INTERVENTIONAL CARDIOLOGY AND SURGERY

Interventional versus conservative treatment in acute non-ST elevation coronary syndrome: time course of patient management and disease events over one year in the RITA 3 trial

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Heart 2006;92:1473–1479. doi: 10.1136/hrt.2005.060541

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Accepted 15 March 2006
Published Online First
18 April 2006

Objective: To determine whether, in acute non-ST elevation coronary syndrome, the benefit from early invasive coronary intervention compared with a conservative strategy of later symptom-guided intervention varies over time.

Methods: In RITA 3 (Randomised Intervention Trial of unstable Angina 3) patients were randomly assigned to coronary angiography (median 2 days after randomisation) and appropriate intervention (n = 895) or to a symptom-guided conservative strategy (n = 915).

Results: In the first week patients in both groups were at highest risk of death, myocardial infarction (MI) or refractory angina (incidence rate 40 times higher than in months 5–12 of follow up). There were 22 MIs and 6 deaths in the intervention group (largely due to procedure-related events, 14 MIs and 3 deaths) versus 17 MIs and 3 deaths in the conservative group. In the rest of the year there were an additional 12 versus 27 MIs, respectively (treatment-time interaction p = 0.021). Over one year in the intervention group there was a 43% reduction in refractory angina; 22% of patients underwent coronary artery bypass surgery and 35% underwent percutaneous coronary intervention only, which reduced refractory angina but provoked some early MIs; and 43% were still treated medically, mostly because of a favourable initial angiogram.

Conclusion: Any intervention policy needs to recognise the high risk of events in the first week and the substantial minority of patients not needing intervention. Intervention may be best targeted at higher risk patients, as the early hazards of the procedure are then offset by reduced subsequent events.

Admissions to hospital of patients with unstable angina or non-ST segment myocardial infarction (MI) are common and costly. The outcome is poor, with a hospital mortality of 2.7% and 5.9%, respectively.¹ Within six months 19% of patients are hospitalised. Almost 22% of deaths occur within 24 h of hospital admission and the median time of death is six days.²

Seven large randomised trials^{3–13} have sought to show a benefit from prompt coronary angiography leading to percutaneous coronary intervention (PCI) or coronary artery bypass graft (CABG) surgery in selected patients. Two early studies^{3,4} failed to show benefit possibly because there was only a small difference in the actual intervention rates in the two arms of the trials. Of the five more recent trials, three^{5–9} did show benefit in terms of reduction in angina, three^{6,7,10} showed a reduction of fatal or non-fatal MI, and one had an increase of MI.¹¹ No trial showed an effect on death at six months. After one year of follow up mortality was reduced in FRISC II (Fragmin and Fast Revascularisation during Instability in Coronary artery disease) (3.9% to 2.2%, p = 0.016)⁵; the absolute benefit was maintained after two years (5.4% to 3.7%, p = 0.038).¹² In RITA 3 (Randomised Intervention Trial of unstable Angina 3) death and the occurrence of MI were reduced after five years.¹³

After one year an interventional strategy in RITA 3⁸ resulted in a 43% reduction in refractory angina but had no effect on death or non-fatal MI. Here we examine the findings in the RITA 3 trial to characterise the time course of

the hazard in these patients and the time-related impact of an early interventional strategy as opposed to later intervention largely guided by symptoms. Such a difference in strategy has been tested in only two formal trials^{10,11} but has substantial implications for the provision of cardiac resources to manage these patients. Current guidelines are not definitive on this issue.^{14,15}

METHODS

Study patients

The design of RITA 3 has been described previously. In brief we enrolled 1810 patients (aged over 18 years) with acute non-ST elevation coronary syndrome from 45 UK hospitals.⁸ Patients were randomly assigned to angiography or conservative management within 48 h of the index episode of cardiac chest pain. Patients assigned to angiography in centres without on-site angiographic facilities were transferred to an appropriate centre. Coronary angiography was to be done as soon as possible after randomisation and ideally within 72 h. The requirement and type of revascularisation

