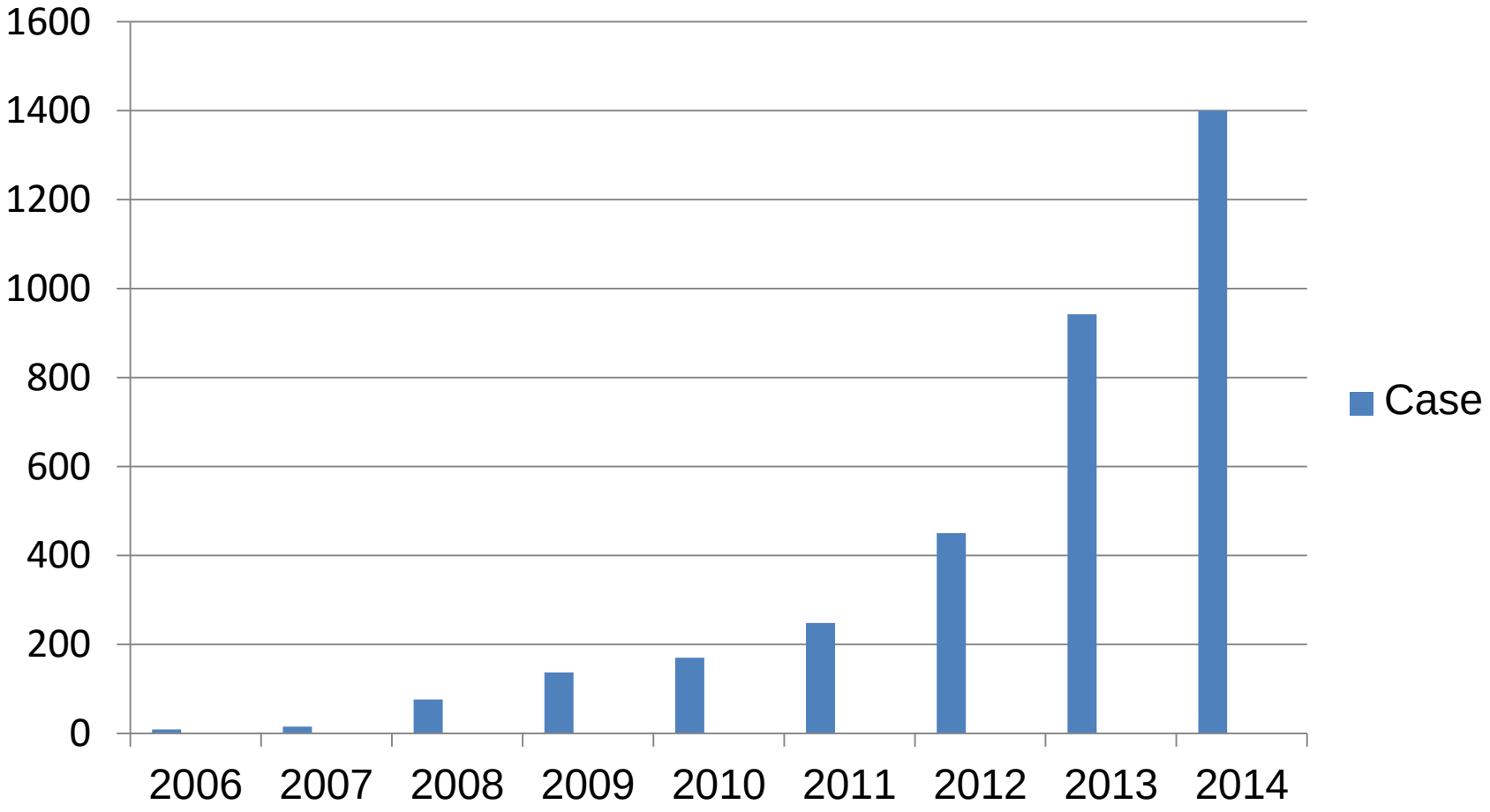
ĐIỀU TRỊ TỐI ƯU TRONG PHÒNG NGỪA ĐỘT QUỴ THỨ PHÁT

TS.BS Nguyễn Huy Thắng
Khoa BLMMN, BV Nhân Dân 115

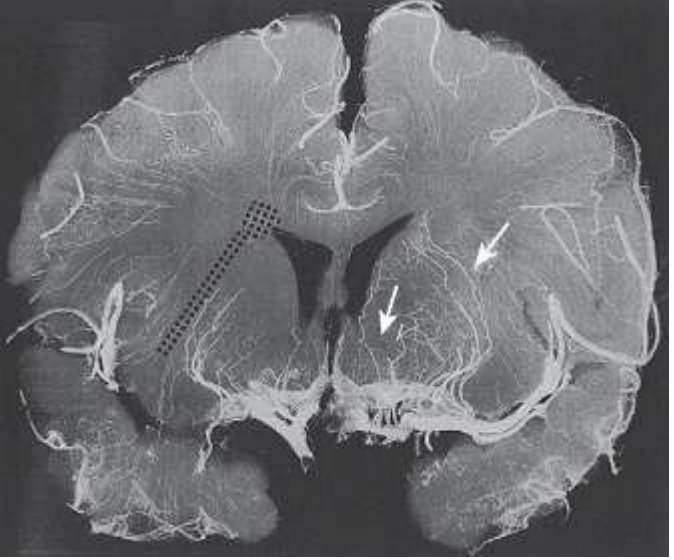
Country Data of Number of Patients treated with IV-rtPA



More than 90% was used in tertiary Hospital

Source BI Vietnam

All Treatment after Acute Stroke are the same ???

