

# Journal Meeting

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## #1 Trauma / Original research

### Immediate and Delayed Traumatic Intracranial Hemorrhage in Patients With Head Trauma and Preinjury Warfarin or Clopidogrel Use

## Article data

- Original article
- Journal : Annals of Emergency Medicine  
Volume 59, No.6 : June 2012
- Authors : Daniel K. Nishijima, MD et al.
- From : 2 trauma centers and 4 community hospitals in Northern California, US

3/32

## 背景

- 服用抗凝血劑、抗血小板製劑會增加頭部外傷腦出血機會，但影響有多大？
- 立即性vs.延遲性腦出血
- 研究目的：給臨床醫師一個動向決策的參考，一個服藥的頭部外傷病人，initial CT沒有ICH，放回家OK嗎？

4/32

## 研究方法

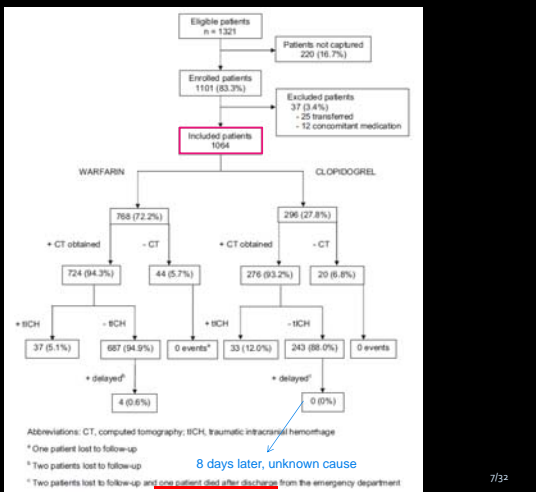
- Prospective, observational study
- 2 trauma centers and 4 community hospitals
- 2009. 04 ~ 2011.01
- 收案條件：頭部鈍傷病人來急診，且：
  - Age  $\geq$  18 y/o
  - 受傷前7日內有用warfarin或者clopidogrel
  - 頭部外傷不論有無LOC, amnesia都算
- 排除條件：
  - 轉院個案
  - 同時服用warfarin and clopidogrel

5/32

## Outcome Measures

- Immediate ICH : initial CT evaluation reported by radiologist
- Delayed ICH : within 14 days after initial normal CT scan, no repeated head injury
- Neurosurgical intervention
  - ICP monitor
  - Brain tissue oxygen probe
  - Burr hole/ craniotomy/ craniectomy
  - Intraventricular catheter / shunt
  - Mannitol use or hypertonic saline

6/32



Characteristic	Patients, No. (%)		
	Total (n=1,064)	Warfarin (n=768)	Clopidogrel (n=296)
<b>Demographics</b>			
Age, mean (SD), y	75.4 (12.7)	75.3 (13.0)	75.7 (11.9)
Male sex	502 (47.1)	362 (47.1)	140 (47.3)
<b>Mechanism of injury</b>			
Ground-level fall	887 (83.3)	644 (83.9)	243 (82.1)
Fall from height	37 (3.5)	23 (3.0)	14 (4.7)
MVC, <35 miles/h	18 (1.7)	12 (1.6)	6 (2.0)
MVC, ≥35 miles/h	24 (2.3)	16 (2.1)	8 (2.7)
MVC, unknown speed	9 (0.8)	4 (0.5)	5 (1.7)
Pedestrian struck by automobile	4 (0.4)	4 (0.5)	0
Bicyclist struck by automobile	4 (0.4)	3 (0.4)	1 (0.3)
Direct blow	59 (5.6)	45 (5.9)	14 (4.7)
Unknown mechanism	16 (1.5)	13 (1.7)	3 (1.0)
Other mechanism	6 (0.5)	4 (0.5)	2 (0.7)
<b>Clinical history</b>			
Vomiting	45 (4.2)	34 (4.4)	11 (3.7)
Headache	357 (33.6)	239 (31.1)	118 (39.9)
Loss of consciousness or amnesia	196 (18.4)	136 (17.7)	60 (20.3)
Concomitant aspirin use	43 (4.0)	19 (2.5)	24 (8.1)
<b>Physical examination</b>			
Alcohol intoxication	33 (3.1)	26 (3.4)	7 (2.4)
<b>Any evidence of trauma above the clavicles</b>	752 (70.7)	531 (69.1)	221 (74.7)
Trauma to face	406 (38.2)	296 (38.5)	110 (37.2)

## The reasons of using medication

- Warfarin
  - Atrial fibrillation (543/768, 70.7%)
- Clopidogrel
  - CAD (158/296, 53.4%)
- 大部分的人(>80%)在受傷前24小時內有服藥

Table 2. Prevalence of traumatic intracranial hemorrhage, neurosurgical intervention, and mortality.

