Coronary Collaterals Function and Clinical Outcome Between Patients With Acute and Chronic Total Occlusion

OBJECTIVES　This study sought to demonstrate how changes in the collateral function and its clinical significance before and after percutaneous coronary interventions (PCIs) are compared between patients with acute coronary syndrome and total or nearly total occlusions (ATOs) and chronic total occlusions (CTOs).

BACKGROUND　The functional relevance of the collateral circulation in patients with ATOs and CTOs has not been fully investigated.

METHODS　The pressure-derived collateral pressure index (CPI), myocardial fractional flow reserve (FFRmyo), and coronary fractional flow reserve (FFRcor) at maximum hyperemia induced by intravenous adenosine were evaluated in occluded vessels at baseline, after the PCI, and at 1 year in 23 ATO and 74 CTO patients.

RESULTS　The FFRmyo and FFRcor were significantly lower, but the CPI was significantly higher in the CTO than ATO patients at baseline and after the PCI. There were significant increases in the FFRmyo (p < 0.001) and FFRcor (p < 0.001), whereas there was no significant change in the CPI immediately after the PCI in both ATO and CTO patients. In the CTO patients, a post-PCI FFRmyo <0.90 (p = 0.01) and post-PCI CPI <0.25 (p = 0.033) were independent predictors of the clinical outcome. Patients with a high post-PCI CPI had better clinical outcomes in CTO patients with a low post-PCI FFRmyo (log-rank p = 0.009), but not a high post-PCI FFRmyo (log-rank p = 0.492).

CONCLUSIONS　Recruitable coronary collateral flow did not regress completely immediately after the PCI both in patients with ATOs and CTOs. Despite good collaterals in CTO patients, aggressive efforts to reduce the ischemic burden might improve the clinical outcome.

急性和慢性冠狀動脈完全阻塞患者之側枝循環功能與臨床預後的相關性

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背景

在冠狀動脈「急性完全阻塞」（ATOs，指急性冠心症合併冠狀動脈完全阻塞或近乎完全阻塞）和「慢性完全阻塞」（CTOs）患者中，其側枝循環的功能差異，和預後的相關性，目前尚未被深入研究。這個研究的主要目的在於了解 ATOs 及 CTOs 患者在經皮冠狀動脈介入（PCIs）術前和術後，側枝循環功能的變化及其臨床意義。

方法

本研究總共收錄了 23 個 ATO 患者及 74 個 CTO 患者，藉由經靜脈注射 adenosine 以達到最大的冠狀動脈血流的狀態下，對阻塞病灶在 PCI 術前、術後及術後一年，偵測其側枝循環壓力指數（pressure-derived collateral pressure index, CPI），心肌血流儲備分數（pressure-derived collateral pressure index, FFRmyo）和冠狀動脈血流儲備分數（coronary fractional flow reserve, FFRcor）【詳見備註】，並評估其對臨床預後的相關性。

結果

1. CTO 患者在 PCI 術前及術後，其 FFRmyo 和 FFRcor 明顯比 ATO 患者低，但 CPI 卻較高。
2. ATO 及 CTO 患者在 PCI 術後，其 FFRmyo（$p < 0.001$）和 FFRcor（$p < 0.001$）均立即有顯著地增加，但 CPI 卻無顯著變化。
3. 在 CTO 患者中，PCI 術後 FFRmyo < 0.90（$p = 0.01$）和 PCI 術後 CPI <0.25（$p = 0.033$）是獨立的臨床預後預測因子。
4. CTO 病兆在 PCI 術後，低 FFRmyo 的患者若合併高 CPI 值（log-rank $p = 0.009$），其臨床預後較佳。

