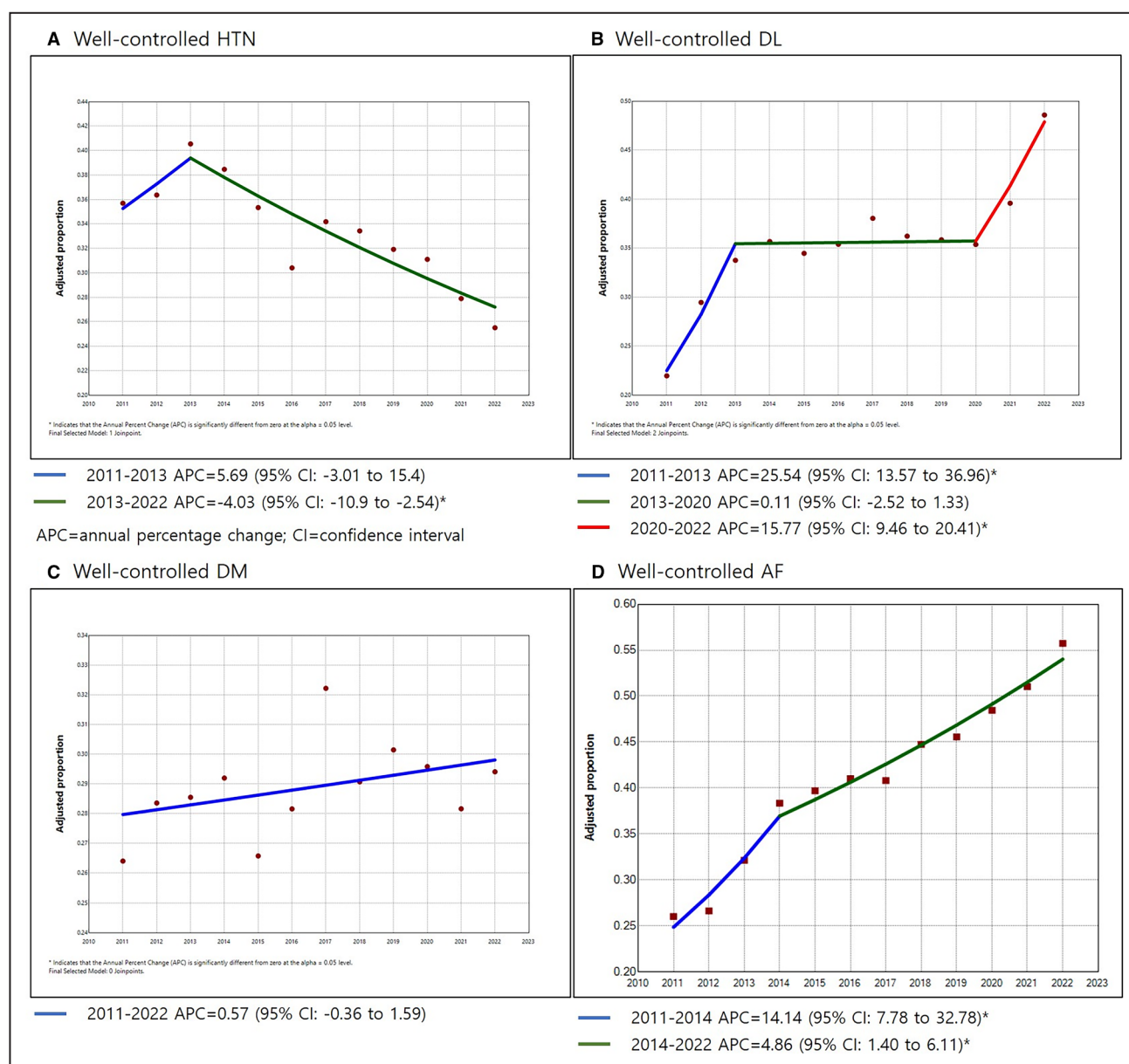


Figure 2. Joinpoint analysis of well-controlled risk factors.

A, Hypertension, **(B)** dyslipidemia, **(C)** diabetes, and **(D)** AF. AF indicates atrial fibrillation; APC, annual percentage change; DL, dyslipidemia; DM, diabetes; and HTN, hypertension.

