

EDITORIAL

Revascularisation for acute coronary syndromes: PCI or CABG?

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Recent advances in both percutaneous coronary intervention and coronary artery bypass grafting emphasise the need for new randomised trials addressing acute coronary syndromes specifically, including a high proportion of patients with truly representative disease

We are in the midst of a steady increase in the number of patients presenting to hospitals with acute coronary syndromes (ACS). This group includes patients with ST segment elevation myocardial infarction (STEMI), non-ST segment elevation myocardial infarction (NSTEMI) and unstable angina (chest pain without electrocardiographic changes or an enzyme rise). The optimal treatment of STEMI (currently thought to be primary percutaneous coronary intervention (PCI) or systemic thrombolysis) will not be discussed further here. For NSTEMI and unstable angina, the consensus of rapidly evolving guidelines is that management should be based upon a system of risk stratification, incorporating an assessment of chest pain, ECG changes and cardiac markers.¹ For patients in the high risk group, recent trials show that an early invasive strategy (coronary angiography followed by revascularisation when appropriate) is superior to a conservative one, in terms of recurrent ischaemic episodes, if not lives saved.²⁻⁴ We are now left with the question of which mode of revascularisation should be selected for individual patients.

NEW PCI VERSUS NEW CABG

Conventional surgical revascularisation, as performed routinely, achieves a combined average risk of < 3% and the prospect of an excellent long term outcome.⁵ This operative risk may be further reduced, particularly in high risk patients, by avoiding cardiopulmonary bypass, using "off-pump" CABG (OPCABG),^{6,7} while total arterial revascularisation may further improve long term outcome.⁸ On the other hand, conventional stents have minimised the periprocedural risk of PCI to < 2%, while drug eluting stents have recently been shown to reduce restenosis rates to single figures in selected lesions.^{9,10}

TRIAL EVIDENCE

What evidence is there to guide our choice? Before we review the trials, it is salutary to recall their limitations. Patients enrolled in these trials comprised a small proportion of all patients

undergoing revascularisation (5-16% in ERACI-II, ARTS, and SoS), and included a high proportion with two vessel disease and normal ventricular function.¹¹⁻¹³ Such patients do not usually gain prognostically from CABG versus medical treatment¹⁴ and are therefore unlikely to demonstrate a survival advantage in comparison to PCI. Furthermore, the precise distribution of coronary artery disease, and the lesion types (both being critical factors in the day-to-day judgment of which mode of revascularisation is best for a particular patient) were generally not specified in any detail. Older trials lacked the widespread use of stents in the PCI group, as well as the routine use of low molecular weight heparin,¹⁵ aspirin and clopidogrel,¹⁶ statins,¹⁷ and glycoprotein IIb/IIIa inhibitors,¹⁸ all of which now contribute to the standard medical care for patients with ACS. For these reasons, most of the trials performed in the early 1990s are now outdated, and are not considered here.

Recent trials which might inform our decision making, and which avoid most of the pitfalls listed above, are summarised in table 1. They fall into two categories: those comparing an invasive and a conservative strategy for the treatment of patients with ACS (FRISC II, TACTICS-TIMI 18, and RITA 3)²⁻⁴; and those comparing PCI and CABG for the treatment of ischaemic heart disease (ERACI II, ARTS, and SoS).¹¹⁻¹³ It will immediately be apparent that neither group addresses the problem in hand directly. In particular, patients in the invasive arm of the former group were allocated, mostly at the discretion of the investigators, to PCI, CABG or continued medical treatment, without randomisation²⁻⁴;

Abbreviations: ACS, acute coronary syndrome; ARTS, arterial revascularization therapies study; AWESOME, angina with extremely serious operative mortality evaluation; CABG, coronary artery bypass grafting; ERACI-II, Argentine randomised study: coronary angioplasty with stenting versus coronary bypass surgery in patients with multiple vessel disease; FRISC-II, Fragmin and fast revascularization during instability in coronary artery disease; NSTEMI, non-ST segment elevation myocardial infarction; OPCABG, "Off-pump" CABG; PCI, percutaneous coronary intervention; PRAIS-UK, prospective registry of acute ischaemic syndromes in the UK; RAVEL, randomised comparison of a sirolimus-eluting stent with a standard stent for coronary revascularization; RITA-3, third randomized intervention trial of unstable angina; SIRIUS, prospective randomised evaluation of the sirolimus-eluting stent in patients with de novo coronary artery lesions; SoS, stent or surgery trial; STEMI, ST segment elevation myocardial infarction; TACTICS-TIMI 18, treat angina with Aggrastat and determine cost of therapy with an invasive or conservative strategy-thrombolysis in myocardial infarction

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Table 1 Summary of significant, recent trial data relevant to the question of treating patients with ACS by PCI or CABG