討論

這個研究的值得注意的發現有二點：

1. 這是第一個利用冠狀動脈 Pressure wire（PressureWire, St. Jude Medical, St. Paul, Minnesota）來比較 ATO 及 CTO 的患者側枝循環功能的研究，同時亦觀察 PCI 打通血管前後，側枝循環血流的變化及其對臨床預後的影響。
2. 另一個有趣的發現是，即使 CTO 患者有良好的側枝循環提供支援，但仍不足以去防止未來重大心血管事件的發生。因此該研究的作者相信，積極地打通 CTO 病兆，將改善患者的臨床預後。
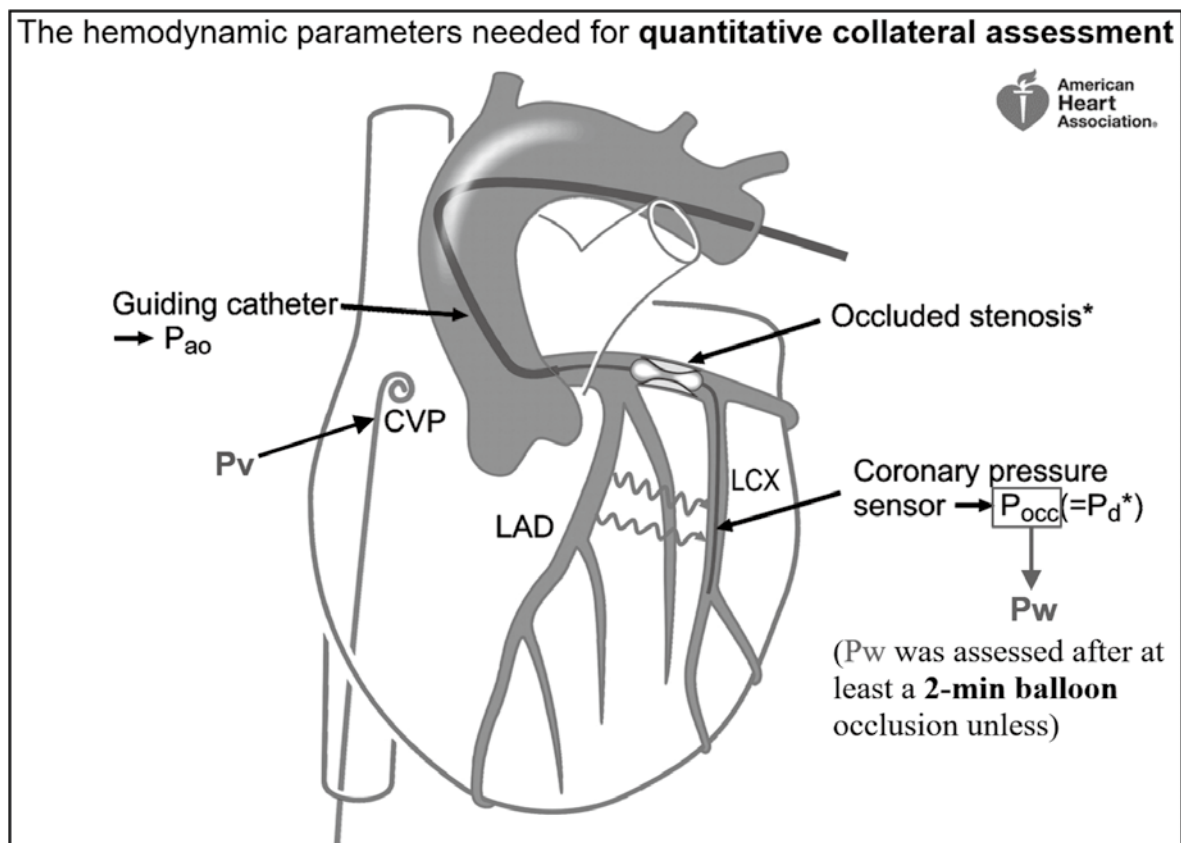
實驗限制

