Q J Med 2009; **102**:369–378
doi:10.1093/qjmed/hcp005 Advance Access publication 13 March 2009

Reviews

QJM

Myocardial infarction after percutaneous coronary intervention: a meta-analysis of troponin elevation applying the new universal definition

L. TESTA[1,2], W.J. VAN GAAL[3], G.G.L. BIONDI ZOCCAI[4], P. AGOSTONI[5], R.A. LATINI[2], F. BEDOGNI[2], I. PORTO[6] and A.P. BANNING[1]

From the [1]Institute of Cardiology, John Radcliffe Hospital, Oxford, UK, [2]Interventional Cardiology Department, Sant'Ambrogio Clinical Institute, Milan, Italy, [3]Institute of Cardiology, The Northern Hospital, Melbourne, Australia, [4]Institute of Cardiology, University of Turin, Turin, Italy, [5]Antwerp Cardiovascular Institute Middelheim, Antwerp, Belgium, and [6]Institute of Cardiology, Catholic University, Rome, Italy

Summary

Aim: Elevation of Troponin after scheduled percutaneous coronary intervention (PCI) is a recognized consequence. We sought to evaluate the prognostic significance and impact of the newly published definition of PCI-related myocardial infarction (MI) according to which any troponin elevation >3 times the upper reference limit identify a peri-procedural MI.

Methods: Search of BioMedCentral, CENTRAL, mRCT and PubMed (updated May 2008). Outcomes of interest were: MACE [the composite of all cause death, MI, repeat target vessel PCI (re-PCI) and coronary artery bypass grafting (CABG)]; single end points were also assessed.

Results: Fifteen studies have been included totalling 7578 patients. Troponin elevation occurred in 28.7% of the procedures. The incidence of PCI-related MI according to the new definition was 14.5%. During the hospitalization, any level of raised troponin was associated with an increased risk of MACE [OR 11.29 (3.00–42.48), Number needed to harm (NNH) 5], death [OR 7.16 (1.95–26.27), NNH = 100], MI [OR 30.85 (6.05–157.38), NNH = 4] and re-PCI [OR 4.13 (1.23–13.88), NNH = 50]. Patients with PCI-related MI had an increased risk of death [OR 17.25 (2.71–109.96), NNH = 100] and re-PCI [OR 10.86 (3.2–36.94), NNH = 25]. At follow up of 18 months any troponin elevation was associated with an increased risk of MACE [OR 1.48 (1.12–1.96), NNH = 20], death [OR 2.19 (1.59–3.00), NNH = 50], MI [OR 3.29 (2.71–6.31), NNH = 33] and re-PCI [OR 1.47 (1.06–2.03), NNH = 25]. In patients with PCI-related MI the risk of MACE was further increased: OR 2.25 (1.26–4.00), NNH = 3. An increase of the troponin level below the cut-off was not associated with MACE.

Conclusion: A diagnosis of MI according to the new guidelines applies to 15% of patients undergoing PCI and these patients are at high risk of further adverse events both during the hospital stay and at 18 months.

Address correspondence to Dr Luca Testa, MD, PhD, Cardiology Ward, Level 2, John Radcliffe Hospital, Headley Way, Oxford, OX3 9DU, UK. email: luctes@gmail.com

Introduction

The incidence of elevated biomarkers of myocardial damage after percutaneous coronary intervention (PCI) is 1–30%. This variation reflects differences in the biomarker measured and the patient population being treated. There is an increasing consensus that troponin is probably the most relevant biomarker but the prognostic impact of troponin elevation after PCI is still debated.[1,2]

The new universal definition of myocardial infarction (MI)[3] arbitrarily defines 'PCI-related MI' as patients with normal baseline levels and a rise of troponin three times the 99th percentile of the upper reference limit (URL).[3] By means of a meta-analytic approach, we sought to comprehensively assess the incidence and the prognostic impact of troponin elevation in patients with normal baseline levels undergoing PCI, and also the incidence, impact and practical implications of this new definition of PCI-related MI.

Methods

Data sources and searches

BioMedCentral, CENTRAL, mRCT and PubMed were searched (updated to May 2008), according to an established method.[4] Pertinent studies were also searched in major recent international cardiology meetings. References of original and review articles were cross-checked. Key words were 'troponin', 'percutaneous' and 'intervention'.

Study selection

Characteristics of included studies were: (i) normal baseline troponin, (ii) scheduled procedure for stable or unstable angina, (iii) post procedure Troponin assessed and (iv) complete reporting of procedural and follow up raw data. Both studies assessing troponin T and I elevation have been included if they fulfilled the above criteria.

Data extraction and end points

Two independent reviewers (L.T., W.v.G.) performed data abstraction. Divergences were resolved by consensus and/or another reviewer. The end points of interest in the overall analysis were: (i) the combined rate of major adverse cardiovascular events (MACE), defined as all cause death, further non-fatal acute MI (both Q and non-Q wave), repeat target vessel PCI (re-PCI), and coronary artery bypass surgery (CABG). Additional analyses were carried out for single end points. In-hospital and follow-up data have been appraised and analysed. The definitions of end point across the included studies were consistent so that they have been accepted in the data abstraction.

We then assessed the risk of overall death and a further MI in patients with raised troponin above and below the cut-off of PCI-related MI according to the new guidelines.[3] We calculated the number needed to harm as 1/Absolute Risk Reduction (ARR).

Data synthesis and analysis

Review Manager freeware package (RevMan 4.2)[5] was used for analysis. Review Manager is a comprehensive statistical and reviewing program, developed and maintained by The Cochrane Collaboration (Oxford, UK), which includes ad hoc statistical tools for pooled estimate calculations, according to several methods.