3.0 while on warfarin was <10%. This low rate of controlled AF likely reflects that many patients receiving subtherapeutic anticoagulation therapy experienced stroke rather than indicating a general failure in risk factor control among all patients with AF. In other words, because this study population consisted of individuals who had already had a stroke, the low rate may reflect selection bias, where inadequately anticoagulated patients were more likely to be represented. Therefore, caution is warranted when interpreting the low rate of risk factor control during this period.

The well-controlled status of diabetes increased with time by 3.0% from 2011 to 2022. The relatively

low absolute control rate may have stemmed from the unclear relationship between diabetes control and outcomes in patients with diabetes. Diabetes control in older age groups tends to be more lenient, with acceptable HbA_{1c} levels of 7.0% to 8.0%,^{31,32} which may have contributed to the modest improvement rates observed. However, with the emergence of new diabetes medications, such as sodium–glucose cotransporter 2 inhibitors, which are associated with a reduction in mortality risk,³³ this trend may gradually change.

Proportions of optimal risk factor control at the time of the index stroke remained notably low at <50% in our study. Despite guidelines emphasizing the importance

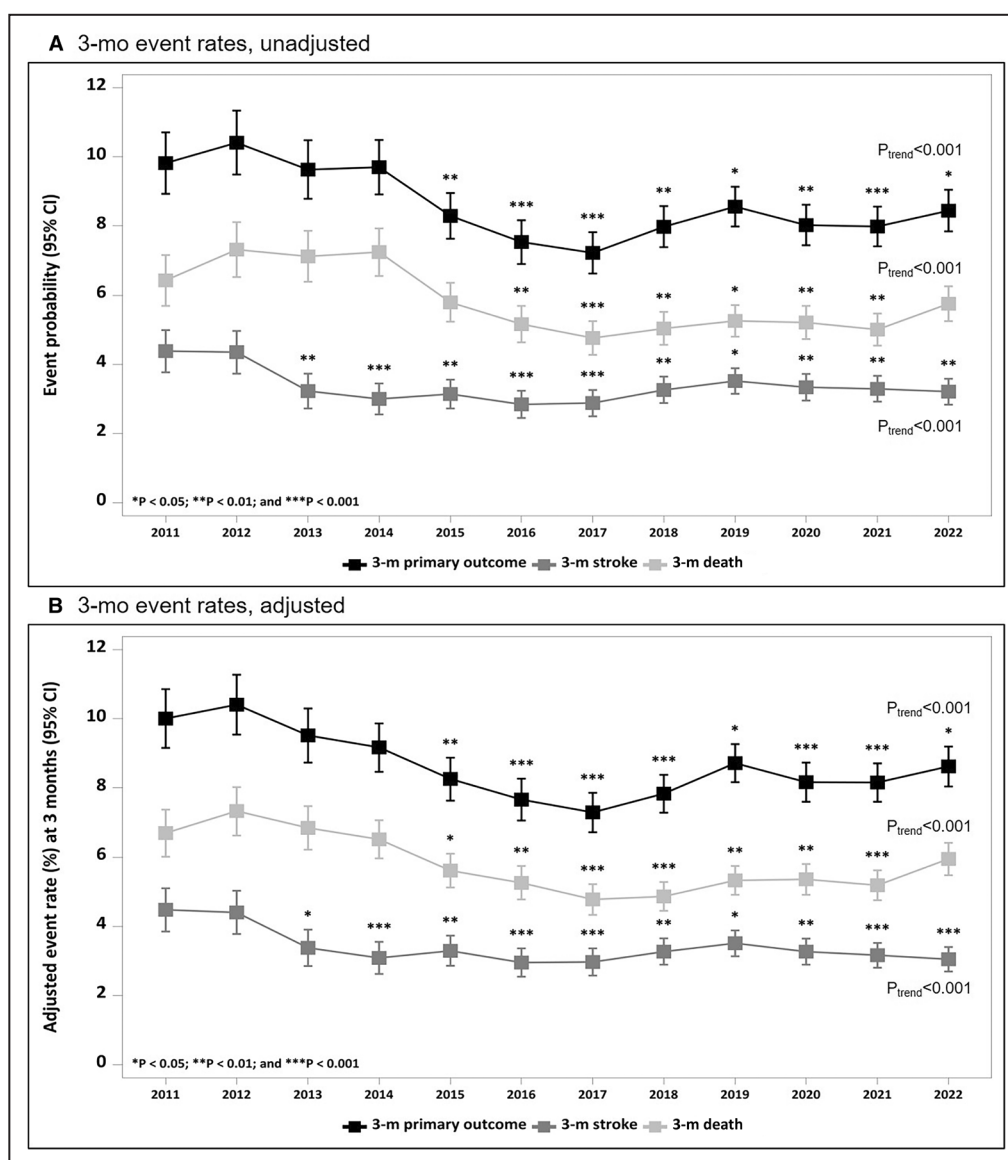


Figure 3. Annual changes in the 3-month event rates of composite of stroke, myocardial infarction, and all-cause death. In unadjusted (A) and adjusted (B) analyses.