Abbreviations: CABG, coronary artery bypass graft; FRISC II, Fragmin and Fast Revascularisation during Instability in Coronary artery disease; ICTUS, Invasive versus Conservative Treatment in Unstable Coronary Syndromes; MI, myocardial infarction; PCI, percutaneous coronary intervention; RITA 3, Randomised Intervention Trial of unstable Angina 3; TACTICS, Treat angina with Aggrastat and determine Cost of Therapy with an Invasive or Conservative Strategy; VANQWISH, Veterans Affairs Non-Q-Wave Infarction Strategies in Hospital

was decided by the patient's physician. Patients assigned to the conservative strategy were managed with optimal angina and thrombosis drugs. Enoxaparin (1 mg/kg subcutaneously twice daily for 2–8 days) was given to all patients. After discharge from hospital coronary angiography could be undertaken for failure of the conservative regimen. The predefined co-primary end points were death, MI and refractory angina within four months, and death and MI within one year. Follow up was planned for five years, with patients seen at four months and each year. Primary end points and cause of death were adjudicated by an independent events committee blinded to treatment according to predefined objective criteria.⁸

Statistical analysis

While the predefined primary end point analyses were according to the intention to treat principle, additional analyses by assigned treatment group were broken down by coronary interventions actually received (or not). Significance tests, risk ratios and their confidence intervals are based on standard methods for binary outcome data by using STATA software (V.7; StataCorp, College Station, Texas, USA).

RESULTS

Characteristics of the 1810 randomly assigned patients (895 intervention, 915 conservative) have been described previously.⁸ The mean age was 62 years and 38% were women. Two thirds of patients had angina before admission, with over half rated grade 3 or 4. Twenty-eight per cent of patients had had a previous MI and 94% patients were taking at least one angina drug. Ninety-two per cent of patients had ECG evidence of ischaemia; 41% had ST depression or transient elevation of at least 0.1 mV. In the intervention group 97% of patients received the intended angiogram at a median of two days after randomisation. During the index admission 44% of patients in the intervention arm underwent a revascularisation procedure compared with 10% in the conservative group. After one year revascularisation procedures had been performed in 57% and 28% of the intervention and conservative groups, respectively.

Time course of primary events over one year

At four months 86 (9.6%) of 895 patients in the intervention group had died or had an MI or refractory angina, compared with 133 (14.5%) of 915 patients in the conservative group (primary end point: risk ratio 0.66, 95% confidence interval (CI) 0.51 to 0.85, $p = 0.001$). This difference was due to a 53% reduction of refractory angina in the intervention group. Death or MI was similar in both treatment groups at one year (co-primary end point: 68 (7.6%) *v* 76 (8.3%), respectively; risk ratio 0.91, 95% CI 0.67 to 1.25, $p = 0.58$). Symptoms of angina were improved and use of angina drugs significantly reduced by the interventional strategy ($p = 0.0006$ for angina symptoms of grade 2+ at one year).

Figure 1 shows the pattern over time for risk of a first primary event of death, MI or refractory angina for each group over time. Risk was high early on, especially in the first three days, in both treatment groups and fell continuously over time so that in months 5 to 12 of follow-up risk was reduced by more than 40-fold compared with the initial three days. In the first week there was little evidence of a treatment difference for a primary event (35 in the intervention group *v* 39 in the conservative group). Likewise in months 4 to 12 after randomisation there was no difference (36 intervention *v* 38 conservative). The treatment difference in primary events is most notable in the period from 8 days to 120 days. During that time 51 patients in the intervention group had a first primary event compared with 94 in the conservative

Figure 1 Rate of occurrence of a first primary event (death, myocardial infarction, refractory angina) by time since randomisation and treatment group. C, conservative group; I, intervention group. Number of events is shown on top of each column and black shading represents events occurring after a revascularisation procedure.

group. During days 0 to 7 a substantial proportion of events occurred after the intervention.

Figure 2 shows the incidence rate by time since randomisation for the predefined co-primary end point of death or MI for each treatment group. In both groups the incidence rate declined markedly with time. In the first 28 days the risk was eight times higher than in the rest of the year. Table 1 shows the incidence of first events in six time intervals since randomisation separately for death, MI and refractory angina.

Deaths during one year

For deaths there was no evidence of a treatment difference at any time point. The death rate declined over time. In both

Figure 2 Rate of occurrence of death or myocardial infarction by time since randomisation and treatment group. C, conservative group; I, intervention group. Number of events is shown on top of each column and black shading represents events occurring after a revascularisation procedure.