Outcome Measures	Total (n=1,064)	Patients, No. (%) [95% CI]		Differences in Proportions, % (95% CI)
		Warfarin (n=768)	Clopidogrel (n=296)	
Immediate tICH*	70/1,000 (7.0) [5.5 to 8.8]	37/724 (5.1) [3.6 to 7.0]	33/276 (12.0) [8.4 to 16.4]	6.8 (2.7 to 11.0)
In-hospital mortality after immediate tICH	15/70 (21.4) [12.5 to 32.9]	8/37 (21.6) [9.8 to 38.2]	7/33 (21.2) [9.0 to 38.9]	-0.4 (-19.7 to 18.8)
Neurosurgical intervention after immediate tICH	12/70 (17.1) [9.2 to 28.0]	5/37 (13.5) [4.5 to 28.8]	7/33 (21.2) [9.0 to 38.9]	7.6 (-10.1 to 25.5)
Delayed tICH†	4/930 (0.4) [0.1 to 1.1]	4/687 (0.6) [0.2 to 1.5]	0/243 (0.0) [0.0 to 1.5]	-0.6 (-1.1 to 0.0)

Table 3. Patients with delayed traumatic intracranial hemorrhage (all with preinjury warfarin use).

Patient Sex and Age, Years	Mechanism of Injury	Initial GCS Score	Initial INR	Repeated Cranial CT Findings (Days After Initial Cranial CT)	Neurosurgical Intervention/ In-hospital Mortality (Days After Initial Cranial CT)	Comments
Man, 63	Ground-level fall, isolated head injury	15	1.50	Small intraparenchymal contusion and subarachnoid hemorrhage (1)	No/no	Patient was admitted to the hospital. Routine repeated cranial CT showed a small tICH. Discharged home HD 4.
Man, 79	Ground-level fall, isolated head injury	15	4.95	Small intraventricular hemorrhage (7)	No/no	Patient was admitted to the hospital. Repeated cranial CT obtained for a <b>change in mental status</b> on HD 7. Patient improved and was discharged home on HD 8.
Man, 91	Ground-level fall, isolated head injury	15	1.90	Large intraparenchymal, subarachnoid, and intraventricular hemorrhage with midline shift of 9.3 mm (3)	No/died (7)	Patient was admitted to the hospital. On HD 3, repeated cranial CT obtained for a <b>change in mental status</b> demonstrated a large tICH, and patient was made DNR. Died on HD 7.

## limitations

### limitations

- 有些人一開始沒切CT
- 同時服用aspirin (warf : clopi = 2.5% : 8.1%)
- 服用warfarin的病人較有出血警覺 → 易於尋求醫療協助

Table 4. Stratified and sensitivity analyses for immediate traumatic intracranial hemorrhage.

Analyses*	Patients, No. (%) [95% CI]		Differences in Proportions, % (95% CI)	Relative Risk (95% CI)
	Warfarin (n=768)	Clopidogrel (n=296)		
Primary analysis	37/724 (5.1) [3.6 to 7.0]	33/276 (12.0) [8.4 to 16.3]	6.8 (2.7 to 11.0)	2.31 (1.48 to 3.63)
Patients 65 y or older	33/554 (5.9) [3.9 to 7.7]	24/217 (11.1) [7.2 to 16.0]	5.5 (3.7 to 7.4)	1.99 (1.20 to 3.29)
Patients with GCS score 13-15	30/703 (4.3) [2.9 to 6.0]	29/268 (10.8) [7.4 to 15.2]	6.6 (2.5 to 10.6)	2.54 (1.55 to 4.14)
Patients with GCS score 15	23/631 (3.6) [2.3 to 5.4]	22/239 (9.2) [5.9 to 13.6]	5.6 (2.2 to 9.5)	2.53 (1.44 to 4.44)
Patients with ground-level fall	30/608 (4.9) [3.4 to 7.0]	27/225 (12.0) [8.1 to 17.0]	7.1 (2.5 to 11.6)	2.43 (1.48 to 4.00)
Patients with evidence of trauma above the clavicles	29/502 (5.7) [3.9 to 8.2]	21/206 (10.2) [6.4 to 15.2]	4.5 (-0.2 to 9.1)	1.77 (1.04 to 3.04)
Patients without concomitant aspirin use	36/705 (5.1) [3.6 to 7.0]	29/252 (11.5) [7.8 to 16.1]	6.4 (2.1 to 10.7)	2.26 (1.41 to 3.60)
Patients evaluated at community hospitals	21/485 (4.3) [2.7 to 6.5]	17/161 (10.6) [6.3 to 16.4]	6.2 (1.1 to 11.3)	2.44 (1.32 to 4.51)
Warfarin patients with INR ≤1.3	35/556 (6.3) [4.4 to 8.6]	33/276 (12.0) [8.4 to 16.3]	5.7 (1.3 to 10.0)	1.90 (1.21 to 2.99)
Warfarin patients with INR ≥2.0	31/441 (7.0) [4.8 to 9.8]	33/276 (12.0) [8.4 to 16.3]	4.9 (0.4 to 9.4)	1.70 (1.07 to 2.71)
Assume patients without cranial CT imaging did not have immediate tICH	37/768 (4.8) [3.4 to 6.6]	33/296 (11.1) [7.8 to 15.3]	6.3 (2.4 to 10.2)	2.31 (1.48 to 3.63)
Assume patients without cranial CT imaging had immediate tICH	81/768 (10.5) [8.5 to 12.9]	53/296 (17.9) [13.7 to 22.8]	7.4 (2.5 to 12.2)	1.70 (1.23 to 2.34)