of risk factor management for primary prevention, real-world studies have revealed challenges in implementing recommended controls.^{7,8} Importantly, the need to improve health care quality is emphasized by the possibility that inadequate control of major vascular risk factors may adversely influence clinical outcomes.

Nevertheless, our findings show a 19.7% absolute increase in management for AF, 26.6% for dyslipidemia, and 3.0% for diabetes, highlighting a growing awareness of the importance of risk factor management in the real world. Furthermore, higher rates of well-controlled risk factors were observed in patients with a history of stroke, with adjusted rates of well-controlled risk factors >50%. Our research underscores the ongoing

need to improve vascular risk factor control, particularly through medication, emphasizing the importance of efforts in both secondary prevention strategies and controlling prestroke risk factors to ensure favorable outcomes in patients with ischemic stroke.

Despite hypertension being the most crucial risk factor for stroke, the annual change in its well-controlled status did not show significant prominence. This finding contrasts with other risk factors and was somewhat unexpected. Although the exact reason is unclear, this may be partly explained by a persistent misconception among the general public that antihypertensive medications, once started, must be taken for life, leading to reluctance in initiating treatment,

particularly among older or frail individuals.³⁴ In addition, the transient fluctuation in hypertension control rates between 2015 and 2017 may partly reflect age-specific changes in hypertension management guidelines. The 2014 Eighth Joint National Committee and subsequent 2015 to 2016 American Heart Association/American College of Cardiology recommendations adopted a more lenient BP target (<150/90 mmHg) for older adults, which may have led to a temporary decrease in treatment intensity.^{35,36} In contrast, the 2017 American Heart Association/American College of Cardiology guideline introduced a lower diagnostic threshold ($\geq$ 130/80 mmHg) and emphasized stricter BP control (<130/80 mmHg) across all age groups,²⁵ likely contributing to the rebound in treatment rates observed thereafter. However, the recent decline in hypertension control rates after 2020 is more difficult to explain, although the indirect impact of the COVID-19 pandemic, such as reduced access to routine medical care and lifestyle disruptions, cannot be excluded. In contrast, with an antihypertensive use of 75% (adjusted rates exceeding 80%), it is understandable why this annual increase was not pronounced, as at least 3 of 4 patients had controlled hypertension. Furthermore, defining well-controlled hypertension at the time of ischemic stroke is inherently challenging. BP typically increases following ischemic stroke, making it difficult to assess whether prestroke hypertension is adequately controlled. Therefore, our findings about hypertension control must be interpreted cautiously.

Our study indirectly supports previous findings that effective management of prestroke risk factors may be associated with favorable outcomes in patients with ischemic stroke. Prestroke statin use has been linked to milder initial stroke severity and improved early prognosis,³⁷ whereas elevated HbA_{1c} levels at admission are associated with worse outcomes and an increased risk of subsequent vascular outcomes in patients with acute ischemic stroke.³⁸ In our study, there was a coincidental similarity between the increasing proportion of well-controlled risk factors and the decreasing risk of early vascular event outcomes, except notably for the COVID-19 pandemic period. These findings suggest that optimal risk factor control may impact subsequent vascular outcomes. Further ongoing research is necessary to explore this relationship.