這個研究的限制有五點：

1. Single center，以及病患收集數量太少。
2. 在 Hemodynamic parameters 方面，因為只使用 Pressure wire 而非 Doppler wire，因此血流量及血管阻力的相關參數付之闕如。

3. CVP 的壓力值使用固定值 10 mmHg 來帶入計算，而非實際測量，對於 ATO 患者的 CPI 值可能導致較大的誤差。

4. 在 PCI 術後，並未執行 Donor vessels 的血管攝影，因此無從比較術後 CPI 值與 angiographic collateral grade 的關聯性。

5. 最後，PCI 術後一年追蹤的 CPI 值，無法排除是否有其他可能的因素及變異去影響 FFR 及 CPI 值的量測。

結論

PCI 術後，不論是 ATO 或 CTO 的患者，其潛在提供救援的側枝血流並不會立即完全地消退。根據研究，CTO 患者的側枝循環比 ATO 患者的側枝循環功能更為強大；然而，即便 CTO 的患者擁有良好的側枝循環，積極的處置去減少心肌缺血的負荷及範圍將有助於改善其臨床預後。當 CTO 患者在 PCI 術後，若其 FFR 仍然偏低，這時一個潛在功能完善的側枝循環，將對病患的長期預後有很大的幫助。

備註【Adapted from Tobias Traupe et al. Circulation. 2010;122:1210-1220】

The hemodynamic parameters needed for **quantitative collateral assessment**

American Heart Association.

Guiding catheter → P_{ao}

Occluded stenosis*

P_v → CVP

LAD　LCX

Coronary pressure sensor → $P_{occ}(=P_d*)$

→ P_w

(Pw was assessed after at least a **2-min balloon** occlusion unless)

$FFRmyo = Pd/Pa$

$FFRcor = (Pd-Pw)/(Pa-Pw)$　代表 the maximum recruitable antegrade perfusion

$CPI = (Pw-Pv)/(Pa-Pv)$

TABLE 1 Baseline Characteristics of Study Subjects

	ATO (n = 23)	CTO (n = 74)	p Value
Age, yrs	56 ± 10	59 ± 11	0.319
Male, %	19 (82.6)	62 (83.8)	0.894
Body mass index (kg/m^2)	25.1 ± 1.9	24.8 ± 2.7	0.616
Coronary risk factors			
Hypertension, %	13 (56.5)	37 (50.0)	0.585
Diabetes mellitus, %	6 (26.1)	25 (33.8)	0.489
Hypercholesterolemia, %	11 (47.8)	27 (36.5)	0.331
Current smoking, %	14 (60.9)	38 (51.4)	0.424
Previous CHD, %	5 (21.7)	30 (40.5)	0.101
Left ventricular ejection fraction, %	57.1 ± 7.1	51.6 ± 12.7	0.011
Medications			
Antiplatelet agents, %	10 (43.5)	38 (55.1)	0.355
Beta-blocker, %	5 (21.7)	32 (47.1)	0.033
ACEIs/ARBs, %	5 (21.7)	12 (17.6)	0.663
Statin, %	6 (26.1)	25 (36.2)	0.373

Values are mean ± SD or n (%).
ACEI = angiotensin-converting enzyme inhibitors; ARBs = angiotensin receptor blockers; ATO = acute coronary syndrome with total or nearly total occlusion; CHD = coronary heart disease; CTO = chronic total coronary occlusion.