At first we calculated random effect odds ratios (OR) with 95% confidence intervals (95% CI), for the comparisons of patients with any raised Troponin vs. patient without raised Troponin, and then we assessed the ORs for patients with levels of raised Troponin above and below the cut-off for PCI-related MI.[3] Binary outcomes from individual studies were combined with Der Simonian and Laird random-effect model, according to an 'intention to treat' analysis. We also carried out the 'z' test with z = estimated effect size/standard error of the estimated effect size, and the OR considered on the log scale. As log(OR) has a unimodal distribution, the reported z values were analysed to obtain a two-tailed 'P', and hypothesis testing results were considered statistically significant at the 0.05 level.[6]

We computed Cochrane Q heterogeneity test (H) by summing the squared deviations of each study's estimate from the overall meta-analytic estimate, weighting each study's contribution in the same manner. Heterogeneity was considered significant at 'P for H' < 0.10.[6]

Sensitivity analysis was performed by excluding studies one at time, in order to assess the contribution of each study to the pooled estimates.[6]

The likelihood of publication bias was assessed graphically by generating a funnel plot for the combined end point of MACE and mathematically by means of Egger's test (P for significant asymmetry < 0.1).[7]

We also subgrouped studies according to the use of IIb/IIIa antagonists, saphenous vein graft intervention $\geqslant$5% of the entire study population, debulking device utilization and extensive (at least 50% of the lesions) stent implantation, and calculated relative ORs for subsequent risk of MACE during follow up.

There is an inevitable link between the detection of elevated troponin and a clinical diagnosis of MI. As one outcome is linked intimately with another, we chose to perform the analysis of in-hospital MACE with and without the end point of MI.

This study is inspired by good practice guidelines,[8] including those from the Cochrane Collaboration, and the Quality of Reporting of Meta-analyses (QUOROM) statement.[6]

Results

Search results and study characteristics

Out of 262 citations, 15 studies totalling 7578 patients have been finally included[1,2,9–21] (Figure 1). Main study characteristics are shown in the tables (Tables 1 and 2). All the included manuscripts were registry/cohort studies. Seven studies included patients with a diagnosis of unstable angina and normal baseline troponin.[1,2,9,10,17,20,21] See appendix for excluded studies.

In-hospital outcome

Regardless its extent, elevation of troponin after scheduled PCI occurred in 28.7% of the procedures. It was associated with an increased risk of subsequent MACE [OR 11.29 (3.00–42.48), $P < 0.001$; P for heterogeneity < 0.001, ARR = 0.23, NNH = 5], death [OR 7.16 (1.95–26.27), $P = 0.003$; P for heterogeneity = 0.82, ARR = 0.01, NNH = 100], MI [OR 30.85 (6.05–157.38), $P < 0.001$, P for heterogeneity = 0.008, ARR = 0.25, NNH = 4], re-PCI [OR 4.13 (1.23–13.88), $P = 0.02$, P for heterogeneity = 0.2, ARR = 0.02, NNH = 50]. No difference was found for the risk of urgent/emergency CABG. The OR for the risk of MACE, excluding MI, was 2.49 (0.96–6.49), $P = 0.06$, P for heterogeneity 0.03.

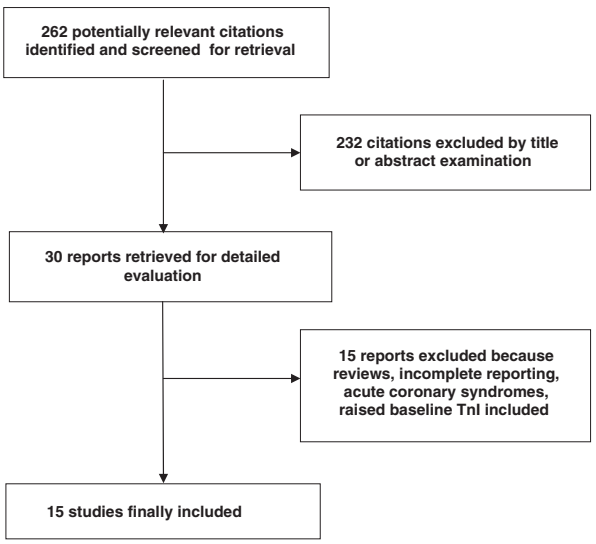

Figure 1. Flow diagram according to QUOROM statement. Inclusion criteria: (1) normal baseline Troponin; (2) scheduled procedure for stable or unstable angina; (3) post-procedure Troponin assessed; (4) complete reporting of procedural and follow up raw data

The incidence of PCI-related MI according to the new definition was 14.5%.

Two studies (about 2000 patients) reported raw data according to the level of raised troponin[16,21]: patients with a raised troponin 3 times URL had an increased risk of death [OR 17.25 (2.71–109.96), $P = 0.003$, P for heterogeneity = 0.73, ARR = 0.01, NNH = 100] and re-PCI [OR 10.86 (3.2–36.94), $P < 0.001$, P for heterogeneity = 0.2, ARR = 0.04, NNH = 25]. No significant difference in the risk of MACE and CABG has been found. One study reported raw data for the risk of in-hospital MI, suggesting that a raised troponin 3 times URL conferred a higher risk.[21]

In patients with raised troponin below the cut-off, no difference has been found in the risk of MACE, death, re-PCI or CABG. One study reported raw data for the risk of in-hospital MI, suggesting that even a raised troponin below 3x URL conferred a higher risk. [21]

Follow-up outcome: overall analysis

At an average follow up of 17.7 months, troponin elevation was associated with an increased risk of MACE [OR 1.48 (1.12–1.96), $P = 0.006$, P for heterogeneity = 0.0001, ARR = 0.05, NNH = 20, Figure 2], overall death [OR 2.19 (1.59–3.00), $P < 0.001$, P for heterogeneity = 0.38, ARR = 0.02, NNH = 50, Figure 3A], MI [OR 3.19 (2.71–6.31), $P = 0.0003$, P for heterogeneity = 0.01, ARD = 0.03, NNH = 33, Figure 3B] and re-PCI [OR 1.47 (1.06–2.03), $P = 0.02$, P for heterogeneity = 0.23, ARR = 0.04, NNH = 25, Figure 3C]. No significant difference in the risk of bypass surgery has been found (Figure 3D).