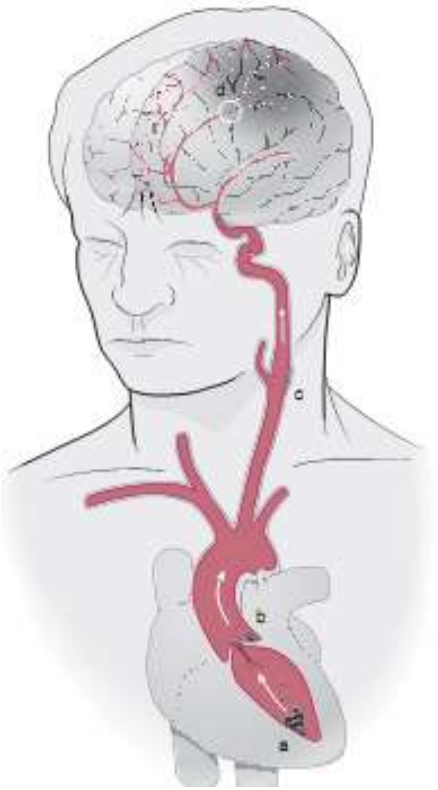


Bệnh Lý Mạch máu Nhỏ

30-40%

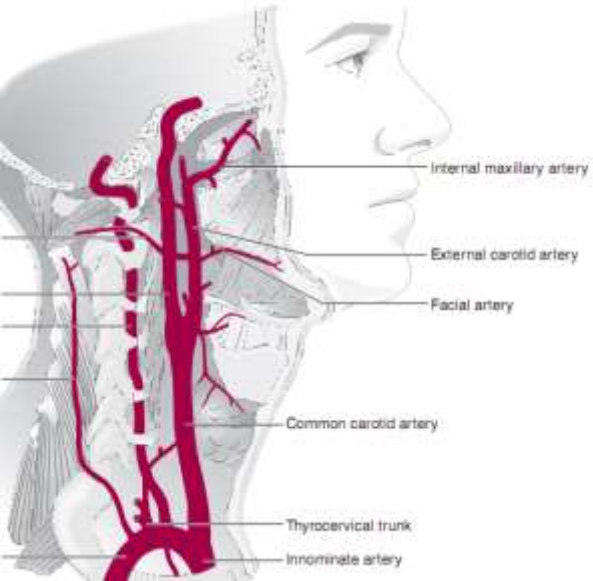
Huyết khối từ tim

10-20%



CÁC NGUYÊN NHÂN ĐỘT QUỴ

Bệnh Lý Mạch máu Lớn



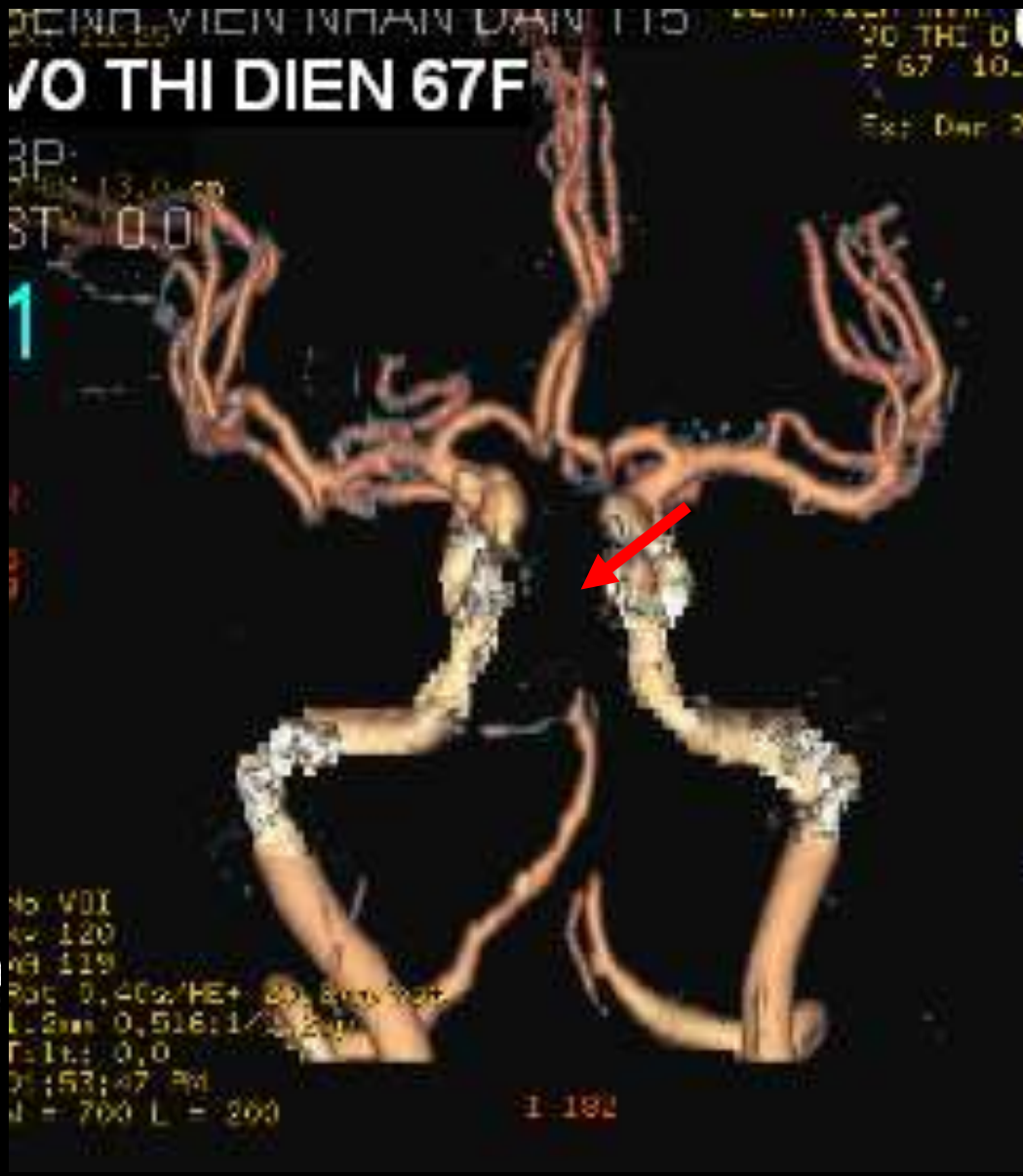
30-40%

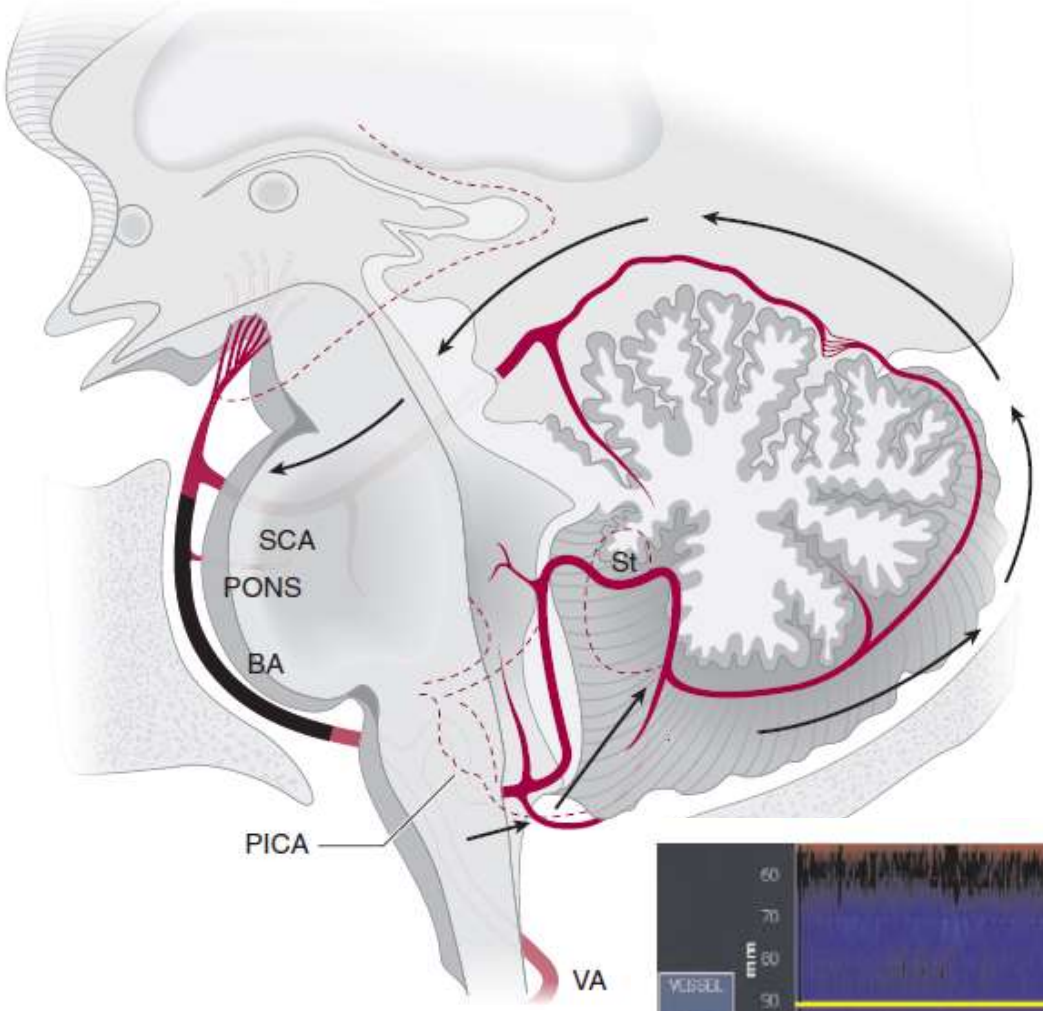
Nguyên Nhân Không Xác Định

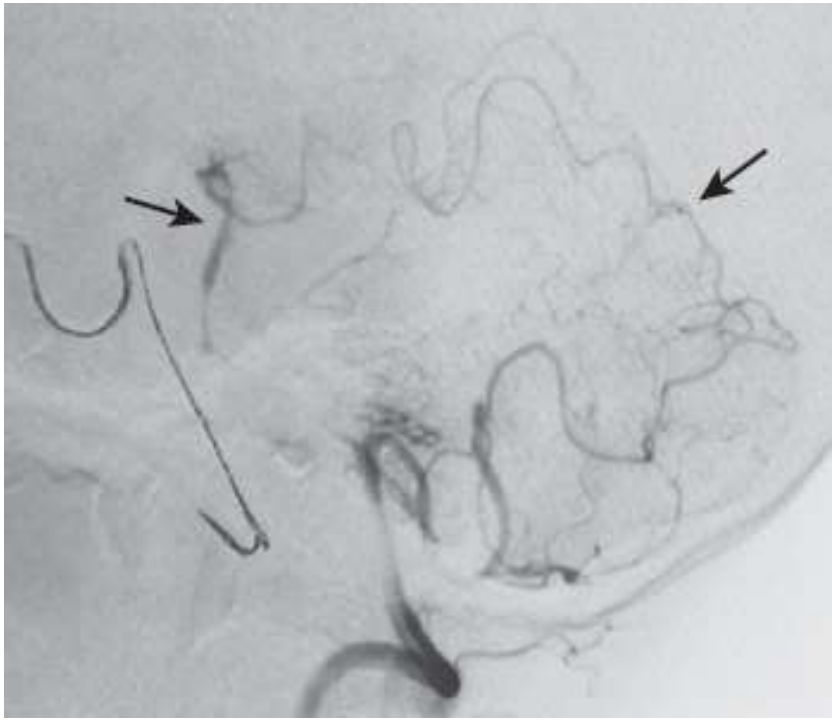
20 - 30%

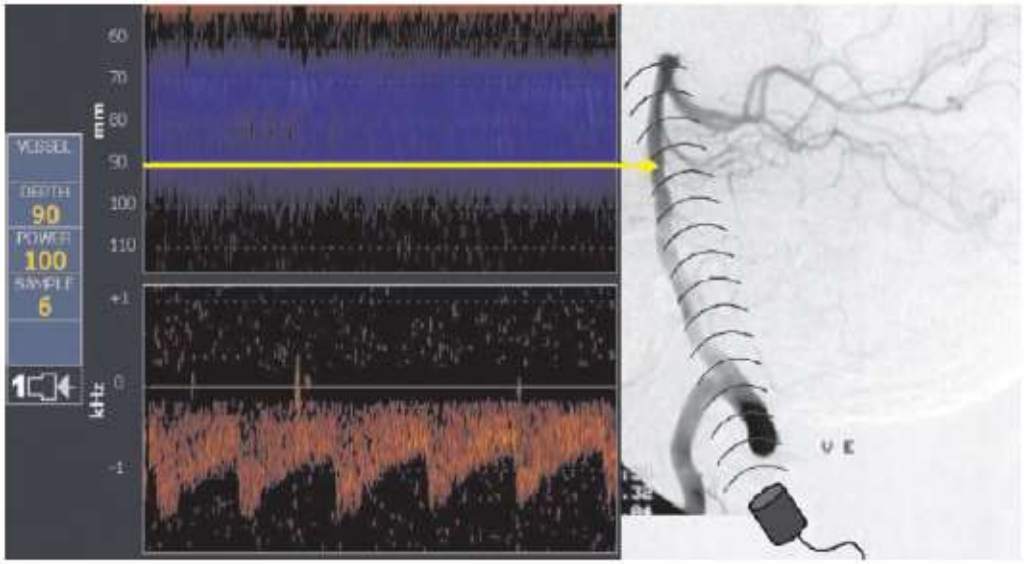
CASE 1

- BN nữ 67T, nhập viện vì hôn mê
- NIHSS 34, nhập viện lúc 12g
- Thời điểm còn bình thường gần nhất 1g sáng.
- T/c: Tăng huyết áp
- ECG nhịp xoang


VO THI DIEN 67F



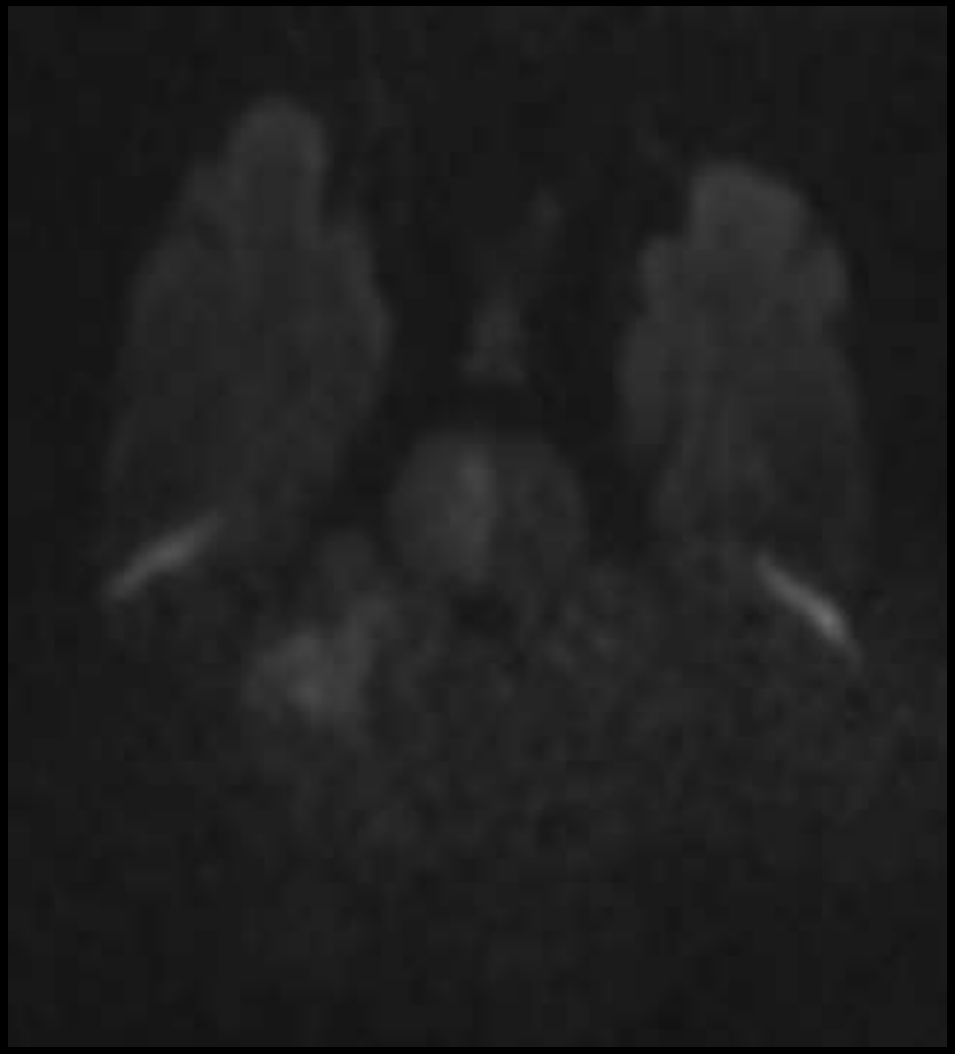




The Caplan ‘s Stroke book

Marc Ribo et al, Stroke

IV rtPA sau 13 giờ tính từ thời điểm BN còn bình thường, NIHSS 8 lúc xuất viện, mRS 3 sau 3 tháng



Pathogenic Mechanisms

	ICAS (n=612)	ECAS (n=224)	P-value
Mechanism			
A to A embolism	333 (54.4)	212 (94.6)	0.000
In situ thrombosis	126 (20.6)	2 (0.9)	0.000
Perforator occlusion	160 (26.1)	0 (0.0)	0.000
Hemodynamic	7 (1.1)	10 (4.5)	0.005

PROSAC registry . Kim JS et al Stroke 2012

AHA/ASA Guideline

Guidelines for the Prevention of Stroke in Patients With Stroke or Transient Ischemic Attack

- Aspirin (50-325mg) Class I, Level A
- Aspirin + Dipyridamole Class I, Level B
- Clopidogrel Class IIa, Level B

Lựa chọn thuốc chống kết tập tiểu cầu nên tùy vào từng cá nhân bệnh nhân với các yếu tố nguy cơ khác nhau

Stroke. 2011;42:227-276

Lựa Chọn Điều Trị Hẹp ĐM Nội Sọ

- Phẩu Thuật EC-IC Bypass
- Điều trị nội khoa: Chống kết tập tiểu cầu & Statin hoặc Warfarin
- Can thiệp nội mạch: đặt Stent

SIZE OF TREATMENT EFFECT

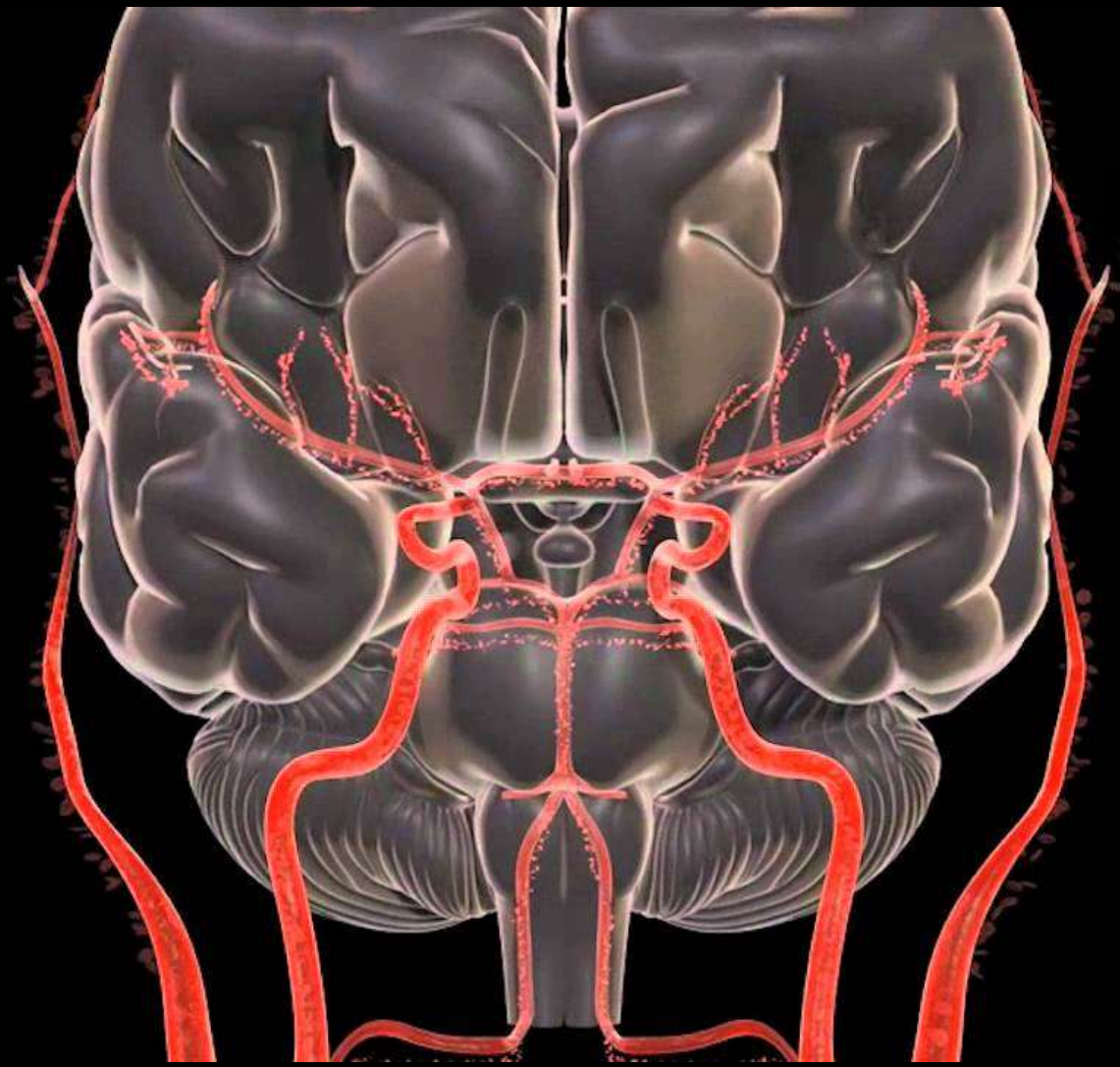
ESTIMATE OF CERTAINTY (PRECISION) OF TREATMENT EFFECT

	CLASS I *Benefit >>> Risk* Procedure/Treatment **SHOULD** be performed/ administered	CLASS IIa *Benefit >> Risk* *Additional studies with focused objectives needed* **IT IS REASONABLE** to perform procedure/administer treatment	CLASS IIb *Benefit ≥ Risk* *Additional studies with broad objectives needed; additional registry data would be helpful* Procedure/Treatment **MAY BE CONSIDERED**	CLASS III *No Benefit* or CLASS III *Harm* COR III: No benefit — Procedure/Test: Not Helpful — Treatment: No Proven Benefit COR III: Harm — Procedure/Test: Excess Cost w/o Benefit or Harmful — Treatment: Harmful to Patients
LEVEL A Multiple populations evaluated* Data derived from multiple randomized clinical trials or meta-analyses	■ Recommendation that procedure or treatment is useful/effective ■ Sufficient evidence from multiple randomized trials or meta-analyses	■ Recommendation in favor of treatment or procedure being useful/effective ■ Some conflicting evidence from multiple randomized trials or meta-analyses	■ Recommendation's usefulness/efficacy less well established ■ Greater conflicting evidence from multiple randomized trials or meta-analyses	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Sufficient evidence from multiple randomized trials or meta-analyses
LEVEL B Limited populations evaluated* Data derived from a single randomized trial or nonrandomized studies	■ Recommendation that procedure or treatment is useful/effective ■ Evidence from single randomized trial or nonrandomized studies	■ Recommendation in favor of treatment or procedure being useful/effective ■ Some conflicting evidence from single randomized trial or nonrandomized studies	■ Recommendation's usefulness/efficacy less well established ■ Greater conflicting evidence from single randomized trial or nonrandomized studies	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Evidence from single randomized trial or nonrandomized studies
LEVEL C Very limited populations evaluated* Only consensus opinion of experts, case studies, or standard of care	■ Recommendation that procedure or treatment is useful/effective ■ Only expert opinion, case studies, or standard of care	■ Recommendation in favor of treatment or procedure being useful/effective ■ Only diverging expert opinion, case studies, or standard of care	■ Recommendation's usefulness/efficacy less well established ■ Only diverging expert opinion, case studies, or standard of care	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Only expert opinion, case studies, or standard of care
	Indicated	**Probably Indicated**	**May consider**	**Not Indicated**