This study has limitations, primarily in the arbitrary definition of risk factor control. While recent guidelines recommend risk-stratified targets, particularly for lipid management, we adopted conservative thresholds (eg, LDL-C <100 mg/dL) to reflect general or moderate-risk populations.²¹ This approach ensured consistency across the cohort, although it may not have fully captured individualized treatment goals. Additionally, in some patients, vascular risk factors

were newly identified or diagnosed during hospitalization. However, for the purpose of this study, such cases were considered preexisting, and control status was determined on the basis of the clinical and laboratory findings at the time of admission. The extent of in-hospital evaluation for AF may have varied among participating centers, which represents a potential limitation. However, most participating hospitals routinely performed electrocardiography, continuous ECG monitoring, and Holter monitoring as part of standard stroke care. Second, the limited information on previous medication use, including dosage and duration, poses a limitation. However, since our study revealed changes in risk factor control over time, the impact of insufficient medication information on the results was likely minimal. Third, smoking, although an important prestroke risk factor, was not included as a major variable in this study, as the primary focus was on pharmacologically modifiable risk factors. This omission may limit the comprehensiveness of our analysis, and the potential mediating effects of smoking on stroke outcomes should be explored in future research. Fourth, conditions such as a history of stroke or coronary artery disease may have a higher recurrence risk despite well-controlled risk factors. Adjusting for risk factors for secondary prevention may have a more significant impact on outcomes than adjusting for risk factor control status at the time of the first-ever stroke. Detailed analyses considering these factors may be necessary in the future. Fifth, caution is needed when interpreting the *P* values in our results. Owing to the large sample size, even minor differences that may not have clinical relevance can result in statistically significant findings (*P*<0.05). It is essential to assess whether the observed statistical significance reflects genuine clinical significance carefully. Sixth, as this was a study conducted in South Korea, even though it was a multicenter, prospective registry analysis, there are limitations to generalizability. Moreover, several hospitals have been added to the CRCS-K-NIH registry since 2011, and the impact of these additions on the observed increase in stroke cases cannot be excluded. The results may differ across countries or races and ethnicities, and the retrospective nature of the analysis makes it challenging to completely control for unmeasured confounders or selection bias. Despite rigorous adjustments, the study may not be entirely free from these limitations. Nevertheless, leveraging a large prospective stroke registry for thorough analysis adds notable value to the study.

In conclusion, our study, which used a comprehensive stroke registry in South Korea over 12 years, confirmed improvements in the management of vascular risk factors such as dyslipidemia and AF at the onset of ischemic stroke. However, we found that the rate of controlling risk factors remained suboptimal in patients

with first-ever ischemic stroke. These longitudinal trends in risk factor control highlight both progress and persistent gaps in stroke prevention practices. These findings may help inform strategies to improve risk factor management by identifying priority areas that warrant targeted intervention in clinical practice and population-level guidelines. Further investigations are warranted to implement effective risk factor control strategies.