Four studies,[11,14,16,21] totalling 2359 patients, follow up ranging between 8 and 72 months (mean 26 months), reported incidence of raised troponin above the cut-off.[3] Such elevation of troponin occurred in 14.5% of the cases. It was associated with a further increased risk of MACE with an OR of 2.25 (1.26–4.00), $P = 0.006$, P for heterogeneity = 0.04, ARR = 0.28, NNH = 3, (Figure 4A).

A raised troponin below the cut-off was associated with a non significant increased risk of MACE: OR 1.85 (0.80–4.28), $P = 0.15$, (Figure 4B).

Table 1 Demographic characteristics of included studies

Study	Year	Design	*N*	FU	M% T+	M% T−	Age T+ (SD)	Age T− (SD)	D (%)	Measurement time points
Bertinchant *et al.*[9]	1999	Cohort study	105	19	78.3	74	63 (11)	60 (11)	27	Baseline, 6, 12, 18, 24, 36, 48 h
Fuchs *et al.*[21]	2000	Cohort study	1129	8	68.5	69	66 (8)	64 (11)	28	Baseline, 6, 18, 24 h
Gruberg *et al.*[10]	2002	Cohort study	116	12	76.0	68.2	73 (9)	69 (10)	48	Baseline, 6, 18, 24 h
Herrmann *et al.*[13]	2002	Cohort study	278	7.8	75.0	80.4	62.3 (7.9)	61.4 (9.2)	19	Baseline, 6, 12, 24 h
Saadeddin *et al.*[12]	2002	Cohort study	96	24	62	81	55 (13)	55 (11)	59	Baseline, 24 h
Nageh *et al.*[15]	2003	Cohort study	109	18	NA	NA	NA	NA	18	Baseline, 6, 12, 24 h
Kizer *et al.*[14]	2003	Cohort study	128	72	87%	71%	58 (39–79)	61 (34–83)	30	Baseline, 0, 8, 12, 24 h
Ramirez-Moreno *et al.*[17]	2004	Cohort study	147	10	75	71	64.8 (7.6)	62.1 (11.4)	31	Baseline, 6, 12, 18, 24 h
Natarajan *et al.*[16]	2004	Cohort study	1128	12	61	68	63.3 (10.5)	60.3 (11.1)	20	Baseline, 8, 16 h
Drzewiecka *et al.*[11]	2004	Cohort study	90	12	NA	NA	NA	NA	24	Baseline, 12, 24 h
Okmen *et al.*[20]	2006	Cohort study	100	21	73	88	57 (9)	55 (10)	28	Baseline, 6, 12, 18, 24 h
Izgi *et al.*[18]	2006	Cohort study	100	12	88.9	89	55.0 (12.8)	54.2 (10.3)	12	Baseline, 24 h
Prasad *et al.*[2]	2006	Cohort study	1949	26	69	72	69.7 (11.1)	65.8 (11.1)	28	Baseline, 8, 16 h
Miller *et al.*[1]	2006	Cohort study	1619	12	NA	NA	NA	NA	26	Baseline, 0, 8, 16 h
Nienhuis *et al.*[19]	2007	Cohort study	713	1	69	74	63.5	63.7	16	Baseline, 12 h

D: diabetes; FU: follow up (months); M: male sex; *N*: cohort size; NA: not available; SD: standard deviation; T+: Troponin positive; T−: Troponin negative.

Table 2 Procedural characteristics of included studies

Study	B2/C lesion (%)	Graft (%)	Debulking device (%)	Success rate	Complications rate[a] (%)	IIb/IIIa inhibitor (%)	Thyenopiridine load	Dual antiplatelet therapy duration	PTCA only (%)
Bertinchant *et al.*[9]	75[b]	1	0	NA	53.2	0	500 mg Ticl	4 weeks	58%
Fuchs *et al.*[21]	NA	8%	28	NA	3.2	10%	NA	NA	17.5
Gruberg *et al.*[10]	NA	24.8	22.8	91	NA	3	No	2–4 weeks	NA
Herrmann *et al.*[13]	42.7	15.5	0	NA	10	16	300 mg Clop	4 weeks	NA
Saadeddin *et al.*[12]	89[b]	0	0	NA	13.5	0	No	NA	28
Nageh *et al.*[15]	70[b]	0	9	94	21.5	6.3	300 mg Clop	4 weeks	40
Kizer *et al.*[14]	12[c]	NA	NA	NA	NA	0	No	NA	91
Ramirez-Moreno *et al.*[17]	16[d]	0.5	0	NA	21.7	22.4	NA	4 weeks	0
Natarajan *et al.*[16]	57	5	NA	NA	3	18	Both	4 weeks	17
Drzewiecka *et al.*[11]	NA	NA	NA	NA	NA	NA	no	4 weeks	NA
Okmen *et al.*[20]	38	0	0	NA	12	42	500 mg Ticl	4 weeks	15
Izgi *et al.*[18]	78[b]	3	0	NA	6	5	300 mg Clop	2 months	8
Prasad *et al.*[2]	33.6[c]	9	12	98	15	50	NA	NA	7.5
Miller *et al.*[1]	NA	0	0	NA	NA	65	300 mg Clop	NA	11
Nienhuis *et al.*[19]	NA	0	NA	NA	1.5	NA	300 mg Clop	4 weeks	NA

NA: not available. PTCA: percutaneous transluminal coronary angioplasty.
[a]Defined according to each study definition.
[b]Including B1 lesions.
[c]C lesions only.
[d]Percentage of lesion longer than 20 mm.

