

SUPPLEMENTAL PUBLICATION MATERIAL

Supplementary figure

Fig. S1. The proportion of patients who received statins before and after diagnosis with moyamoya disease (MMD)

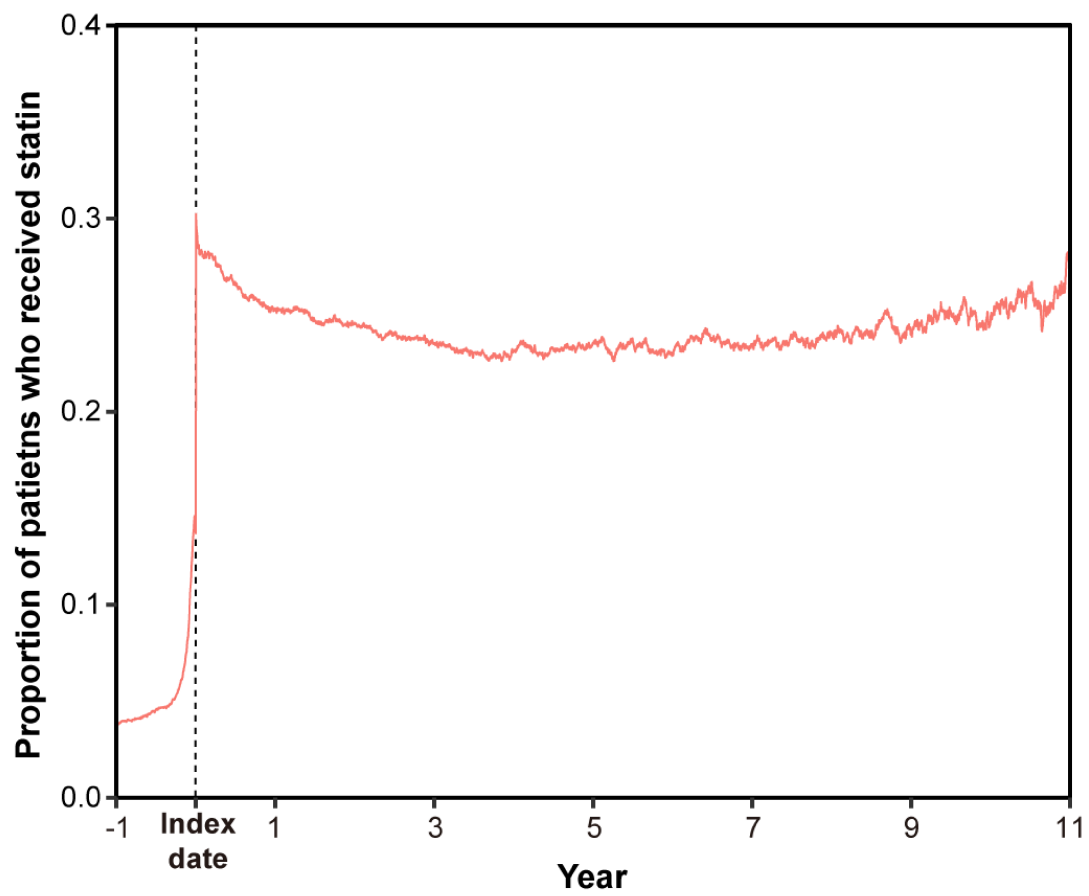
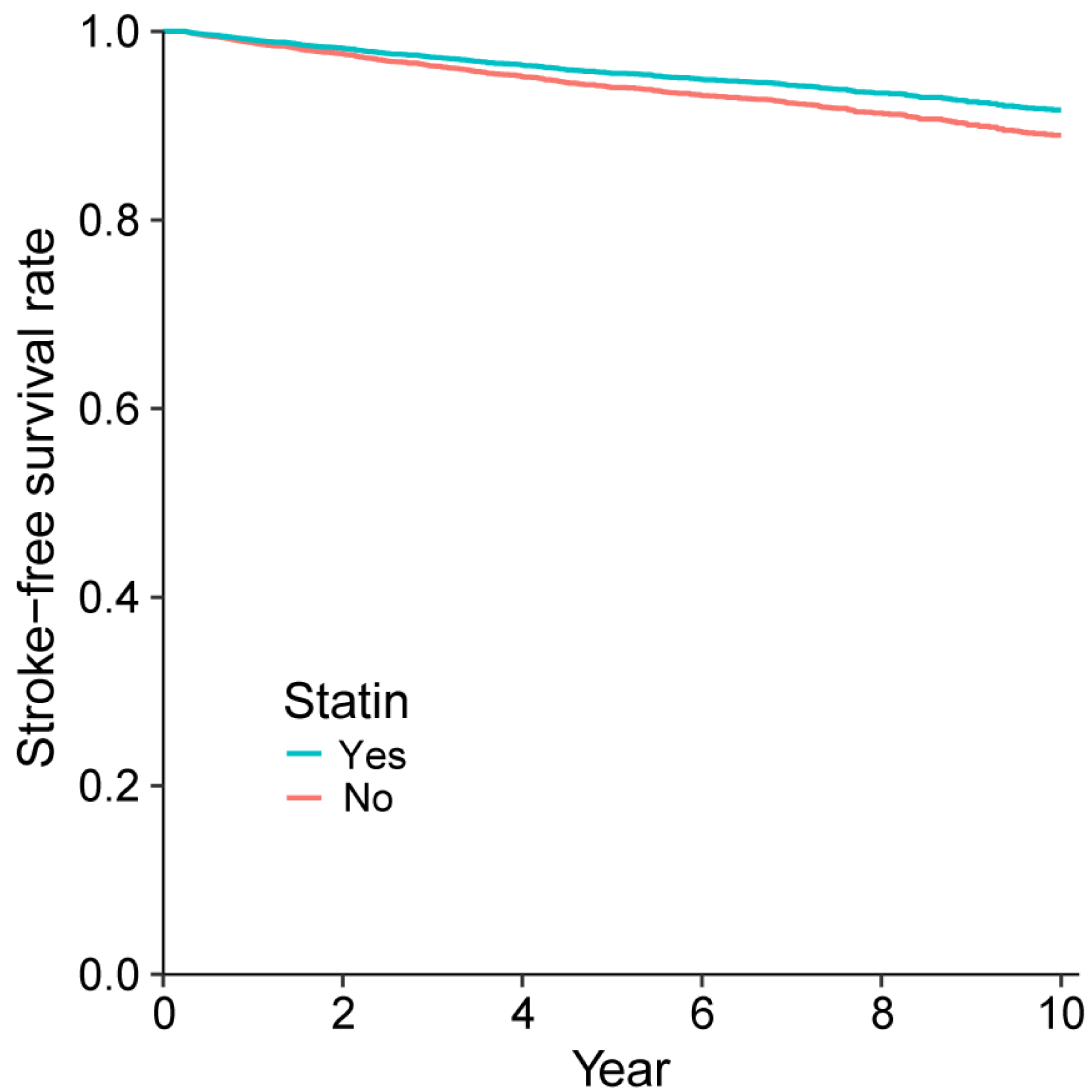