ARTICLE INFORMATION

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Supplemental Material

Tables S1–S7

Figures S1–S4

REFERENCES

- Meschia JF, Bushnell C, Boden-Albala B, Braun LT, Bravata DM, Chaturvedi S, Creager MA, Eckel RH, Elkind MS, Fornage M, et al. Guidelines for the primary prevention of stroke: a statement for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2014;45:3754–3832. doi: [10.1161/STR.0000000000000046](https://doi.org/10.1161/STR.0000000000000046)
- Powers WJ, Rabinstein AA, Ackerson T, Adeoye OM, Bambakidis NC, Becker K, Biller J, Brown M, Demaerschalk BM, Hoh B, et al. Guidelines for the early Management of Patients with Acute Ischemic Stroke: 2019 update to the 2018 guidelines for the early Management of Acute Ischemic Stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2019;50:e344–e418. doi: [10.1161/STR.0000000000000211](https://doi.org/10.1161/STR.0000000000000211)
- Ryu WS, Schellingerhout D, Hong KS, Jeong SW, Kim BJ, Kim JT, Lee KB, Park TH, Park SS, Park JM, et al. Relation of pre-stroke aspirin use with cerebral infarct volume and functional outcomes. *Ann Neurol*. 2021;90:763–776. doi: [10.1002/ana.26219](https://doi.org/10.1002/ana.26219)
- Park JM, Kang K, Cho YJ, Hong KS, Lee KB, Park TH, Lee SJ, Ko Y, Han MK, Lee J, et al. Comparative effectiveness of Prestroke aspirin on stroke severity and outcome. *Ann Neurol*. 2016;79:560–568. doi: [10.1002/ana.24602](https://doi.org/10.1002/ana.24602)
- Westphal LP, Widmer R, Held U, Steigmiller K, Hametner C, Ringleb P, Curtze S, Martinez-Majander N, Tiainen M, Nolte CH, et al. Association of prestroke metformin use, stroke severity, and thrombolysis outcome. *Neurology*. 2020;95:e362–e373. doi: [10.1212/WNL.00000000000009951](https://doi.org/10.1212/WNL.00000000000009951)
- Hong KS, Lee JS. Statins in acute ischemic stroke: a systematic review. *J Stroke*. 2015;17:282–301. doi: [10.5853/jos.2015.17.3.282](https://doi.org/10.5853/jos.2015.17.3.282)
- Yang Q, Cogswell ME, Flanders WD, Hong Y, Zhang Z, Loustalot F, Gillespie C, Merritt R, Hu FB. Trends in cardiovascular health metrics and associations with all-cause and CVD mortality among US adults. *JAMA*. 2012;307:1273–1283. doi: [10.1001/jama.2012.339](https://doi.org/10.1001/jama.2012.339)
- Han L, You D, Ma W, Astell-Burt T, Feng X, Duan S, Qi L. National Trends in American Heart Association revised Life's simple 7 metrics associated with risk of mortality among US adults. *JAMA Netw Open*. 2019;2:e1913131. doi: [10.1001/jamanetworkopen.2019.13131](https://doi.org/10.1001/jamanetworkopen.2019.13131)
- Collaboration NCDRF. Worldwide trends in hypertension prevalence and progress in treatment and control from 1990 to 2019: a pooled analysis of 1201 population-representative studies with 104 million participants. *Lancet*. 2021;398:957–980. doi: [10.1016/S0140-6736\(21\)01330-1](https://doi.org/10.1016/S0140-6736(21)01330-1)
- Marcus ME, Manne-Goehler J, Theilmann M, Farzadfar F, Moghaddam SS, Keykhaei M, Hajebi A, Tschida S, Lemp JM, Aryal KK, et al. Use of statins for the prevention of cardiovascular disease in 41 low-income and middle-income countries: a cross-sectional study of nationally representative, individual-level data. *Lancet Glob Health*. 2022;10:e369–e379. doi: [10.1016/S2214-109X\(21\)00551-9](https://doi.org/10.1016/S2214-109X(21)00551-9)
- Joseph P, Lanas F, Roth G, Lopez-Jaramillo P, Lonn E, Miller V, Mente A, Leong D, Schwalm JD, Yusuf S. Cardiovascular disease in the Americas: the epidemiology of cardiovascular disease and its risk factors. *Lancet Reg Health Am*. 2025;42:100960. doi: [10.1016/j.lana.2024.100960](https://doi.org/10.1016/j.lana.2024.100960)
- Kim BJ, Park JM, Kang K, Lee SJ, Ko Y, Kim JG, Cha JK, Kim DH, Nah HW, Han MK, et al. Case characteristics, hyperacute treatment, and outcome information from the clinical research center for stroke-fifth division registry in South Korea. *J Stroke*. 2015;17:38–53. doi: [10.5853/jos.2015.17.1.38](https://doi.org/10.5853/jos.2015.17.1.38)
- Kim BJ, Han MK, Park TH, Park SS, Lee KB, Lee BC, Yu KH, Cha JK, Kim DH, Lee J, et al. Current status of acute stroke management in Korea: a report on a multicenter, comprehensive acute stroke registry. *Int J Stroke*. 2014;9:514–518. doi: [10.1111/ijls.12199](https://doi.org/10.1111/ijls.12199)
- Williams B, Mancia G, Spiering W, Agabiti Rosei E, Azizi M, Burnier M, Clement DL, Coca A, de Simone G, Dominiczak A, et al. 2018 ESC/ESH guidelines for the management of arterial hypertension. *Eur Heart J*. 2018;39:3021–3104. doi: [10.1093/eurheartj/ehy339](https://doi.org/10.1093/eurheartj/ehy339)
- Goldstein LB, Bushnell CD, Adams RJ, Appel LJ, Braun LT, Chaturvedi S, Creager MA, Culebras A, Eckel RH, Hart RG, et al. Guidelines for the primary prevention of stroke: a guideline for healthcare professionals