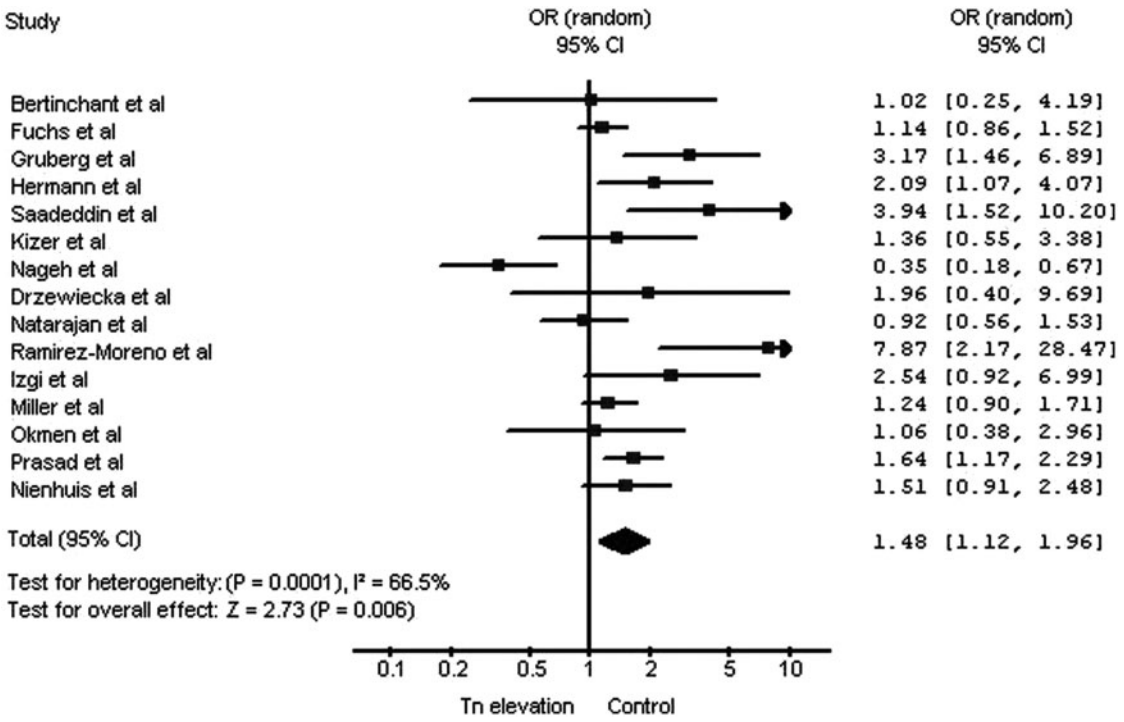

Figure 2. Individual and summary ORs for major adverse cardiac events in the overall analysis (all cause death/non-fatal MI/repeat PCI/coronary artery bypass graft).

Follow-up outcome: subgroup analysis

Only one of the pre-specified subgroup analyses reached statistical significance. In studies in which ⩾5% of the population underwent saphenous vein graft treatment,[2,10,13,16,21] the risk of mid-long-term MACE was higher in troponin positive patients than those patients with normal post procedure troponin [OR 1.49 (1.06–2.10), $P = 0.02$].

Seven studies[1,2,9,10,17,20,21] included patients with normal baseline troponin and stable or unstable angina perhaps not providing separate patient-level data according to the indication of the procedure, therefore any further statistical inspection of the impact of the clinical status and admission diagnosis seemed unreliable.

Sensitivity analysis and publication bias

In the analysis for any level of increased troponin, the sequential exclusion of each trial from the computation of the OR for MACE did not affect the overall result (Table 3).

The funnel plot according to the overall risk of MACE shows clear symmetry, further confirmed by the Egger's test as '*P* for asymmetry' was 0.885, (Figure 5). The presence of four studies outside the boundaries of the 95% CI is a further confirmation of the usefulness of pooling data as the overall result takes into account all the included trials and gives a summary of the evidences beyond specific limitations of any single studies. In particular there are two studies, Nageh *et al.*[15] and Ramirez- Moreno *et al.*,[17] which lie far outside. Possible explanations relate to the features of such studies, in particular the sample size, the definition of the end points and the characteristics of the study population. Moreover, differences in the management of the complications and/or the technical approaches might play a part in this finding.

Discussion

A raised troponin from a normal baseline level after scheduled PCI is a common finding as it occurred in almost a third of patients. Overall, elevation of troponin affected mid-long-term prognosis as it is associated with significantly increased risk of MACE, specifically with a doubled risk of overall death and a 3-fold risk of subsequent MI. After PCI, patients with a raised troponin >3 times the 99th percentile of the URL have further increased risk of MACE compared to those patients without troponin elevation at an average follow up of about 17.7 months. Smaller levels of troponin elevation <3 times the

