Dr. Giampaolo Niccoli, MD, PhD, FESc Institute of Cardiology Catholic University of Rome, Italy







P. T.

Age: 60 years

Sex: female.

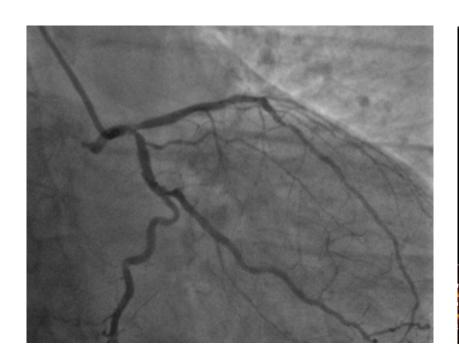
Cardiological risk factors: diabetes mellitus type II, dyslipidemia.

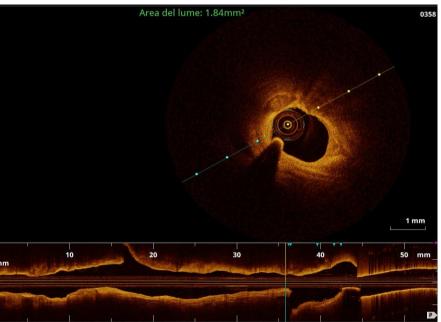
Cardiological History: chest pain on effort (CCS II), positive exercise stress test.

Coronary angiography: left main (65%), ostial ADA (70%), ostial Cx (70%).





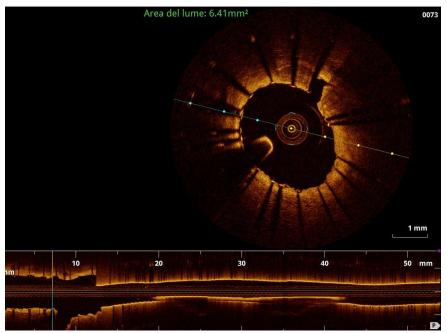






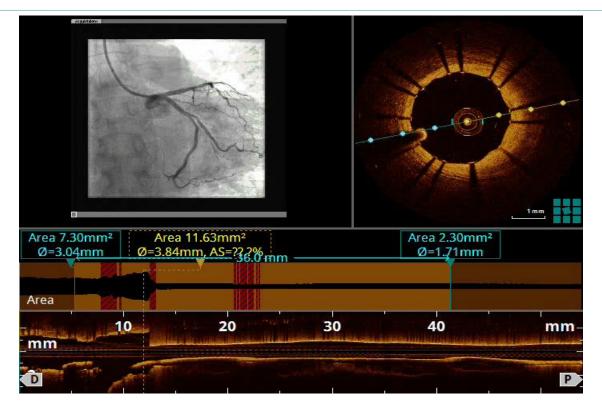
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PTCA on Left Main-ADA-Cx with stent implantation (Resolute Onyx 3.5 x 22 mm on Left Main-Cx; Resolute Onyx 3.0 x 12 mm on IVA with final kissing balloon).





### **Final result**



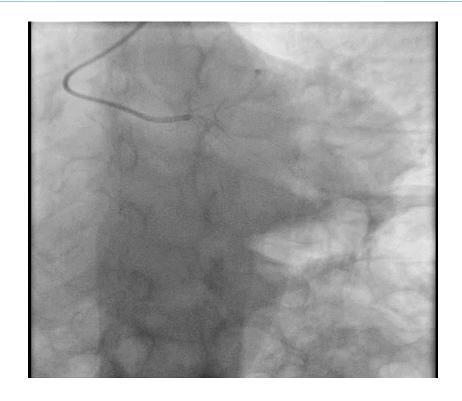




- Therapy on discharge: Clopidogrel 75 mg/die, ASA 100 mg/die, Carvedilol 6,25 mg x 2, Tresiba 20 UI x 1, Novorapid x 3, Atorvastatin 20 mg/die.
- The patient became asymptomatic for chest pain after revascularization.
- At 1 year follow up, clopidogrel was interrupted without any changing of the of the remaining therapy.
- After about 1 year and half, the patient presented to our Emergency Department for typical chest pain at rest. At EKG: 2 mm ST-depression in lateral leads.
- Coronary angiography was performed.