▲ 表 1

TABLE 2 Angiographic Findings of Study Subjects

	ATO (n = 23)	CTO (n = 74)	p Value
Measured vessel lesion, %			0.460
Left anterior descending artery	12 (52.2)	39 (52.7)	
Left circumflex artery	5 (21.7)	9 (12.2)	
Right coronary artery	6 (26.1)	26 (35.1)	
Vessels diseased, %			0.716
1	13 (56.5)	38 (51.4)	
2	6 (26.1)	17 (23.0)	
3	4 (17.4)	19 (25.7)	
Collateral flow grade			0.071
1	8 (34.8)	13 (17.6)	
2	6 (26.1)	19 (25.7)	
3	9 (39.1)	42 (56.8)	
Anatomic collateral pathway			0.002
Epicardial	5 (21.7)	16 (21.6)	
Intramyocardial	15 (65.2)	24 (32.4)	
Coexistence	3 (13.0)	34 (45.9)	
Stent type, %			0.471
Sirolimus-eluting stent	0 (0.0)	1 (1.4)	
Zotarolimus-eluting stent	5 (21.7)	25 (33.8)	
Everolimus-eluting stent	9 (39.1)	18 (24.3)	
Biolimus-eluting stent	9 (39.1)	30 (40.5)	
Total number of stents	1.3 ± 0.6	1.8 ± 1.0	0.003
Stent size, mm	3.19 ± 0.29	2.98 ± 0.33	0.009
Stent length, mm	26.0 ± 8.6	36.4 ± 13.5	<0.001

Values are n (%) or mean ± SD.
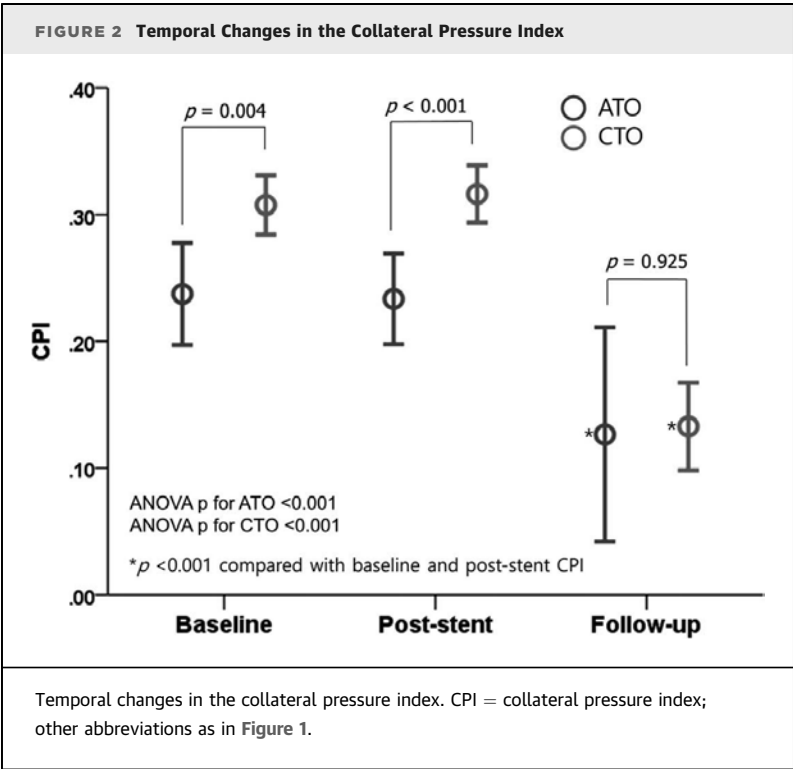Abbreviations as in Table 1.