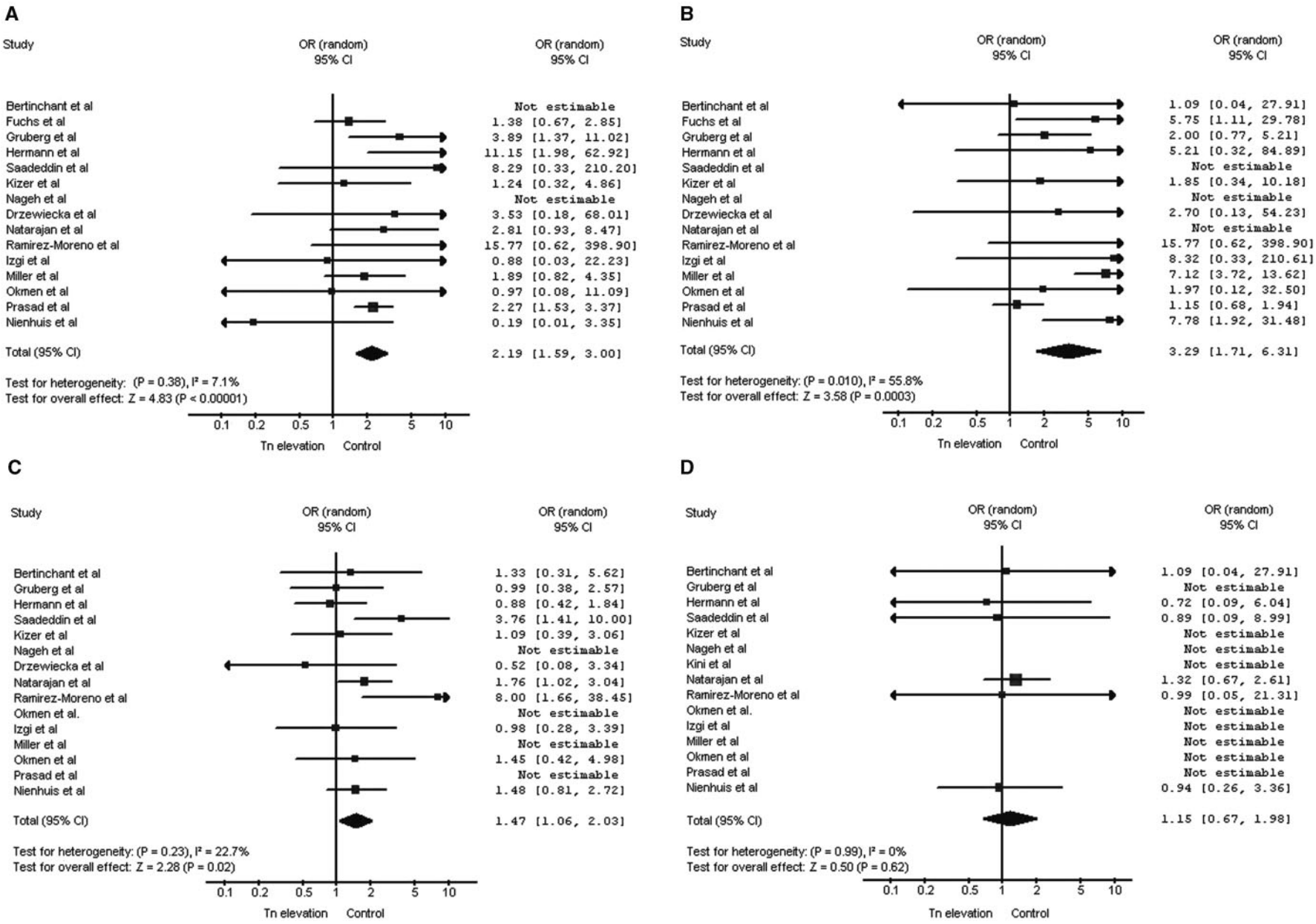

Figure 3. Individual and summary ORs for the risk of single end points. (**A**) All-cause death. (**B**) Non-fatal MI. (**C**) Repeat PCI. (**D**) Coronary artery bypass graft.

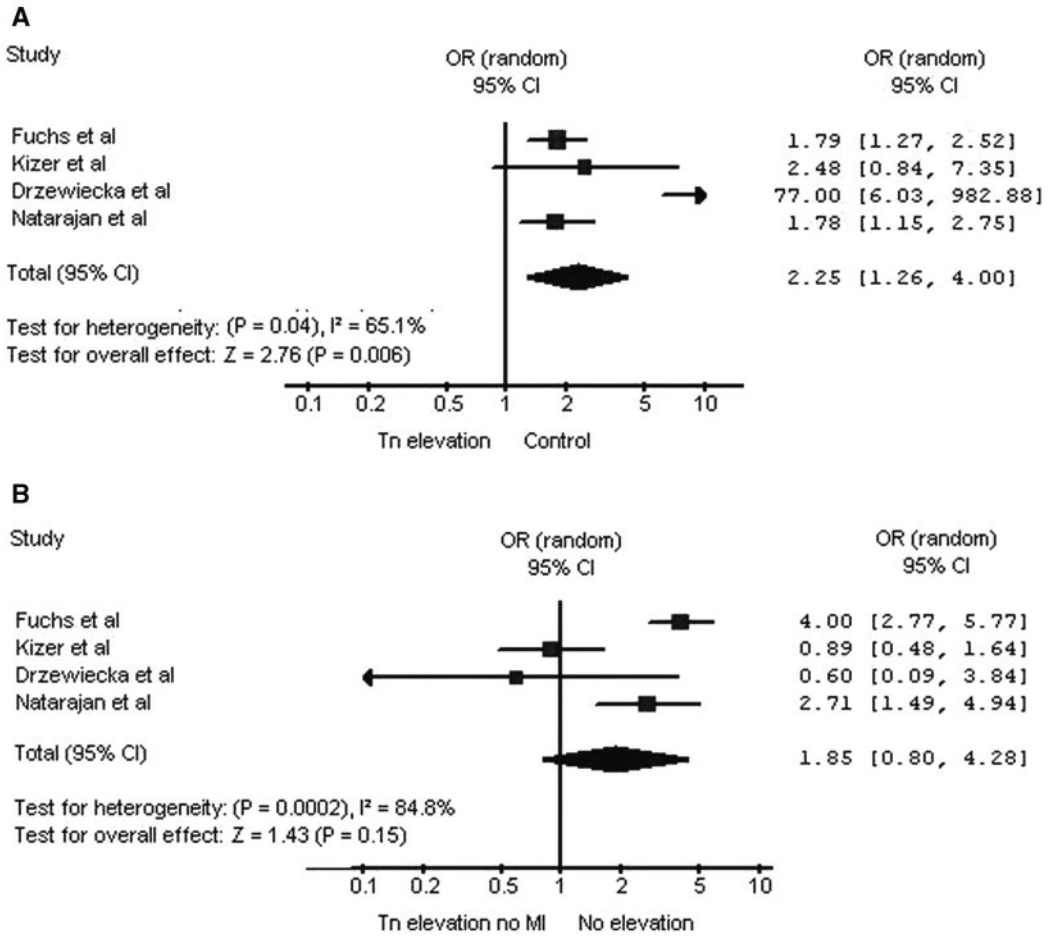

Figure 4. Individual and summary ORs for major adverse cardiac events (all-cause death/non-fatal MI/repeat PCI/coronary artery bypass graft) according to levels of raised troponin. (**A**) Raised troponin above the cut-off of the new universal definition. (**B**) Raised troponin below the cut off of the new universal definition.

