

JOURNAL READING

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ORIGINAL ARTICLE

Clopidogrel with Aspirin in Acute Minor Stroke or Transient Ischemic Attack

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Clopidogrel with Aspirin in Acute Minor Stroke or Transient Ischemic Attack

背景

- 在transient ischemic attack (TIA) 或 minor ischemic stroke後中風是很常見
- Combination therapy with clopidogrel and aspirin相較於只用aspirin也許能對之後發生的中風提供更多保護效果

研究目的

- 已知抗血小板治療對於預防次級中風的角色，但aspirin是唯一有在中風急性期被研究過的藥物，其效果不太高(modest)
- Aspirin和clopidogrel均可抑制血小板，同時使用還可降低缺血性ACS的發生率
- 儘管combination therapy對於中風後預防缺血性事件的發生率沒有效果，但中風後早期(高危險期)並沒有研究過
- 在Clopidogrel in High-Risk Patients with Acute Nondisabling Cerebrovascular Events (CHANCE)的trial中測試：在3個月內combination therapy(相較於只用aspirin)是否可以減少復發性中風(在一群acute high-risk TIA或minor ischemic stroke的人之中)

方法

- 研究設計: randomized, double-blind, placebo-controlled clinical trial, 114 所大陸的臨床醫學中心, 5170 patients → 2584: combination ; 2586: aspirin
- Inclusion criteria:
 - 40歲以上
 - 診斷為acute minor ischemic stroke或TIA
 - 可以在症狀發生後24hr內使用研究用藥物
- Exclusion criteria:
 - 出血
 - 本身除了此次中風外還有其他腦血管病變者 (某些腦部相關症狀)
 - 使用會影響血小板凝集的藥物
 - 明顯有在使用或不可使用clopidogrel or aspirin的人
- 用藥方式: clopidogrel for 90 days + aspirin on first 21 days (placebo + aspirin) for 90 days

BASELINE CHARACTERISTICS

- No obvious difference

Table 1. Baseline Characteristics of the Patients.*			
Characteristic	Aspirin (N=2586)	Clopidogrel and Aspirin (N=2584)	
Age — yr			
Median	62	63	
Interquartile range	54–71	55–72	
Female sex — no. (%)	898 (34.7)	872 (33.8)	
Systolic pressure — mm Hg			
Median	150	150	
Interquartile range	136–161	136–161	
Diastolic pressure — mm Hg			
Median	90	90	
Interquartile range	80–100	80–98	
Body-mass index†			
Median	23	23	
Interquartile range	23–27	23–26	
Medical history — no. (%)			
Ischemic stroke	517 (20.0)	516 (20.0)	
TIA	80 (3.1)	94 (3.6)	
Myocardial infarction	53 (2.0)	43 (1.7)	
Angina	87 (3.4)	87 (3.3)	
Congestive heart failure	38 (1.5)	42 (1.6)	
Known atrial fibrillation or flutter	48 (1.9)	48 (1.9)	
Valvular heart disease	10 (0.4)	4 (0.2)	
Hypertension	1483 (57.3)	1716 (66.4)	
Diabetes mellitus	145 (5.6)	150 (5.8)	
Hypercholesterolemia	283 (10.9)	290 (11.2)	
Pulmonary embolism	3 (<0.1)	0	
Current or previous smoking — no. (%)			
At least time to randomization — hr	13	13	
Time to randomization — no. (%)			
<12 hr	3280 (49.3)	3291 (50.0)	
≥12 hr	3306 (50.3)	3291 (50.0)	
Qualifying event — no. (%)			
TIA	728 (28.2)	717 (27.7)	
Minor stroke	1858 (71.8)	1867 (72.3)	
ABCD ² score‡			
Median	4	4	
Interquartile range	4–5	4–5	

結果

- Stroke → $p < 0.001$ (esp. ischemic)
- Stroke, myocardial infarction, or death from cardiovascular causes → $p < 0.001$
- Bleeding events → no obvious difference