▲ 表 2

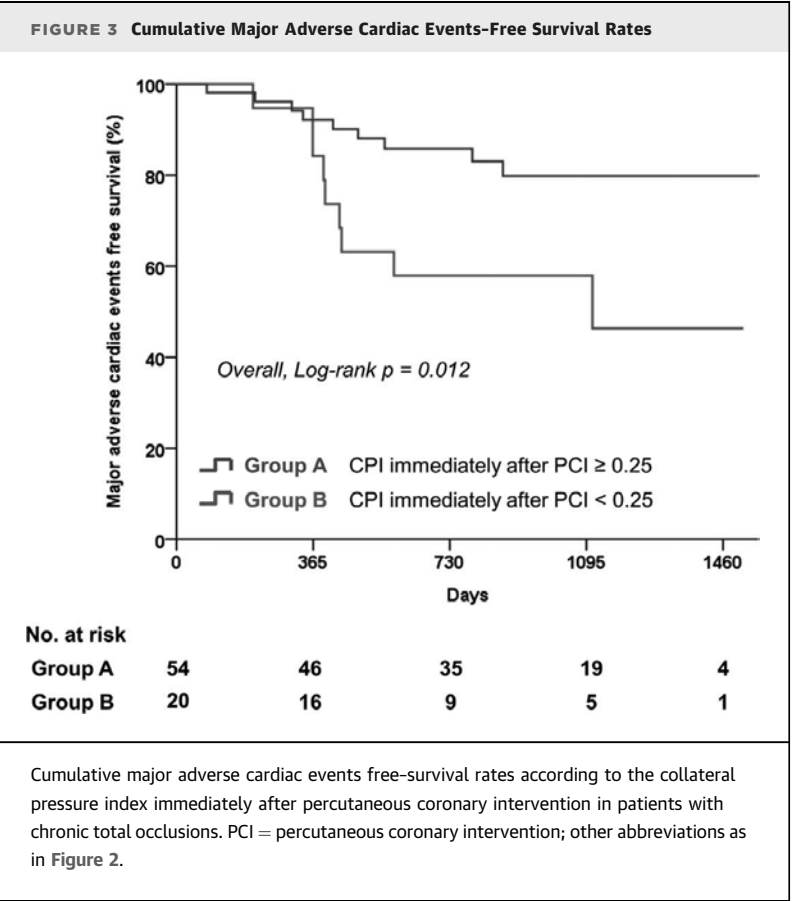**FIGURE 1 Temporal Changes in the Fractional Flow Reserve**
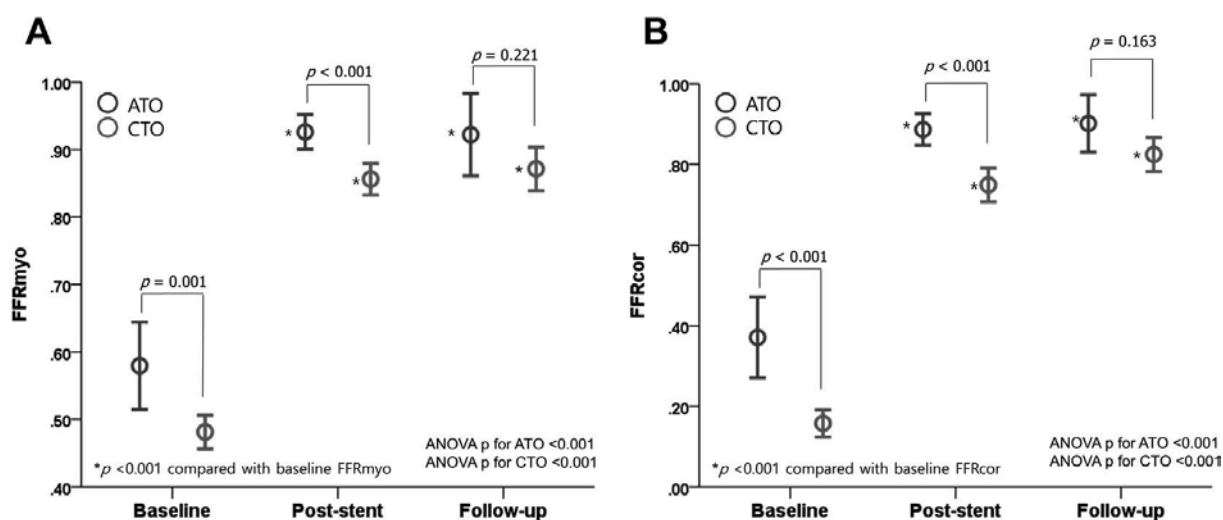
Temporal changes in the myocardial fractional flow reserve **(A)** and coronary fractional flow reserve **(B)**. ANOVA = analysis of variance; ATO = acute coronary syndrome with total or nearly total occlusion; CTO = chronic total occlusion; FFRcor = coronary fractional flow reserve; FFRmyo = myocardial fractional flow reserve.

