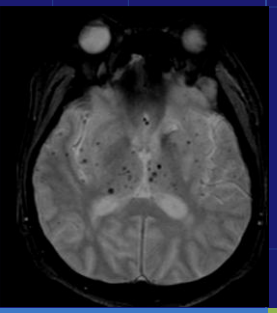
Silent cerebrovascular diseases and their significance



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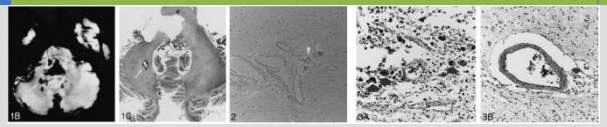


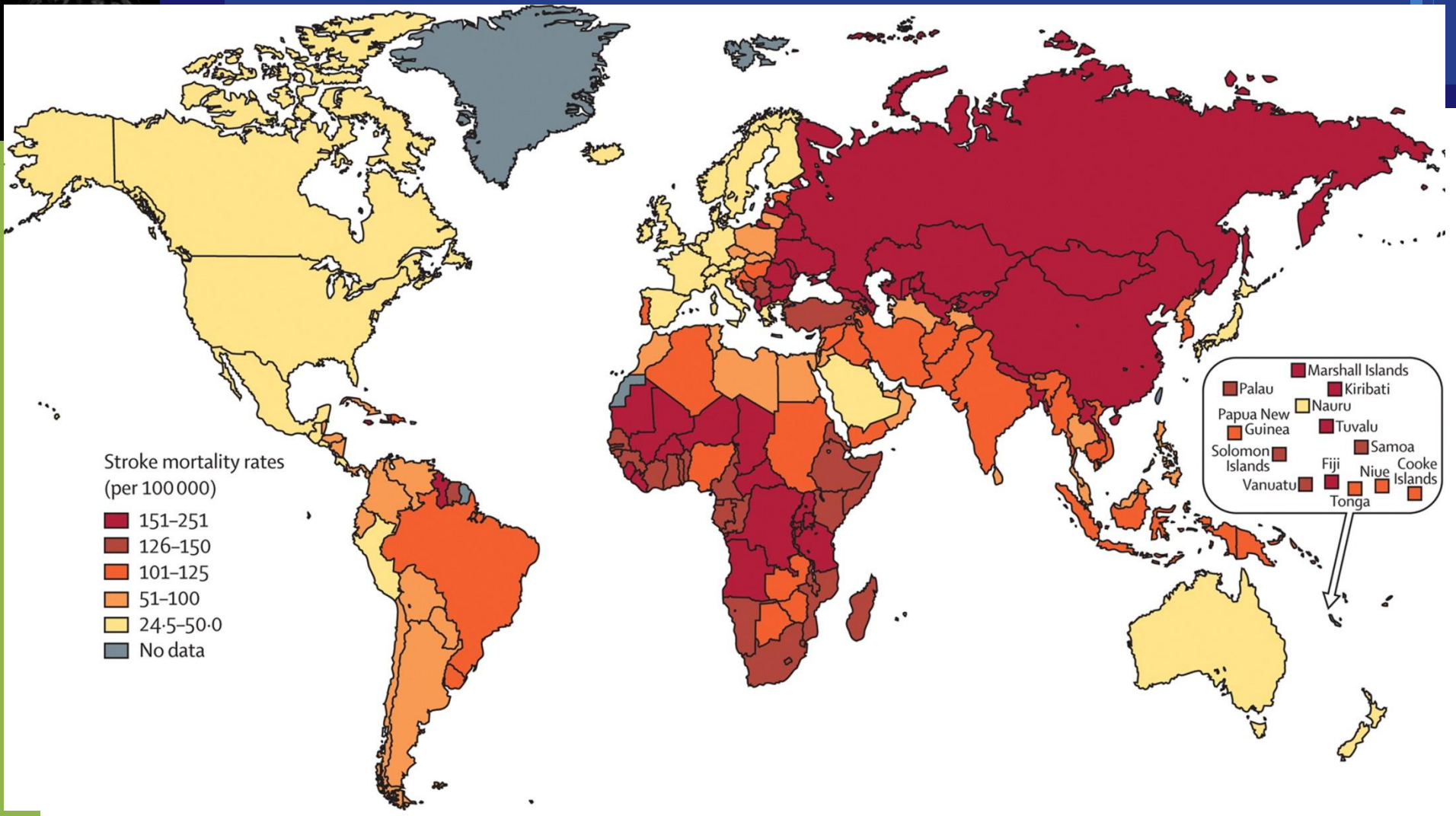
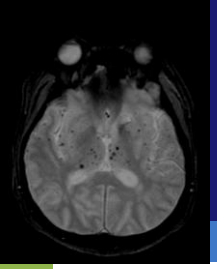


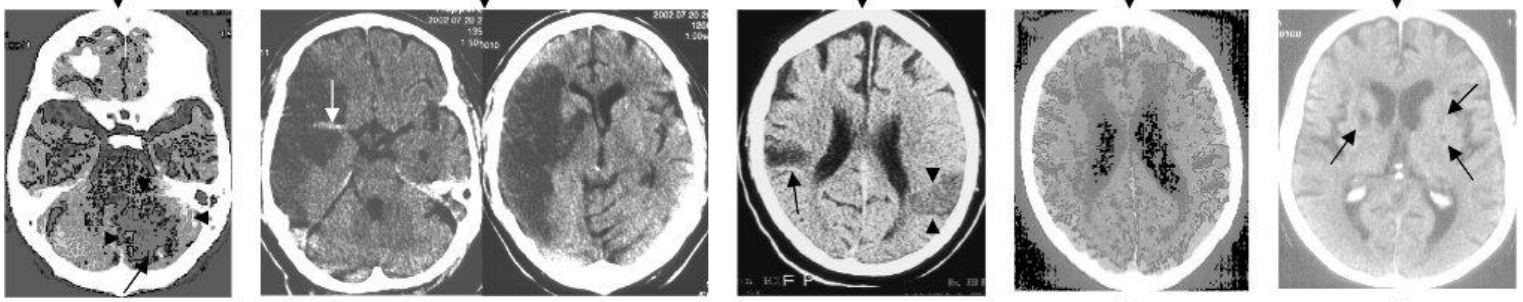
Figure . Age-adjusted and sex-adjusted stroke mortality rates are highest in eastern Europe, north Asia, central Africa, and the south Pacific.



Stroke Subtype

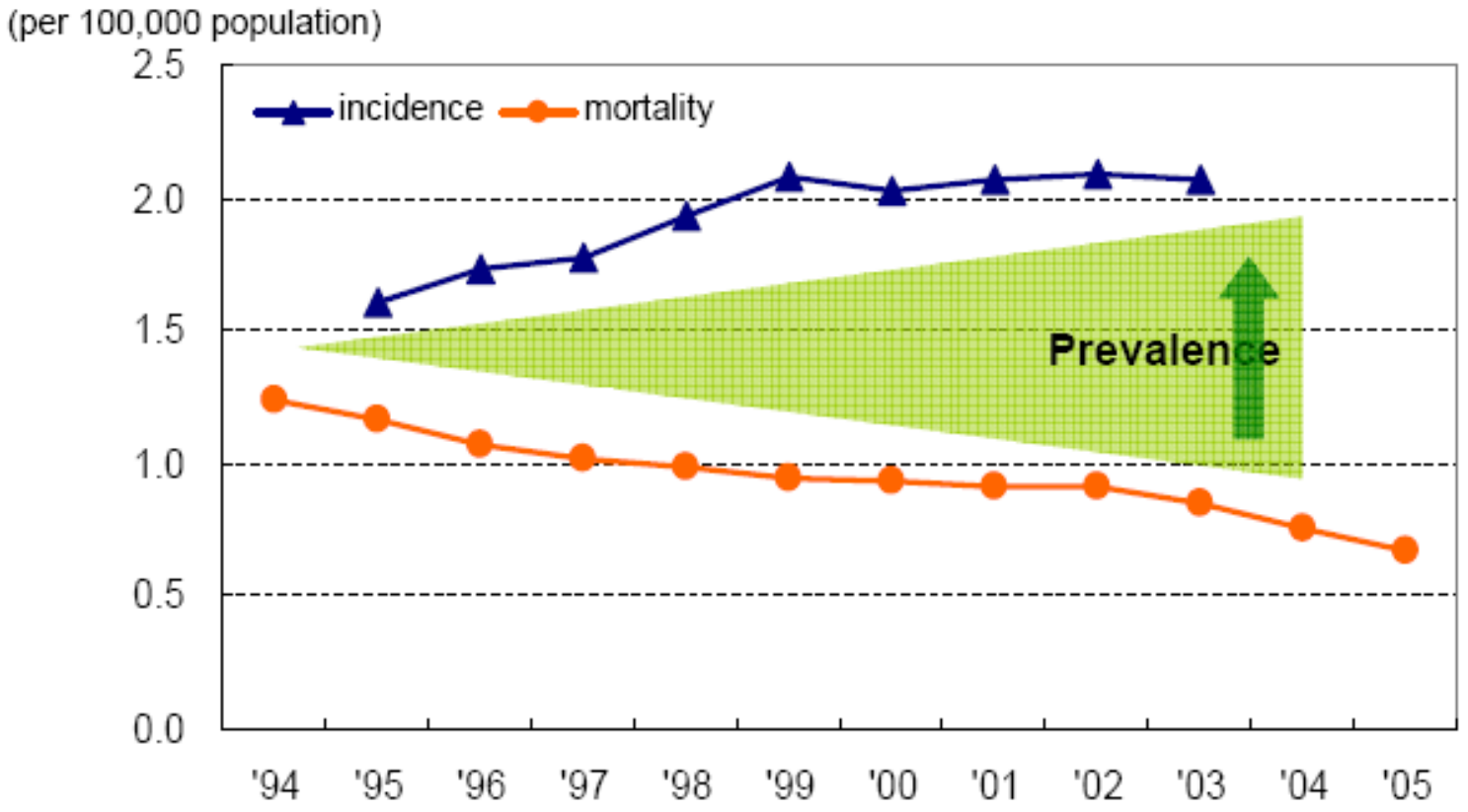
Ischaemic stroke

20%	20–25%	20–25%	5%	25–30%
Large-artery atherosclerosis • Extracranial ~12% (including aortic arch) • Intracranial ~8%	**Cardiac disease** • Atrial fibrillation • Ventricular thrombi • Valve disease • Reduced ventricular contractility	**Small-artery disease** Penetrating artery occlusion due to • Lipohyalinosis • Atherosclerosis	**Other causes** • Dissection • Hypercoagulability • Vasculitis • Migraineous stroke • Drug abuse	**Cryptogenic stroke**
Haemodynamic failure with borderzone infarction (rare; not shown)	Cardiogenic embolism	Lacunar infarction (Leukoaraiosis)	Various mechanisms of infarction Various infarct morphology	
Artery-to-artery embolism or autochthonous athero-thrombosis (common)				