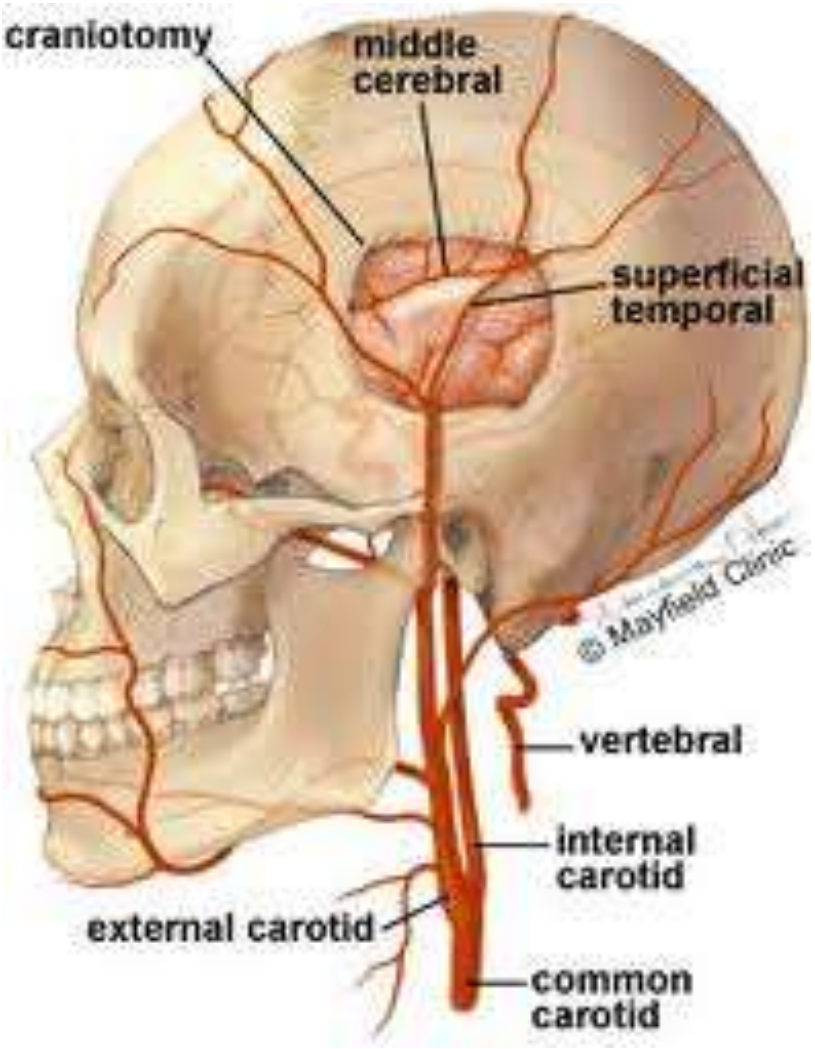
Lựa Chọn Điều Trị Hẹp ĐM Nội Sọ

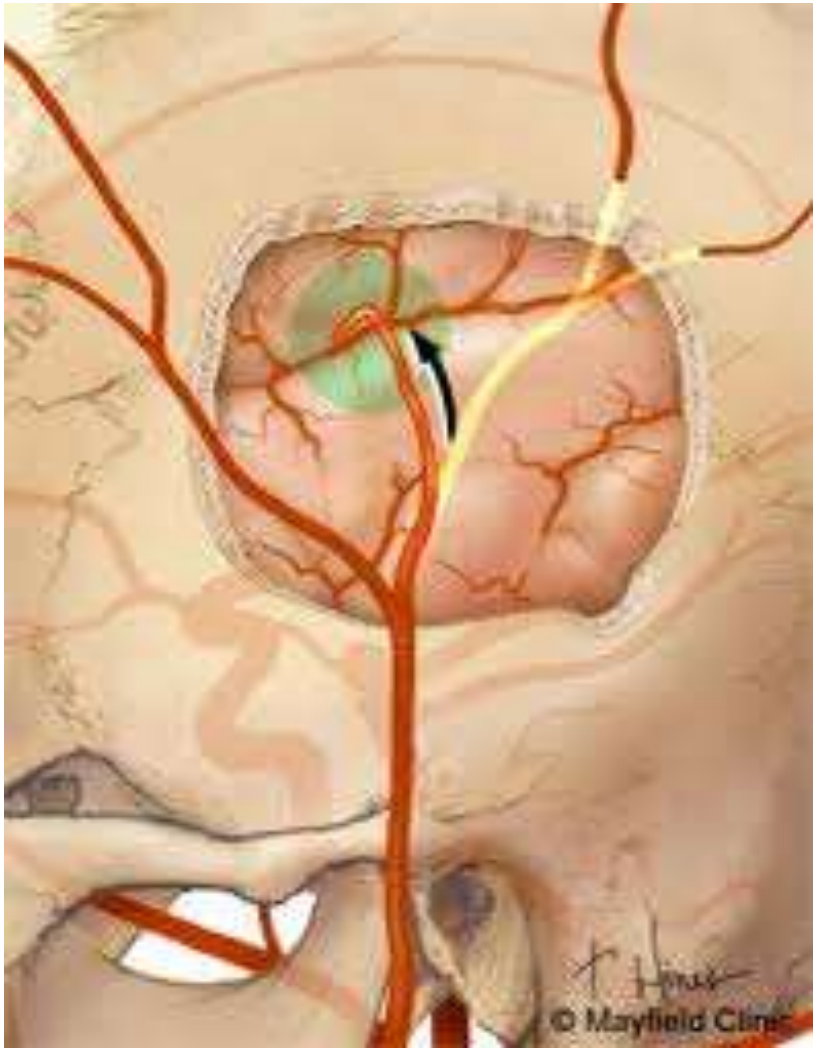
- **Phẩu Thuật EC-IC Bypass**
- Điều trị nội khoa: Chống kết tập tiểu cầu & Statin hoặc Warfarin
- Can thiệp nội mạch: đặt Stent

Extracranial-Intracranial Bypass Surgery



Extracranial-Intracranial Bypass Surgery





Failure of Extracranial–Intracranial Arterial Bypass to Reduce the Risk of Ischemic Stroke — Results of an International Randomized Trial

The EC/IC Bypass Study Group*

N Engl J Med 1985; 313:1191-1200 | November 7, 1985

- 1377 BN có tiền căn NNM có kèm hẹp nặng ĐM não giữa hay ĐM cảnh trong cùng bên.
- 714 BN được chọn lựa ngẫu nhiên ĐT nội khoa.
- 663 BN được phẫu thuật bypass (STA-MCA), kèm chế độ ĐT nội khoa tương tự.
- Kết quả: Tỷ lệ ĐQ tái phát xảy ra cao hơn rõ rệt ở nhóm BN điều trị phẫu thuật.

N Engl J Med. 1985; 313: 1191–1200

Treatment of Intracranial Stenosis
EC-IC Bypass Surgery

Tỷ lệ Đột quỵ	**Nội Khoa**	**PT Bypass**	
Hẹp ĐMN giữa ≥ 70%	14/59 **(24%)**	22/50 **(44%)**	p<0,05
Hẹp ĐMC trong ≥ 70%	26/72 **(36%)**	29/77 **(38%)**	NS

Furlan et al 1980, Awad et al 1984

EC-IC Bypass Surgery Conclusion

Phẫu thuật Bypass không làm giảm nguy cơ Đột qụy tái phát trên BN tắc/ hẹp Động mạch lớn !!!

AHA/ASA Guideline

Guidelines for Prevention of Stroke in Patients With Ischemic Stroke or Transient Ischemic Attack

Extracranial-intracranial (EC/IC) bypass surgery was not found to provide any benefit for patients with carotid occlusion or those with carotid artery narrowing distal to the carotid bifurcation.[176] New efforts using more sensitive imaging to select patients with the greatest hemodynamic compromise for RCTs using EC/IC bypass surgery are ongoing.[177,178]

Among patients with symptomatic carotid occlusion, EC/IC bypass surgery is not routinely recommended (Class III, Level of Evidence A).

AHA/ASA Guideline 2007

SIZE OF TREATMENT EFFECT

ESTIMATE OF CERTAINTY (PRECISION) OF TREATMENT EFFECT

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Lựa Chọn Điều Trị Hẹp ĐM Nội Sọ

- Phẩu Thuật EC-IC Bypass
- **Điều trị nội khoa: Chống kết tập tiểu cầu hoặc Warfarin**
- Can thiệp nội mạch: đặt Stent

Warfarin-Aspirin Symptomatic Intracranial Disease (WASID) Trial

- Bao gồm các BN thiếu máu não thoáng qua hoặc ĐQ do nguyên nhân hẹp ĐM nội sọ (50-99%)
- Lựa chọn ĐT ngẫu nhiên: Warfarin (INR 2-3) vs. Aspirin 1300 mg.
- 569 BN được theo dỏi trong thời gian 1.8 năm

Chimowitz. NEJM 2005

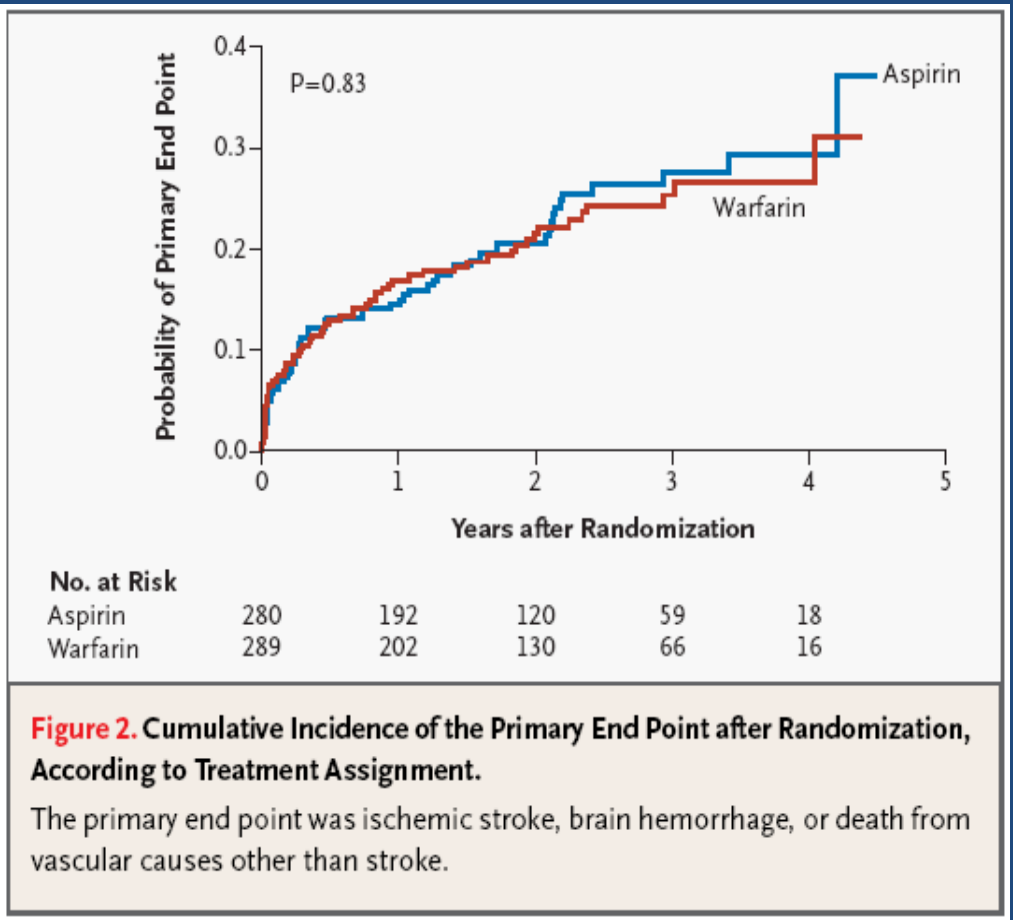


Figure 2. Cumulative Incidence of the Primary End Point after Randomization, According to Treatment Assignment.

The primary end point was ischemic stroke, brain hemorrhage, or death from vascular causes other than stroke.

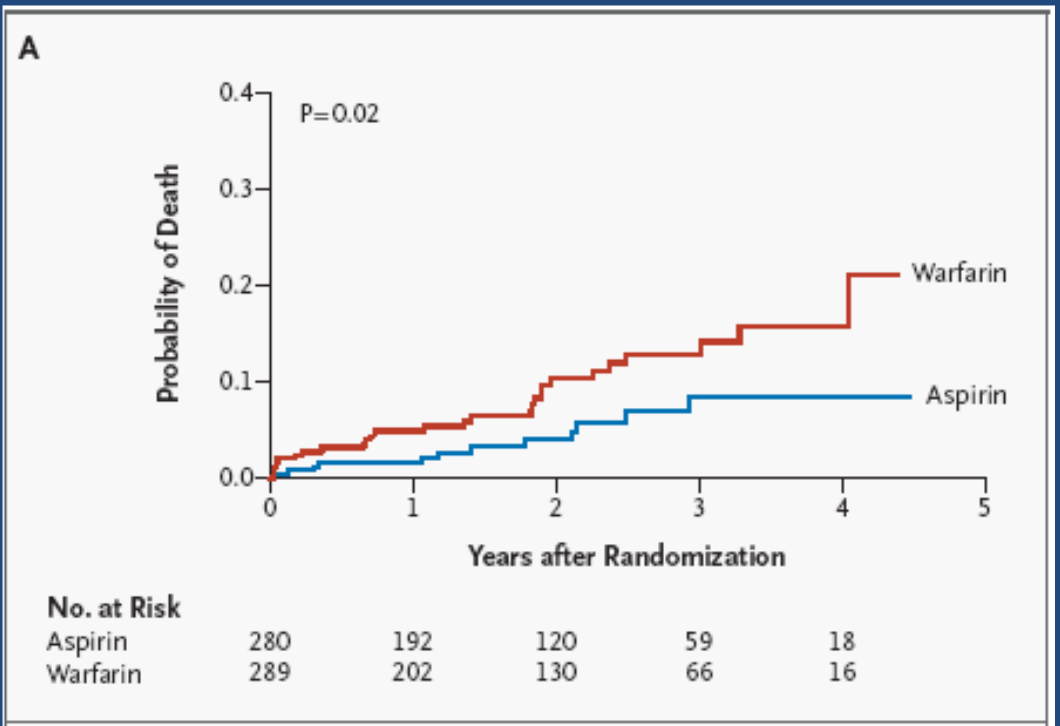
Stroke & Vascular Death

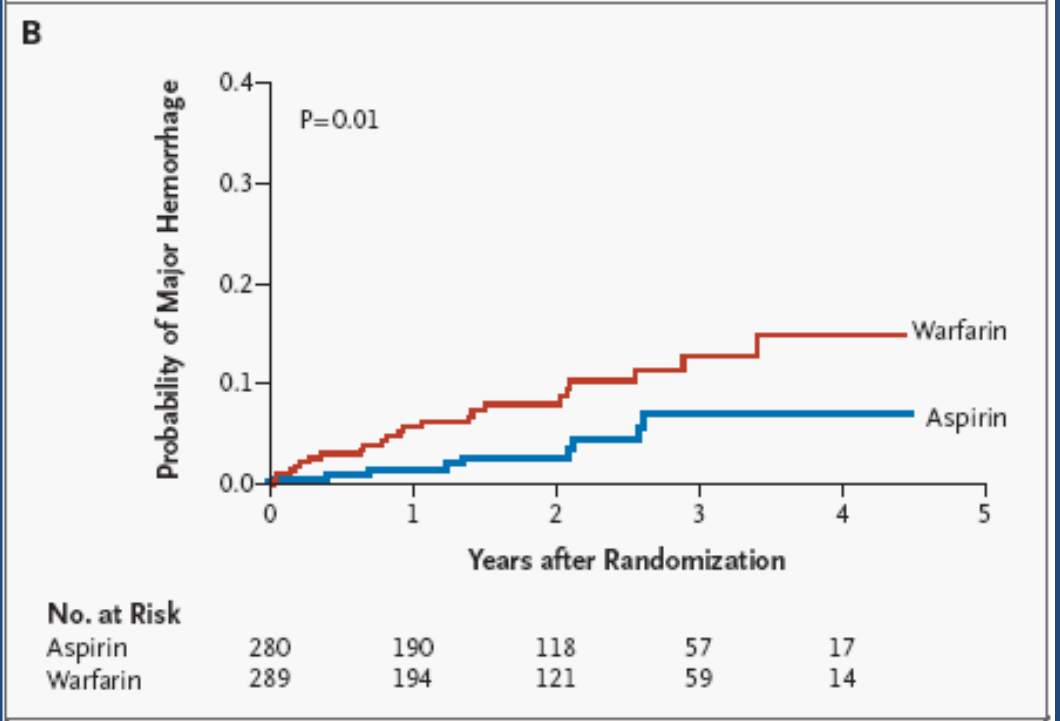
Aspirin	Warfarin	
22.1%	21.8%	p 0.82

-

Tiêu chí kết quả chính bao gồm ĐQ thiếu máu, Xuất huyết não hay tử vong do nguyên nhân mạch máu: 21.8% (warfarin) vs. 22.1% (aspirin).