\*Based on patients who received a cranial CT scan on initial evaluation after head injury.

## Discussion

- 若一開始CT沒出血，則延遲性出血的機會非常低(<1%)，留院觀察或是輸血correct coagulopathy是非必要的
- 現行guideline建議有服用warfarin的病人頭部外傷要routine切CT (基於理論)
- > 60 %出血病人沒有ILOC / amnesia
- 11-18 %出血病人外觀看不出有頭部外傷  
→ 有吃抗凝血的病人還是切下去吧！！

13/32

## Conclusion

- 關於延遲性出血，若一開始CT沒事，則延遲性出血機會很低(<1%)，可以考慮衛教回家，也不必積極輸FFP
- Discharge from ER is "reasonable"
- Routine follow up and discharge instructions are necessary

14/32



15/32

## #2 Original article

Can early cardiac troponin I measurement help to predict recent coronary occlusion in out-of-hospital cardiac arrest survivors?

## Article data

- Original article
- Journal : Crit Care Med  
2012 Vol. 40, No. 6
- Authors : Florence Dumas, MD, MPH et al.
- From : Paris Cardiovascular Research Centre, Paris, France

17/32

## Intro

- AMI (acute occlusion of coronary artery)仍是造成OHCA的主因
- PCI可能改善outcome
- History of chest pain不明確
- EKG predictive value不高
- Troponin I是最準的biomarker
  - Postresuscitatio triage
- Troponin I在非心因性OHCA也會上升？

18/32

## 研究設計

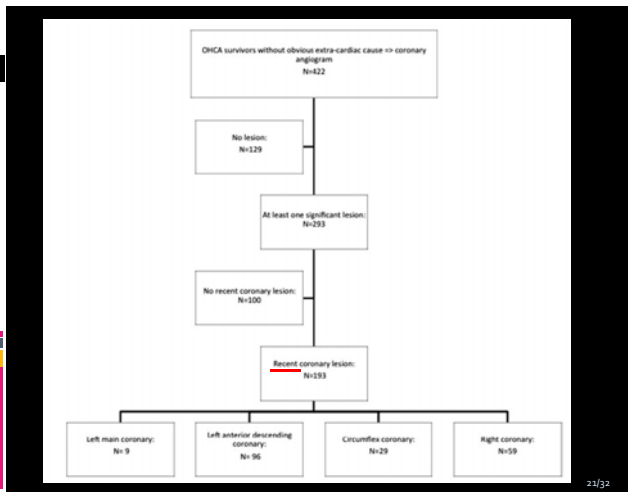
- Retrospective
- Out-of-hospital resuscitation by emergency team (含一位emergency physician)
- 無明顯extra-cardiac cause of arrest，一律做cath，不論臨床及EKG findings
- Percutaneous intervention (PCI) if indicated
- 視情況做therapeutic hypothermia
- 2003.01~2008.12
- Check troponin I level and EKG

19/32

## Abnormal data

- Troponin I > 0.15 ng/mL
- Post-ROSC EKG
  - ST elevation >1 mm in standard leads
  - ST elevation >2 mm in precordial leads
- Outcome assessment
  - To detect a **recent** coronary occlusion or unstable lesion by CAG
  - PCI successful when residual stenosis < 50%
  - LVEF was recorded