A B C D E

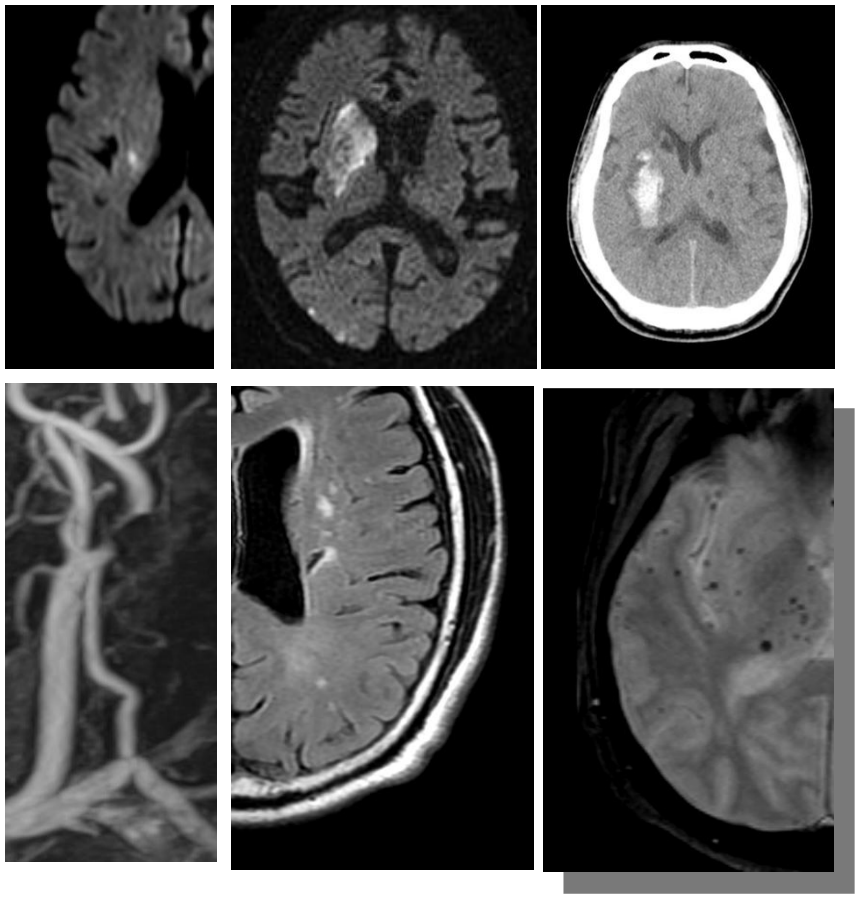
Increased proportion of disabled survivors (1995 – 2003)

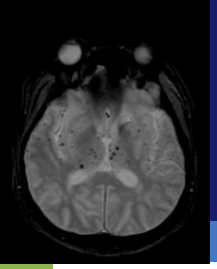


Source : 1) incidence : KCDC(2004), 2) mortality : KNSO mortality data(1994~2005)

Brain Lesions

- **Symptomatic**
  - **Ischemic stroke**
    - Lacunar infarction
    - Large artery atherosclerosis
  - **Hemorrhagic stroke**
- **Asymptomatic**
  - **Vascular lesion**
    - Asymptomatic vascular stenosis
  - **Ischemic cerebral lesions**
    - White matter lesions (leukoaraiosis)
    - **Silent infarction**
  - **Hemorrhagic cerebral lesions**
    - **Microbleeds**

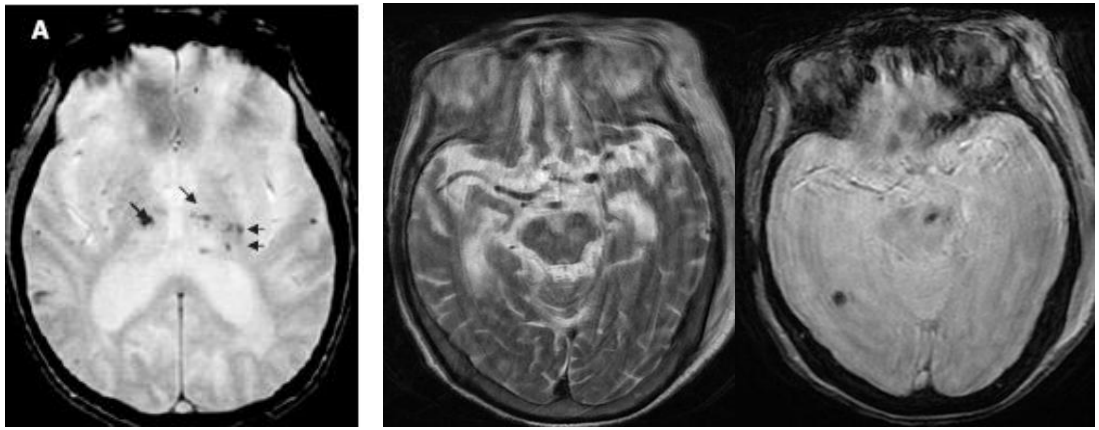




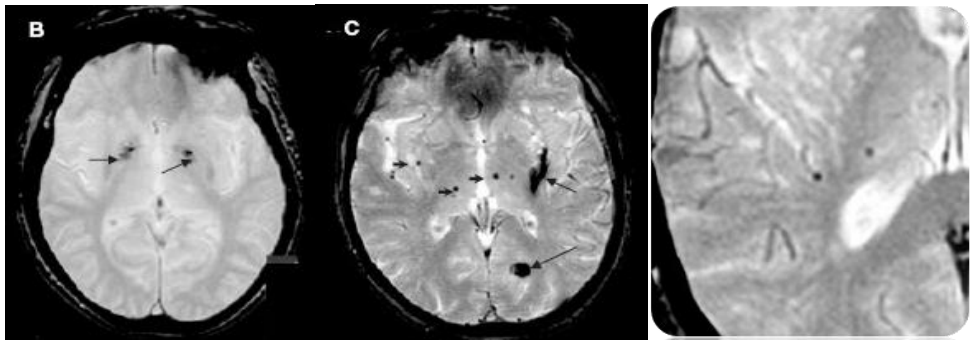
Cerebral Microbleeds

Cerebral Microbleeds (CMB)

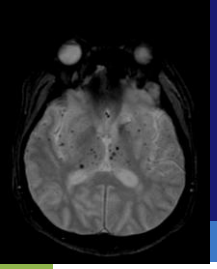
- Visualized by **GRE** sequence: Susceptibility effect
- **Small round dark lesion (<5 mm)**
- Throughout the whole brain areas



- Mimicking lesions
  - Calcification
  - Old hemorrhage
  - Vessel signal void



Cordonnier et al. *Brain* (2007), **130**, 1988–2003

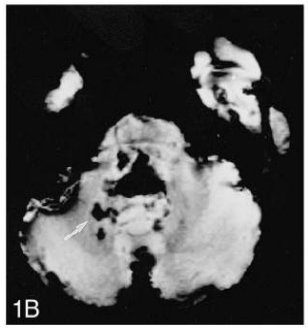


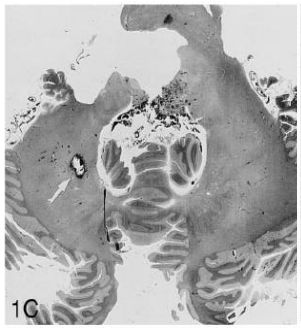
Meaning of CMB?

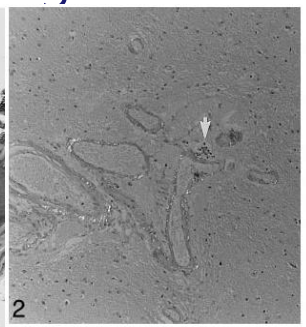
- **CMB is related with ICH** **Offenbacher et al., *AJNR* 1996**
  - In 120 patients with ICH,
  - 33% had "microbleeds" (33%)
- **CMB is related with chronic HT** **Chan et al., *AJNR* 1996**

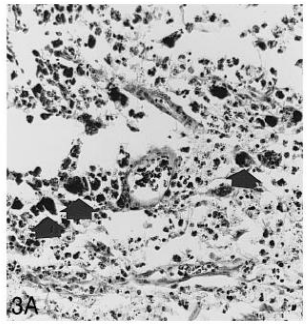
Fazekas et al., *AJNR* 1999

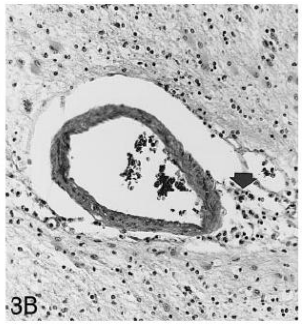
- **Pathology of CMB**
  - Hallmark of old hemorrhage
  -