WASID Trial. NEJM 2005





- Death

Aspirin	Warfarin	
2.4 %	5.2 %	p 0.02

- Major Hemorrhage

Aspirin	Warfarin	
1.8 %	5.0 %	p 0.01

WASID Trial. NEJM 2005

- 8/ 2003, Wasid phải dừng lại sớm sau BN thứ 569 vì lo ngại tỷ lệ xuất huyết và tử vong cao ở nhóm điều trị Warfarin

WASID Conclusion

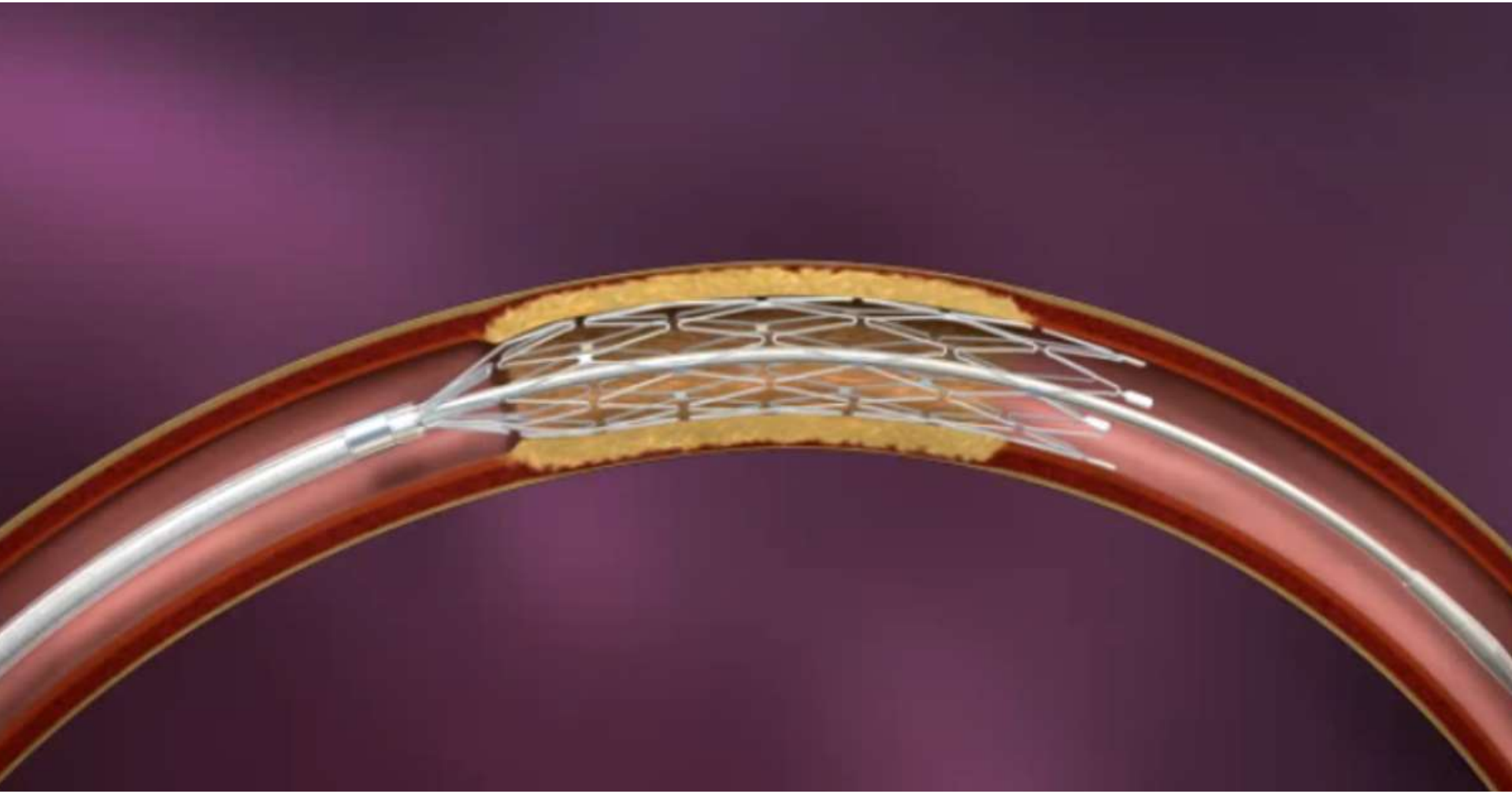
Đối với BN đột quỵ liên quan đến hẹp ĐM nội sọ:

- Warfarin **KHÔNG HIỆU QUẢ** hơn Aspirin
- Warfarin **LÀM TĂNG NGUY CƠ** xuất huyết não quan trọng và nguy cơ tử vong so với aspirin

Lựa Chọn Điều Trị Hẹp ĐM Nội Sọ

- Phẩu Thuật EC-IC Bypass
- Điều trị nội khoa: Antiplatelet & Statin hoặc Warfarin
- **Can thiệp nội mạch: đặt Stent**

Wingspan Stent



Cơ Sở Chỉ Định Đặt Stent

- Tỷ lệ Đột quỵ tái phát cao ở nhóm hẹp nặng ĐM nội sọ 70-99% (# 19%) mặc dù đang được điều trị nội khoa (Wasid 2005).
- Kỹ thuật đặt stent ĐM nội sọ thành công 96.7%
- Nguy cơ Đột quỵ tái phát tương đối thấp

(14%/ năm) qua các số liệu đặt stent Wingspan ban đầu.

The NEW ENGLAND JOURNAL of MEDICINE

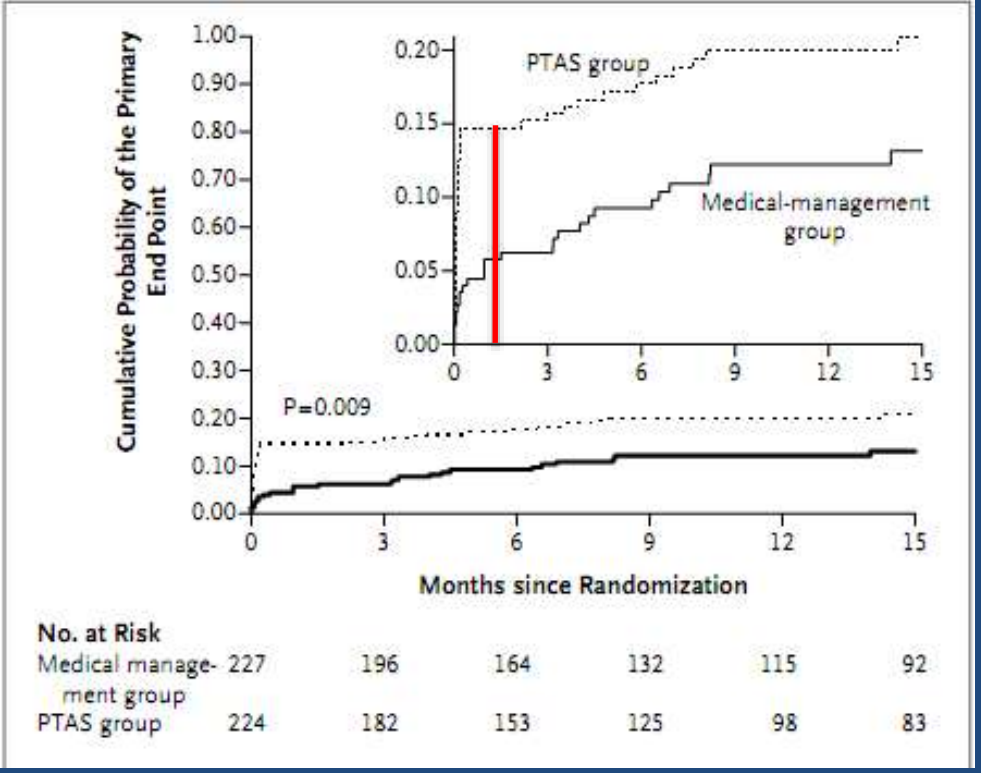
ORIGINAL ARTICLE

Stenting versus Aggressive Medical Therapy for Intracranial Arterial Stenosis

Marc I. Chimowitz, M.B., Ch.B., Michael J. Lynn, M.S., Colin P. Derdeyn, M.D.,

- Bao gồm 451/ 764 Bn đột quỵ/ TIA có hẹp 70-99% ĐM nội sọ tại 50 trung tâm Đột quỵ tại Hoa Kỳ.
- Lựa chọn ngẫu nhiên điều trị nội khoa & đặt stent kèm theo điều trị nội khoa sau đó.
- Kết quả chính: tỷ lệ ĐQ/ tử vong trong 30 ngày

SAMMPRIS Trial. NEJM 2011



Medical Treatment : ASP + Clopidogrel
Rosuvastatin 20mg

- Stroke & Vascular Death/ 30 days
- Medical Treatment — Stent

  5.8% — **14.7%** — p 0.002
- Ischemic Stroke in territory of qualifying artery > 30 days
- 13 (5.7%) — 13 (5.8%) — NS

SAMMPRIS CONCLUSION

CONCLUSIONS

In patients with intracranial arterial stenosis, aggressive medical management was superior to PTAS with the use of the Wingspan stent system, both because the risk of early stroke after PTAS was high and because the risk of stroke with aggressive medical therapy alone was lower than expected. (Funded by the National Institute of Neurological Disorders and Stroke and others; SAMMPRIS ClinicalTrials.gov number, NCT00576693.)

SAMMPRIS Trial. NEJM 2011

Original Investigation

Effect of a Balloon-Expandable Intracranial Stent vs Medical Therapy on Risk of Stroke in Patients With Symptomatic Intracranial Stenosis

The VISSIT Randomized Clinical Trial

Osama O. Zaidat, MD, MS; Brian-Fred Fitzsimmons, MD; Britton Keith Woodward, MD; Zhigang Wang, MD; Monika Killer-Oberpfalzer, MD; Ajay Wakhloo, MD, PhD; Rishi Gupta, MD, MBA; Howard Kirshner, MD; J. Thomas Megerian, MD, PhD; James Lesko, PhD; Pamela Pitzer; Jandira Ramos, MPH; Alicia C. Castonguay, PhD; Stanley Barnwell, MD; Wade S. Smith, MD; Daryl R. Gress, MD; for the VISSIT Trial Investigators

• VISSIT (the Vitesse Intracranial Stent Study for IS Therapy) trial is an international, multicenter, 1:1 randomized, parallel group trial that enrolled patients from 27 sites (2009-2012) with last follow-up in May 2013.

• Primary outcome measure: a composite of stroke in the same territory within 12 months of randomization or hard transient ischemic attack (TIA) in the same territory day 2 through month 12 post randomization.

JAMA. 2015;313(12):1240-1248

MEDICAL MANAGEMENT

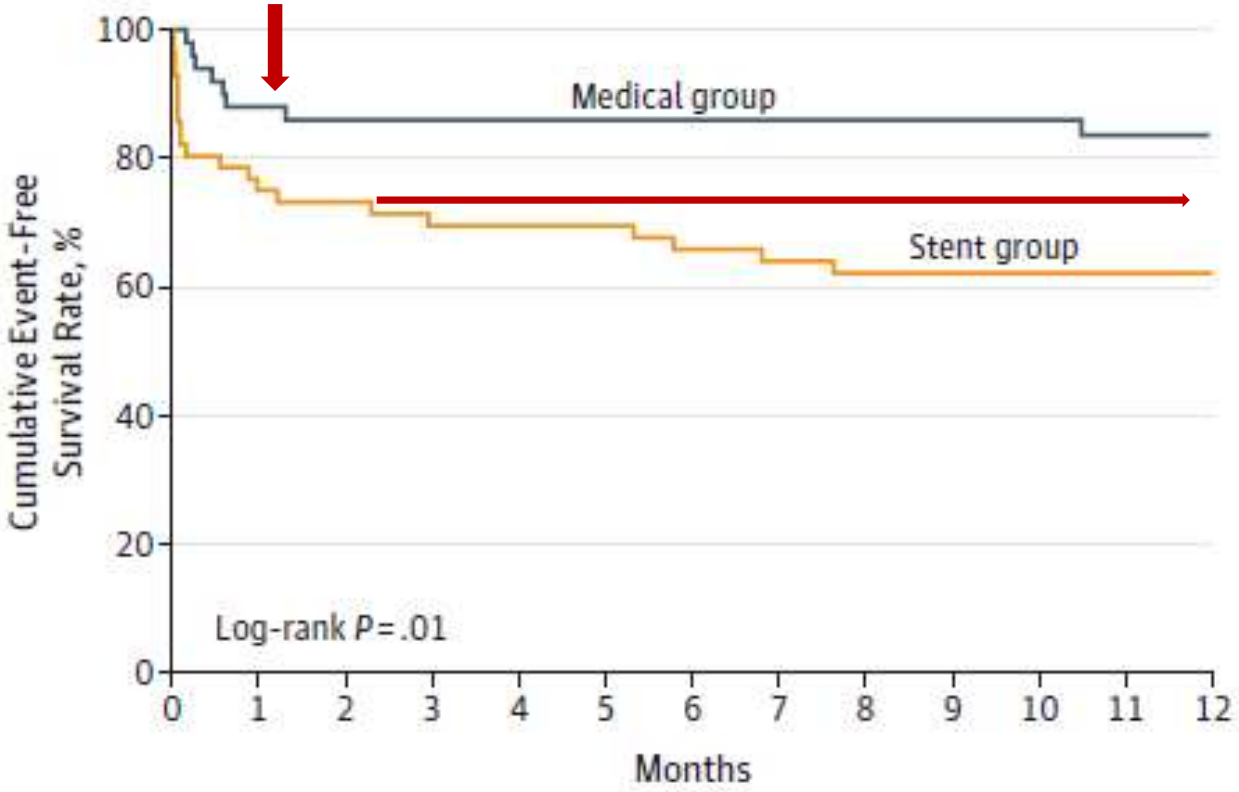
1. Clopidogrel (75mg daily) and aspirin (81-325 mg daily) for the first 3 months after enrollment.
2. Statin: (20-80mg daily) to lower low-density lipoprotein cholesterol (LDL) levels to less than 100mg/dL.
3. Antihypertensive regimen to control systolic blood pressure to ≤ 140mmHg.