## **Angiography of ST**

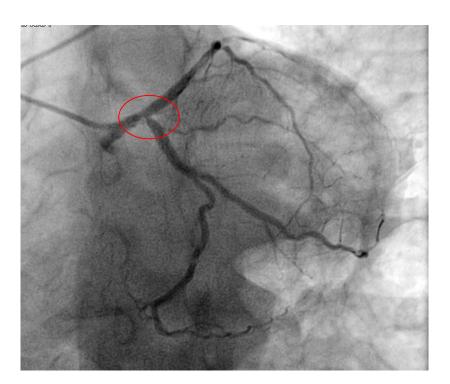


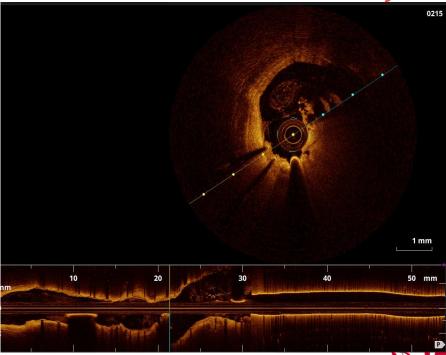


Dr. Giampaolo Niccoli



Thrombosis ESC Working Group







 PCI on Left main-ADA-Cx: intracoronary Reopro bolus, kissing dilatation with Trek NC 3.5x20 mm (Cx) and 3.25x15 mm (ADA) (14 atm); final "POT" finale with Trek 4.5x12 mm (10 atm).

 Therapy on discharge: Cardioaspirin 100 mg/die, Efient 10 mg/die, Carvedilol 6,25 mg x 2, Tresiba 20 UI x 1, Novorapid x 3, Atorvastatin 80 mg/die.





### **Guidelines on myocardial revascularization**

	European guidelines 4,5,34		US guidelines <sup>6,35</sup>				
	BMS	DES	BMS	DES			
Stable coronary art	ery disease						
DAPT (P2Y <sub>12</sub> inhibitor plus aspirin)	≥1 month (class IA)	6 months (class IB) with new-generation DES Shorter DAPT duration (<6 months) in patients at high bleeding risk (class IIb, A) <sup>4</sup>	Clopidogrel 75 mg/day for ≥1 month and ideally up to 12 months in patients not at high risk of bleeding (class IB) <sup>6</sup>	Clopidogrel 75 mg/day for ≥1 months in patients not at hig risk of bleeding (class IB) <sup>6</sup>			
Aspirin	Lifelong single antiplat 75–100 mg/day) (c	telet therapy (usually aspirin tlass IA)	Aspirin 81–325 mg/day indefinitely (cla	ss IA)			



## **Short vs prolonged DAPT after DES**

#### 6-12 Months vs. 18-48 Months

A Mortality									
	Prof	onged		Short		Otida Ratio	(OR)		
Study	Events	Total	Events	Total		11		OR	96% C
DES-LATE (12 vs. 36 mo)	46	2531	32	2514			_	1.44	(0.91-2.26
PRODIGY (6 vs. 24 mo)	49	750		751		-		1.10	
ARCTIC (12 vs. 18 mo)	7	635		624			_	0.76	0.29 - 2.06
ITALIC (6 vs. 24 mc)	7	910	8	912			_	0.88	[0.32 - 2.43]
DAPT (12 vs. 30 mo)	98	5020	74	4941		-	-	1.31	(0.97-1.78
OPTIDUAL (12 vs. 48 mc)	16	695	24	690				0.65	(0.34 - 1.24)
Bayesian hierarchical me	ta-onolys	is				- 11		1.12	(0.81 - 1.45)
Fixed effect model	223	10541	192	10432		+		1.16	(0.95 - 1.41)
Random effects model						+		1.14	[0.92 - 1.42]
Meterogeneity: I-squared=10.2	7%, New-eq	uared-6	10078, p-4	0.2660					
							1 1		
				q	1 0.2	0.5 1	2 5	10	
					Bunkana	ad botter	Short by	ottor	