Hemosiderin laden macrophage

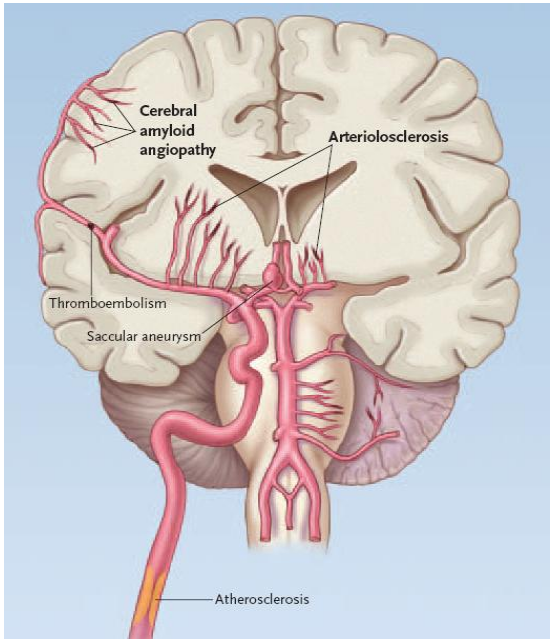
Ischemic Stroke Subtype

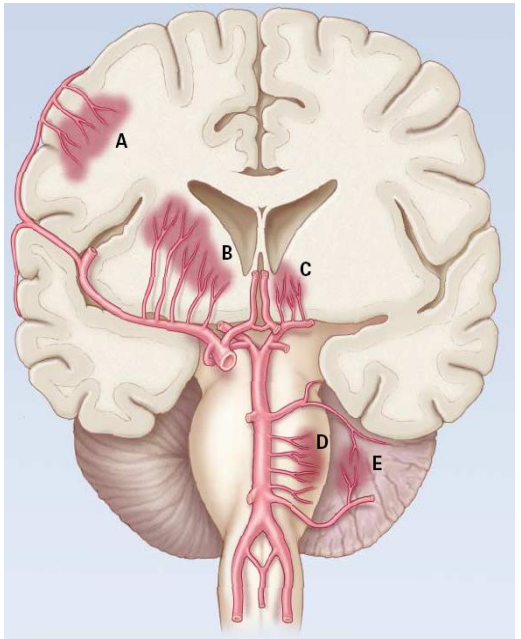
TABLE 2. Prevalence of Silent Microbleeds on T2*-Weighted MRI in Different Subtypes of Stroke

	Microbleeds			
Stroke Subtype	%	n	Range	PVH Grade
Cerebral infarction				
Atherothrombotic	20.8	0.63±1.53	0–6	1.3±0.90**
Cardioembolic	30.4*	2.5±5.6	0–21	1.3±0.82**
Lacunar	62.1**	7.4±16.1**	0–119	1.7±0.99**
Intracerebral hemorrhage	71.4**	9.1±13.8**	0–61	1.6±0.98**
Control	7.7	0.09±0.34	0–2	0.62±0.68

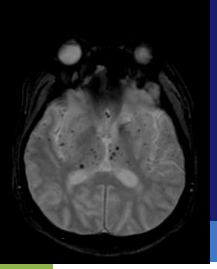
Values are mean±SD. PVHs are graded 0 (normal) through 3 (severe).
*$P<0.05$, **$P<0.01$ vs control.

Kato et al., *Stroke 2002*





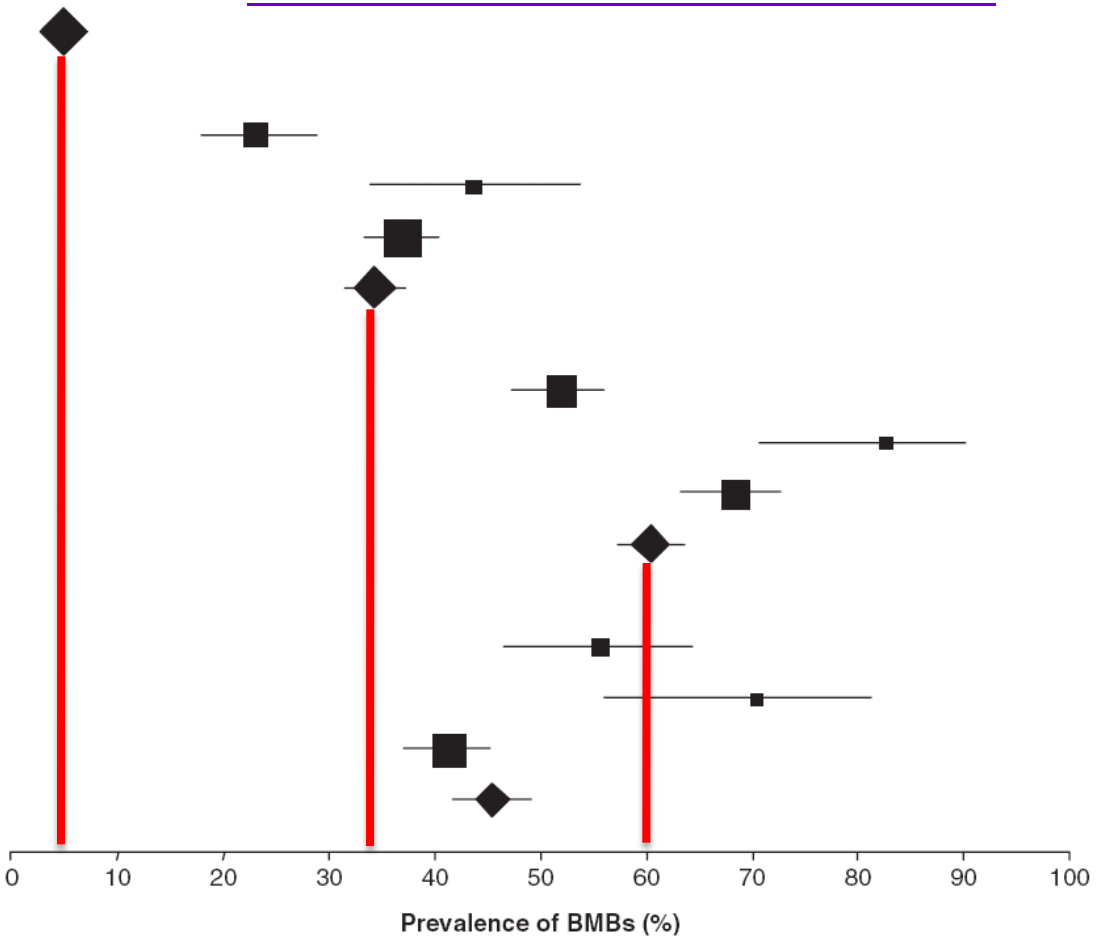
NEJM 2006



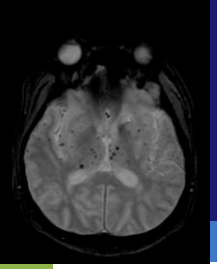
Prevalence of CMB

Group	n/N	Prevalence % (95%CI)
Healthy adults		
All studies	70/1411	5.0 (3.9–6.2)
Ischaemic stroke		
First-ever	53/231	22.9 (18.0–28.8)
Prior stroke	41/94	43.6 (34.0–53.7)
Not distinguished	266/750	35.5 (32.1–39.0)
All studies	360/1075	33.5 (30.7–36.4)
Non-traumatic intracerebral haemorrhage		
First-ever	246/475	51.8 (47.3–56.0)
Prior stroke	47/57	82.5 (70.6–90.2)
Not distinguished	247/362	68.2 (63.3–72.8)
All studies	540/894	60.4 (57.2–63.6)
Ischaemic and haemorrhagic stroke (mixed)		
First-ever	65/117	55.6 (46.5–64.2)
Prior stroke	33/47	70.2 (56.0–81.3)
Not distinguished	229/556	41.2 (37.2–45.3)
All studies	327/720	45.4 (41.8–49.1)

SNUH health care clinic data: 5%



Brain 2007;130:1988-2003



Risk Factors for Microbleeds

Table 3 Influence of comorbid conditions on the prevalence of BMBs

Risk factor	Healthy adults			Adults with cerebrovascular diseases		
	Studies	Sample size	Odds ratio, 95% CI	Studies	Sample size	Odds ratio, 95% CI
Male gender	4	1411	1.4, 0.9–2.3	16	1275	1.2, 0.98–1.5
Hypertension	4	1411	3.9, 2.4–6.4	12	1037	2.3, 1.7–3.0
Smoking	4	1411	1.0, 0.5–2.0	11	1107	0.7, 0.5–0.9
Ischaemic heart disease	2	730	1.9, 0.8–4.4	7	628	0.6, 0.4–1.02
Diabetes mellitus	4	1411	2.2, 1.2–4.2	14	1303	0.9, 0.7–1.1

Close relationship

- Tanaka et al (1999): ICH
- Roob et al (1999): Healthy
- Tsushima et al (2003): Healthy
- Lee et al (2002): NR Adm
- Chan et al. (1996): NR Adm

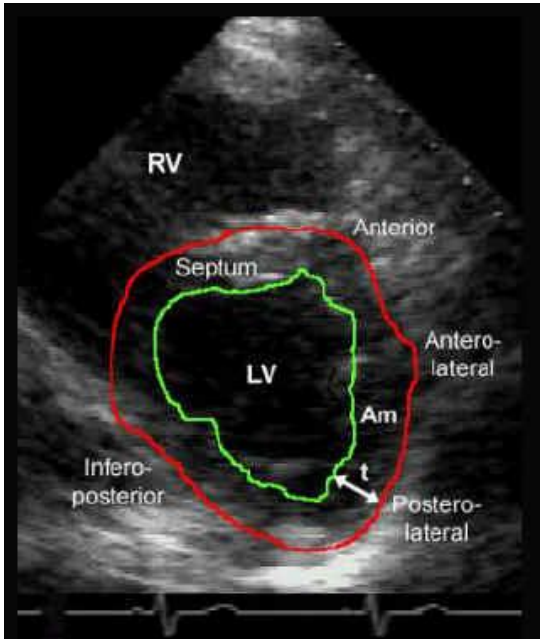
No relationship

- Jeerakathil et al (2003): Framingham
- Roob et al (2000): ICH
- Jeong et al (2004): ICH
- Greenberg et al (2004): Lobar ICH
- Fan et al. (2003): Acute ischemic stroke

Quantitative measurement of HT

HT severity and LVMI

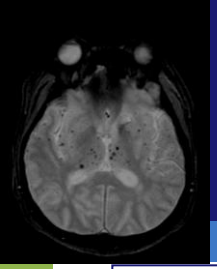
- HT severity is reflected by **left ventricular (LV) hypertrophy**
- **LV mass index (LVMI)**
  - **Calculation using parameters in TTE**
  - Devereux and Reicheck (1977)