99th percentile of the URL were not associated with a worse prognosis.

In the studies included in this analysis, few clearly report angiographic success and definitions of procedural complication were quite different. Unsurprisingly MACE is highly linked to the diagnosis of in-hospital MI. According to these data, the risk of PCI-related MI is about 15% and the number needed to harm for further MACE is three. So for every 100 coronary interventions about 15 patients would receive a diagnosis of PCI-related MI. Among these 15, five will experience a further MACE in the next 18 months.

The relevance of cardiac marker elevation during and after PCI has been debated by interventionalists for some years. However, using CK-MB it became clear that patients with enzyme elevation >5 times URL clearly had an impact on subsequent prognosis.[23] The impact of elevation of CPK to levels <5 times URL was less clear. The introduction of troponin measurement has reinvigorated the debate particularly because enzyme elevation appeared more frequent. More recently detailed studies have shown the link between elevated troponin post PCI and areas of new myonecrosis on MRI scanning. These studies have definitively shown that the issue of troponin elevation is not an epiphenomenon and cannot be ignored.[24]

There are broadly two circumstances where troponin elevation occurs after PCI. The first is where a procedure appears to be complication free and in these circumstances the troponin elevation is considered surprising and occult. When review of the angiogram fails to elucidate any compromise of small vessels the most likely cause for this is embolised atheromatous material displaced downstream during stent expansion. Procedurally, this may be evident as slower antegrade flow but the ultimate consequence is a limited area of downstream infarction. The second circumstance occurs in cases where the index PCI procedure may have involved procedural side branch occlusion and/or coronary dissection. These patients are usually more complex with more atheroma and procedural risk

Table 3 Sensitivity analysis

Excluded studies	OR	CI
Bertinchant *et al.*[9]	1.49	1.09–2.02
Fuchs *et al.*[21]	1.45	1.10–1.98
Gruberg *et al.*[10]	1.38	1.03–1.86
Herrmann *et al.*[13]	1.50	1.09–2.06
Saadeddin *et al.*[12]	1.38	1.03–1.85
Nageh *et al.*[15]	1.58	1.25–2.01
Kizer *et al.*[14]	1.48	1.08–2.02
Ramirez-Moreno *et al.*[17]	1.37	1.03–1.81
Natarajan *et al.*[16]	1.52	1.12–2.11
Drzewiecka *et al.*[11]	1.46	1.07–2.03
Okmen *et al.*[20]	1.49	1.10–2.04
Izgi *et al.*[18]	1.42	1.05–1.93
Prasad *et al.*[2]	1.46	1.04–2.05
Miller *et al.*[1]	1.52	1.08–2.13
Nienhuis *et al.*[19]	1.47	1.06–2.04

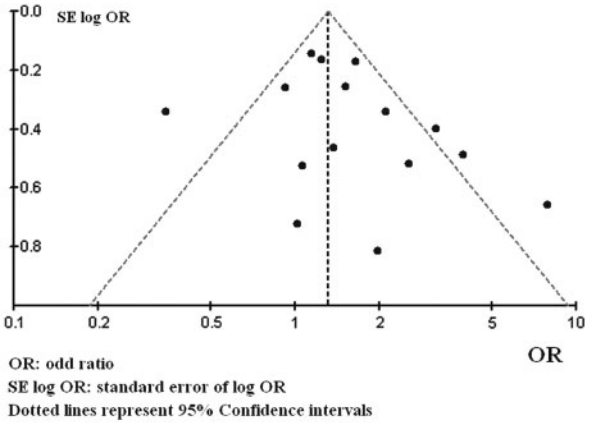

Figure 5. Funnel plot of included studies according to the risk of MACE. Dotted lines show the 95% CI.

factors including diabetes and renal dysfunction etc. In these cases despite the operators' intention, a suboptimal outcome may result with residual stenosis or impaired antegrade flow to side branches. Differentiation between these two different circumstances in most published studies is not possible. As a consequence we cannot definitively define whether troponin elevation reflects a difficult procedure with inadequate procedural results or whether it is a marker of a highest risk group undergoing PCI treatment. But, it is probably not surprising that these patients appear to be more likely to have further events.

The lack of prognostic significance of small increases of troponin after PCI, despite a clear trend, could be to due to the relatively small sample size, i.e. it is conceivable that to distinguish between the prognostic impact of a small increase of troponin and the impact of other clinical variables a larger population would be required. From the sub-group studies, in troponin positive patients saphenous vein graft treatment appeared to confer a higher risk of subsequent events compared to patients with no troponin rise. High rates of subsequent MACE are well recognised following vein graft intervention. This is in part due to a higher angioplasty restenosis rate but also a higher rate of disease progression in other areas of the vein graft compared to native coronary artery disease.[25]

Several studies published in the last few years suggested different approaches aiming at reducing the risk of myocardial damage after elective PCI. Pre-treatment with high dose statins appeared to significantly reduce procedural myocardial injury in elective coronary intervention.[26,27] Also pre-treatment with 50 mcg of adenosine appears to decreases the incidence of myonecrosis after non-urgent PCI compared with patients not undergoing pre-treatment.[28]

Historically the subsequent management of patients after a successful PCI did not take in great account the prognostic implications of a raised troponin. However, the new universal definition of PCI-related MI clearly identifies a population of patients at high risk of adverse events. This should be discussed in the consent process for PCI and when troponin is elevated >3 times URL, adopting similar management of patients with spontaneous acute MI should be considered. Assessment of left ventricle function and direction of social and employment decisions as highlighted by the guide-line[3] is probably reasonable as the patient has a higher risk of future events than those patients where troponin is not elevated after PCI.