Fig. S2. Estimated stroke-free survival curve according to the use of statins



The X-axis indicates the time (year) from the diagnosis of moyamoya disease (index date). The plot indicates estimated stroke-free survival curves according to the use of statins based on the multivariate time-dependent Cox regression model (Table 2).

Supplementary tables**Supplementary table S1.** Baseline characteristics of the included and excluded patients in the study

Variable	Total (N=23,310)	Included (N=13,373)	Excluded (N=9,937)	P value
Sex, male	8,210 (35.2)	4,657 (34.8)	3,553 (35.8)	0.141
Age, year	40.1 ±18.7	38.7 ± 18.2	41.9 ± 19.1	<0.001
Concurrent stroke	7,472 (32.1)	5,454 (40.8)	2,018 (20.3)	<0.001
Revascularization surgery	5,199 (22.3)	3,877 (29.0)	1322 (13.3)	<0.001
Comorbidity				
Hypertension	9,375 (40.2)	4,800 (35.9)	4,575 (46.0)	<0.001
Diabetes mellitus	2,616 (11.2)	1,377 (10.3)	1,239 (12.5)	<0.001
Atrial fibrillation	677 (2.9)	340 (2.5)	337 (3.4)	<0.001
Renal disease	1,005 (4.3)	439 (3.3)	566 (5.7)	<0.001
Malignancy	662 (2.8)	372 (2.8)	290 (2.9)	0.535

The data are represented as numbers (%) or mean ± standard deviation. P value is derived from chi-square test for categorical variables and independent t-test for continuous variable.