JAMA. 2015;313(12):1240-1248

Outcome	Proportion, (%) [95% CI]		Difference (95% CI)[a]	*P* Value
	Medical Group (n = 53)	Stent Group (n = 58)		
Safety outcomes within 30 d				
Any stroke within 30 d or hard TIA between 2 d and 30 d of randomization	5/53 (9.4) [3.1-20.7]	14/58 (24.1) [13.9-37.2]	14.7 (1.2-28.2)	.05
Primary effectiveness end points				
Stroke in the same territory (distal to the target lesion) within 1 y or hard TIA in the same territory between 2 d and 1 y of randomization	8/53 (15.1) [6.7-27.6]	21/58 (36.2) [24.0-49.9]	21.1 (5.4-36.8)	.02
Stroke in the same territory within 1 y of randomization	5/53 (9.4) [3.1-20.7]	20/58 (34.5) [22.5-48.1]	25.1 (10.5-39.6)	.003
NIHSS at 12 mo, No.	41	48		
Mean (SD)	0.46 (0.90)	1.35 (2.02)		.02
Median (IQR) [range]	0 (0-1) [0-4]	0.5 (0-2) [0-10]	0.89 (0.21-1.57)	
NIHSS worse by 4 points, baseline-12 mo	0/53 (0) [0-5.5]	3/58 (5.2) [1.1-14.4]	5.2 (−0.5 to 10.9)	.25
mRS worse, baseline-12 mo	6/53 (11.3) [4.3-23.0]	14/58 (24.1) [13.9-37.2]	12.8 (−1.1 to 26.7)	.09
Restenosis				
≥50%[d]		9/34 (26.5) [12.9-44.4]		
≥70%[d]		1/34 (2.9) [0.1-15.3]		
Other safety end points				
Death from any cause within 30 d of randomization	0/53 (0) [0-5.5]	3/58 (5.2) [1.1-14.4]	5.2 (−0.5 to 10.9)	.25

JAMA. 2015;313(12):1240-1248

PRIMARY OUTCOME

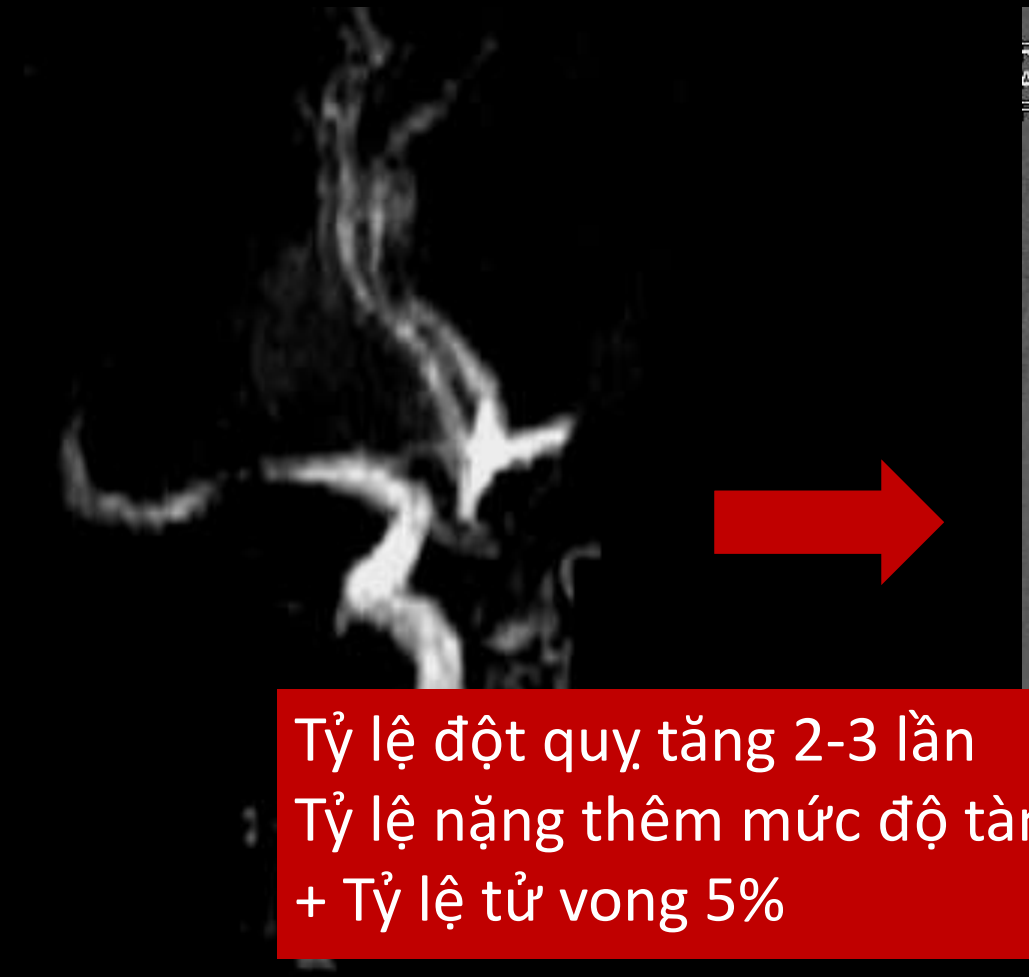


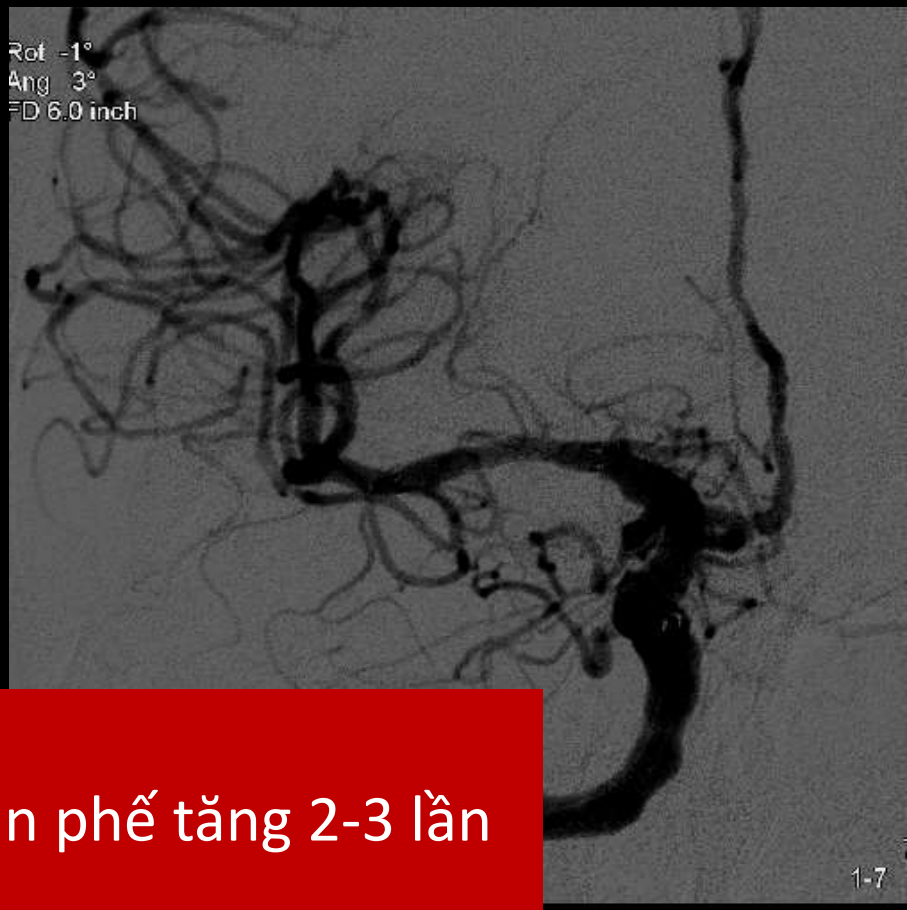
No. at risk

Medical group	53	44	43	43	41	40	39	38	38	38	38	33	20
Stent group	57	42	40	38	38	38	36	35	34	33	33	31	21

JAMA. 2015;313(12):1240-1248

Intracranial stenosis: Stent or Angioplasty for What?





Tỷ lệ đột quỵ tăng 2-3 lần
Tỷ lệ nặng thêm mức độ tàn phế tăng 2-3 lần
+ Tỷ lệ tử vong 5%

VISSIT CONCLUSION

CONCLUSIONS AND RELEVANCE Among patients with symptomatic intracranial arterial stenosis, the use of a balloon-expandable stent compared with medical therapy resulted in an increased 12-month risk of added stroke or TIA in the same territory, and increased 30-day risk of any stroke or TIA. These findings do not support the use of a balloon-expandable stent for patients with symptomatic intracranial arterial stenosis.

JAMA. 2015;313(12):1240-1248

Stroke
JOURNAL OF THE AMERICAN HEART ASSOCIATION

American Stroke Association

Guidelines for the Prevention of Stroke in Patie… Transient Ischemic Attack: A Guideline for Healthcare Pr… American Heart Association/Ameri…on

Không Chỉ Định

For patients with stroke c… able to severe stenosis (70%–99%) of a mai… artery, **stenting with the Wingspan ste… ot recommended as an initial treatment**

(Class III; Level of Evidence B).

***Stroke*. 2014**

For patients with recent stroke o days)
attributable to severe steno of a major
intracranial artery, the pidogrel 75 mg/d
to aspirin for 90 d asonable
ss IIb; Level of Evidence B).

Cân Nhắc Chỉ Định
Lợi ích > nguy cơ

AHA Guidelines 2014

For patients with a stroke or TIA a 50% to 99% stenosis of a major intr

maintenance of systol mm Hg and high-intensity sta recommended

(Class I; Lev).

Gần như chắc chắn mang lại lợi ích cho BN

AHA Guidelines 2014

Tiến Bộ Vượt Bậc của Điều [illegible] Nội Khoa

Nghiên cứu	[illegible] quỵ tái phát
EC/IC bypass study [illegible]	24%
Wasid (2005)	19%
Sampris (20[illegible]	12.2%
VISSIT (2015)	9.4%

Điều Trị Nội Khoa Đã Làm Giảm > 50% nguy cơ ĐQ tái phát

LARGE VESSEL DISEASE

1. Chống Kết tập tiểu cầu:

   Aspirin 325mg + Clopidogrel 75mg (3 tháng)

2. Kiểm soát yếu tố nguy cơ:

   Huyết áp tâm thu < 140mmHg

   High dose of Statin : LDL < 70 mg/dl

   (Rosuvastatin 20mg hoặc Atorvastatin 80mg)

CASE 2

- BN nam 37 tuổi
- Cao huyết áp, tiểu đường type 2
- 11/2013: Nhồi máu não bán cầu P – di chứng yếu ½ thân T. mRS 3
- Đang được điều trị:

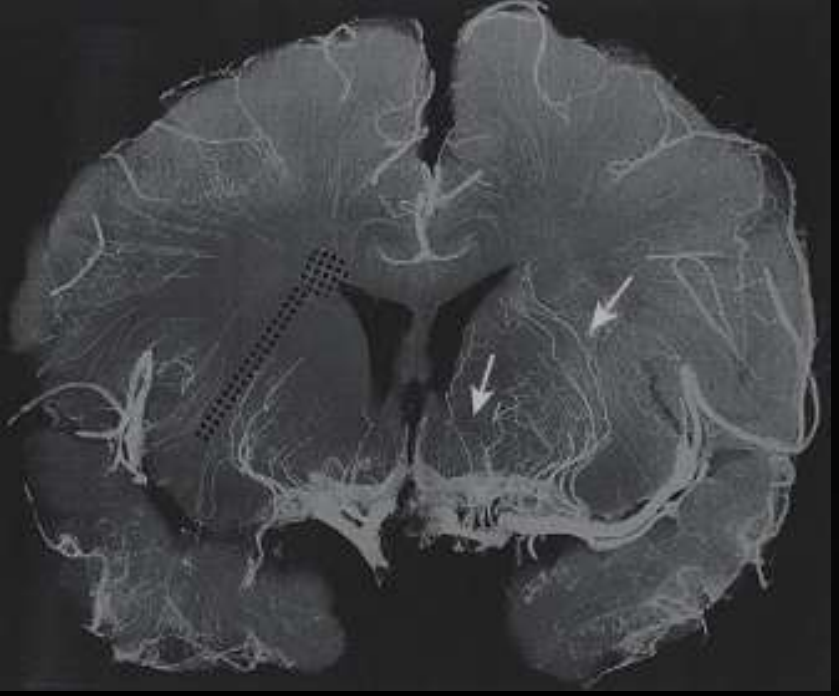
aspirin, perindopril, diamicron, atorvastatin.

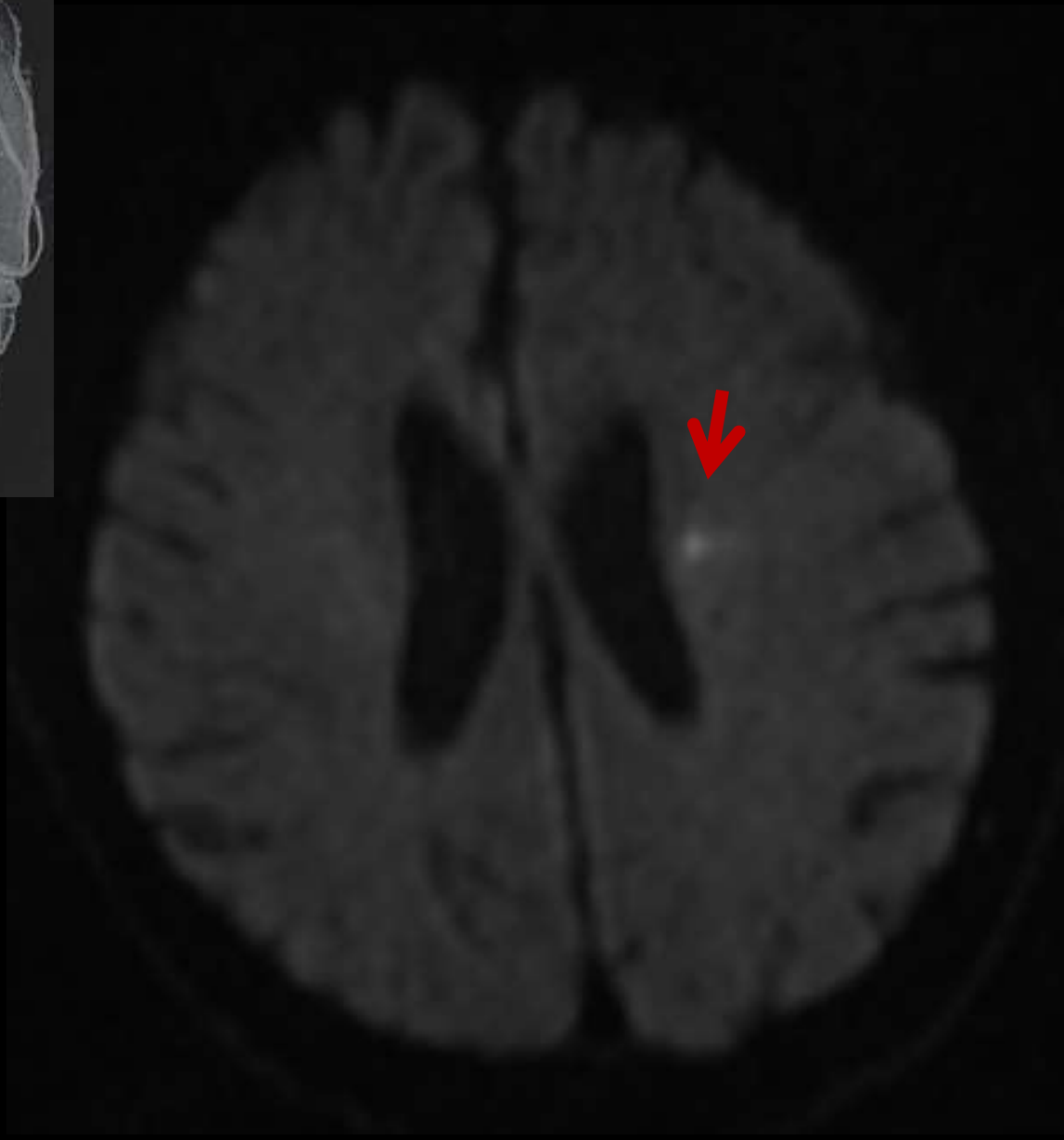
- 7/2014: Nhập viện vì nói khó, yếu ½ thân P
- HA 130/ 80, ECG nhịp xoang
- Glucose 6.8 mmol/l, Hba1c 6.6%
- Cholesterol 210, TG 180, HDL-C 35, LDL-C 80 mg%.
- Siêu âm tim trong giới hạn bình thường.
- Duplex: Không ghi nhận tắc hẹp có ý nghĩa


Current
A
LE VAN LUONG 37M
50
R


Current
A
LE VAN LUONG 37M
72
R


LE VAN LUONG 37M
27.07.2014
21.42
A
82
L
R





Treatment Plan ?