#### B Major hemorrhage

	Prok	onged		Short		Odds Ratio (C	OR)	
Study	Events		Events	Total			OR	95% C
DES-LATE (12 vs. 36 mo)	34	2531	24	2514		14	1.41	(0.84- 2.39
PRODIGY (6 vs. 24 mo)	13	750	5	751			2.63	(0.93 - 7.42)
ARCTIC (12 vs. 18 mc)	7	635	1	624		++-	→ 6.94	(0.85- 56.6)
ITALIC (5 vs. 24 mo)	3	910	0	912		$\rightarrow$	7.04	(0.36-136.5
DAPT (12 vs. 30 mo)	119	5020	73	4941		-	1.62	(1.21 - 2.17)
OPTIDUAL (12 vs. 48 mo)	14	695	14	690		<b>→</b> ∓	0.99	(0.47 - 2.10)
Bayesian hierarchical met	te-analysi	is				1 :	1.58	(1.14 - 2.45)
Fixed effect model	190	10541	117	10432			1.61	(1.20 - 2.04)
Random effects model						-	1.58	(1.20- 2.09)
Hoterogeneity: I-aguareduk@	i, tev-ega	erealud.d	1198, pull.	2547		1 :		
				ſ				
				0.	1 0.2	0.5 1 2	5 10	
					lendouse	od hattor St	vart halfor	

#### C Myocardial infarction

	Profor	naed		Short		Odds Rat	io (OR)			
Study	Events 1							OF	95% CI	
DES-LATE (12 vs. 36 mg)	19 2	2531	27	2514				0.70	(0.39-1.26)	
PRODIGY (6 vs. 24 mo)	25	750	26	751			_	0.96		
ARCTIC (12 vs. 17 mo)	9	635	9	624		-!:+		0.98	forms minds	
ITALIC (5 vs. 24 mo)	.4	910	6	912	_			0.67		
DAPT (12 vs. 30 mo)		5020	198	4941		-			(0.38-0.62)	
Bayesian hierarchical m Fixed effect model	eta-anaty 156 f		266	9742		4			(0.45-1.09) (0.47-0.70)	
Random effects model						4			(0.47-0.96)	
Heterogeneity: I-aquared=42	BN, tou-o	gaare	d-0.0629,	p=0.136	52					
				0.	1 0.2	0.5 1	2 :	5 10		
					Protonos	ed better	Short	better		

#### D Stent thrombosis

	Prolong	ed	Short	Odds Ratio (OR)	
Study	Events To	tal Events	Total		OR 95% CI
DES-LATE (12 vs. 36 mc PRODIGY (6 vs. 24 mc)		31 11 50 10		-	0.63 (0.24-1.63) 0.80 (0.31-2.04)
ARCTIC (12 vs. 18 mo) (TALIC (8 vs. 24 mo)	0 6	35 3	624 3 912		0.14 (0.01-2.71)
DAPT (12 vs. 30 mo)	19 50	20 65	5 4941		0.29 (0.17-0.48)
Bayesian hierarchical m Fixed effect model	ata-analysi 34 98		9742	+	0.45 (0.19-0.87) 0.37 (0.25-0.55)
Random effects model Helerogeneity: I—squared::2	8.9%, tnu-squ	aredu0.1193	ξ, ρυθ.25	**	0.42 (0.24-0.74)
				0.1 0.2 0.5 1 2 5	10
				Prolonged better Short be	tler

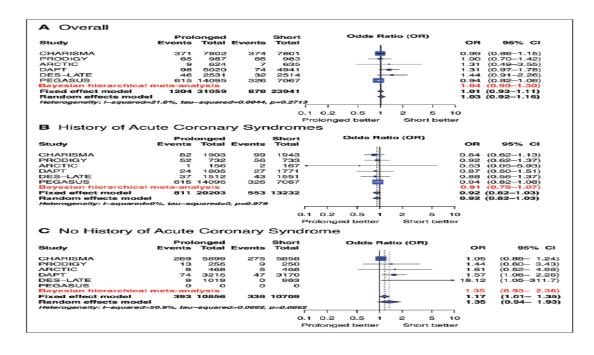
Bittl JA et al, Circulation, 2016





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# **Short vs prolonged DAPT according to previous ACS**