20/32



21/32

Table 1. Baseline characteristics

	Overall n = 422 (%)	Recent Occlusion n = 193 (%)	No Occlusion n = 229 (%)	p <sup>a</sup>	
Male gender	349 (83)	167 (87)	182 (79)	.64	
Smoking	176 (45)	94 (61)	82 (46)	.007	
Diabetes	70 (18)	28 (16)	42 (18)	.22	
Hypertension	167 (42)	74 (41)	93 (44)	.49	
Coronary disease history	101 (26)	42 (23)	59 (28)	.24	
Age >59 yrs <sup>b</sup>	214 (51)	95 (49)	119 (52)	.57	
Time between collapse and base life support <4 min <sup>c</sup>	200 (50)	104 (56)	96 (45)	.03	
Time between base life support and return of spontaneous circulation ≤15 min <sup>d</sup>	220 (53)	111 (58)	109 (49)	.05	
ST segment elevation	127 (30)	104 (54)	23 (10)	<.001	
Shockable initial rhythm	285 (68)	146 (76)	139 (61)	<.001	
Overall number of electrical shocks ± SD	3.4 ± 3.3	3.5 ± 3.3	3.3 ± 3.3	.36	
Epinephrine ≥2 mg <sup>e</sup>	218 (52)	112 (58)	106 (46)	.02	
<2	101 (24)	44 (23)	57 (25)		
Blood lactate (mmol L <sup>-1</sup> ) <sup>f</sup>	2-4.2	104 (25)	51 (26)	53 (23)	.61
4.2-7.9	96 (23)	39 (20)	56 (24)		
>7.9	122 (29)	59 (31)	63 (28)		
Creatinine (μmol L <sup>-1</sup> ) <sup>g</sup>	>114	217 (51)	96 (50)	121 (53)	.52
<0.79	105 (25)	22 (11)	83 (36)		
0.79-4.32	105 (25)	40 (21)	65 (28)		
4.32-17.48	107 (25)	58 (30)	49 (21)	<.001	
>17.48	105 (25)	73 (38)	32 (14)		
<40%	106 (24)	22 (12)	84 (36)		
40-60%	117 (28)	60 (31)	56 (24)	.001	
>60%	85 (28)	50 (26)	35 (15)		
Hospital survival	171 (41)	92 (48)	79 (34)	.006	

Mean 20.4  
Median 4.3

22/32

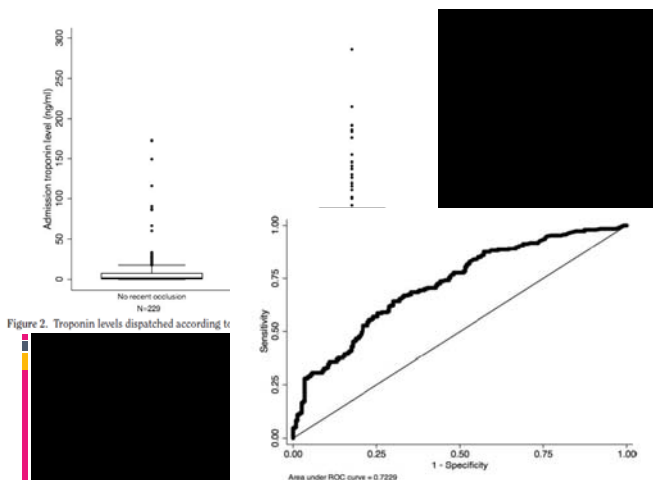


Figure 3. Troponin I receiving operating characteristic (ROC) curve predicting a recent coronary lesion.

## 生統小複習

- Receiver operating characteristic curve
- ROC曲線：對角線→無鑑別度  
愈往左上角→敏感度愈高
- Area under curve：曲線下的面積
  - 0~1：數值愈大愈好

AUC=0.5	幾乎沒有判別力 (no discrimination)
0.7 ≤ AUC < 0.8	可接受的判別力 (acceptable discrimination)
0.8 ≤ AUC < 0.9	好的判別力 (excellent discrimination)
AUC ≥ 0.9	非常好的判別力 (outstanding discrimination)