- from the American Heart Association/American Stroke Association. *Stroke*. 2011;42:517–584. doi: [10.1161/STR.0b013e3181fcb238](https://doi.org/10.1161/STR.0b013e3181fcb238)
16. Cosentino F, Grant PJ, Aboyans V, Bailey CJ, Ceriello A, Delgado V, Federici M, Filippatos G, Grobbee DE, Hansen TB, et al. 2019 ESC guidelines on diabetes, pre-diabetes, and cardiovascular diseases developed in collaboration with the EASD. *Eur Heart J*. 2020;41:255–323. doi: [10.1093/eurheartj/ehz486](https://doi.org/10.1093/eurheartj/ehz486)
 17. Authors/Task Force M, Guidelines ESCCfP, Societies ESCNC. 2019 ESC/EAS guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk. *Atherosclerosis*. 2019;290:140–205. doi: [10.1016/j.atherosclerosis.2019.08.014](https://doi.org/10.1016/j.atherosclerosis.2019.08.014)
 18. Arguedas JA, Leiva V, Wright JM. Blood pressure targets in adults with hypertension. *Cochrane Database Syst Rev*. 2020;12:CD004349. doi: [10.1002/14651858.CD004349.pub3](https://doi.org/10.1002/14651858.CD004349.pub3)
 19. Saiz LC, Gorricho J, Garjon J, Celaya MC, Erviti J, Leache L. Blood pressure targets for the treatment of people with hypertension and cardiovascular disease. *Cochrane Database Syst Rev*. 2022;11:CD010315. doi: [10.1002/14651858.CD010315.pub5](https://doi.org/10.1002/14651858.CD010315.pub5)
 20. American Diabetes A. 6. Glycemic targets: standards of medical Care in Diabetes-2021. *Diabetes Care*. 2021;44:S73–S84. doi: [10.2337/dc21-S006](https://doi.org/10.2337/dc21-S006)
 21. Mach F, Baigent C, Catapano AL, Koskinas KC, Casula M, Badimon L, Chapman MJ, De Backer GG, Delgado V, Ference BA, et al. 2019 ESC/EAS guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk. *Eur Heart J*. 2020;41:111–188. doi: [10.1093/eurheartj/ehz455](https://doi.org/10.1093/eurheartj/ehz455)
 22. Kim HJ, Fay MP, Feuer EJ, Midthune DN. Permutation tests for joinpoint regression with application to cancer rates. *Stat Med*. 2000;19:335–351. doi: [10.1002/\(sici\)1097-0258\(20000215\)19:3<335::aid-sim336>3.0.co;2-z](https://doi.org/10.1002/(sici)1097-0258(20000215)19:3<335::aid-sim336>3.0.co;2-z)
 23. Lin DY. Cox regression analysis of multivariate failure time data: the marginal approach. *Stat Med*. 1994;13:2233–2247. doi: [10.1002/sim.4780132105](https://doi.org/10.1002/sim.4780132105)
 24. Grundy SM, Stone NJ, Bailey AL, Beam C, Birtcher KK, Blumenthal RS, Braun LT, de Ferranti S, Faiella-Tommasino J, Forman DE, et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA guideline on the Management of Blood Cholesterol: executive summary: a report of the American College of Cardiology/American Heart Association task force on clinical practice guidelines. *Circulation*. 2019;139:e1046–e1081. doi: [10.1161/CIR.0000000000000624](https://doi.org/10.1161/CIR.0000000000000624)
 25. Whelton PK, Carey RM, Aronow WS, Casey DE Jr, Collins KJ, Dennison Himmelfarb C, DePalma SM, Gidding S, Jamerson KA, Jones DW, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and Management of High Blood Pressure in adults: a report of the American College of Cardiology/American Heart Association task force on clinical practice guidelines. *Circulation*. 2018;138:e484–e594. doi: [10.1161/CIR.0000000000000596](https://doi.org/10.1161/CIR.0000000000000596)
 26. Arnett DK, Blumenthal RS, Albert MA, Buroker AB, Goldberger ZD, Hahn EJ, Himmelfarb CD, Khera A, Lloyd-Jones D, McEvoy JW, et al. 2019 ACC/AHA guideline on the primary prevention of cardiovascular disease: a report of the American College of Cardiology/American Heart Association task force on clinical practice guidelines. *Circulation*. 2019;140:e596–e646. doi: [10.1161/CIR.0000000000000678](https://doi.org/10.1161/CIR.0000000000000678)