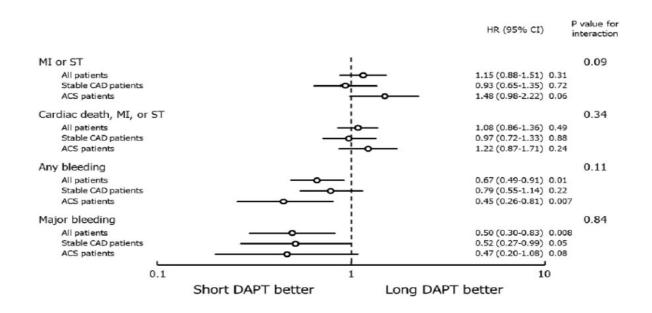


Bittl JA et al, Circulation, 2016



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# Short vs prolonged DAPT after DES according to previous ACS

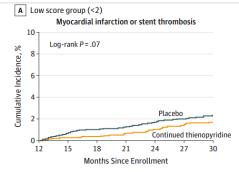


Palmerini T et al, EHJ, 2017



# Late stent thrombosis: a clinical case DAPT score

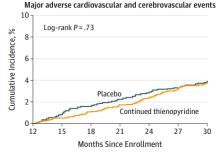
Clinical Prediction Score	
Variable	Points
Age, y	
≥75	-2
65-<75	-1
<65	0
Cigarette smoking	1
Diabetes mellitus	1
MI at presentation	1
Prior PCI or prior MI	1
Paclitaxel-eluting stent	1
Stent diameter <3 mm	1
CHF or LVEF <30%	2
Vein graft stent	2
Total score range: -2 t	o 10



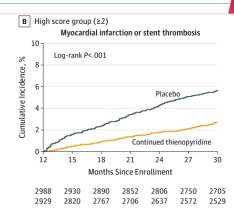
No. at risk

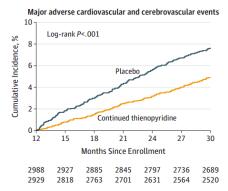
Continued thienopyridine 2874 2817 2770 2742 2706 2659 2637

Placebo 2857 2806 2769 2745 2711 2684 2659



No. at risk
Continued thienopyridine 2874 2814 2762 2734 2695 2646 2624
Placebo 2857 2804 2759 2730 2692 2664 2637





ESC Working Group



Dr. Giampaolo Niccoli



TABLE 4 Clinical U	tility of MI Status Ver	sus DAPT Score Stratification			
	NNTB for MI/ST Before Stratification	NNTH for GUSTO Moderate or Severe Bleeding Before Stratification	<b>→</b>	NNTB After Stratification	NNTH After Stratification
No MI (n = 6,308)	84	103	DAPT score <2 (n = 4,098)	203	74
			DAPT score $\ge 2$ (n = 2,210)	40	389
Any MI (n = 5,340)	39	106	DAPT score <2 (n = 1,633)	91	48
			DAPT score $\ge 2$ (n = 3,707)	31	226

Kereiakes DJ et al, JACC 2016





### Something else to consider?

### Angiographic variables

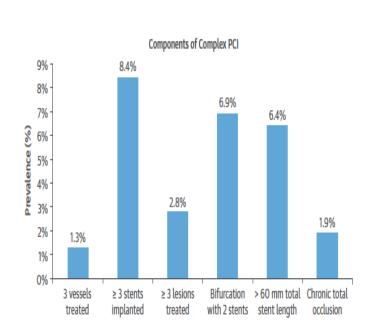
- Complexity of lesions
- Proximal coronary segment involvement
- Severe and diffuse Coronary Disease (Sullivan Score, Bogaty Score)
- Stent number, length and overlap

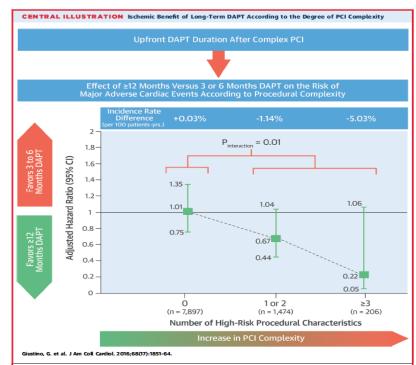
### Imaging Variables (IVUS or OCT).