24/32

Table 2. Predictive values of Troponin I and ST elevation (isolated or combined)

	cTnI Cutoff			Isolated ST-Segment Elevation	cTnI >4.66 ng mL <sup>-1</sup> or ST-Segment Elevation	Combination of cTnI >4.66 ng mL <sup>-1</sup> and ST-Segment Elevation
	>0.38 ng mL <sup>-1</sup>	>4.66 ng mL <sup>-1</sup>	>31.83 ng mL <sup>-1</sup>			
	n = 355 (85%)	n = 204 (49%)	n = 67 (15%)	n = 127 (30%)	n = 243 (58%)	n = 88 (21%)
Sensitivity	94.3%	66.8%	29.0%	53.9%	81.4%	39.4%
Specificity	24.5%	66.8%	95.2%	90.0%	62.9%	94.8%
Positive predictive value	51.3%	62.9%	83.6%	81.9%	64.3%	86.4%
Negative predictive value	83.6%	70.5%	61.4%	69.8%	79.8%	65.0%
Youden index	0.19	0.34	0.24	0.44	0.43	0.34
Yule coefficient Q	0.69	0.6	0.78	0.83	0.73	0.84

- 33/422 (8%) had a normal TnI (<0.15 ng/mL)
- 89/295 (30%) had no ST elevation but presented a recent coronary lesion
- 53 of the above 89 (60%) had a TnI level higher than 4.66 ng/mL

25/32

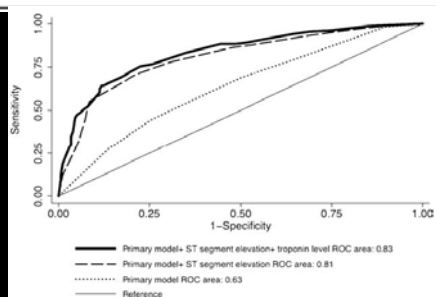
Table 3. Multivariate analysis of factors associated with an increase of troponin level according to optimum threshold (>4.66 ng mL<sup>-1</sup>)

	Odds Ratio	95% Confidence Interval	p <sup>a</sup>
Recent occlusion	4.05	1.99-8.25	<.001
Male gender	0.83	0.34-2.05	.69
Age >59 yrs <sup>b</sup>	0.43	0.22-0.83	.01
Time from collapse to base life support <4 mins <sup>b</sup>	1.28	0.67-2.45	.46
Time from base life support to return of spontaneous circulation <15 mins <sup>b</sup>	0.59	0.28-1.23	.16
Ejection fraction (per category increase)	1.32	0.86-2.03	.21
Epinephrine <2 mg <sup>b</sup>	0.46	0.22-0.98	.04
Ventricular fibrillation/ventricular tachycardia as initial cardiac rhythm	4.96	2.31-10.65	<.001
Smoking	0.69	0.35-1.34	.27
Creatinine >114 µg L <sup>-1</sup> <sup>b</sup>	1.78	0.85-3.71	.13
Lactate (per quartile increase)	1.07	0.77-1.48	.70
ST-segment elevation	1.59	0.73-3.38	.23

26/32

Table 4. Early independent predictive factors for recent occlusion

	Odds Ratio	95% Confidence Interval	p Value <sup>a</sup>
Epinephrine <2 mg <sup>b</sup>	2.11	1.20-3.73	.01
Ventricular fibrillation/ventricular tachycardia	1.68	0.91-3.12	.10
Smoking	1.98	1.15-3.40	.01
Cardiac troponin I >4.66 ng mL <sup>-1</sup>	3.58	2.03-6.32	<.001
ST-segment elevation	10.19	5.39-19.26	<.001



27/32

## Discussion

- 單獨看TnI上升，要預測coronary occlusion 效果很差
- 可能被急救中的其他因子影響
  - Defibrillation → TnI release
- 即便合併其他factor，TnI仍不適合拿來預測recent occlusion，也不適合拿來當作是否要做cath的決定因子
- Multiple variables to predict occlusion

28/32

## Elevated Troponin I

- Cardiac resuscitation本身就會使TnI上升
- 先前已有人study表示有相關
- False positive
  - CHF
  - Tachycardia
  - Sepsis
  - Kidney failure
- Initial shockable rhythm → TnI較高
- 但也可能是電擊之後造成的...

29/32

## Coronary angiography

- 293/422 (70%) were have at least 1 coronary lesion
- 193/422 (46%) were considered for responsible of the OHCA
- 有找到coronary lesion，做PCI → survival 46%，比起一般的survival 31%好太多了
- emergent PCI 對於cardiogenic OHCA還是很有價值的

30/32

## 結論

- 單獨的Tnl上升用在心因性的OHCA病人，是不足以拿來當作緊急做cath的marker的
- Tnl上升雖有其價值在，但同時要參考其他的factor(age, smoking, initial rhythm, EKG finding....)

32/32



32/32