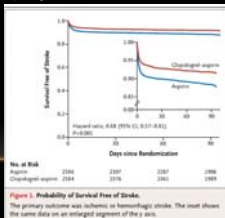
Outcomes	Aspirin (n=2048)	Clopidogrel and Aspirin (n=2048)	Hazard Ratio (95% CI)	P Value
	Patients with Event n(%)	Patients with Event n(%)		
Primary outcomes				
Stroke	302	212	0.68 (0.57-0.81)	<0.001
Secondary outcomes				
Stroke, myocardial infarction, or death from cardiovascular causes	307	216	0.68 (0.58-0.80)	<0.001
Ischemic stroke	295	204	0.67 (0.56-0.81)	<0.001
Myorrhagic stroke	8	8	1.00 (0.28-3.76)	0.99
Myocardial infarction	2	3	1.44 (0.24-8.61)	0.69
Death from cardiovascular causes	5	6	1.34 (0.35-5.78)	0.67
Death from any cause	10	10	0.97 (0.40-2.33)	0.94
Transient ischemic attack	47	39	0.82 (0.53-1.26)	0.34
Safety outcomes				
Bleeding*				
Severe	4	4	0.94 (0.24-3.78)	0.94
Moderate	4	3	0.73 (0.26-2.06)	0.60
Any bleeding	19	15	1.07 (0.68-1.70)	0.79

結論

- 在有TIA或minor ischemic stroke高風險且症狀發生後24hr內有被發現的人之中，使用combination therapy比只用aspirin更可降低之後中風的發生率
- 使用combination therapy相較只用aspirin治療者比起來，不會造成更多的hemorrhagic events

討論

- 先前的試驗，患者病情較嚴重且輕微中風和TIA病患沒有在第一時間收住院，所以不但沒有顯示減少缺血的风险，而且還增加出血的风险
- 從生存曲線圖看來，隨機分組後24小時內出現症狀者，幾乎一半都是在12小時內就收住院了。儘管沒有看到12小時內和更長時間之間的差異，但絕對事件發生率在12小時內是比較高的
- 大陸中風的亞型和其他發展中國家不同，大陸有較高的顱內大動脈粥狀硬化發生率以及在影響clopidogrel的代謝方面有基因多型性



討論

- 建議高危險TIA或acute minor stroke的病人發病24小時內，給予combination therapy

Original Investigation

Prehospital Triage to Primary Stroke Centers and Rate of Stroke Thrombolysis

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Prehospital Triage to Primary Stroke Centers and Rate of Stroke Thrombolysis

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背景

- 由於IV tPA是唯一有證據背景的reperfusion治療，但使用率低(1%-5%)
- Primary stroke centers (PSCs)的建立，希望能將懷疑有中風的病人直接送至PSCs，使tPA發揮其功效
- 藉由prehospital檢傷的實施，評估此政策對於急性中風照護的影響

研究目的

- 為了評估Chicago, Illinois城市方針：對於prehospital檢傷，讓疑似中風的病人至primary stroke center接受IV tPA治療的建議

方法

- Retrospective multicenter cohort study [在2011/3/1-intervention前後六個月(September 1, 2010, to August 31, 2011)]
- 10所 primary stroke center hospitals in Chicago
- 收院病人均有stroke和transient ischemic attack
- Intervention:** 對於有中風送去primary stroke centers實施prehospital檢傷
- Main outcomes and measures:** IV tPA use (部分有缺血性中風而自ED進來的人)

結果

- 有1075個中風或TIA的人在prehospital檢傷期間，另外1172人在posttriage periods
- 病患人口特質包括年齡、性別、危險因素等在此兩期間非常相似 (平均年齡65歲；53%女性).
- 檢傷實施後，相較於未實施檢傷前：
 - 急診醫療設施的使用程度增加 [30.2%→38.1% ($P < .001$)]
 - 急診醫療設施的提前通知也增加 [65.5%→76.5% ($P = .001$)]
 - IV tPA的使用率分別為3.8%和10.1% ($P < .001$)
 - 開始治療時機更快 [減少171.7至145.7分鐘 ($P = .03$)] in the pretriage and posttriage periods, respectively.
 - Stroke unit admission, symptomatic intracranial hemorrhage rates, and in-hospital mortality →無明顯差異
 - Adjusting for mode of arrival, prehospital notification, and onset-to-arrival time, posttriage periods獨立地與增加tPA被缺血性中風病人使用有關 (adjusted odds ratio = 2.21; 95%CI, 1.34-3.64).