LVMI (g/m2)=[1.05x{(LVEDD+IVSTd+PWTd])3-(LVEDD)3}-13.6]/BSA

-BSA confounder adjustment

-Accurate LVH index



CMB and LVMI

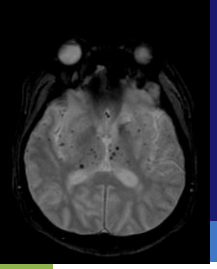
Left ventricular hypertrophy is associated with cerebral microbleeds in hypertensive patients

S.-H. Lee, MD; J.-M. Park, MD; S.-J. Kwon, MD; H. Kim, PhD; Y.-H. Kim, MPH; J.-K. Roh, MD, PhD; and B.-W. Yoon, MD, PhD

Neurology 2004;63:16-21

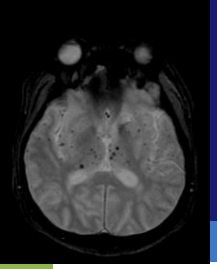
Table 5 *Ordinal logistic regression analysis*

Parameter	Odds ratio	95% CI	*p*
CMB in whole-brain area			
Grade of LV mass index	1.53	1.09–2.14	0.01
Previous stroke	2.47	1.17–5.22	0.02
Leukoaraiosis			
Grade of LV mass index	1.51	1.07–2.12	0.02
Old age, >75 y	1.06	1.02–1.1	0.01
Diabetes	3.67	1.07–2.12	0.01
CMB in subcortical white matter			
Previous stroke	2.31	1.05–5.06	0.04
CMB in central gray matter			
Body mass index	0.87	0.76–0.99	0.03
Grade of LV mass index	2.14	1.48–3.10	<0.01
Previous stroke	2.19	1.01–4.73	0.04
CMB in infratentorial area			
Grade of LV mass index	2.13	1.40–3.22	<0.01



The Other Risk Factors

- **Old age**
  - Roob et al., *Neurology* 1999; Jeerakathil et al., *Stroke* 2004
- **Cerebral amyloid angiopathy (CAA)**
  - Greenberg et al., *Neurology* 1996
- **Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL)**
  - A hereditary form of small-vessel disease
  - Lesnik Oberstein et al., *Neurology* 2001; Dichgans et al., *Stroke* 2002
- **Low serum cholesterol**
  - Lee et al., *Stroke* 2002
  - The lowest quartile of **total cholesterol (< 165 mg/dL**; OR = 10.9)



CMB and low cholesterol

Low Concentration of Serum Total Cholesterol Is Associated With Multifocal Signal Loss Lesions on Gradient-Echo Magnetic Resonance Imaging

Analysis of Risk Factors for Multifocal Signal Loss Lesions

Seung-Hoon Lee, MD; Hee-Joon Bae, MD; Byung-Woo Yoon, MD, PhD; Ho Kim, PhD; Dong-Eog Kim, MD; Jae-Kyu Roh, MD, PhD

Stroke. 2002;33:2845-2849.

TABLE 3. Comparison of Lipid Profiles Among the Groups of MSLLs

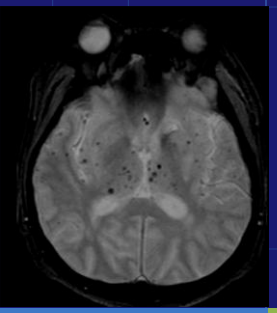
	Grade of MSLL				
	Absent	Mild	Moderate	Severe	*P**
TC, mmol/L	4.97±0.98	4.78±1.09	5.01±1.01	4.16±0.72	0.019
LDLC, mmol/L	3.02±0.86	2.85±0.95	3.18±0.39	2.30±0.62	0.009
HDLC, mmol/L	1.24±0.36	1.38±0.49	1.33±0.41	1.11±0.34	0.241†
TG, mmol/L	1.57±0.87	1.19±0.73	1.06±0.55	1.69±1.17	0.083†

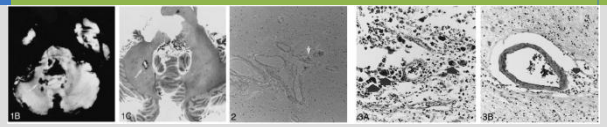
TABLE 5. Multivariate Analysis

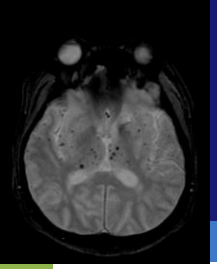
	OR	95% CI
Hypertension	3.42	1.17–9.97
Leukoaraiosis	4.62	2.87–7.41
TC <25th percentile	10.91	3.98–25.57
TC >75th percentile	2.45	0.96–6.26
HDLC <25th percentile	0.92	0.37–2.33
HDLC >75th percentile	3.46	1.45–8.29

Cumulative logits model.

Clinical Implications

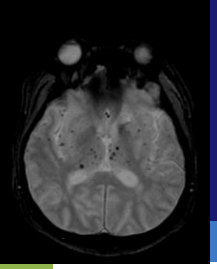






Clinical Implications

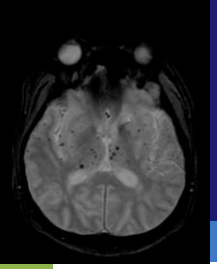
1. Prediction of ICH
2. Prediction of hemorrhagic transformation
3. Caution with antiplatelet or anticoagulant treatment



Prediction of ICH

Patients with HT

- Who will have **ischemic** vs **hemorrhagic** stroke?
- **Microbleeds** might be a prediction tool for future event?



Regional Association

Cerebral microbleeds are regionally associated with intracerebral hemorrhage

S.H. Lee, MD; H.J. Bae, MD; S.J. Kwon, MD; H. Kim, PhD; Y.H. Kim, MPH; B.W. Yoon, MD, PhD

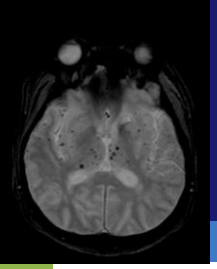
Neurology 2004;62:72-76

- Cross-sectional design
- 227 stroke patients (144 ischemic; 83 hemorrhagic)
- *In situ* correlation of distribution

Table 3 *Logistic regression analysis for ICH in CSC and DGM*

	CSC			DGM		
Variable	*p*	OR	(95% CI)	*p*	OR	(95% CI)
Leukoaraiosis	0.46	0.78	(0.41–1.50)	0.78	1.07	(0.66–1.75)
CMB location						
CSC CMB	<0.01	5.50	(2.68–11.27)	0.27	1.33	(0.80–2.21)
DGM CMB	0.09	0.51	(0.24–1.11)	<0.01	2.55	(1.46–4.45)
IT CMB	0.73	1.13	(0.56–2.31)	0.10	0.60	(0.32–1.10)
Old lacune location						
CSC lacune	0.49	0.74	(0.32–1.73)	0.95	1.02	(0.58–1.80)
DGM lacune	0.32	1.35	(0.74–2.48)	0.88	0.97	(0.63–1.48)
IT lacune	0.29	0.60	(0.24–1.54)	<0.01	0.36	(0.17–0.77)

ICH = intracerebral hemorrhage; CSC = corticosubcortical area; DGM = deep gray matter; OR = odds ratio; IT = infratentorial area.



Evidences in Prospective Data

Cerebral Microbleeds as a Risk Factor for Subsequent Intracerebral Hemorrhages Among Patients With Acute Ischemic Stroke

Fan et al. Stroke 2003

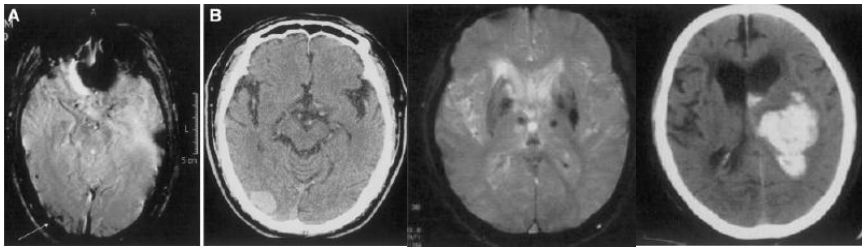


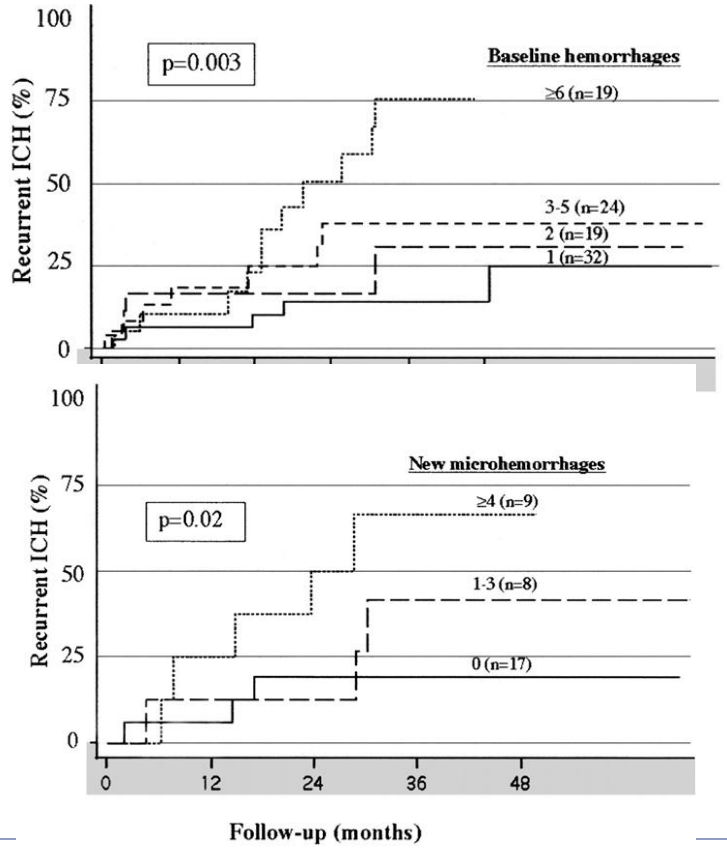
TABLE 2. Vascular Events During Follow-Up of 121 Patients

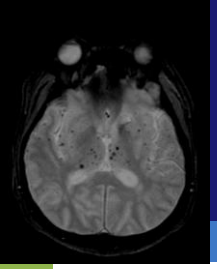
	Total (n=121), n (%)	MBs(+) (n=43), n (%)	MBs(−) (n=78), n (%)	*P*
Recurrent stroke	16 (13.2)	9 (20.9)	7 (9.0)	0.157
Intracerebral hemorrhage	5 (4.13)	4 (9.3)	1 (1.28)	0.053*
Cerebral infarction	11 (9.01)	5 (11.6)	6 (7.7)	0.747*
Ischemic heart disease	5 (4.13)	1 (2.33)	4 (5.13)	0.654*
Death	14 (11.6)	5 (11.6)	9 (11.5)	1.0*

*Fisher's exact test.