Dates	Number unstable	Number treated invasively	n		Subset of patients with ACS			
			n PCI	n CABG	Mortality (% at 1 year)	MI (% at 1 year)	Revascularisation (% at 1 year)	
Trials of invasive v conservative strategy for ACS								
FRISC II	1996–98	2457	1222	530 425	PCI CABG	~1 ~3	~15 ~9	14.3 1.6
TACTICS-TIMI 18	1997–99	2220	1114	459 220	PCI CABG	8.7 9.1		14.8 6.9
RITA 3	1997–2001	1810	895	311 184	PCI CABG	4.6	3.8	?
Trials of PCI v CABG for IHD								
ERACI II	1996–98	411	450	207 204	PCI CABG	0.9 5.7	0.9 5.7	16.8 4.8
ARTS	1997–99	450	450	226 224	PCI CABG	2.7 2.2	5.8 5.8	16.9 3.6
SoS	1996–99	451	451	210 241	PCI CABG	?	?	?

ACS, acute coronary syndrome; CABG, coronary artery bypass grafting; IHD, ischaemic heart disease; MI, myocardial infarction; PCI, percutaneous coronary intervention.

and, in the latter group, patients with ACS comprised only a subset of the whole patient cohort (92%, 37%, and 20%, respectively).^{11–13}

TRIALS OF INVASIVE VERSUS CONSERVATIVE MANAGEMENT

In the FRISC II trial, comparing invasive and non-invasive strategies to treat ACS, PCI was recommended for one vessel or two vessel disease and CABG for three vessel disease or left main stenosis.² Two year follow up has been published for this study.¹⁹ There was a slight excess of deaths at one year after CABG (~3%) versus PCI (~1%), the difference emerging at the time of the procedure (the equivalent figure for the non-invasively managed patients being ~4%). Conversely, there was an excess of myocardial infarctions after PCI (~15%) versus CABG (~9%), although most of these were “enzyme leaks” associated with the revascularisation procedure, rather than late, “spontaneous” myocardial infarctions (which occurred twice as frequently as this in the non-invasively managed patients). The most significant difference between the two treatments was in the incidence of repeat revascularisation; 14.3% for PCI versus 1.6% for CABG (table 1). Interestingly, there were more episodes of late revascularisation in the non-invasively managed patients than there were repeat revascularisations in the invasively managed patients.¹⁹ As can also be seen from table 1, it is more difficult to obtain such clarity in differentiating the results of PCI and CABG in TACTICS-TIMI-18, because one year rates of death and myocardial infarction were not separated into the two treatment subgroups in the presentation of the results. The combined figure was similar for both PCI and CABG in this trial, at 8–9%. Again, there was a higher repeat revascularisation rate for PCI (14.8%) than CABG (6.9%).³ In RITA 3, separate death, myocardial infarction, and repeat revascularisation rates for the PCI and CABG subsets were not reported.⁴

TRIALS OF STENT VERSUS SURGERY

The ERACI II trial randomised patients with multivessel disease to PCI or CABG.¹¹ Significantly, from the point of view of treating ACS, no less than 92% of patients in this trial presented with “unstable angina” (Braunwald classes II and IIIC). The one year death rate favoured PCI (0.9%) versus

CABG (5.7%), and the myocardial infarction rate was distributed similarly (0.9% v 5.7%). Again, repeat revascularisation was more common after PCI (16.8%) than CABG (4.8%).¹¹ The results for the subset of 37% of patients with ACS in the ARTS study have been published separately.²⁰ There was no difference in terms of death (2–3%) or myocardial infarction (5–6%) for PCI versus CABG; but, again, revascularisation was more frequent after PCI (16.9%) versus CABG (3.6%), with almost exactly the same rates as seen in ERACI-II.²⁰ The SoS trial has not, as yet, provided a breakdown of outcomes for the subset of patients with ACS.¹³

THE CURRENT POSITION

In summary, there is a sound evidence base to support an invasive strategy for patients with an ACS and a high risk profile. If the trials are to be followed beyond this point, there should be a preference for PCI for one or two vessel disease, and for CABG for three vessel or left main stem disease. For a select population of patients with two or three vessel (“easily randomised”) disease, the rate of hard clinical end points is similar for PCI and CABG, if the patient is willing to accept a modest restenosis rate. There are, however, other important, pragmatic factors (the physician preference mentioned in the trials) affecting the selection of PCI or CABG, and not fully addressed in the trials.