The practical first step is a consensus of the timing of biomarker sampling. A normal level at 6 h following the procedure makes significant elevation unlikely but sampling of troponin I 24 h after PCI correlates well with the magnitude of procedural myocardial necrosis.[29] Subsequently a robust audit mechanism to review cases where troponin is elevated is appropriate. This will influence practice in cases where troponin was raised and act as a spur for further research.

Contribution of the present study to the current context

There is no previous meta-analytic assessment of the prognostic impact of troponin after scheduled PCI according to the new definition of PCI-related MI. Additionally, these data differ from a previous meta-analysis about the prognostic significance of troponin[30] as only publications in which raw data were available for independent OR calculation were

selected (Figure 1). Morevoer, the ORs were calculated according to the random effect model, as required by the Cochrane collaboration criteria in the presence of significant heterogeneity, and the risk of several hard end-points was assessed in order to fully depict a clinical scenario.

Limitation of the present study

A limitation inherent to all meta-analyses is the potential heterogeneity among studies that might lead to inaccurate conclusions. However, the Cochrane Q heterogeneity test (which assesses heterogeneity among ORs and the validity of pooling the results), indicated significant heterogeneity for the overall ORs of MACE and MI. This could be related to the fact that we included in the definition of MACE also the risk of re-PCI and CABG: such risk has not been assessed by all the included studies. However, we overcame this issue analysing single end points separately. We also included in the analysis both Troponin I and T, this might have introduced heterogeneity. Finally, some the included studies are dated so they represent a range of several years in which the approach to patients undergoing PCI progressively but steadily changed across time. However the incidence of periprocedural damage was similar and the aim of the present manuscript was to investigate the outcome of patients with raised troponin rather than to evaluate possible preventive strategies and management.

Conclusion

Troponin measurement after PCI should be mandatory. The risk of PCI-related MI is about 15%. The occurrence of a PCI procedural MI defined by the new universal definition confers an adverse prognosis both in hospital and over the next 18 months.

Acknowledgements

All the authors had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Funding

Dr Banning is partially funded by the Oxford Biomedical Research Centre Programme. This study is part of a senior investigator project of the Center for Overview, Meta-analysis, and Evidence-based medicine Training based in Oxford, UK (http://www.metcardio.org).

Conflict of interest: None declared.

References

1. Miller WL, Garratt KN, Burritt MF, Lennon RJ, Reeder GS, Jaffe AS. Baseline troponin level: key to understanding the importance of post-PCI troponin elevations. *Eur Heart J* 2006; **27**:1061–9.
2. Prasad A, Singh M, Lerman A, Lennon RJ, Holmes DR Jr, Rihal CS. Isolated elevation in troponin T after percutaneous coronary intervention is associated with higher long-term mortality. *J Am Coll Cardiol* 2006; **48**:1765–70.
3. Thygesen K, Alpert JS, White HD. Joint ESC/ACCF/AHA/WHF task force for the redefinition of myocardial infarction. Universal definition of myocardial infarction. *Eur Heart J* 2007; **28**:2525–38.
4. Biondi Zoccai GG, Agostoni P, Abbate A, Testa L, Burzotta F. A simple hint to improve Robinson and Dickersin's highly sensitive PubMed search strategy for controlled clinical trials. *Int J Epidemiol* 2005; **34**:224–5.
5. Review Manager 4.2.2. Available from The Cochrane Collaboration at http://www.cochrane.org/ Accessed 20 October 2008.
6. Clarke M, Oxman AD, eds. Cochrane Reviewers' Handbook 4.1.3. In: The Cochrane Library, Issue 3, 2001. Oxford, UK: Update Software. Updated quarterly.
7. Egger M, Smith GD, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. *Br Med J* 1997; **315**:629–34.
8. Biondi-Zoccai GGL, Testa L, Agostoni P. A practical algorithm for systematic reviews in cardiovascular medicine. *Ital Heart J* 2004; **5**:486–7.
9. Bertinchant JP, Polge A, Ledermann B, Genet L, Fabbro-Peray P, Raczka F, *et al*. Relation of minor cardiac troponin I elevation to late cardiac events after uncomplicated elective successful percutaneous transluminal coronary angioplasty for angina pectoris. *Am J Cardiol* 1999; **84**:51–7.
10. Gruberg L, Fuchs S, Waksman R, Pichard AD, Kent KM, Laird JR, *et al*. Prognostic value of cardiac troponin I elevation after percutaneous coronary intervention in patients with chronic renal insufficiency: a 12-month outcome analysis. *Catheter Cardiovasc Interv* 2002; **55(2)**:174–9.
11. Drzewiecka-Gerber A, Drzewiecki J, Wita K, Krauze J, Jaklik A, Trusz-Gluza M, *et al*. Prognostic value of troponin I after elective percutaneous coronary interventions. *Kardiol Pol* 2004; **61**:117–26.
12. Saadeddin SM, Habbab MA, Sobki SH, Ferns GA. Biochemical detection of minor myocardial injury after elective, uncomplicated, successful percutaneous coronary intervention in patients with stable angina: clinical outcome. *Ann Clin Biochem* 2002; **39**:392–7.
13. Herrmann J, Von Birgelen C, Haude M, Volbracht L, Malyar N, Eggebrecht H, *et al*. Prognostic implication of cardiac troponin T increase following stent implantation. *Heart* 2002; **87**:549–53.
14. Kizer JR, Muttrej MR, Matthai WH, McConnell J, Nardone H, Sonel AF, *et al*. Role of cardiac troponin T in the long-term risk stratification of patients undergoing percutaneous coronary intervention. *Eur Heart J* 2003; **24**:1314–22.
15. Nageh T, Sherwood RA, Harris BM, Byrne JA, Thomas MR. Cardiac troponin T and I and creatine kinase-MB as markers of myocardial injury and predictors of outcome following percutaneous coronary intervention. *Int J Cardiol* 2003; **92**:285–93.