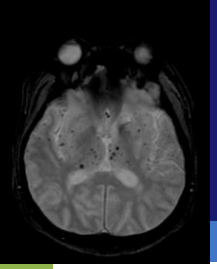
Hemorrhage Burden Predicts Recurrent Intracerebral Hemorrhage After Lobar Hemorrhage

Greenberg et al. Stroke 2004



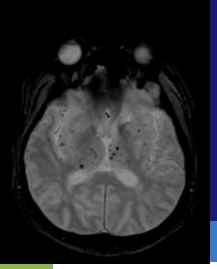


1. Prediction of ICH
2. **Prediction of hemorrhagic transformation**
3. Caution with antiplatelet or anticoagulant treatment



The First Suggestions

- **After thrombolysis**
  - Kidwell et al., *Stroke 2002*
  - Pretreatment GRE MRI before IA thrombolysis (n=41)
  - 5 patients with microbleeds
  - Major symptomatic hemorrhage (n=5)
  - **Patients with microbleeds: n=1 (p = 0.049)**
- **After acute stroke in general**
  - Nighoghossian et al., *Stroke 2002*
  - 100 patients with acute ischemic stroke: 20 patients with microbleeds
  - Early hemorrhagic transformation was occurred 26 patients in F/U GRE or CT: 10 patients with microbleeds
  - **Microbleeds are an independent risk factor for early hemorrhagic transformation (p<0.0001)**



Contradictory Data

Thrombolysis for Ischemic Stroke in Patients with Old Microbleeds on Pretreatment MRI

Laurent Derex[a, d] Norbert Nighoghossian[a, d] Marc Hermier[c, d]
Patrice Adeleine[b] Frédéric Philippeau[a] Jérôme Honnorat[a] Hasan Yilmaz[c]
Pascal Dardel[c] Jean-Claude Froment[c, d] Paul Trouillas[a]

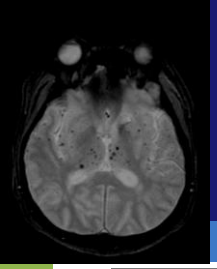
Cerebrovasc Dis 2004;17:238–241

CME

Clinical importance of microbleeds in patients receiving IV thrombolysis

W. Kakuda, MD; V.N. Thijs, MD, PhD; M.G. Lansberg, MD, PhD; R. Bammer, PhD; L. Wechsler, MD;
S. Kemp, BS; M.E. Moseley, PhD; M.P. Marks, MD; and G.W. Albers, MD, for the DEFUSE Investigators*

NEUROLOGY 2005;65:1175–1178



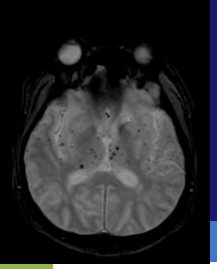
After Thrombolysis

*B*leeding *R*isk *A*nalysis in *S*troke *I*maging Before Thrombo*L*ysis (BRASIL)

Pooled Analysis of T2*-Weighted Magnetic Resonance Imaging Data From 570 Patients

Fiehler et al., *Stroke* 2007

- A pooled analysis of 570 patients in 13 centers in Europe, North America, and Asia
- Microbleeds within 6 hours from onset
- No controlled, no randomized study, retrospective sampling in some centers
- Proportions of patients with symptomatic hemorrhage
  - **5.8%** (95% CI, 1.9 to 13.0) in the presence of microbleeds
  - **2.7%** (95% CI, 1.4 to 4.5) in patients without CMB
  - **No significant absolute increase (P=0.170, Fisher's exact test)**
- **If there is any increased risk of ICH attributable to microbleeds, it is likely to be small and unlikely to exceed the benefits of thrombolytic therapy.**



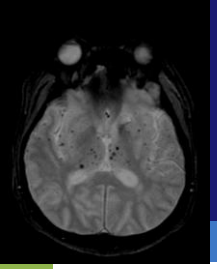
Without Thrombolysis

Does microbleed predict haemorrhagic transformation after acute atherothrombotic or cardioembolic stroke?

S-H Lee,[1,2] B-S Kang,[1] N Kim,[1] J *J Neurol Neurosurg Psychiatry* 2008;**79**:913–916.

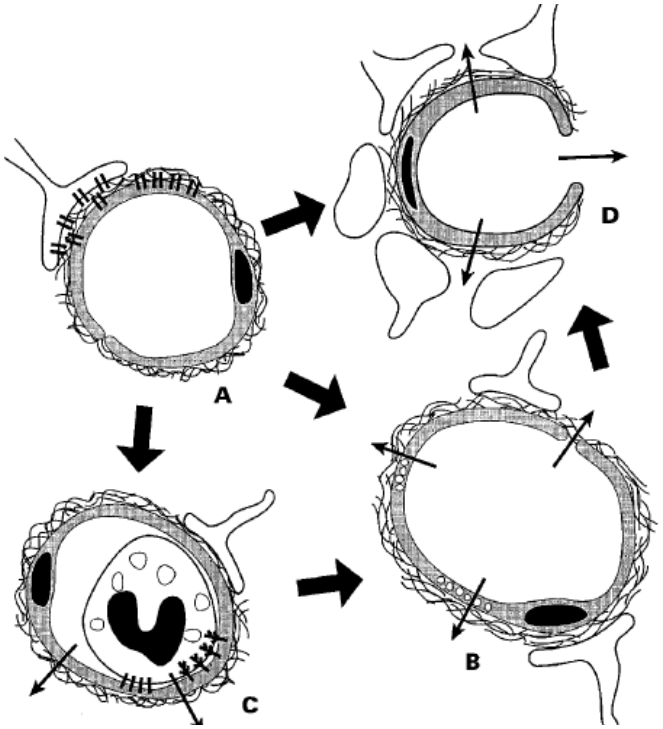
SNUH study

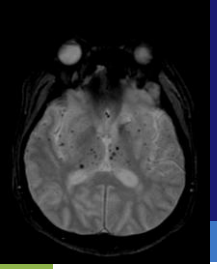
- Study population : 380 among 1,034 acute ischemic stroke
  - Large artery atherosclerosis (n=219)
  - Cardioembolism (n=161)
- lack of significance between MBs and HTf
  - Presence vs absence of CMB
  - Number of CMB
  - Stroke mechanism
- **Conclusion**
  - **Underlying MBs do not predict incident HTf after acute ischemic stroke.**



Difference in ICH Mechanism

- **ICH**
  - ICH was associated with **chronic hypertensive microangiopathy** such as lipohyalinosis, microartheroma, and microaneurysm
  - Microbleeds:
- **Hemorrhagic transformation**
  - Associated with **ischemic injury to the microvasculature** such as loss of basal laminar in extensive brain infarction





1. Prediction of ICH
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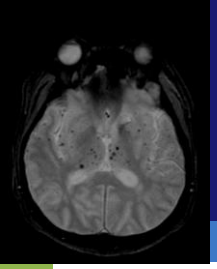


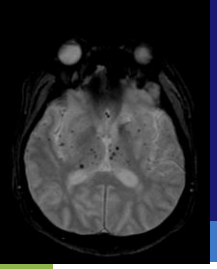
Association

AFTER ASPIRIN MEDICATION

Asymptomatic microbleeds as a risk factor for aspirin-associated intracerebral hemorrhages

Wong et al, *Neurology* 2003;60:511-513

	Symptomatic intracerebral hemorrhage		
Characteristics	Yes (n = 21)	No (n = 21)	*p* Value
Aspirin users	21	21	
	Asymptomatic microhemorrhages on GRE MRI		
Presence	19	7	<0.001
Mean no. (range)	13.3 (0–54)	0.4 (0–2)	<0.001
Distribution			
Lobar region	16	5	0.002
Basal ganglia	13	3	0.002
Thalamus	13	0	<0.001
Pons	10	0	<0.001
Cerebellum	10	0	<0.001



Association

AFTER WARFARIN MEDICATION

Cerebral microbleeds are a risk factor for warfarin-related intracerebral hemorrhage

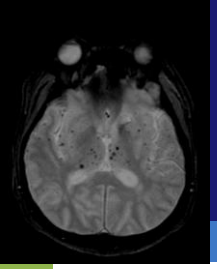
Lee SH et al. Neurology® 2009;72:171-176

SNUH study population

Case 24 vs. control 48

Table 3 Conditional logistic regression analysis

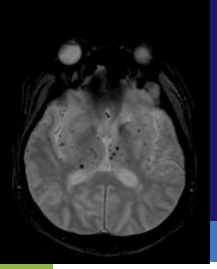
Variables	OR	95% CI	*p* Value
PT-INR	4.13	1.40-12.77	0.011
Presence of microbleeds	83.12	5.96-1,159.10	0.001
WMH	3.60	0.70-113.64	0.093



Another question

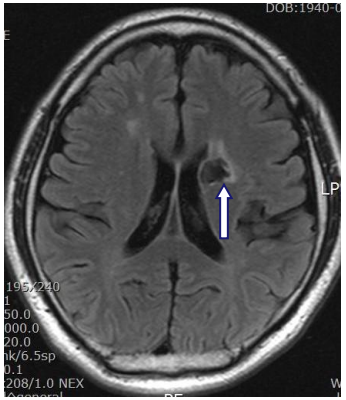
Is antiplatelet or anticoagulant treatment associated with a higher prevalence of CMBs?