First, there is a pragmatic bias towards performing PCI where it is feasible and safe to do so. For example, for a single “culprit” lesion, or two significantly stenosed vessels, PCI is usually straightforward, quick, convenient, and performed at low risk; whereas multi-vessel disease with one or more chronically occluded vessels usually favours CABG, chiefly because of the low chance of PCI achieving full revascularisation (chronic total occlusions continue to have a high failure rate) and because multiple angioplasty sites increase the restenosis risk. Left main stem lesions involving the bifurcation and technically adverse, proximal coronary artery lesions are indications for surgery on the grounds of safety. Depressed left ventricular function generally biases towards CABG, except when it is extremely poor, when PCI may be preferred. The presence of serious co-morbidity also usually steers the choice towards PCI, unless there is an OPCABG enthusiast in the hospital. Indeed, recent trial data support the safety and efficacy of PCI versus CABG for patients at high risk for

CABG.²¹ PCI may also be used to “buy time” and delay CABG until a young patient reaches the optimal age to have a single operation, thereby avoiding a high risk “re-do” late in life.

The second pragmatic factor affecting the choice of PCI or CABG is the constraint, in many centres, upon the resources available for CABG, particularly when scheduling urgent operations. It is logistically generally easier to proceed immediately with PCI at the same sitting as the angiogram than to wait for an operation. In RITA 3, PCI was performed after a median of three days, and CABG after 22 days.⁴ In an everyday, “non-trial” environment, the waits are likely to be considerably longer than these. As shown in table 1, the proportion of patients with ACS receiving CABG versus PCI in the trials of an invasive strategy for ACS was, on average, 26% v 40%, respectively.²⁻⁴ This is a target which is not achieved in the “real world”, however; for patients with ACS in the UK, only 27% undergo coronary angiography, and 15% revascularisation of all types, by as late as six months after presentation.²²

IMPACT OF NEW DEVELOPMENTS

None of the trials listed includes the very latest developments in CABG or PCI. In particular, in the surgical field, there are increasing trends towards OPCABG and complete arterial revascularisation. OPCABG, in which grafts are anastomosed to the coronary arteries on the beating, normothermic heart, without the use of cardiopulmonary bypass, avoids the problems inherent in aortic cannulation and extracorporeal circulation (in particular, the risk of stroke). There is now considerable evidence that OPCABG reduces mortality and morbidity in higher risk patients.⁶⁻⁸ “Total arterial” grafting (based on both internal mammary arteries ± a radial artery) minimises the consequences associated with the premature failure of venous conduits.²³ Use of both internal mammary arteries may also confer a survival advantage. In a meta-analysis of several large, observational studies, the hazard ratio for death was 0.81 (95% confidence interval 0.72 to 0.94) for patients with bilateral rather than single internal mammary artery grafts after matching for age, sex, ejection fraction, and diabetes.⁸ The use of composite arterial grafts based upon the internal mammary arteries (when additional arterial grafts are anastomosed to the mammary arteries) eliminates the need for anastomosing grafts to the aorta, permitting a true “no touch” aortic technique, further reducing the risk of stroke.²⁴

With respect to PCI, polymer coated, drug eluting stents show great promise. Data from the RAVEL and SIRIUS trials, which included > 40% patients with ACS, using a stent eluting the antiproliferative, anti-inflammatory, and anti-migratory drug sirolimus, report < 2% mortality, < 9% target vessel failure, and < 3% in-stent restenosis rates at six months,⁹⁻¹⁰ marking the drug eluting stent out as a significant advance over conventional stents. The full implications of this advance are not yet clear. It may be that, if the promise of this new technology is realised, many more patterns of coronary artery disease may be amenable to PCI than at present.

THE FUTURE

If drug eluting stents and total arterial and OPCABG deliver sustained, long term results, both forms of revascularisation will gain in safety and efficacy. There will be continued, substantial expansion of PCI, both because of the increased incidence of ACS, and because of the broadening of the indications for performing the procedure. With respect to CABG, there is likely to be a continued, but more modest increase in numbers, generated by patients with patterns of disease unsuitable for PCI and by those with coexistent valvar or aortic disease. The aim of increasing operations from 500 to 750 per million of population, for both PCI and CABG, as

recommended in the National Service Framework for coronary heart disease in the UK, seems appropriate, but still lags considerably behind the 1000–1500 per million currently performed in Europe and the USA, respectively.

There are also several new trials to perform. One would be a randomised study of PCI and CABG in ACS in patients with (patent, but stenosed) multivessel disease, incorporating the best medical treatment in both arms, plus drug eluting stents in the PCI arm and modern CABG (as outlined above) in the other, and with appropriate follow up. For the results to be widely applicable it is important that such a trial includes a high proportion of patients with true multi-vessel disease. Another appropriate new trial would be to compare PCI versus CABG for diabetic patients with ACS, using the new techniques outlined above in both treatment groups.