AHA/ASA Guideline

Guidelines for the Prevention of Stroke in Patients With Stroke or Transient Ischemic Attack

- Aspirin (50-325mg) Class I, Level A
- Aspirin + Dipyridamole Class I, Level B
- Clopidogrel Class IIa, Level B

Lựa chọn thuốc chống kết tập tiểu cầu nên tùy vào từng cá nhân bệnh nhân với các yếu tố nguy cơ khác nhau

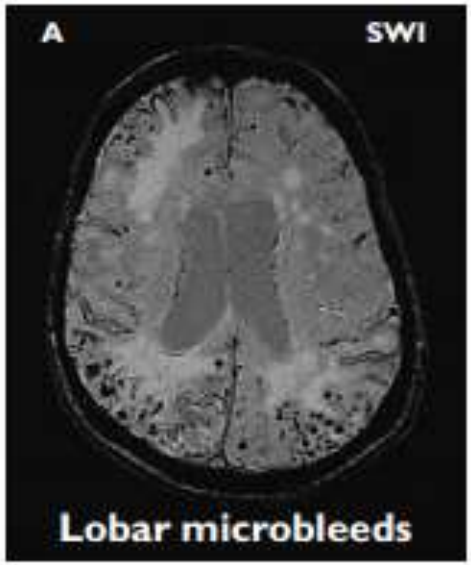
Stroke. 2011;42:227-276

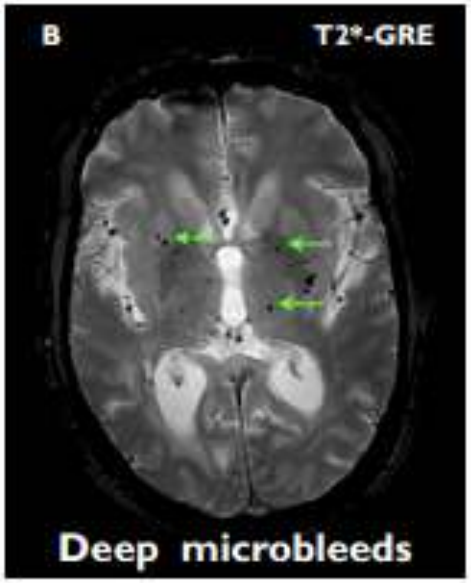
But ….

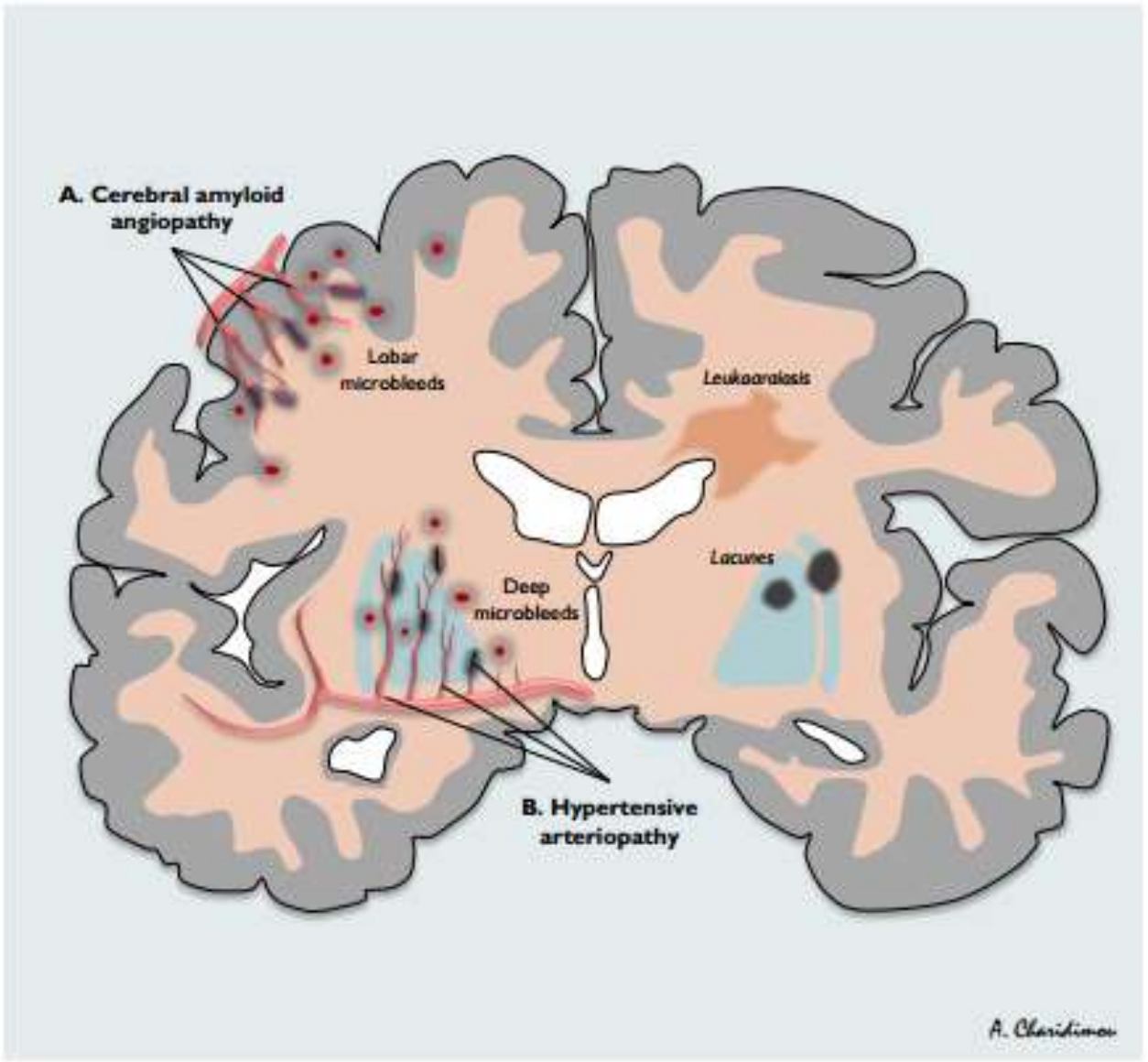
His Gradient Echo

Chúng ta sẽ chọn chống kết tập nào cho BN ???

Small Vessel Disease & Microbleeds







Vi xuất huyết não (Cerebral Microbleeds - CMBs)

Neurology 2006;66;165

Tỉ lệ cao hơn của CMBs đối với các bệnh nhân gốc Châu Á (43%) so với bệnh nhân da trắng (25%)

Tỉ lệ CMBs : từ 20% đến 70%

Tỉ lệ CMBs :

- Gắn liền với cao tuổi, cao huyết áp mạn tính, CAA, CADASIL và mức cholesterol huyết thanh thấp
- Tăng nguy cơ tương lai của ICH
- Tăng tỉ lệ ICH sau khi sử dụng aspirin

Sự liên quan giữa phân nhóm đột quỵ thiếu máu & tỉ lệ vi xuất huyết não

Neurology 2006;66;165

Tỉ lệ vi xuất huyết não trong các bệnh nhân bệnh lý thiếu máu não

Reference	Cohort characteristics	Max. CMB size, mm	Age ± SD (range), y	% HTN	n	% CMB
16	Patients with multiple lacunes and hypertension	NR	69 (55–88)	100	68	71
17	Acute or chronic ischemic stroke	NR				
	Lacunar		74 ± 9	71	66	62
	Atherothrombotic		74 ± 10	46	24	21
	Cardioembolic		77 ± 6	39	23	30
36	Vascular dementia and microangiopathic lesions on MRI	NR	74 ± 6	79	67	78
20	History of ischemic stroke	10	NR	NR	232	18
19	Patients with multiple lacunes or Binswanger's disease	NR	76 ± 8	77	81	60
39	Consecutive patients with acute ischemic stroke	NR	68 ± 11	69	121	36
25	Consecutive patients with acute ischemic stroke and HTN	5	65 ± 9	100	113	65
26	Consecutive patients with acute ischemic stroke	5	65 ± 9	84	144	35
28	Acute first ever ischemic stroke	NR	69 ± 13	NR		
	Lacunar				31	23
	Atherothrombotic				22	23
	Cardioembolic				13	0
29	Acute lacunar infarction	7	66 ± 9	72	138	51
40	Acute TIA or ischemic stroke	NR	>50 y	NR	203	25
Total					1,346	40

HTN = hypertension; NR = not reported.

Vi xuất huyết không triệu chứng là một yếu tố nguy cơ của ICH liên quan với aspirin

Characteristics	Symptomatic intracerebral hemorrhage: Yes (n = 21)	No (n = 21)	p Value
Age, y ± SD	72 ± 7.8	71.5 ± 7.2	
M/F	14/7	14/7	
Hypertension	14	14	
Systolic BP, mm Hg ± SD	164 ± 20	156 ± 25	0.19
Diastolic BP, mm Hg ± SD	89 ± 14	84 ± 10	0.13
Diabetes	5	10	0.09
Ischemic heart disease	8	6	0.37
Atrial fibrillation	3	1	0.3
Previous stroke	11	14	0.27
Smoking	7	10	0.27
Aspirin users	21	21	
Daily dose, mg	114 ± 40.6	124 ± 40.8	0.45
Duration, mo.	18.6 ± 16.3	22.2 ± 22.3	0.29
	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

BP = blood pressure; GRE = gradient recall-echo.

Sự hiện diện và mức độ của Vi xuất huyết không triệu chứng trên GRE trong 21 bệnh nhân dùng aspirin có bị ICH và 21 bệnh nhân dùng aspirin không có tiền sử của ICH

Vi xuất huyết xảy ra thường xuyên hơn (19 vs 7, p <0.001) và rộng hơn (số lượng chảy máu trung bình 13.3 vs 0.4, p<0.001) ở nhóm ICH so với nhóm đối chứng.

Wong KS, et al Neurology 2003;60;511-513

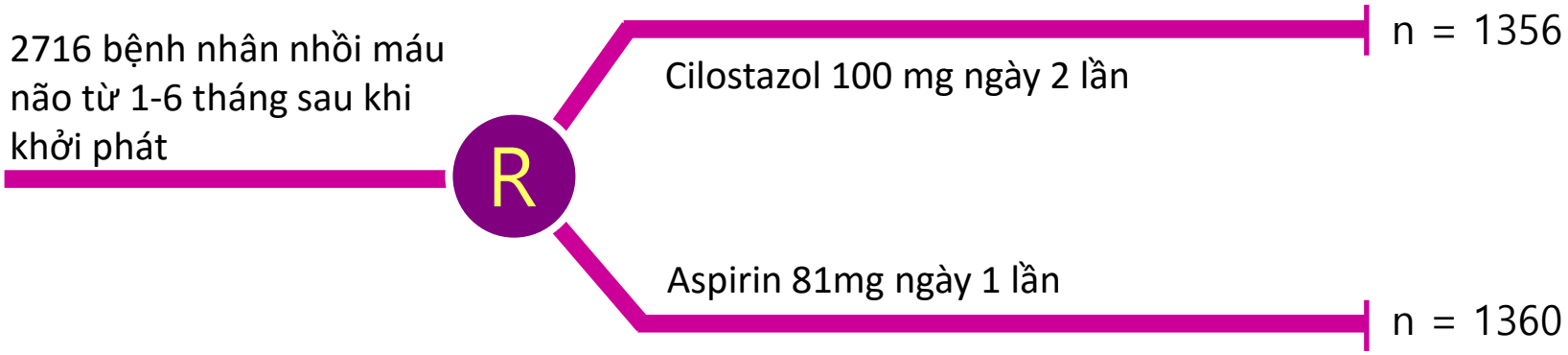
Mục Tiêu Điều Trị

Giảm Nguy Cơ Nhồi máu Não tái phát

Aspirin ???