- Some studies provide data about the use of antiplatelet/anticoagulant agents at the time of brain MRI examination.
- No association with **antiplatelet agents** and increased risk of possessing CMBs
  - Ischemic stroke (Nighoghossian et al., 2002; Schonewille et al., 2005), ICH (Jeong et al., 2004; Lee et al., 2006), CADASIL (Lesnik Oberstein et al., 2001)
- No association with **anticoagulant** treatment and increased risk of possessing CMBs
  - Ischemic stroke (Schonewille et al., 2005), ICH (Jeong et al., 2004)

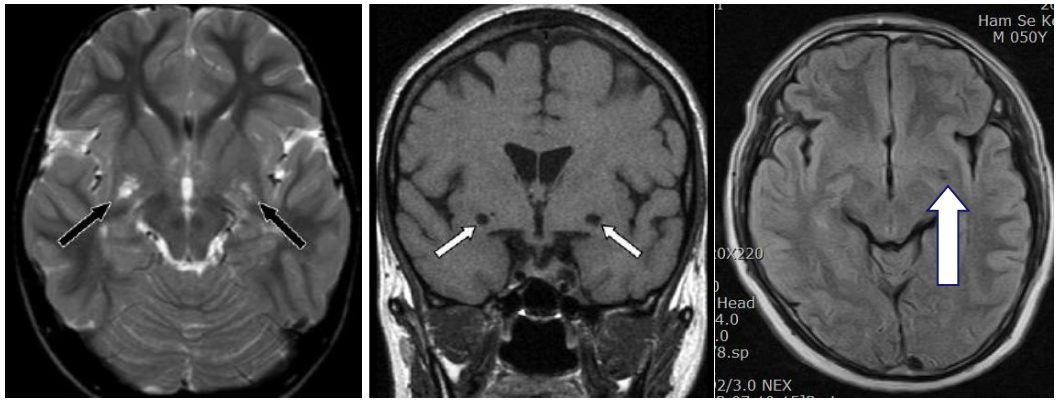


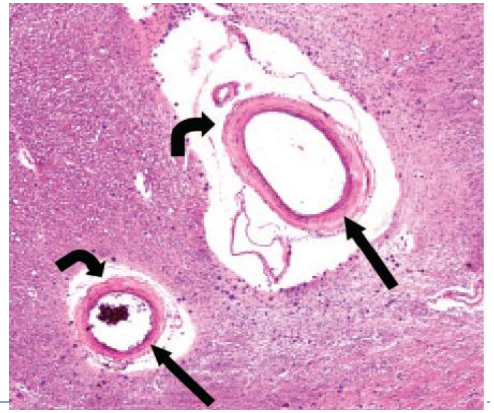
Silent infarction

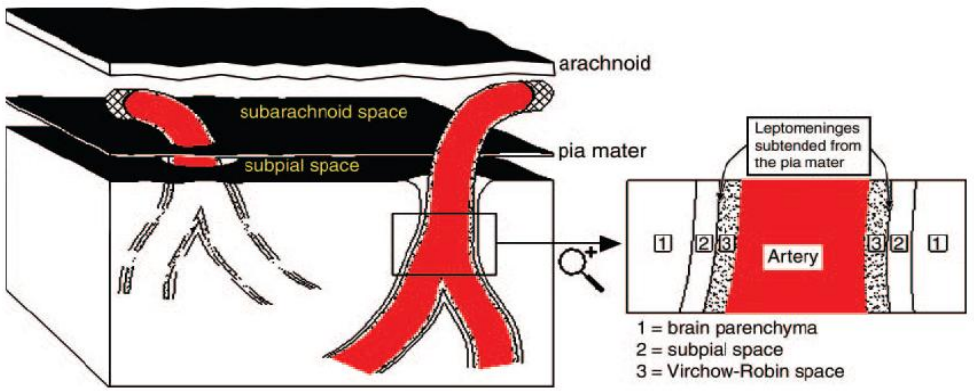
Silent infarct

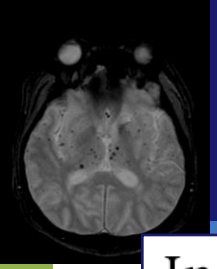


- Infarct occurred at non-eloquent area
- Perilesional gliosis (+)
- Differential point: Dilated perivascular space









Prevalence

Incidental Findings on Brain MRI in the General Population

N Engl J Med 2007;357:1821-8.

- As a related study of Rotterdam Scan Study
- Age > 45Y

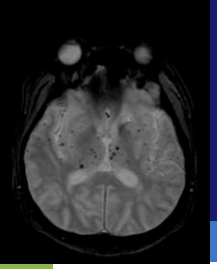
Table 1. Incidental Findings on 2000 MRI Scans.*

Finding	No. (%)
Asymptomatic brain infarct†	145 (7.2)
Lacunar infarct	112 (5.6)
Cortical infarct	41 (2.0)
Primary tumors, benign	31 (1.6)
Meningioma	18 (0.9)
Vestibular schwannoma	4 (0.2)
Intracranial lipoma‡	2 (0.1)
Trigeminal schwannoma	1 (<0.1)
Pituitary adenoma	6 (0.3)

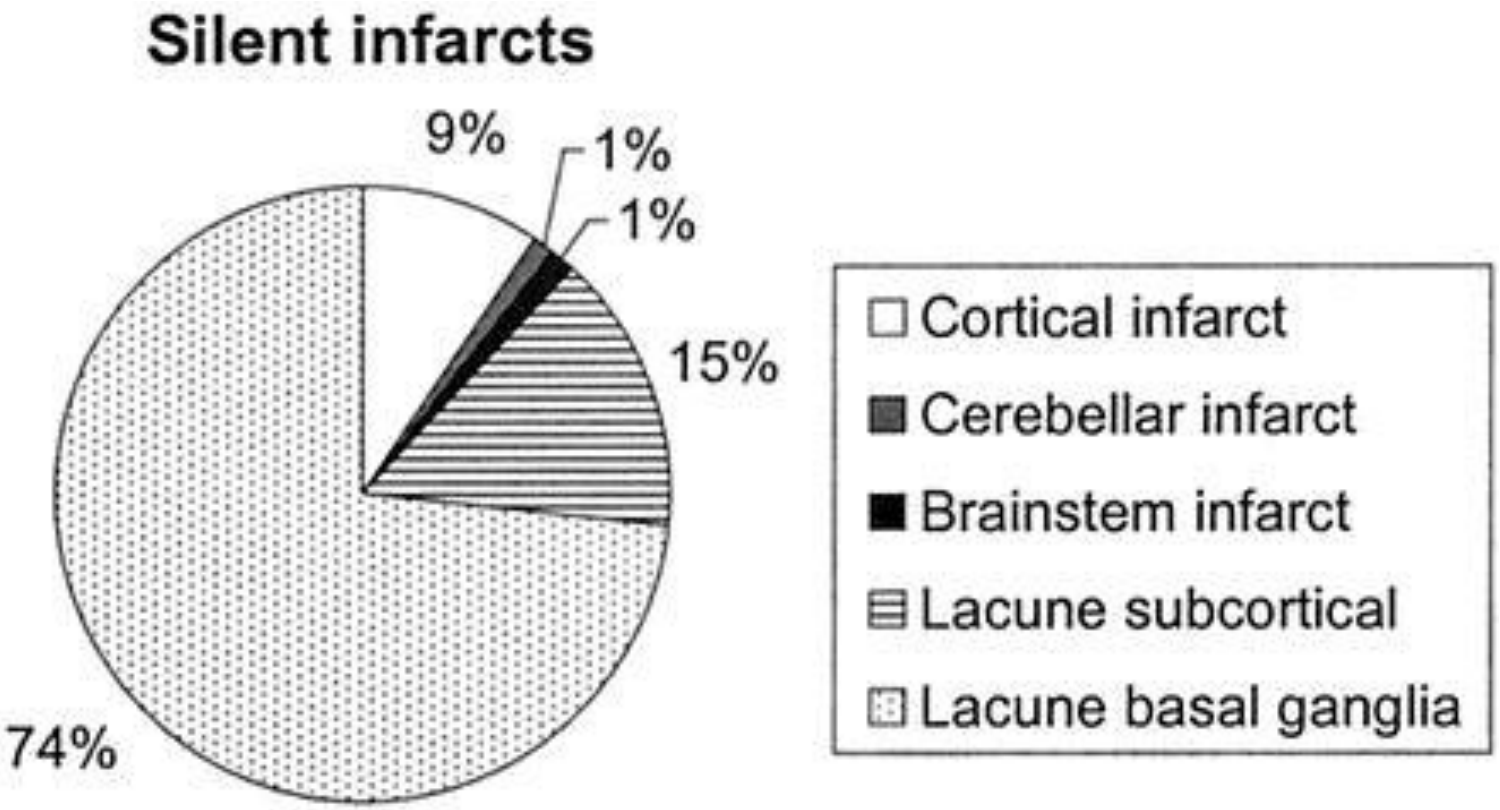
Silent brain infarcts: a systematic review

	Mean age (range), years	SBI, %
Helsinki Aging Brain Study (HABS), 1995[9]	72 (56–88)	16
Cardiovascular Health Study (CHS), 1997[10]	75 (65–97)	28
Atherosclerosis Risk in Communities (ARIC) Study, 1998[11]	63 (55–72)	11
Rotterdam Scan Study (RSS), 2002[12]	72 (60–90)	20
National Institute for Longevity Sciences - Longitudinal Study of Aging (NILS-LSA), 2003[13]	59 (40–79)	10
Memory and Morbidity in Augsburg Elderly (MEMO) study, 2004[14]	72 (65–83)	13
Framingham Heart Study (FHS), 2005[15]	62 (34–97)	12
Austrian Stroke Prevention Study (ASPS), 2006[16]	64 (50–75)	8