The pace of change and advancement in the techniques of revascularisation for ACS has never been greater. It is therefore important that the optimal treatment for such patients is decided after *joint* consultation between an interventional cardiologist and a cardiac surgeon. We can be sure that the majority of patients with ACS will benefit from two complementary strategies that continue to advance and improve.

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IMAGES IN CARDIOLOGY

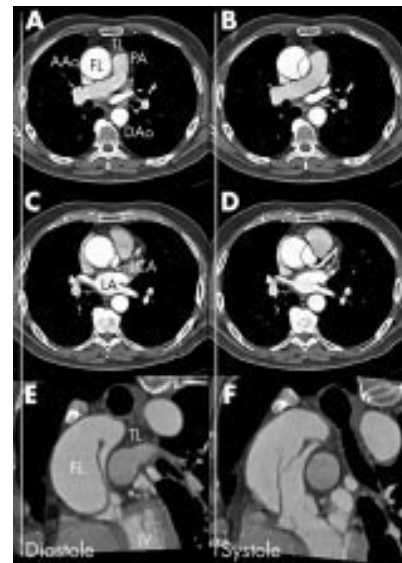
The dynamics of an ascending aorta dissection by 16 row multislice computed tomography

A 65 year old man was referred for follow up of a dissected ascending aorta. The study was performed with a 16 slice spiral computed tomography scanner (Sensation 16, Siemens, Germany) after the intravenous administration of 100 ml of iodinated contrast material with the following protocol: detector collimation 12 × 1.5 mm, rotation time 0.42 s, scan time 19 s. The scan was retrospectively reconstructed using the ECG track to create iso-cardio-phasic datasets. Main datasets were reconstructed in the diastolic phase and systolic phase (80% and 20% of the RR interval, respectively). The false lumen, in the diastolic phase, occupies almost the entire volume of the ascending aorta (below, panel A). The dynamics of the dissected flap are shown during the diastolic and systolic phase of the cardiac cycle (right, panels A–F). During the diastolic (A, C, E) phase the true lumen collapses while the false lumen is widely expanded. This configuration is caused by the higher blood pressure in the false lumen during diastole, which compresses the true lumen. In the systolic phase (B, D, F) the true lumen is maximally expanded because of the high systolic pressure during the ventricular systolic ejection phase.

The patient did not undergo surgery because of the severely impaired heart function.



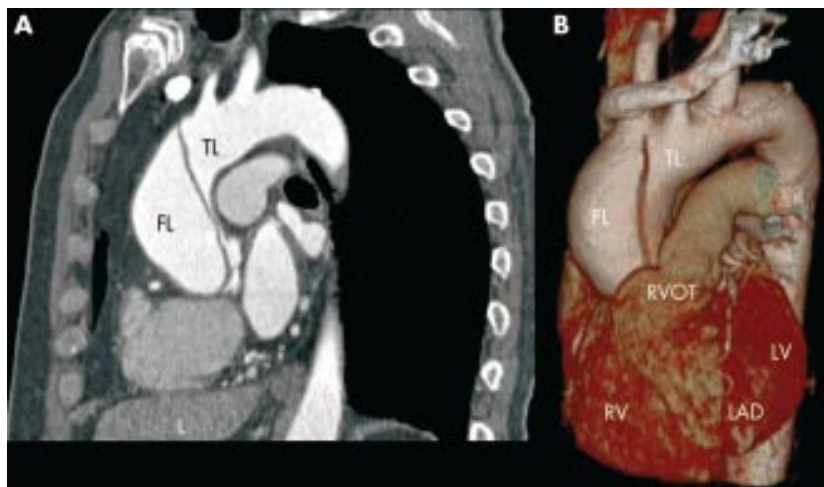
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Comparison between diastolic (left column—A, C, E) and systolic (right column—B, D, F) configuration of the dissected flap. The axial slices performed at the level of the right pulmonary artery (A, B) and at the level of the origin of the left coronary artery (C, D) show how the dissected flap shifts between the diastolic and systolic phase. The sagittal oblique multiplanar reconstructed images (E, F), display the same behaviour of the flap (white arrowheads) along the ascending aorta. During the diastolic phase the dissected flap tends to cover the origin of the left coronary artery. Also clearly displayed is the closed and open aortic valve during the diastolic and systolic phase, respectively (E and F). FL, false lumen; TL, true lumen; LV, left ventricle; RV, right ventricle; RVOT, right ventricular outflow tract; L, liver; LAD, left anterior descending; LCA, left coronary artery; LA, left atrium; AAo, ascending aorta; DAo, descending aorta; PA, pulmonary artery.

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Panoramic images reconstructed in the diastolic phase. The sagittal oblique multiplanar reformatted image (A) and the three dimensional volume rendering reconstruction (B), show the configuration of the dissected flap. The false lumen in the ascending tract of the thoracic aorta occupies most of the transverse diameter of the vessel at this level.