Table 1 Numbers of patients who died or had a first MI or incident refractory angina, by time since randomisation and treatment group

Time (days)	Death		MI		Refractory angina		Combined	
	I	C	I	C	I	C	I	C
0-3	3(1.1)	0(0.0)	13(4.9)	10(3.7)	7(2.6)	16(5.9)	20	24
4-7	3(0.8)	3(0.8)	9(2.6)	7(1.9)	4(1.1)	7(2.0)	15	15
8-14	5(0.8)	2(0.3)	2(0.3)	6(1.0)	9(1.5)	14(2.3)	14	21
15-28	4(0.3)	4(0.3)	0(0.0)	2(0.2)	7(0.6)	17(1.4)	10	23
29-120	11(0.14)	14(0.17)	6(0.08)	9(0.11)	12(0.2)	31(0.4)	27	50
121-365	15(0.07)	13(0.06)	4(0.02)	10(0.05)	20(0.10)	21(0.11)	36	38
Total	41	36	34	44	59	106	122	171

Numbers in brackets are the event rates/1000 days of follow up.

C, conservative group; I, intervention group; MI, myocardial infarction.

groups combined, the death rate in months 1, 2 to 4 and 5 to 12 was 0.48, 0.15 and 0.07 deaths/1000 days of follow up, respectively.

Within the first seven days after randomisation nine patients died. Six were in the intervention group, four deaths were related to angiography or intervention and two deaths were sudden. In the conservative group all three deaths were sudden deaths associated with MI.

Within 28 days 24 patients died. Of the 15 in the intervention group, seven deaths were procedure related (two at angiography, three in patients assigned to percutaneous transluminal coronary angioplasty and two in patients assigned to coronary surgery). Of the eight other deaths three were sudden, four were associated with an MI and one was in a patient with no evidence of MI. The nine conservative group deaths were due to four MIs, three sudden death, one coronary artery disease with no acute event and one spontaneous retroperitoneal haemorrhage.

MI during one year

Over the whole year the incidence of MI was non-significantly higher in the conservative group (34 MIs in the intervention group *v* 44 MIs in the conservative group, $p = 0.29$) (fig 3). There was evidence of a treatment-time interaction ($p = 0.021$), in that MIs in the first week were somewhat more common in the intervention group (22

intervention *v* 17 conservative), whereas in the rest of the year MIs were substantially more common in the conservative group (12 intervention *v* 27 conservative). There was a pronounced trend in risk of MI over time. For both groups combined the rate of a first MI in 1000 days of follow up in week 1, the rest of month 1, months 2 to 4 and months 5 to 12 was 3.11, 0.27, 0.09 and 0.03, respectively.

Of the 22 MIs at seven days in the intervention group 10 were definite procedure-related infarctions, six were definite MIs, four were probable MIs related to the procedure and two were probable MIs not related to the procedure. In the conservative arm of the 17 MIs, nine were definite MIs, five were probable MIs, two were procedure-related MIs after non-assigned treatment (one probable and one definite), and one was a fatal MI.

At 28 days the number of MIs had increased by 10 to a total of 29: 24 in the intervention arm and 25 in the conservative arm. In the intervention arm there was one additional definite MI and one additional probable MI related to a procedure. In the conservative arm there were four additional definite MIs, three further probable MIs, and one further MI related to a non-assigned procedure.

Refractory angina over one year

The incidence of refractory angina was more pronounced in the conservative group at all times over the first four months

Figure 3 Rate of occurrence of myocardial infarction by time since randomisation and treatment group. C, conservative group; I, intervention group. Number of events is shown on top of each column and black shading represents events occurring after a revascularisation procedure.

Figure 4 Rate of occurrence of refractory angina by time since randomisation and treatment group. C, conservative group; I, intervention group. Number of events is shown on top of each column and black shading represents events occurring after a revascularisation procedure.

of follow up (39 cases (4.4%) in intervention group *v* 85 (9.3%) in conservative group, $p < 0.0001$) (fig 4). In the subsequent months 5 to 12 there was no difference in incident refractory angina (20 cases *v* 21 cases in the intervention and conservative groups, respectively). In both treatment groups there was a continuous pronounced reduction in risk of incident refractory angina over time.