Table 1. Cohort Demographic Characteristics, Medical History, Clinical Data, and Outcomes

Variable	No. (%)		P Value
	Pretriage (n = 1075)	Posttriage (n = 1172)	
Age, mean (SD), y	64.9 (15.5)	64.5 (15.0)	.53
Female	590 (54.9)	617 (52.6)	.29
Race			
White	421 (39.2)	443 (38.0)	
Black	559 (52.1)	586 (50.3)	.04
Asian or other	95 (8.8)	143 (12.2)	
Hispanic	107 (10.0)	131 (11.2)	.37
Diagnosis			
Ischemic stroke	719 (66.9)	787 (67.2)	
Intracerebral hemorrhage	175 (16.3)	174 (14.8)	
Subarachnoid hemorrhage	96 (8.9)	90 (7.7)	.10
Transient ischemic attack	81 (7.5)	108 (9.2)	
Undetermined	4 (0.4)	13 (1.1)	
Hypertension	807 (75.1)	888 (75.8)	.73
Diabetes mellitus	311 (28.9)	376 (32.1)	.11
Dyslipidemia	347 (32.3)	367 (31.3)	.72
Coronary artery disease	201 (18.7)	224 (19.1)	.83
Atrial fibrillation or flutter	116 (10.8)	118 (10.1)	.53
Prior stroke	236 (22.0)	262 (22.4)	.83
Current smoking	204 (19.0)	247 (21.1)	.22
Mode of arrival			
EMS from scene to ED	325 (30.2)	447 (38.1)	
Private transport to ED	401 (37.3)	381 (32.5)	
Transfer from other institution	321 (30.0)	333 (28.4)	<.001
Unknown	28 (2.6)	11 (0.9)	
EMS prenotification	213 (65.5)	342 (76.5)	.001
Stroke unit admission	900 (83.7)	948 (80.9)	.09
In-hospital mortality	76 (7.1)	93 (7.9)	.47

Table 2. Characteristics Among Subset of Patients With Diagnosis of Ischemic Stroke

Variable	No. (%)		P Value
	Pretriage (n = 738)	Posttriage (n = 787)	
Age, mean (SD), y	66.7 (15.1)	65.9 (14.5)	.30
Female	400 (55.6)	424 (53.9)	.72
Race			
White	257 (35.7)	286 (36.3)	
Black	401 (55.8)	413 (52.5)	.17
Asian or other	61 (8.5)	88 (11.2)	
Hispanic	50 (7.0)	75 (9.5)	.08
Hypertension	552 (76.7)	619 (78.7)	.39
Diabetes mellitus	224 (31.2)	278 (35.3)	.09
Dyslipidemia	269 (37.4)	268 (33.8)	.15
Coronary artery disease	159 (21.8)	180 (22.9)	.30
Atrial fibrillation or flutter	84 (11.5)	87 (11.0)	.34
Prior stroke	190 (26.4)	185 (23.5)	.36
Current smoking	146 (20.3)	180 (22.8)	.24
Mode of arrival			
EMS from scene to ED	266 (37.8)	367 (46.6)	
Private transport to ED	301 (41.8)	266 (33.7)	
Transfer from other institution	141 (19.6)	150 (19.1)	<.001
Unknown	11 (1.5)	4 (0.8)	
EMS prenotification	165 (22.8)	288 (36.5)	<.001
Onset-to-ED arrival time, min			
0-60	54 (7.5)	108 (13.7)	
61-120	47 (6.5)	58 (7.4)	
121-180	33 (4.6)	38 (4.8)	
181-270	24 (3.3)	31 (3.9)	<.001
271-360	27 (3.8)	26 (3.3)	
>360	108 (15.8)	117 (14.9)	
Not documented or unknown	426 (59.2)	479 (60.8)	
Stroke unit admission	601 (84.4)	628 (80.1)	.09
In-hospital mortality	30 (4.2)	34 (4.3)	.90
Overall IV tPA use for IS	23 (3.2)	69 (8.8)	<.001
OTI time, mean (SD), min	171.7 (46.2)	145.7 (35.7)	.01
Symptomatic intracranial hemorrhage	0	2 (2.8)	>.99
IV tPA use for IS, ED only	22 (3.8)	64 (8.1)	<.001
OTI time, mean (SD), min ^a	102.9 (26)	89.5 (47.3)	.14

結論

- 在Chicago，prehospital中風檢傷實施在emergency medical services use和prenotification方面有顯著的改進，而且more doubled IV tPA在primary stroke centers被使用

討論

- 先前study: 在ischemic stroke的病人・有檢傷的話tPA使用率可達23.4%；有一個analysis：有10%病人使用tPA對於中風結果和costs有助益
- 提早到院：全國25%的病人在症狀後‘黃金’一小時送達通常較有機會接受tPA
- Pre-notification：by EMS→減少評估時間→有利於盡早thrombolysis
- Confounding factors to thrombolysis: hospital size, teaching status, duration of time

討論

- Limitations:
 - (1)有PSCs的data但沒有non-PSCs的data
 - (2)無法評估prehospital對於stroke的screening標準
 - (3)可能產生selection bias和retrospective data collection error

THANKS FOR YOUR ATTENTION !!