 27. Amarenco P, Kim JS, Labreuche J, Charles H, Abtan J, Bejot Y, Cabrejo L, Cha JK, Ducrocq G, Giroud M, et al. A comparison of two LDL cholesterol targets after ischemic stroke. *N Engl J Med*. 2020;382:9. doi: [10.1056/NEJMoa1910355](https://doi.org/10.1056/NEJMoa1910355)
 28. Cholesterol Treatment Trialists C, Baigent C, Blackwell L, Emberson J, Holland LE, Reith C, Bhalra N, Peto R, Barnes EH, Keech A, et al. Efficacy and safety of more intensive lowering of LDL cholesterol: a meta-analysis of data from 170,000 participants in 26 randomised trials. *Lancet*. 2010;376:1670–1681. doi: [10.1016/S0140-6736\(10\)61350-5](https://doi.org/10.1016/S0140-6736(10)61350-5)
 29. Amarenco P, Labreuche J. Lipid management in the prevention of stroke: review and updated meta-analysis of statins for stroke prevention. *Lancet Neurol*. 2009;8:453–463. doi: [10.1016/S1474-4422\(09\)70058-4](https://doi.org/10.1016/S1474-4422(09)70058-4)
 30. Lee M, Lee BC, Yu KH, Oh MS, Kim BJ, Kim JY, Kang J, Lee KJ, Kim DY, Park JM, et al. Secular trends in outcomes and impact of novel Oral anticoagulants in atrial fibrillation-related acute ischemic stroke. *Stroke*. 2024;55:625–633. doi: [10.1161/STROKEAHA.123.044487](https://doi.org/10.1161/STROKEAHA.123.044487)
 31. American Diabetes Association Professional Practice C. 13. Older adults: standards of Care in Diabetes-2024. *Diabetes Care*. 2024;47:S244–S257. doi: [10.2337/dc24-S013](https://doi.org/10.2337/dc24-S013)
 32. LeRoith D, Biessels GJ, Braithwaite SS, Casanueva FF, Draznin B, Halter JB, Hirsch IB, McDonnell ME, Molitch ME, Murad MH, et al. Treatment of diabetes in older adults: an Endocrine Society* clinical practice guideline. *J Clin Endocrinol Metab*. 2019;104:1520–1574. doi: [10.1210/je.2019-00198](https://doi.org/10.1210/je.2019-00198)
 33. Zinman B, Wanner C, Lachin JM, Fitchett D, Bluhmki E, Hantel S, Mattheus M, Devins T, Johansen OE, Woerle HJ, et al. Empagliflozin, cardiovascular outcomes, and mortality in type 2 diabetes. *N Engl J Med*. 2015;373:2117–2128. doi: [10.1056/NEJMoa1504720](https://doi.org/10.1056/NEJMoa1504720)
 34. Marshall IJ, Wolfe CD, McKevitt C. Lay perspectives on hypertension and drug adherence: systematic review of qualitative research. *BMJ*. 2012;345:e3953. doi: [10.1136/bmj.e3953](https://doi.org/10.1136/bmj.e3953)
 35. James PA, Oparil S, Carter BL, Cushman WC, Dennison-Himmelfarb C, Handler J, Lackland DT, LeFevre ML, MacKenzie TD, Ogedegbe O, et al. 2014 evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the eighth joint National Committee (JNC 8). *JAMA*. 2014;311:507–520. doi: [10.1001/jama.2013.284427](https://doi.org/10.1001/jama.2013.284427)
 36. Rosendorff C, Lackland DT, Allison M, Aronow WS, Black HR, Blumenthal RS, Cannon CP, de Lemos JA, Elliott WJ, Findeiss L, et al. Treatment of hypertension in patients with coronary artery disease: a scientific statement from the American Heart Association, American College of Cardiology, and American Society of Hypertension. *Hypertension*. 2015;65:1372–1407. doi: [10.1161/HYP.0000000000000018](https://doi.org/10.1161/HYP.0000000000000018)
 37. Choi JC, Lee JS, Park TH, Cho YJ, Park JM, Kang K, Lee KB, Lee SJ, Ko Y, Lee J, et al. Effect of pre-stroke statin use on stroke severity and early functional recovery: a retrospective cohort study. *BMC Neurol*. 2015;15:120. doi: [10.1186/s12883-015-0376-3](https://doi.org/10.1186/s12883-015-0376-3)
 38. Chang JY, Kim WJ, Kwon JH, Lee JS, Kim BJ, Kim JT, Lee J, Cha JK, Kim DH, Cho YJ, et al. Association of Prestroke Glycemic Control with Vascular Events during 1-year follow-up. *Neurology*. 2021;97:e1717–e1726. doi: [10.1212/WNL.00000000000012729](https://doi.org/10.1212/WNL.00000000000012729)