- Stent underexpansion or malapposition
- Edge dissections
- Residual thrombus burden or plaque prolapse



### **Procedure complexity**



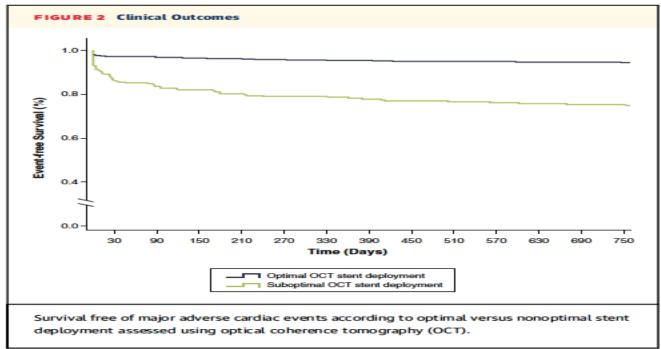


Giustino G et al, JACC 2016



### **OCT** guidance of PCI



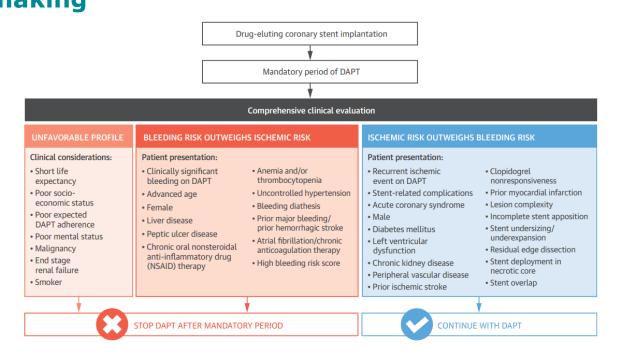


Prati F et al, JACC imaging 2015



# Late stent thrombosis: a clinical case Decision making





Montalescot, G. et al. J Am Coll Cardiol. 2015; 66(7):832-47.



### **Conclusions**



- The decision to prolong DAPT after DES is complex
- Clinical factors are not always of utility
- Pocedural data as well imaging informations may be of help
- Scores should include both clinical and procedural data



## Thank you for your attention



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### **Ongoing Studies**

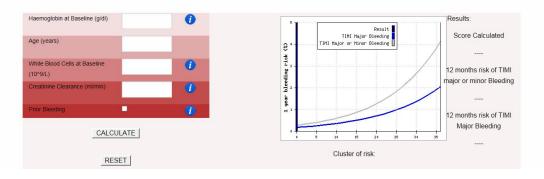
Study (Ref. #)	Design	Size	Active (Months)	Control (Months)	Population	Primary EP
GLOBAL LEADERS (NCTO1813435)	RCT (Biomatrix stent)	16,000	1	12	DES	Composite of all-cause mortality or nonfatal new Q-wave MI up to 2 yrs post-randomization
REDUCE (NCTO2118870)	RCT (COMBO dual therapy stent)	1,500	3	12	ACS	Composite of all-cause mortality, MI, ST, stroke, or bleeding at 12 months
SMART-CHOICE (NCTO2079194)	RCT	5,100	3	12	DES	Composite of death, MI, cerebrovascular events, or bleeding over 3-12 months after the index procedure
SMART-DATE (NCT01701453)	RCT	3,000	6	12	ACS	Composite of death, MI, CVA, ST, or major bleeding over 6-18 months post-hospitalization
DAPT-STEMI (NCT01459627)	RCT	1,100	6	12	STEMI	Composite of death, MI, revascularization, CVA, or bleeding at 18 months post-randomization
TWILIGHT (NCTO2270242)	RCT	8,000	3	12	complex PCI with DES	Major bleeding at 15 months post-PCI



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# Late stent thrombosis: a clinical case PRECISE DAPT-score





- To Predict the risk of bleeding in individual patients with coronary artery disease, treated coronary stenting and subsequent dual antiplatelet therapy
- Dataset including 14,963 patients from 8 randomized clinical trials, enrolled in more than 130 clinical sites and 12 countries worldwide.

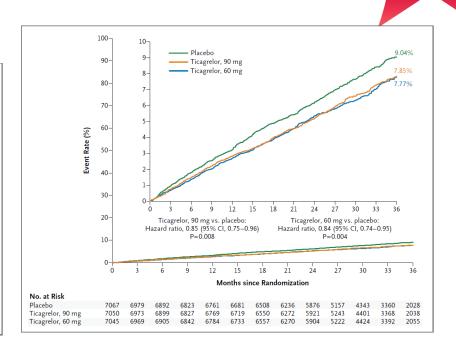
The PRECISE-DAPT Risk Score has been externally validated in two independent datasets. Data analysis, derivation and validation of the PRECISE-DAPT score were performed at the Erasmus Medical Center public health department.