16. Natarajan MK, Kreatsoulas C, Velianou JL, Mehta SR, Pericak D, Goodhart DM. Incidence, predictors, and clinical significance of troponin-I elevation without creatine kinase elevation following percutaneous coronary interventions. *Am J Cardiol* 2004; **93**:750–3.
17. Ramírez-Moreno A, Cardenal R, Pera C, Pagola C, Guzmán M, Vázquez E, *et al.* Predictors and prognostic value of myocardial injury following stent implantation. *Int J Cardiol* 2004; **97**:193–8.
18. Izgi A, Tanalp AC, Kirma C, Dundar C, Oduncu V, Akcakoyun M, *et al.* Predictors and prognostic significance of troponin-I release following elective coronary angioplasty. *J Int Med Res* 2006; **34**:612–23.
19. Nienhuis MB, Ottervanger JP, Dikkeschei B, Suryapranata H, de Boer MJ, Dambrink JH, *et al.* Prognostic importance of troponin T and creatine kinase after elective angioplasty. *Int J Cardiol* 2007; **120**:242–7.
20. Okmen E, Cam N, Sanli A, Unal S, Tartan Z, Vural M. Cardiac troponin I increase after successful percutaneous coronary angioplasty: predictors and long-term prognostic value. *Angiology* 2006; **57**:161–9.
21. Fuchs S, Kornowski R, Mehran R, Lansky AJ, Satler LF, Pichard AD, *et al.* Prognostic value of cardiac troponin-I levels following catheter-based coronary interventions. *Am J Cardiol* 2000; **85**:1077–82.
22. ACC/AHA/SCAI 2005 Guideline Update for Percutaneous Coronary Intervention A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (ACC/AHA/SCAI Writing Committee to Update the 2001 Guidelines for Percutaneous Coronary Intervention). Available at www.acc.org.
23. Ellis SG, Chew D, Chan A, Whitlow PL, Schneider JP, Topol EJ. Death following creatine kinase-MB elevation after coronary intervention: identification of an early risk period: importance of creatine kinase-MB level, completeness of revascularization, ventricular function, and probable benefit of statin therapy. *Circulation* 2002; **106**:1205–10.
24. Selvanayagam JB, Porto I, Channon K, Petersen SE, Francis JM, Neubauer S, *et al.* Troponin elevation after percutaneous coronary intervention directly represents the extent of irreversible myocardial injury: insights from cardiovascular magnetic resonance imaging. *Circulation* 2005; **111**:1027–32.
25. Mehta SK, Frutkin AD, Milford-Beland S, Klein LW, Shaw RE, Weintraub WS, *et al.* American College of Cardiology-National Cardiovascular Data Registry. Utilization of distal embolic protection in saphenous vein graft interventions (an analysis of 19,546 patients in the American College of Cardiology-National Cardiovascular Data Registry). *Am J Cardiol* 2007; **100(7)**:1114–8.
26. Pasceri V, Patti G, Nusca A, Pristipino C, Richichi G, Di Sciascio G, ARMYDA Investigators. Randomized trial of atorvastatin for reduction of myocardial damage during coronary intervention: results from the ARMYDA (Atorvastatin for Reduction of MYocardial Damage during Angioplasty) study. *Circulation* 2004; **110(6)**:674–8.
27. Briguori C, Colombo A, Airoldi F, Violante A, Focaccio A, Balestrieri P, *et al.* Statin administration before percutaneous coronary intervention: impact on periprocedural myocardial infarction. *Eur Heart J* 2004; **25**:1822–8.
28. Lee CH, Low A, Tai BC, Co M, Chan MY, Lim J, *et al.* Pretreatment with intracoronary adenosine reduces the incidence of myonecrosis after non-urgent percutaneous coronary intervention: a prospective randomized study. *Eur Heart J* 2007; **28**:19–25.
29. Selvanayagam JB, Cheng AS, Jerosch-Herold M, Rahimi K, Porto I, van Gaal W, *et al.* Effect of distal embolization on myocardial perfusion reserve after percutaneous coronary intervention: a quantitative magnetic resonance perfusion study. *Circulation* 2007; **116**:1458–64.
30. Nienhuis MB, Ottervanger JP, Bilo HJ, Dikkeschei BD, Zijlstra F. Prognostic value of troponin after elective percutaneous coronary intervention: A meta-analysis. *Catheter Cardiovasc Interv* 2008; **71**:318–24.

Appendix Excluded studies

Study	Criteria for exclusion
Karim *et al. Am J Cardiol* 1995	• No raw data available for OR calculation
Attali P *et al. Clin Cardiol* 1998	• No raw data available for OR calculation
Shyu *et al. Am Heart J* 1998	• Stent vs. balloon comparison
Garbarz *et al. Am J Cardiol* 1999	• Baseline + TnI patients included. • No separate raw data provided for patients with baseline—TnI.
Ricchiuti *et al. Clin Chim Acta* 2000	• PTCA vs. Stent vs. Atherectomy comparison
Cantor *et al. JACC* 2002	• Not scheduled PCI included. • Patient with MI within the previous 7 days included
Wu *et al. Am J Cardiol* 2002	• No raw data available for OR calculation
Ricciardi *et al. Am Heart J* 2003	• No raw data for group with –Tn after procedure
Nallamothu *et al. Am J Cardiol* 2003	• No raw data available for OR calculation
Kini *et al. Am J Cardiol* 2004	• No raw data available for OR calculation
Okmen *et al. J Invasive Cardiol* 2005	• No raw data available for OR calculation
Newby *et al. JACC* 2006	• Baseline + TnI/Ck-MB patients included. • No separate raw data provided for patients with baseline –TnI. • PCI not performed routinely
Cavallini *et al. Eur Heart J* 2007	• Baseline + TnI patients included. • No separate raw data provided for patients with baseline –TnI.