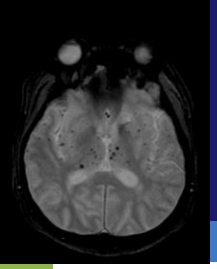
Lancet Neurol 2007; 6: 611–19



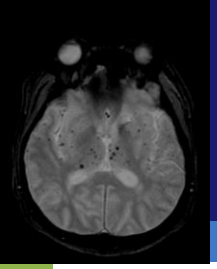
Location



Vermeer, NEJM 2003

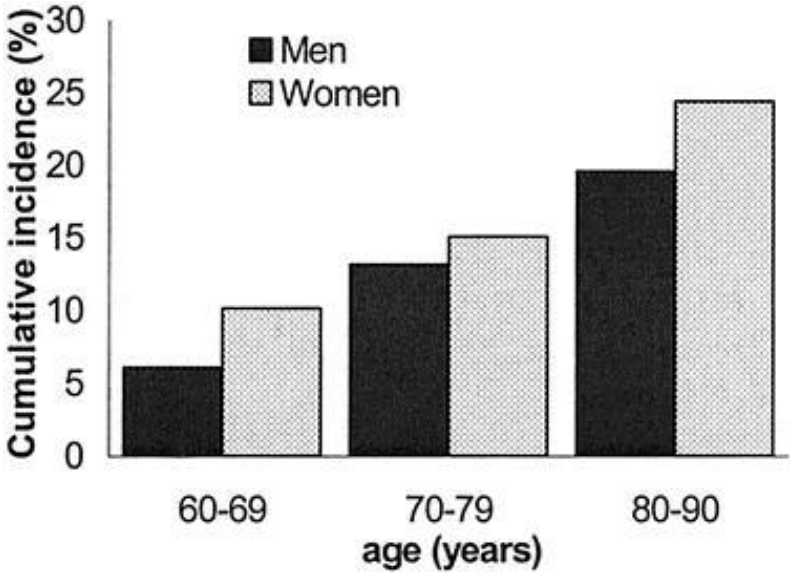


Risk factors

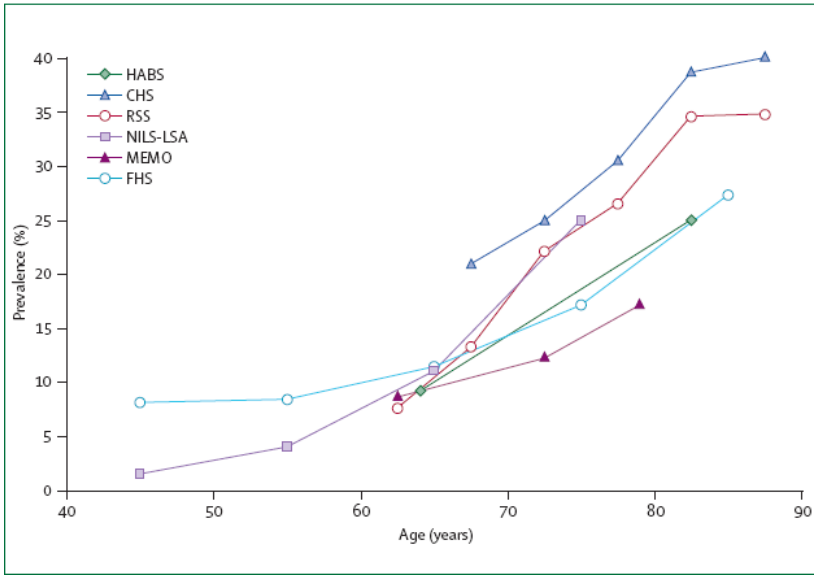


Age

- Rotterdam study
- Age 60-90
- MRI: mean 3.4 yr later (n=668)
- At least 1 new infarct in 14% (87% of these silent)



Vermeer et al. Stroke 2003



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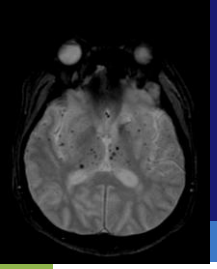
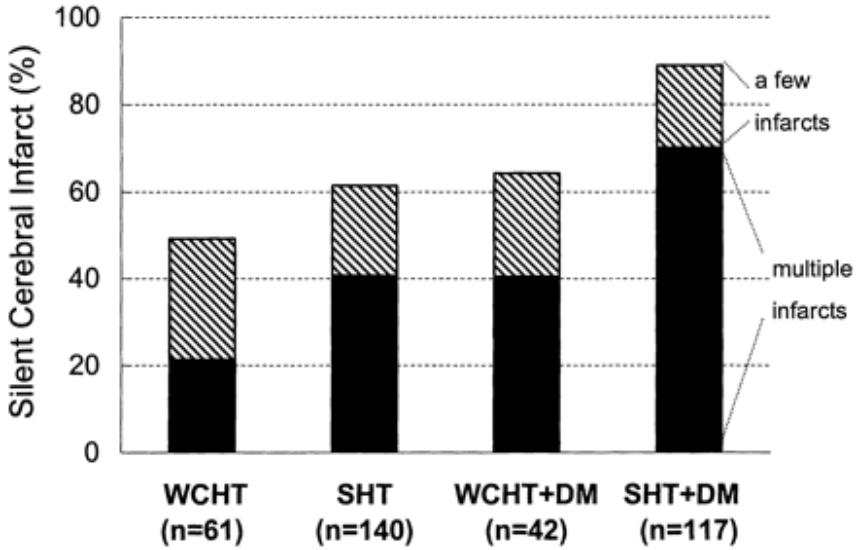


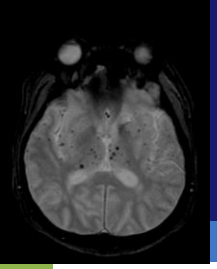
Coexistence of risk factors

- In asymptomatic HT pts. (n=360)
- Infarcts more common if DM also present

	DM + HT	Just HT
≧ 1 infarct	82%	58%
≧ 3 infarct	62%	35%



Eguchi et al. Stroke 2003



Blood pressure fluctuation

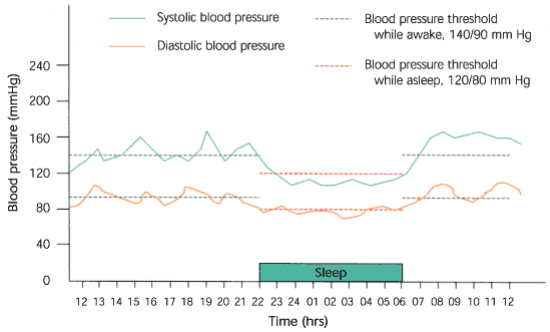
A) Dipper : noctural BP decrease (10-19%) compared to daytime BP

B) Non-Dipper: noctural BP decrease less than 10% compared to daytime BP

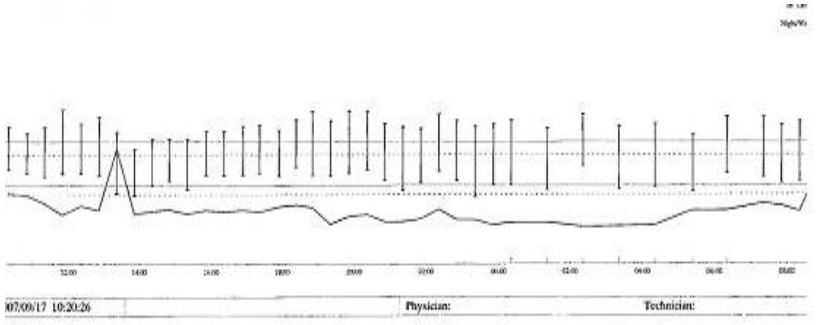
C) Extreme dipper: nocturnal BP decrease more than 20%

