Ischaemia and infarction in STEMI patients with multivessel disease. Insights from the Complete versus Lesion-only PRimary PCI Trial (CvLPRIT) Nuclear Substudy

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Abbreviations

ACEI	=	angiotensin converting enzyme inhibitor
ARB	=	angiotensin receptor blocker
CvLPRIT	=	Complete versus Lesion-only PRimary PCI Trial
IRA	=	infarct-related artery
LV	=	left ventricle/ventricular
MPS	=	myocardial perfusion scintigraphy
OMT	=	optimal medical therapy
PPCI	=	primary percutaneous coronary intervention
QCA	=	quantitative coronary angiography
STEMI	=	ST-elevation myocardial infarction

The Complete versus Lesion-only PRimary PCI Trial (CvLPRIT) was undertaken in seven United Kingdom centres.[1,2] Patients with ST-elevation myocardial infarction (STEMI) and multivessel coronary stenoses were randomized to primary percutaneous coronary intervention (PPCI) to the infarct-related artery (IRA) only, or complete revascularization. At 12 month follow-up, the rate of the combined primary endpoint (all-cause mortality, recurrent MI, heart failure, ischaemia-driven revascularization) was lower after complete revascularization. All surviving patients were asked to undergo myocardial perfusion scintigraphy (MPS) 6-8 weeks post admission. It was expected that this *a priori* nuclear substudy would provide mechanistic insights into the outcome of the main trial, and help to define the clinical role of MPS in the PPCI era.

Stress-rest MPS was performed according to local departmental practice: technetium-99m-tetrofosmin 95%, two-day protocol 84%, vasodilator stress 84%, glyceryl trinitrate at rest 59%. Blinded semiquantitative analysis was performed in a central core-lab (ADK), and summed scores were expressed as percentages of the left ventricular myocardium (%LV). Separate scores were calculated for IRA and non-IRA territories. Supervising physicians were blinded to the results of MPS unless inducible hypoperfusion exceeded 20%LV (no patient), or symptoms developed within one month such that another ischaemia test would otherwise have been required (3 patients, all IRA-only, no significant inducible hypoperfusion, no further revascularization).

Of 296 CvLPRIT patients, 205 (69%) underwent MPS as intended; they were broadly similar to those in the overall study cohort.[1] The vast majority were asymptomatic and on optimal medical therapy (OMT) at the time of MPS (Table). IRA-only patients had more extensive resting defects (infarction) than complete revascularization patients (Table). This was associated with a non-significant trend towards more extensive infarction in the territory of the index IRA rather than that of a non-IRA. The extent of inducible hypoperfusion (ischaemia) was small, and exceeded 10%LV in only 14 patients (7%). There was no difference between the IRA-only and complete revascularization groups (Table).

Sixteen patients suffered a late cardiac event following MPS. No scintigraphic variable was predictive of the combined primary end-point. However, the extent of infarction was greater in patients suffering death, MI or heart failure than in those who had no event or a revascularization event – 23.5 (19.1-35.3) *versus* 8.8 (4.4-16.2) *versus* 7.4 (2.9-10.3) %LV, $P<0.01$ – whilst resting LV ejection fraction was lower – 43 (30-45) *versus* 57 (51-62) *versus* 59 (46-62) %, $P=0.01$. The extent of inducible hypoperfusion was similar – 0 (0-1.5) *versus* 1.5 (0-4.4) *versus* 2.9 (0-7.4) %LV, $P=0.26$.

The reduction in infarct size after complete revascularization might represent early improvement in collateral perfusion from treated non-IRAs to the watershed of the IRA territory. "Hard" cardiac events (as opposed to revascularization) occurring after MPS were associated with more extensive infarction and more severely impaired LV systolic function. It is therefore plausible that a small reduction in median infarct size explains the lower rate of early heart failure events and death seen in the complete revascularization arm of CvLPRIT.[1,3] Interestingly, the CvLPRIT cardiac magnetic resonance substudy showed no significant difference in infarct size between the randomized groups prior to hospital discharge.[2] This discrepancy probably reflects differences in the substudy populations, and the likelihood that early imaging overestimated infarct size.

All patients had undergone PPCI to the IRA and were receiving contemporary OMT. This may explain the limited inducible hypoperfusion seen even in the IRA-only group, and the inability of complete revascularization to reduce it further.[4] Therefore residual ischaemia is unlikely to be an important driver of further events post-PPCI for STEMI, and its suppression alone cannot explain the reduced event rate in the complete revascularization arm of CvLPRIT. Finally, routine ischaemia testing in asymptomatic patients following hospital discharge after PPCI for STEMI may have a limited yield, even in those with unrevascularized non-IRAs.

References

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Table. Characteristics of patients in the CvLPRIT Nuclear Substudy.

Variable		IRA-only	Complete	p
Number		101	104	
Clinical status at time of MPS at 6-8 weeks				
Canadian Cardiovascular Society class 0-1		87/91 (96)	96/96 (100)	0.054
New York Heart Association class 1		78/89 (88)	84/93 (90)	0.56
Beta-blocker		86/100 (86)	96/104 (92)	0.15
Statin		98/100 (98)	103/104 (99)	0.62
ACEI or ARB		95/99 (96)	99/104 (95)	0.99
MPS variables				
Stress defect (%LV)		13.2 (7.4-19.1)	13.2 (7.4-16.2)	0.16
Rest defect (%LV)	Overall	10.3 (5.9-17.6)	8.8 (4.4-14.7)	0.049
	IRA territory	8.8 (3.3-14.0)	5.9 (2.9-11.8)	0.09
	Non-IRA territory	0 (0-4.4)	0 (0-4.0)	0.70
Inducible hypoperfusion (%LV)		1.5 (0-4.4)	1.5 (0-5.9)	0.70
Resting ejection fraction (%)		58 (49-62)	57 (50-64)	0.84
Primary clinical end-points				
Early events (pre-MPS or <6 weeks)		9 (9)	1 (1)	<0.01
Late events (post-MPS or >6 weeks)	All events	12 (12)	4 (4)	0.04
	Death	1 (1)	0 (0)	
	Recurrent MI	1 (1)	0 (0)	
	Heart failure	2 (2)	1 (1)	
	Revascularization	8 (8)	3 (3)	

Results shown as mean (SD), median (IQR), or number of patients (%).

ACEI – angiotensin converting enzyme inhibitor; ARB – angiotensin receptor blocker.