Supplementary table S2. Type and daily dose of statin in the patients at 90 days after the index date

Type of statin	Dose per day, mg									
	1	2	2.5	4	5	10	20	40	60	80
Atorvastatin	0	0	0	0	24	1036	661	285	53	0
Fluvastatin	0	0	0	0	0	0	0	2	0	17
Lovastatin	0	0	0	0	0	0	1	0	1	0
Pitavastatin	7	101	0	52	0	0	0	0	0	0
Pravastatin	0	0	0	0	3	21	22	49	0	0
Rosuvastatin	0	0	3	0	231	597	182	1	0	0
Simvastatin	0	0	0	0	1	77	142	16	0	0

Data are number of patients taking the statin at 90 days from the diagnosis of moyamoya disease.

Supplementary table S3. Characteristics of the patients at 90 days after the index date

Variable	Total (n = 13,373)	No statin (n=9,788)	Statin (n=3,585)	P value
Sex, male	4,657 (34.8)	3,376 (34.5)	1,281 (35.7)	0.182
Age, year	38.7 ± 18.2	34.9 ± 18.7	49.0 ± 11.7	<0.001
Concurrent stroke	5,454 (40.8)	3,645 (37.2)	1,809 (50.5)	<0.001
Revascularization surgery	3,877 (29.0)	3,272 (33.4)	605 (16.9)	
Comorbidity				
Hypertension	4,800 (35.9)	2,773 (28.3)	2,027 (56.5)	<0.001
Diabetes mellitus	1,377 (10.3)	602 (6.2)	775 (21.6)	<0.001
Atrial fibrillation	340 (2.5)	208 (2.1)	132 (3.7)	<0.001
Renal disease	439 (3.3)	248 (2.5)	191 (5.3)	<0.001
Malignancy	372 (2.8)	251 (2.6)	121 (3.4)	0.535

The data are represented as numbers (%) or mean ± standard deviation. P value is derived from chi-square test for categorical variables and independent t-test for continuous variable.

Supplementary table S4. Risk factors for the primary outcome regarding the statin intensity in MMD patients

Variable	Adjusted HR (95% CI)*	P value
Sex, male	0.89 (0.75–1.06)	0.198
Age, years	1.02 (1.02–1.03)	<0.001
Concurrent stroke [†]	1.28 (1.08–1.50)	0.004
Revascularization surgery	0.67 (0.54–0.85)	<0.001
Comorbidities		
Hypertension	0.85 (0.71–1.02)	0.086
Diabetes mellitus	1.03 (0.80–1.34)	0.803
Atrial fibrillation	0.79 (0.44–1.40)	0.415
Renal disease	1.31 (0.90–1.92)	0.163
Malignancy	1.25 (0.82–1.93)	0.302
Medication		
Antiplatelet		
No antiplatelet	1 (ref)	
Single antiplatelet	1.00 (0.83–1.19)	0.974
Dual antiplatelet	1.24 (0.90–1.69)	0.184
Statin intensity [‡]		
No statin	1 (ref)	
Low	0.63 (0.28–1.41)	0.263
High	0.75 (0.61–0.92)	0.006

Data were obtained from the multivariable time-dependent Cox proportional hazards regression model for the development of stroke.

MMD, moyamoya disease; HR, hazard ratio; CI, confidence interval

*Adjusted for the covariates listed in this table.

[†]Stroke within 3 months before or after the diagnosis of moyamoya disease

[‡]'Low intensity statin' was determined according to the 2013 American Heart

Association/American College of Cardiology guidelines on the management of blood cholesterol.¹ Statins above the dosage of 'low intensity' was determined as 'high-intensity'.

References

- 1 Stone NJ, Robinson JG, Lichtenstein AH, *et al.* 2013 ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation* 2014;**129**:S1-45. doi:10.1161/01.cir.0000437738.63853.7a