Relation of primary events to interventions actually received

In the intervention group 865 patients (97%) did receive their intended angiogram, of whom 491 (55%) went on to a planned revascularisation procedure within a year of randomisation. A further 18 patients underwent unplanned PCI or CABG in the first year, which leaves 386 patients (43%) in the intervention group who did not receive a revascularisation procedure in a year. Within a year, 196 intervention group patients had CABG and 325 had PCI (12 of whom also had CABG, including two who had CABG and subsequent PCI).

In contrast, 258 patients (28%) in the conservative group did undergo an unplanned revascularisation procedure at some point in the year after randomisation, 113 of whom had CABG. It is relevant to explore the incidence of primary events in both treatment groups in relation to the coronary revascularisation procedures they actually received:

Deaths and procedure undertaken

In the intervention group 41 patients died within one year, nine of them after PCI (one of them after having an MI on the same day as PCI) and eight after CABG. Thus, 24 intervention group patients who died did not receive a revascularisation procedure; one of them was to receive PCI and three CABG. In the intervention group four patients died within one week of randomisation as a result of a planned procedure: two were considered related to angiography and two to PCI. No patient assigned to the conservative group died from a procedure in the first week.

In the conservative group five of the 36 deaths occurred after CABG (all at least one month after randomisation). No patients died after percutaneous transluminal coronary angioplasty; thus, 31 patients who died had not received a revascularisation procedure.

MI and procedure undertaken

In the intervention group, 17 of the 34 MIs within a year occurred in patients who did not receive a revascularisation procedure: 15 MIs were after PCI and two after CABG. In the first seven days after randomisation the risk of MI was highest: 22 of the 34 intervention group MIs were in this first week. Eleven of these occurred shortly after PCI, none after CABG, four in patients awaiting planned PCI, four in patients awaiting planned CABG, and two in patients under planned medical management. In this first week the rate of MIs after PCI was over four times higher than the rate among intervention group patients still under medical management.

In the conservative group, there were five MIs after PCI (two on the day of PCI) and one MI on the day of CABG, the other 38 MIs within a year being among patients still under medical management. Two of the MIs after PCI were within a week of randomisation.

Of the 21 of 68 events (deaths or MI within one year) occurring in the intervention group after PCI, 10 were in patients who received a glycoprotein IIb/IIIa inhibitor and 11 in patients who did not. Of the four of 75 events in the conservative group after PCI two were in patients who had received a glycoprotein IIb/IIIa inhibitor and two who had not.

Table 2 Baseline and angiographic predictors of the planned procedure in the intervention group

	Medical (n=355)	PCI (n=314)	CABG (n=194)
Number of significantly diseased vessels			
0	183 (98%)	3 (2%)	0 (0%)
1	80 (29%)	194 (69%)	6 (2%)
2	47 (23%)	97 (47%)	63 (30%)
3	43 (24%)	20 (11%)	124 (66%)
Age (years)			
<60	157 (47%)	122 (37%)	52 (16%)
60–69	113 (37%)	122 (40%)	73 (24%)
≥70	85 (38%)	70 (31%)	69 (31%)
Sex			
Men	166 (32%)	202 (39%)	154 (30%)
Women	189 (55%)	112 (33%)	40 (12%)
Smoker			
Never	110 (52%)	65 (31%)	38 (18%)
Former	143 (36%)	144 (37%)	106 (27%)
Current	102 (40%)	105 (41%)	50 (19%)
Angina grade before admission			
0	119 (43%)	109 (39%)	48 (17%)
1–2	111 (39%)	103 (36%)	69 (24%)
3–4	124 (41%)	102 (34%)	77 (25%)
Previous myocardial infarction			
No	251 (41%)	242 (40%)	119 (19%)
Yes	104 (41%)	72 (29%)	75 (30%)
Diabetes			
No	316 (43%)	266 (36%)	158 (21%)
Yes	39 (32%)	48 (39%)	36 (29%)

Of the 865 with angiogram, one patient died and one had a major cerebrovascular accident and then died. Hence no procedure was planned. The denominator for this table is therefore 863. A further three had no details of the extent of the disease.

CABG, coronary artery bypass graft; PCI, percutaneous coronary intervention.

Refractory angina and procedure undertaken

In the intervention group, there were 59 cases of refractory angina within one year of which 19 were after PCI and four after CABG. That leaves 36 cases of refractory angina in patients still under medical management, of whom six were awaiting planned PCI and seven were awaiting planned CABG. After CABG the rate of refractory angina was consistently lower over time than in other intervention group patients.