Giảm Nguy Cơ Xuất Huyết não

Nghiên cứu CSPS 2



- Mục tiêu: So sánh Cilostazol & Aspirin trong phòng ngừa ĐQ tái phát ở các BN ĐQ thiếu máu não không do nguyên nhân tim.
- Thiết kế nghiên cứu: Tiền cứu, đa trung tâm, ngẫu nhiên, mù đôi.
- Kết cục chính: đột quị (ĐQ thiếu máu não, XHN, XHDN).
- Kết cục phụ: đột quỵ bất kỳ, tử vong do tất cả các nguyên nhân, đau thắt ngực, nhồi máu cơ tim, suy tim, xuất huyết cần nhập viện.
- Theo dõi: 1 - 5 năm

Lancet Neurol 2010; 9: 959–68

CSPS II- Dân số nghiên cứu

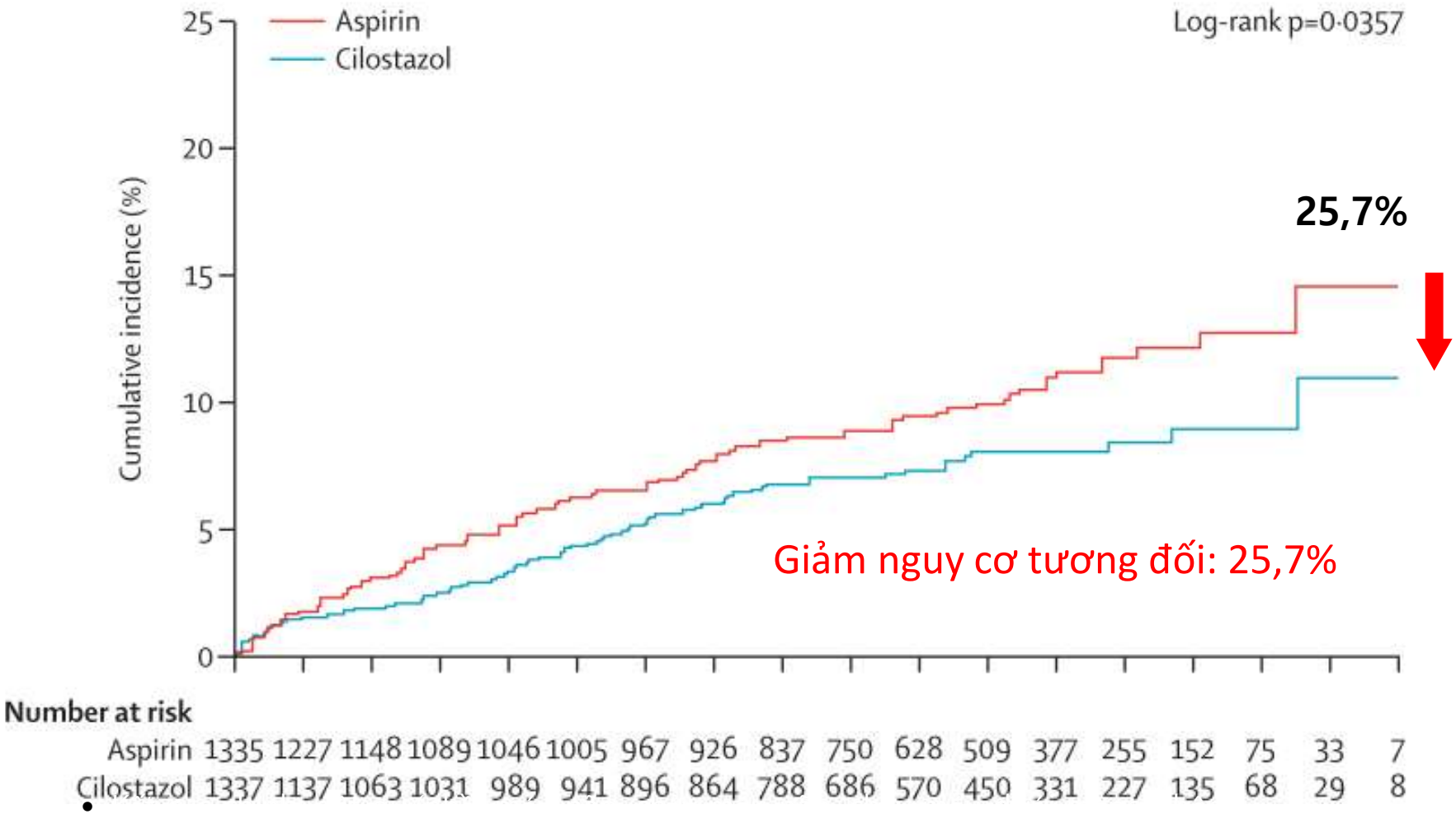
	Cilostazol (n=1337)	Aspirin (n=1335)
Men	959 (72%)	957 (72%)
Age (years)	63·5 (9·2)	63·4 (9·0)
Body-mass index (kg/m²)	24·0 (3·1)	23·9 (3·1)
Stroke subtype		
Atherothrombotic	435 (33%)	420 (31%)
Lacunar	869 (65%)	874 (65%)
Undetermined	33 (3%)	41 (3%)
Days after onset*		
≤28	414 (31%)	419 (31%)
29–56	354 (26%)	338 (25%)
57–112	343 (26%)	320 (24%)
>113	226 (17%)	258 (19%)
Stroke severity (modified Rankin scale)		
0	207 (15%)	186 (14%)
1	612 (46%)	613 (46%)
2	406 (30%)	432 (32%)
3	73 (5%)	69 (5%)
4	39 (3%)	35 (3%)
Drug use		
Cilostazol	304 (23%)	358 (27%)
Aspirin	794 (59%)	749 (56%)
Present smoker	385 (29%)	403 (30%)
Does not abstain from drinking alcohol	640 (48%)	624 (47%)
Complications		
Hypertension	976 (73%)	991 (74%)
Ischaemic heart disease	11 (1%)	18 (1%)
Diabetes mellitus	382 (29%)	393 (29%)
Dyslipidaemia	560 (42%)	599 (45%)

Data are number (%) or mean (SD). *Days from onset of cerebral infarction to start of treatment.

Table 1: **Demographic and clinical characteristics at baseline**

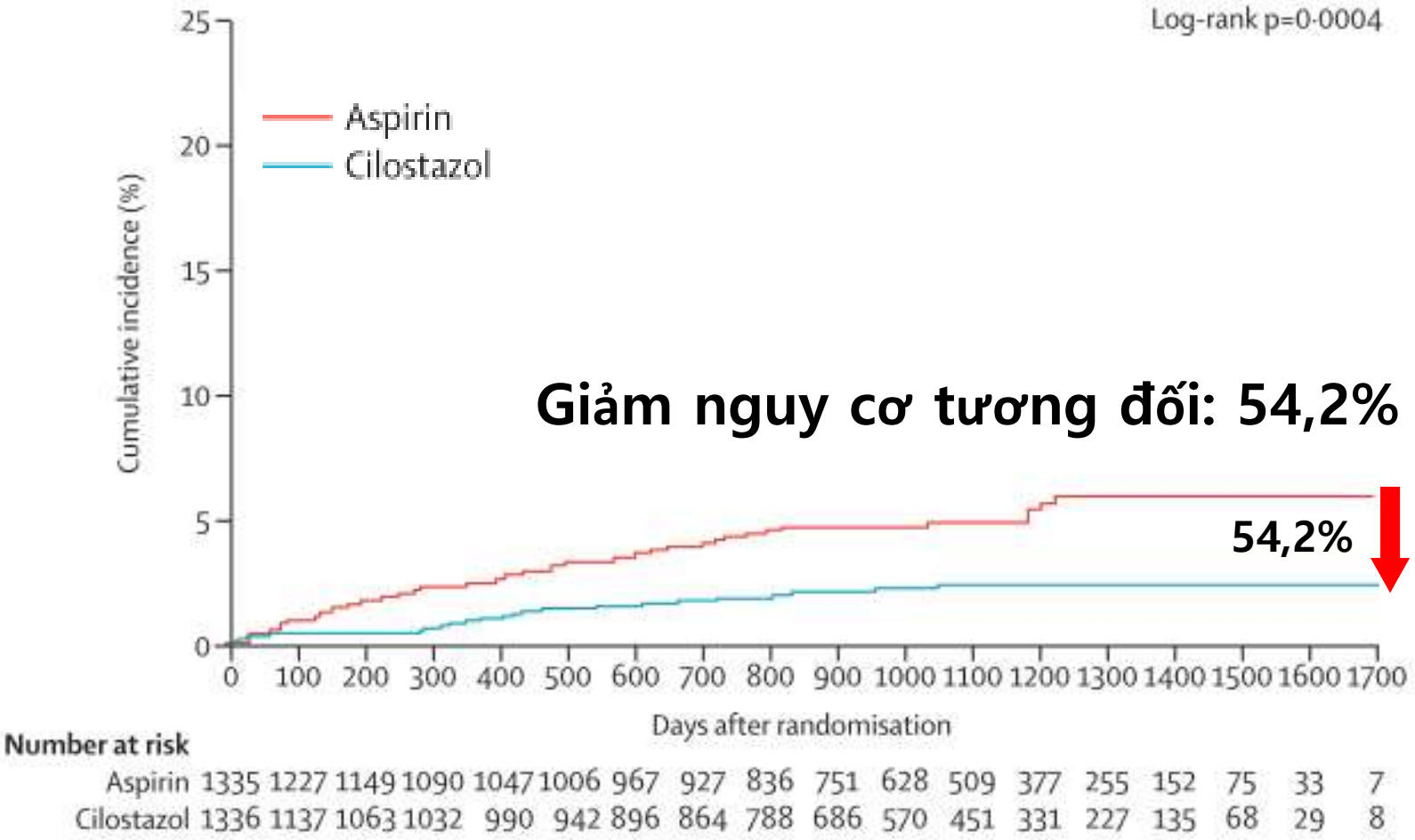
Lancet Neurol 2010; 9: 959–68.

Kết Quả Chính



Lancet Neurol 2010; 9: 959–68.

Biến Cố Xuất Huyết



Can We Do Better ?

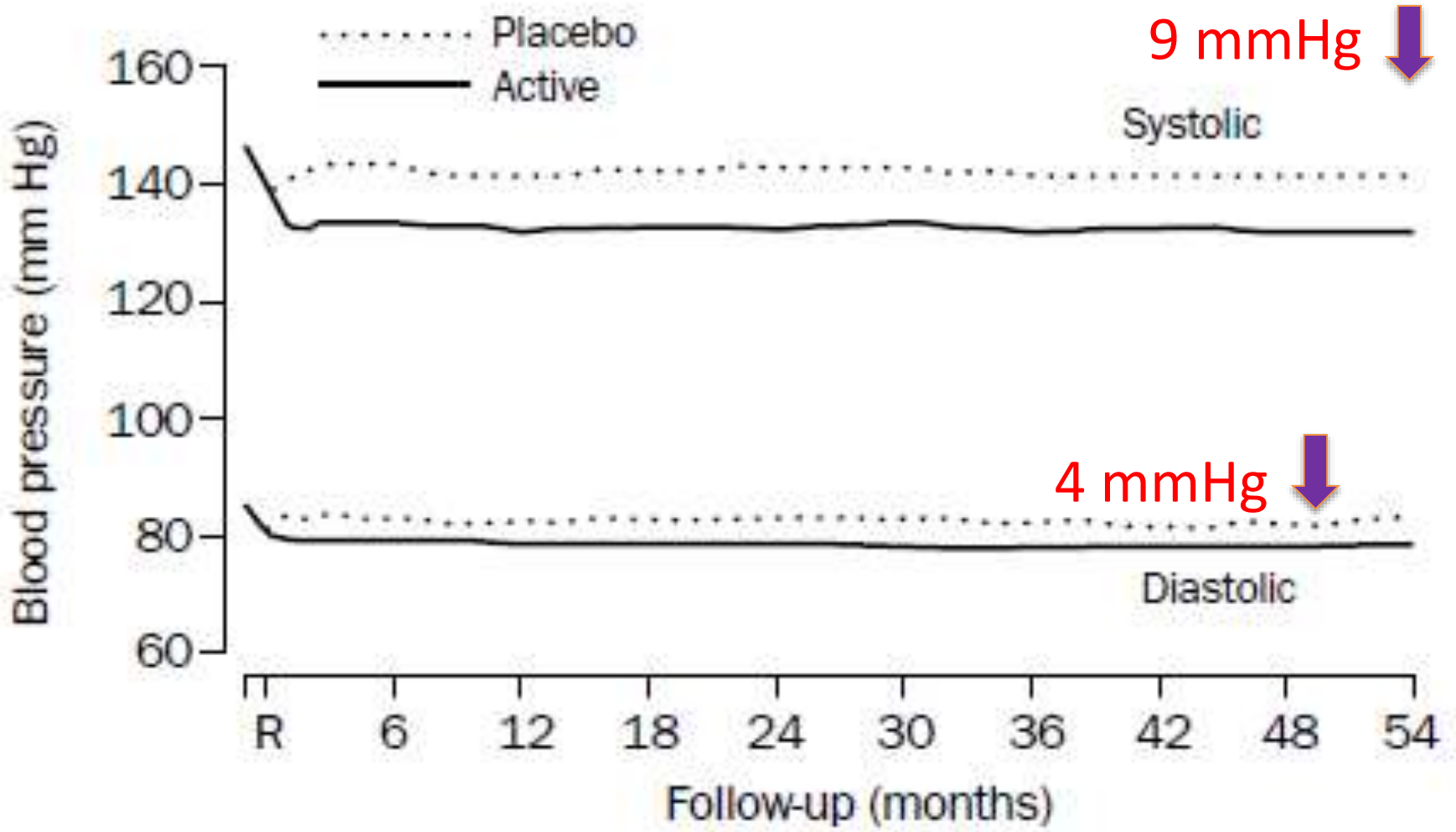
Blood Pressure Target for SVD ?

Randomised trial of a perindopril-based blood-pressure-lowering regimen among 6105 individuals with previous stroke or transient ischaemic attack

- Bao gồm 6105 BN có tiền sử ĐQ hay TIA, lựa chọn ngẫu nhiên Perindopril 4mg (+ Indapamide) hoặc Placebo.
- 40% BN có mức huyết áp < 140/ 90 mmHg
- Tiêu chí kết quả chính: đột quỵ tử vong và không tử vong