D) Reverse dipper : noctural BP increase

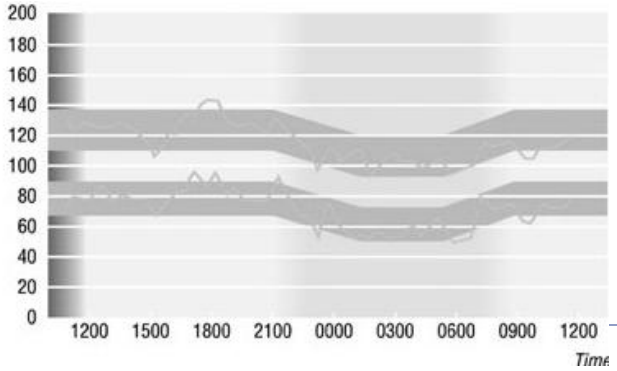
A



B



C



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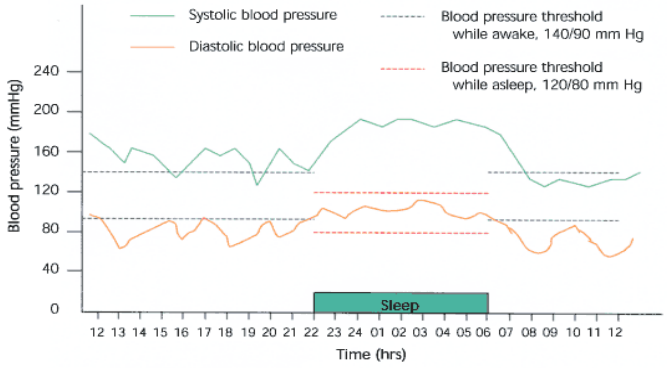
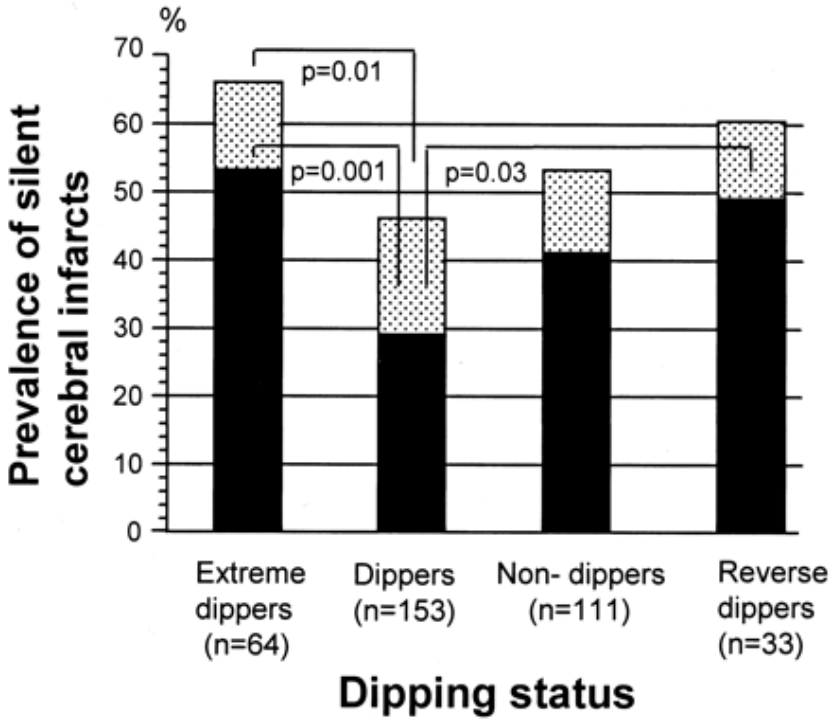
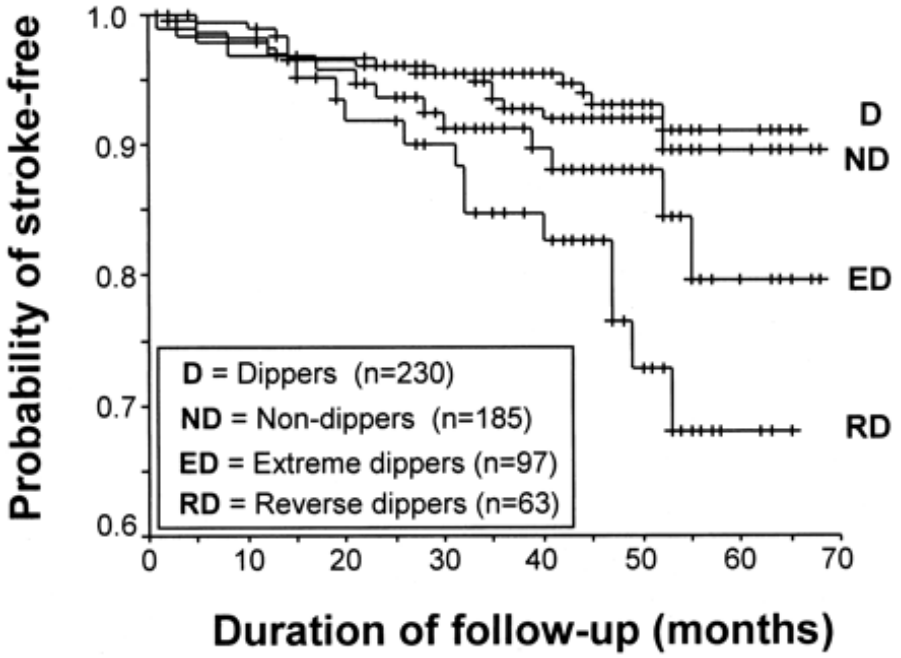
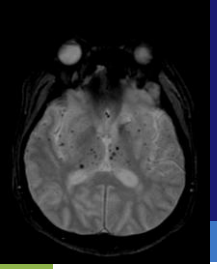


Blood pressure fluctuation





Kario et al. Hypertension 2001



Metabolic syndrome

Metabolic Syndrome as an Independent Risk Factor of Silent Brain Infarction in Healthy People

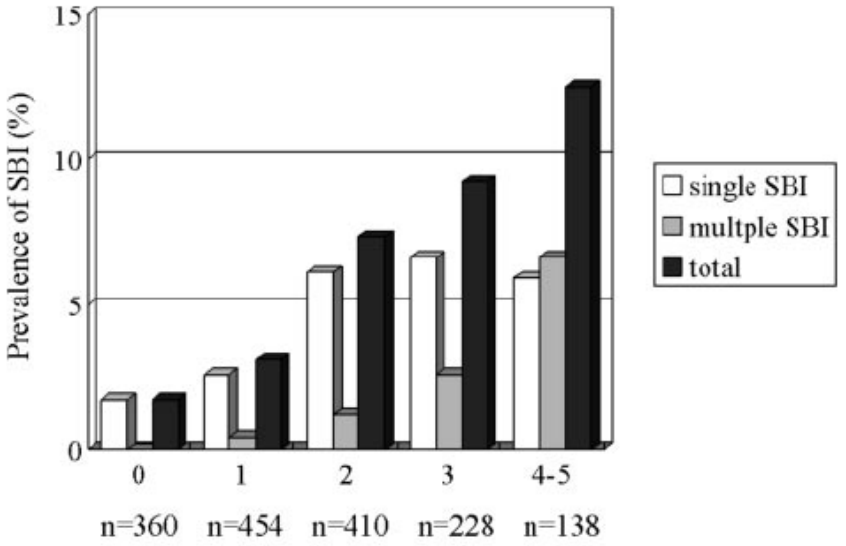
Hyung-Min Kwon, MD; Beom Joon Kim, MD; Seung-Hoon Lee, MD; Seung Ho Choi, MD; Byung-Hee Oh, MD, PhD; Byung-Woo Yoon, MD, PhD

- 88/1588 = 5.5%, (5.9%, >40Y)

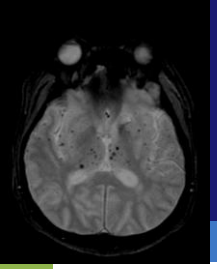
TABLE 1. Demographic Data of Study Subjects and Prevalence of SBI

	Prevalence		
Age, y	Male	Female	Total
<40	1/86 (1.2)	1/57 (1.8)	2/143 (1.4)
40–49	8/247 (3.2)	4/159 (2.5)	12/406 (3.0)
50–59	12/315 (3.8)	8/240 (3.3)	20/555 (3.6)
60–69	21/217 (9.7)	15/164 (9.1)	36/381 (9.4)
≥70	11/62 (17.7)	7/41 (17.1)	18/103 (17.5)

Values in parentheses represent percentages.



MetS factor



A marker for further stroke

Silent Brain Infarcts and White Matter Lesions Increase Stroke Risk in the General Population

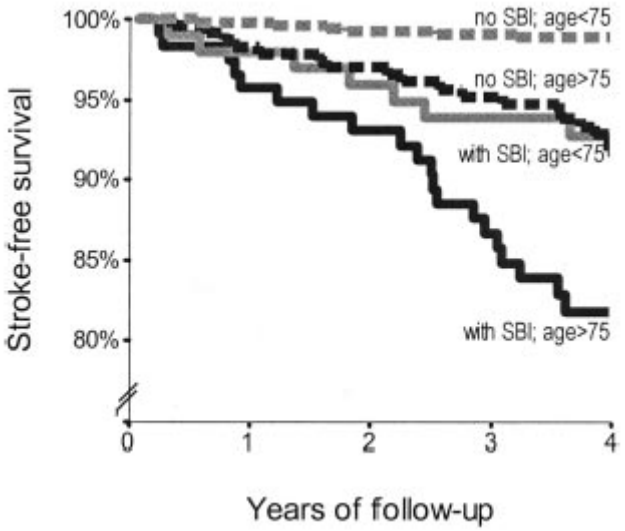
The Rotterdam Scan Study

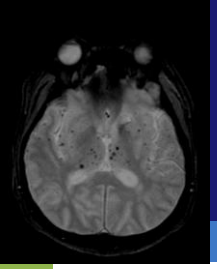
Sarah E. Vermeer, MD; Monika Hollander, MD; Ewoud J. van Dijk, MD;
Albert Hofman, MD; Peter J. Koudstaal, MD; Monique M.B. Breteler, MD

(*Stroke*. 2003;34:1126-1129.)

TABLE 2. Relationship Between the Presence of Silent Brain Infarcts, Tertiles of Periventricular, and Subcortical White Matter Lesions (WML) on MRI and the Risk of Stroke

	Risk of Stroke (Hazard Ratio [95% CI])		
	Adjusted for Age and Sex	Adjusted for Stroke Risk Factors*	Adjusted for MRI Lesions†
Silent brain infarcts			
Absent	1 (reference)	1 (reference)	1 (reference)
Present	3.6 (2.1–6.1)	3.9 (2.3–6.8)	3.3 (1.8–5.9)





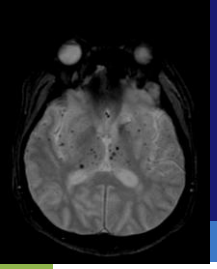
Silent infarction and cognitive decline

- Infarction occurred at the area of non-motor and non-sensory area
- Mainly frontal subcortex and basal ganglia
- Frontal executive function

Table 2. Relation between the Presence of Silent Brain Infarcts at Base Line, the Severity of Periventricular and Subcortical White-Matter Lesions, and the Risk of Dementia.

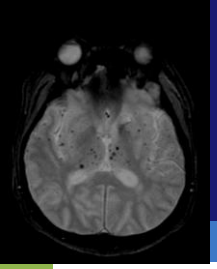
Variable	Hazard Ratio (95% Confidence Interval)	
	Adjusted for Age, Sex, and Level of Education	Adjusted for Age, Sex, Level of Education, and MRI Measures*
Silent brain infarcts (yes vs. no)	2.26 (1.09–4.70)	2.03 (0.91–4.55)
Severity of periventricular white-matter lesions (per SD increase)	1.59 (1.13–2.25)	1.47 (0.92–2.35)
Severity of subcortical white-matter lesions (per SD increase)	1.21 (0.96–1.53)	0.92 (0.65–1.29)

Vermeer et al, NEJM 2003



Summary (1)

- **Microbleeds are associated with…**
  1. ICH in the patients with ischemic stroke
  2. Recurrent ICH
  3. ICH occurred in the patients with aspirin/warfarin(?)
- **Microbleeds are NOT associated with…**
  1. Hemorrhagic transformation after thrombolysis
  2. Early hemorrhagic transformation in the acute phase of ischemic stroke
- Microbleeds may **reflect baseline status of BBB disruption**.



Summary (2)

- **Silent infarction**
  - Associated with stroke risk factors
  - associated with metabolic syndrome

  - Predicts future stroke risk (HR 3.3)
  - Is associated with cognitive decline

  - **Future studies will have to show whether screening and treating high-risk patients can effectively reduce the risk of further infarcts, stroke, and dementia.**

Thank You !