In the conservative group, 100 of the 106 cases of refractory angina within one year occurred in patients still under medical management. There were five cases after PCI and one after CABG.

Predictors of planned procedure in the intervention group

For the 865 (97%) patients in the intervention group who did receive their intended coronary angiogram, the consequent planned procedure was PCI for 314 patients and CABG for 194 patients, which leaves 357 planned to continue with medical treatment only. Table 2 shows the angiographic and other baseline features by these three management options.

The strongest predictor of planned intervention was the number of significant diseased vessels. Most with no significant disease had medical treatment (table 2). Most patients with single-vessel disease had PCI (69%) and six (2%) had CABG. Of those patients with two-vessel disease 23% had planned medical care, 47% had PCI and 30% had CABG. By comparison 66% of patients with triple-vessel disease underwent CABG. Planned CABG was more likely in older patients and patients with previous MI, and was less likely in women and patients with no angina before admission. Planned medical management was more likely in younger patients, women and patients without diabetes.

Table 3 Baseline predictors of coronary revascularisation being done within one year in conservative group patients

	None (n = 657)	PCI only (n = 145)	CABG or both (n = 113)
Age (years)			
<60	292 (76%)	59 (15%)	33 (9%)
60–69	205 (67%)	54 (18%)	47 (15%)
≥70	160 (71%)	32 (14%)	33 (15%)
Sex			
Men	401 (69%)	90 (15%)	92 (16%)
Women	256 (77%)	55 (17%)	21 (6%)
Smoking			
Never	139 (71%)	30 (15%)	28 (14%)
Former	283 (70%)	66 (16%)	55 (14%)
Current	235 (75%)	49 (16%)	30 (10%)
Angina grade			
0	227 (79%)	45 (15%)	16 (6%)
1–2	211 (72%)	40 (14%)	43 (13%)
3–4	175 (66%)	60 (18%)	54 (16%)
Previous myocardial infarction			
No	482 (71%)	121 (18%)	78 (11%)
Yes	175 (75%)	24 (10%)	35 (15%)
Diabetes			
No	571 (71%)	134 (14%)	96 (12%)
Yes	86 (75%)	11 (10%)	17 (15%)

CABG, coronary artery bypass graft; PCI, percutaneous coronary intervention.

Predictors of the need for intervention in conservative group patients

In the conservative group 258 patients (28%) required a revascularisation procedure within one year, 113 of whom had CABG. Table 3 shows how occurrence of these revascularisation procedures related to baseline features. Younger patients, women and patients without angina before admission were less likely to have any revascularisation, and especially CABG. By design the conservative group did not get a planned coronary angiogram.

Use of glycoprotein IIb/IIIa inhibitors

Among patients who underwent angioplasty before discharge, 70 of 291 (24%) received glycoprotein IIb/IIIa inhibitors in the intervention arm and 17 of 61 (28%) in the conservative arm. Of the 35 of 120 primary events occurring after angioplasty in the first year, 15 (four within 72 h, seven within the first week) were in patients who received glycoprotein IIb/IIIa inhibitors and 20 (two within 72 h, seven within the first week) in patients who did not.

DISCUSSION

The RITA 3 trial⁸ showed that, in patients with unstable angina or non-ST elevation MI, early coronary angiography followed by an appropriate revascularisation procedure substantially reduced recurrent refractory angina (53% at four months and 43% over one year). There were no differences in death or MI over one year. More detailed examination of the findings found a notable time dependence of events. Patients were at greatest risk of any event in the first week. Deaths and MI were higher during the first week in the intervention group than in the conservative group (not significant and small numbers) but that potentially adverse outcome was counterbalanced by a lower rate of death and MI in later months, so that after one year there was little overall difference. Thus, the major impact of intervention in RITA 3 over one year was on the occurrence of refractory angina. After five years death and the occurrence of MI were reduced.¹³