▲ 圖 1

FIGURE 2 Temporal Changes in the Collateral Pressure Index

Temporal changes in the collateral pressure index. CPI = collateral pressure index; other abbreviations as in **Figure 1**.

▲ 圖 2

FIGURE 3 Cumulative Major Adverse Cardiac Events-Free Survival Rates

Cumulative major adverse cardiac events free-survival rates according to the collateral pressure index immediately after percutaneous coronary intervention in patients with chronic total occlusions. PCI = percutaneous coronary intervention; other abbreviations as in **Figure 2**.

▲ 圖 3

TABLE 3 Cox Proportional Hazards Model for Major Adverse Cardiac Events

	Hazard Ratio	95% CI	p Value
CPI post-PCI <0.25	3.73	1.11–12.5	0.033
FFRmyo post-PCI <0.9	7.07	1.60–31.2	0.01
Body mass index ≥25 kg/m^2	2.99	0.95–9.38	0.061
Left ventricular ejection fraction	1.03	0.98–1.09	0.246
Statin use	0.30	0.08–1.09	0.068

CI = confidence interval; CPI = collateral pressure index; FFRmyo = myocardial fractional flow reserve; PCI = percutaneous coronary intervention.

▲ 表 3

CENTRAL ILLUSTRATION Cumulative Major Adverse Cardiac Events-Free Survival Rates by Subgroup
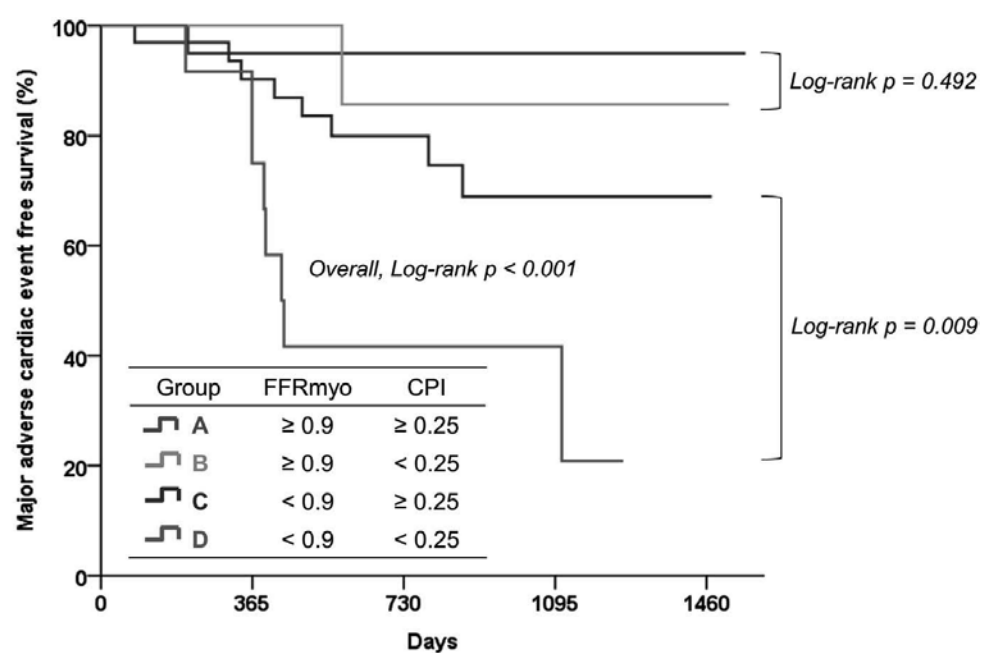
Lee, J.H. et al. J Am Coll Cardiol Intv. 2017;10(6):585–93.

Cumulative major adverse cardiac event-free survival rates according to the myocardial fractional flow reserve and collateral pressure index immediately after percutaneous coronary intervention in patients with chronic total occlusions. CPI = collateral pressure index; FFRmyo = myocardial fractional flow reserve.

▲ 圖 4