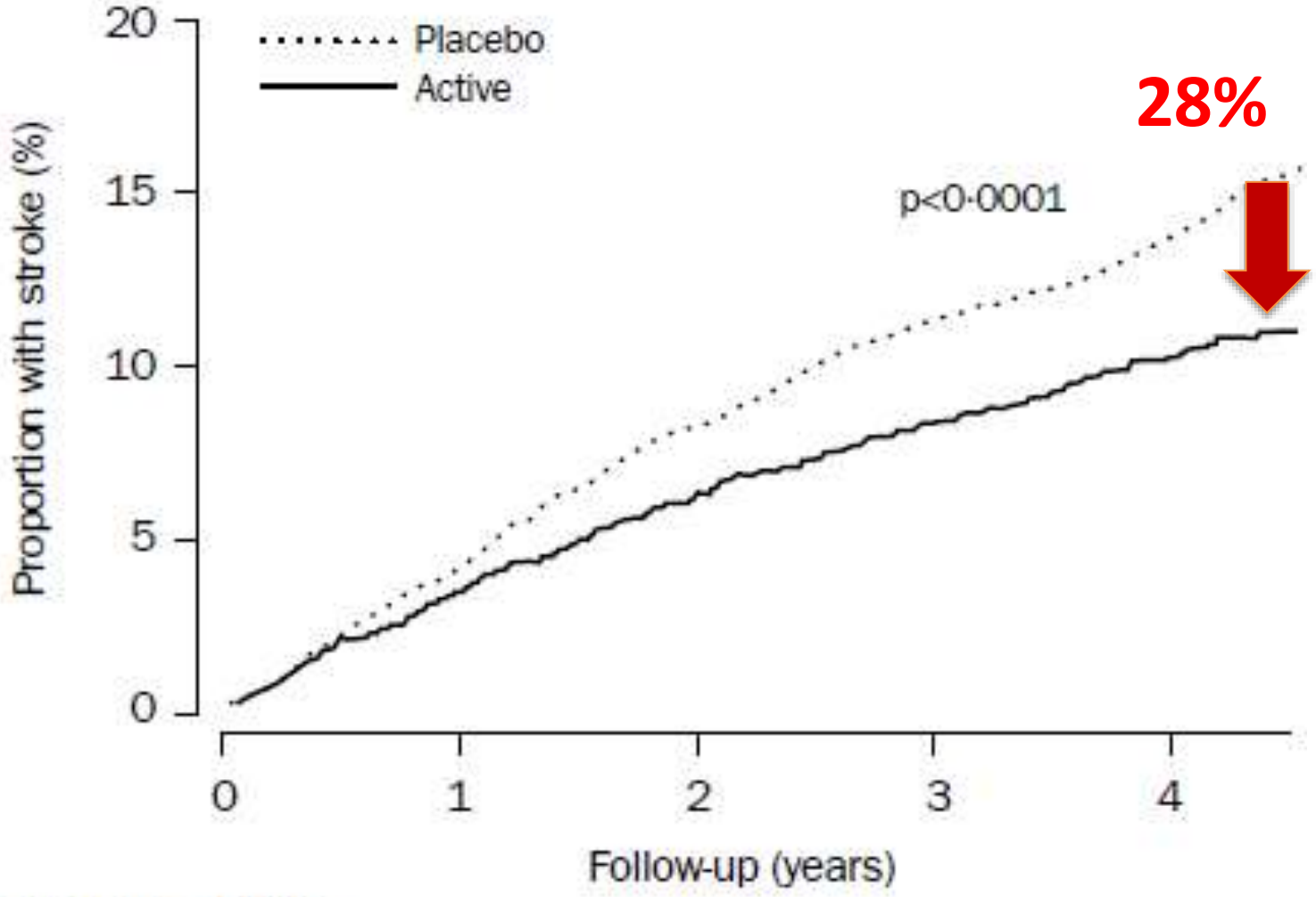
PROGRESS - Lancet 2001; 358: 1033–41

Hiệu Quả Giảm Huyết Áp



Progress. Lancet 2001; 358: 1033

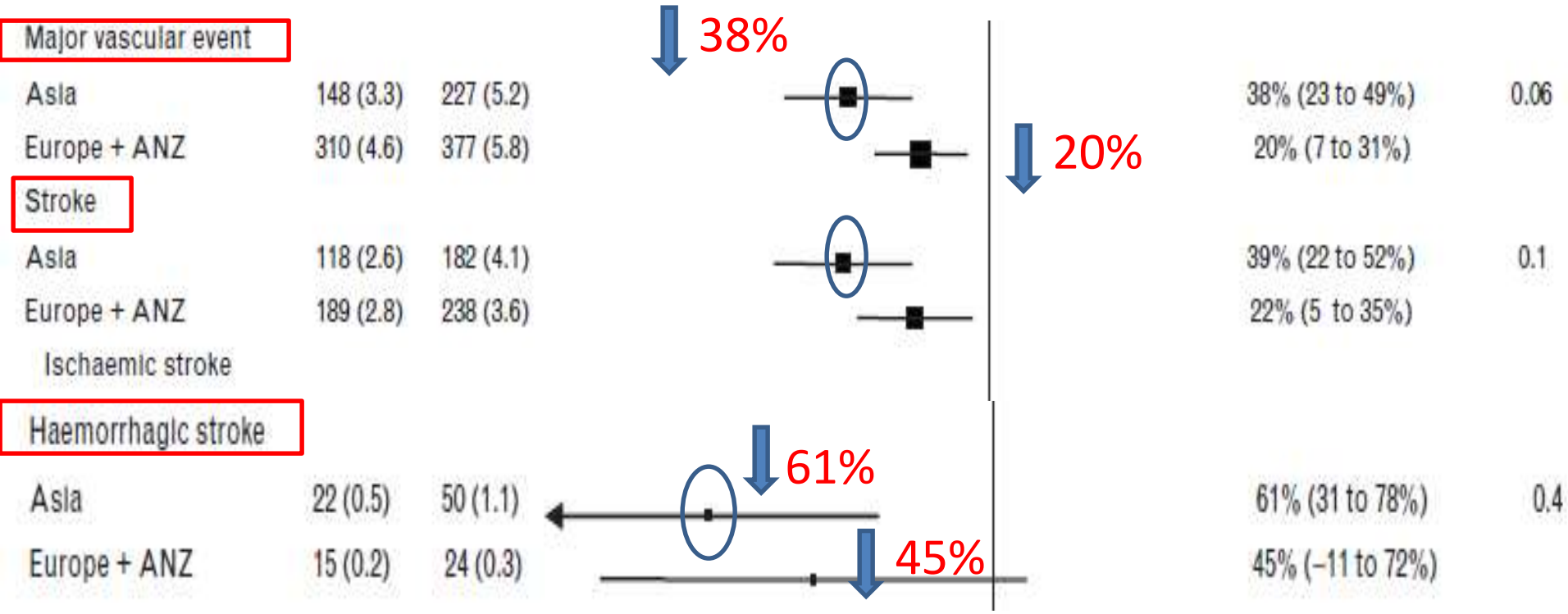
Nguy Cơ Đột Quỵ Tái Phát



Numbers at risk

Active	3051	2902	2765	2634	1595
Placebo	3054	2880	2707	2551	1533

Active treatment reduced BP by 10.3/4.6mmHg in Asian, and by 8.1/3.6mmHg in Western articipants



Journal of Hypertension 2009, 27

BP Target for Lacunar Infarct ?

- **Goals for target BP level or reduction from pretreatment baseline are uncertain and should be individualized, but it is reasonable to achieve a systolic pressure <140 mm Hg and a diastolic pressure <90 mm Hg**

(Class IIa; Level of Evidence B).

AHA/ASA Guidelines for Stroke 2011

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Effects of Clopidogrel Added to Aspirin in Patients with Recent Lacunar Stroke

The SPS3 Investigators*

- SPS3 enrolled 3020 patients with lacunar to 2 different target levels of SBP control, <150 versus <130 mmHg.
- Mean time from qualifying event to randomization was 62 days. At baseline, mean SBP was 145 mm Hg in the higher-target group and 144 mm Hg in the lower-target group.

NEJM 2012 367;9

Systolic BP	<150 mmHg	<130 mmHg
12 months	138 mm Hg	127 mm Hg
Recurrent stroke	2.8 %	2.3 %
	HR 21 %	
Ischemic stroke	2.4 %	2.0 %
	HR 16 %	
Hemorrhagic stroke	0.29 %	0.11 %
	HR 63%	

AHA/ASA Guidelines for Stroke 2014

- **For patients with a recent lacunar stroke, it might be reasonable to target an SBP of <130 mm Hg**

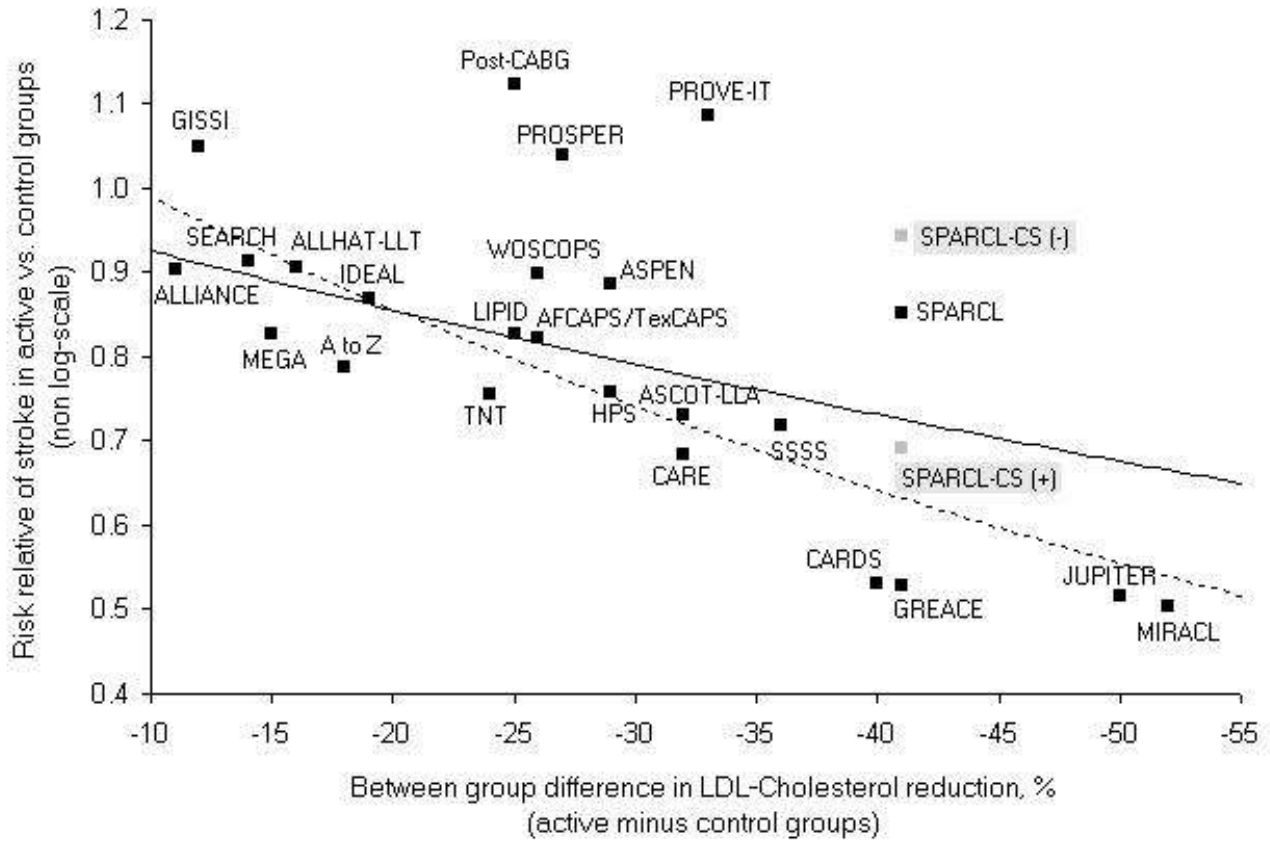
(Class IIb; Level of Evidence B).

And Much More …

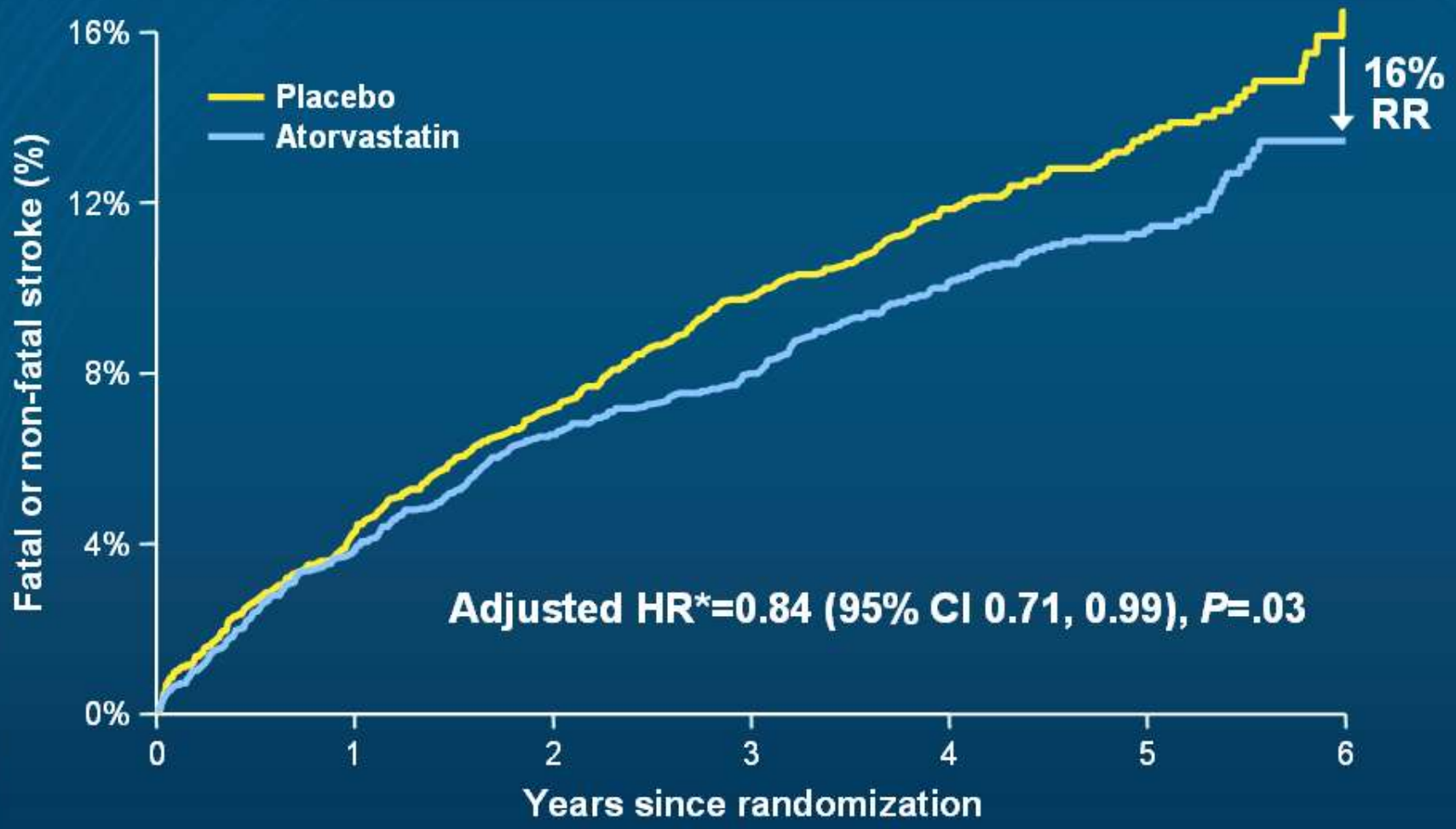
Stroke Risk and LDL Lowering

Each 1 mmol (39 mg) LDL-C reduction reduced the risk of stroke by 21% (95% CI 6.3 to 33.5%, p<0.001)

Total n=165,732



SPARCL: Kết Quả Chính



* Treatment effect from Cox proportional hazards models with pre-specified adjustment for geographical region, entry event, time since entry event, gender, and baseline age.

RR, risk reduction; HR, hazard ratio; CI, confidence interval.

The SPARCL Investigators. *N Engl J Med*. 2006;355:549-559.

SPARCL

Guidelines for Prevention of Stroke in Patients With Ischemic Stroke or Transient Ischemic Attack: A Statement for Healthcare Professionals From the American Heart Association/American Stroke Association Council on Stroke: Co-Sponsored by the Council on Cardiovascular Radiology and Intervention: The American Academy of Neurology affirms the value of this guideline.

Ralph L. Sacco, Robert Adams, Greg Albers, Mark J. Alberts, Oscar Benavente, Karen Furie, Larry B. Goldstein, Philip Gorelick, Jonathan Halperin, Robert Harbaugh, S. Claiborne Johnston, Irene Katzan, Margaret Kelly-Hayes, Edgar J. Kenton, Michael Marks, Lee H. Schwamm and Thomas Tomsick

Cholesterol	Ischemic stroke or TIA patients with elevated cholesterol, comorbid CAD, or evidence of an atherosclerotic origin should be managed according to NCEP III guidelines, which include lifestyle modification, dietary guidelines, and medication recommendations.	Class I, Level A
	Statin agents are recommended, and the target goal for cholesterol lowering for those with CHD or symptomatic atherosclerotic disease is an LDL-C of <100 mg/dL and LDL-C <70 mg/dL for very-high-risk persons with multiple risk factors.	Class I, Level A
	Patients with ischemic stroke or TIA presumed to be due to an atherosclerotic origin but with no preexisting indications for statins (normal cholesterol levels, no comorbid CAD, or no evidence of atherosclerosis) are reasonable to consider for treatment with a statin agent to reduce the risk of vascular events.	Class IIa, Level B

SMALL VESSEL DISEASE

1. Chống Kết tập tiểu cầu:

   Aspirin 325mg/ Clopidogrel/ C… …eed)

2. Kiểm soát yếu tố …

   Huyết á… …ng

3. Statin **L… …mg/dl**

4. **Hba1c < 7mg%**

Don't Combine Antiplatelets for SVD

“To treat the stroke patient optimally, the physician must identify the correct mechanism of stroke…”

The Caplan ‘s Stroke book


Thank You!

Hội Nghị Hội Đột Quỵ TpHCM lần 2
24-25/ 9 /2016