The results of RITA 3 are broadly in keeping with two other large recent trials in that the major impact was on symptoms,

refractory angina or hospital readmission.^{6–9} In TACTICS (Treat Angina with aggrastat and determine Cost of Therapy with an Invasive or Conservative Strategy)⁷ death was not affected at 30 days or six months but the composite end point of non-fatal MI or death was reduced at 30 days. In FRISC II the composite end point of non-fatal MI or death was reduced at six months.⁶ Mortality did not differ significantly at six months but after one and two years of follow-up mortality was reduced.^{5 12} In TACTICS hospital readmission at 30 days was reduced by 39% and in FRISC II at six weeks by 38%. The median time from randomisation to coronary angiography in these two studies was one and four days, respectively, compared with two days in RITA 3. Large registry studies have not shown a benefit in mortality in patients who attend hospitals with catheter facilities or where intervention is done earlier.^{16–18}

A meta-analysis of the large trials⁸ and of recent trials where glycoprotein IIb/IIIa inhibitors and stents were used¹⁹ show an overall favourable clinical response to intervention in terms of death or non-fatal MI. In the first analysis⁸ a beneficial effect on death or non-fatal MI was apparent at one year and in the second¹⁹ reduced mortality was evident at two years with borderline significance. MI was significantly reduced¹⁹ but such analyses are flawed because of the different definitions of MI used in the interventional and conservative arms in FRISC II and TACTICS. A more recent meta-analysis²⁰ showed over 17 months a reduction in severe angina, hospitalisation and MI with a trend to a reduction in mortality. Routine intervention was associated with an early hazard.

As the greatest benefit is on the recurrence of refractory angina and much of the putative reduction of MI occurs not in the first few days but over several weeks, a key question is the timing of the early intervention. The trials, including the current study, were designed to compare early intervention with a conservative treatment strategy in which the need for intervention was largely determined by recurrent symptoms. As the observed benefit was predominantly on the occurrence of angina symptoms over many weeks, one interpretation of the findings is that an invasive strategy, beginning with a coronary angiogram, does not necessarily have to be pursued immediately after the diagnosis of a non-ST segment acute coronary syndrome but should instead begin after a short period of medical stabilisation such as 7–28 days. Some physicians may even argue for intervention only when symptoms recur and that has substantial implications for the provision of cardiac resources to manage these patients. Such a difference in the planning of angiography and intervention has been tested in only one small trial.⁹ The more recently reported ICTUS (Invasive versus Conservative Treatment in Unstable Coronary Syndromes) trial,¹¹ which included 1201 patients, showed no overall benefit from early intervention on a combined end point; a reduction in the later need for rehospitalisation with an acute coronary syndrome was offset by an increase in MI in the early intervention group.¹¹

RITA 3 showed that the rate of occurrence of an event falls steeply with time (figs 1–4) in accordance with data from large registries.^{1 2} Mortality in the trials varies considerably probably due to differences in entry criteria. The critical question is not whether immediate intervention should be undertaken because the risk of events is high early after the onset of symptoms, but rather whether intervention at any chosen time is advantageous to the patient. In the VANQWISH trial⁴ the frequency of death or non-fatal MI was higher in the intervention group than in the conservative group before hospital discharge (36 v 15 events, $p = 0.004$) and at one month (48 v 26 events, $p = 0.012$). The same was true for death (21 v 6 deaths, $p = 0.007$; 23 v 9, $p = 0.21$).

Likewise in FRISC II the event rate was higher in the intervention group at two weeks; there appeared to be an early hazard of intervention. The same observation was made in ICTUS¹¹ and in RITA 3 as reported here.

Reasons for this early mortality and morbidity and the contrasting results between trials²⁰ may relate to the technology for PCI and the concurrent use of thrombosis drugs and stents, or to advances in medical treatment over the years. In RITA 3 selected patients were given glycoprotein IIb/IIIa inhibitors but use did not relate closely to outcome, although the numbers for comparison were small. An observational study has indicated a possible advantage in patients undergoing PCI from concurrent use of a glycoprotein IIb/IIIa inhibitor.²¹ The number of early events in RITA 3 is insufficient to permit a detailed analysis of the impact of these inhibitors. A further difficulty in predicting the optimal time for intervention is the lack of understanding of the detailed pathophysiology of acute coronary syndrome in individual patients. If the initial event is triggered by plaque disruption followed by platelet accumulation on an exposed surface, repair processes will be activated and will be evolving over the ensuing few days. Whether intervention has the same risk to benefit ratio if undertaken almost immediately (< 3 days) or between 7 and 14 days, when the pathological features may have changed, remains largely unknown. Only one trial¹⁰ has attempted to answer that question. The trial was small with 410 patients randomly allocated to immediate angiography (2.4 h) or to delayed angiography (86 h). Both groups received high doses of multiple thrombosis drugs. The 30 day death rate was low as in other recent trials. The combined end point of death or MI was significantly different in favour of early angiography. The difference in the rate of MI was seen in the first 86 h and not subsequently when all patients had undergone angiography. This finding is different from the results of RITA 3 in that in the first week in RITA 3 MI was not reduced in the intervention group. One explanation may be the regimen Neumann *et al*¹⁰ used as antithrombotic treatment. Another is that the time from the onset of symptoms to angiography may have been long because of the referral procedure; if interventions had been undertaken late in all patients, the early hazard would not have been observed and the results would be compatible with the findings in RITA 3.