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# Late stent thrombosis: a clinical case PEGASUS TIMI 54 study

End Point	Ticagrelor	Placebo			Hazard	d Ratio (95	% CI)	P Value
	3-yr Kaplan–Meie	er event rate (%)						
Cardiovascular death, myocardial infarction, or stroke								
Ticagrelor, 90 mg	7.85	9.04			-	-	0.85 (0.75-0.96)	0.008
Ticagrelor, 60 mg	7.77	9.04			-	-	0.84 (0.74-0.95)	0.004
Ticagrelor pooled	7.81	9.04			•	-	0.84 (0.76-0.94)	0.001
Cardiovascular death								
Ticagrelor, 90 mg	2.94	3.39			-	<del></del>	0.87 (0.71-1.06)	0.15
Ticagrelor, 60 mg	2.86	3.39		-	•	<del>_</del>	0.83 (0.68-1.01)	0.07
Ticagrelor pooled	2.90	3.39			-	-	0.85 (0.71-1.00)	0.06
Myocardial infarction								
Ticagrelor, 90 mg	4.40	5.25			-	-	0.81 (0.69-0.95)	0.01
Ticagrelor, 60 mg	4.53	5.25			-		0.84 (0.72-0.98)	0.03
Ticagrelor pooled	4.47	5.25			•	-	0.83 (0.72-0.95)	0.005
Stroke								
Ticagrelor, 90 mg	1.61	1.94		_		+	0.82 (0.63-1.07)	0.14
Ticagrelor, 60 mg	1.47	1.94		_	•	- <u> </u>	0.75 (0.57-0.98)	0.03
Ticagrelor pooled	1.54	1.94		_	-		0.78 (0.62-0.98)	0.03
			0.4	0.6	0.8	1.0 1.25	1.67	
		`	v.∓ <b></b> —	0.0	0.0	1.0 1.23		

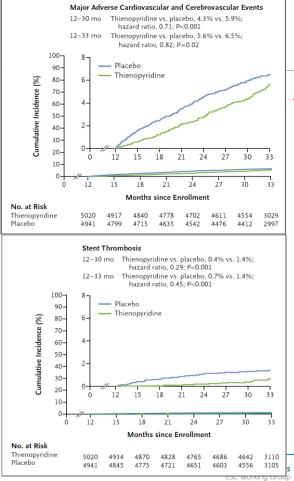




### Late stent thrombosis: a clinical case **DAPT study**

Outcome	Continued Thienopyridine (N = 5020)	Placebo (N = 4941)	Hazard Ratio, Thienopyridine vs. Placebo (95% CI)†	P Value†
	no. of patients (	%)		
Stent thrombosis;	19 (0.4)	65 (1.4)	0.29 (0.17-0.48)	< 0.001
Definite	15 (0.3)	58 (1.2)	0.26 (0.14-0.45)	< 0.001
Probable	5 (0.1)	7 (0.1)	0.71 (0.22-2.23)	0.55
Major adverse cardiovascular and cerebrovascular events∫	211 (4.3)	285 (5.9)	0.71 (0.59–0.85)	<0.001
Death	98 (2.0)	74 (1.5)	1.36 (1.00-1.85)	0.05
Cardiac	45 (0.9)	47 (1.0)	1.00 (0.66-1.52)	0.98
Vascular	5 (0.1)	5 (0.1)	0.98 (0.28-3.39)	0.98
Noncardiovascular	48 (1.0)	22 (0.5)	2.23 (1.32-3.78)	0.002
Myocardial infarction	99 (2.1)	198 (4.1)	0.47 (0.37-0.61)	< 0.001
Stroke	37 (0.8)	43 (0.9)	0.80 (0.51-1.25)	0.32
Ischemic	24 (0.5)	34 (0.7)	0.68 (0.40-1.17)	0.16
Hemorrhagic	13 (0.3)	9 (0.2)	1.20 (0.50–2.91)	0.68
Type uncertain	0	1 (<0.1)	_	0.32

Mauri L et al, NEJM, 2014







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