The predictors of intervention in RITA 3⁸ are, as expected, the number of diseased vessels, previous MI, presence of angina, and old age. These relationships can mostly be explained by associations of the number of significantly diseased vessels with both planned management and baseline features. The lack of benefit among women in RITA 3 is in accord with the findings in FRISC II.⁶ The extent to which women were less likely to have planned revascularisation (especially CABG) was more than could be attributed to women tending to have fewer diseased vessels on an angiogram.

RITA 3,⁸ like VANQWISH,⁴ FRISC II,^{5,6} and ICTUS,¹¹ provides some evidence of early adverse effects related to coronary intervention. That harm is offset by a later advantage. The physician is faced with a dilemma. Non-ST elevation MI and unstable angina carry a high early hazard, which decreases rapidly with time. And yet immediate intervention or intervention in the first seven days may not necessarily be advantageous. As technology advances the balance may favour more immediate intervention. From the current data it is not possible to argue that immediate intervention is mandatory but equally it is not possible to show unequivocally that a more measured approach to intervention is advantageous. The RITA 3 findings raise important questions that are critical to the provision of an effective health system, but the answers will need to come

from randomised clinical trials, not of a strategy as in RITA 3, but comparing alternative timings of coronary angiography. Patients will probably continue to undergo procedures in a timely manner on the basis of clinical assessment of long-term risk linked to the immediate evidence of continuing ischaemia. Intervention may best be targeted at high risk patients, as the early hazards of the procedure are offset by a reduced risk of subsequent events.

ACKNOWLEDGEMENTS

We thank all the investigators and coordinators of the RITA 3 trial and all the medical and nursing staff in the recruitment and intervention centres who made the trial possible. Most of all, we thank all the patients who participated in the trial. RITA 3 was funded by a competitive grant from the British Heart Foundation, and the British Heart Foundation received a donation from Aventis Pharma. Additional governmental support (Culyer) was obtained to reimburse interventional centres for part of the costs of PCI catheters and stents.

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IMAGES IN CARDIOLOGY

doi: 10.1136/hrt.2005.082826

Intramycocardial echinococcal cyst demonstrated by multislice computed tomography

A 52-year-old man was admitted to our hospital because of palpitations and fatigue. The physical examination was normal. A 12 lead ECG showed sinus tachycardia. The indirect haemagglutination test was negative but there was pronounced eosinophilia. Transthoracic echocardiography showed a suspicious lesion in the left ventricular apex, which could have been a cardiac hydatid cyst. Transoesophageal echocardiography was proposed but the patient was unable to tolerate it. Enhanced multislice computed tomography (MCT) was performed. Volume rendered images revealed a 3 × 2.5 cm cystic structure planed in left ventricular apex (panel A: C, cyst; D1, diagonal artery; LAD, left anterior descending artery). An axial maximal intensity projection image clearly showed septates within the cyst (panel B: LV, left ventricle; RV, right ventricle). With a diagnosis of echinococcosis, the patient was referred for surgical resection of the mass. Analysis of the resected specimen revealed it to be a hydatid cyst.

Transthoracic echocardiography is usually the initial diagnostic test in patients with a suspected cardiac mass. However, this technique is restricted by its small field of views and insufficient acoustic window in some patients. MCT allows for detailed delineation of intra- and pericardiac masses. As a result, we wanted to present the MCT images of the left ventricular cyst that we could not evaluate echocardiographically.

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