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SYSTEMATIC REVIEW

The efficacy of statin administration prior to elective percutaneous coronary intervention in reducing the incidence of post-procedural myocardial infarction or all-cause mortality: a systematic review

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Abstract

BACKGROUND

Observational studies show that statin-naïve patients presenting with acute coronary syndrome (ACS) or stable angina that undergo elective percutaneous coronary infusion (PCI) have significantly higher rates of myocardial infarction (MI) and mortality. This systematic review will appraise the evidence for giving statin-naïve patients statins 24 hours pre-PCI, with the aim of reducing post-procedural MI and mortality.

OBJECTIVE

To critically evaluate and appraise primary and secondary literature that investigates the efficacy of pre-treatment loading with a statin in improving outcomes for patients with ACS or stable angina undergoing PCI.

METHODS

The Cochrane Database of Systemic Reviews and National Institute for Health and Care Excellence Clinical Knowledge Summaries (NICE CKS) database were searched for relevant guidelines. MEDLINE database and Cochrane Central Register of Controlled Trial (CENTRAL) were then searched for randomized controlled trials (RCTs). Our search was limited to peer-reviewed papers published in the last 10 years, between 1 February 2006 and 1 February 2016. Exclusion criteria: patients previously on statin therapy; statin administration outside 24 hours of pre-PCI; unsuitable outcomes measured; and non-randomized trials.

RESULTS

The literature search yielded 86 papers. Of these, 80 were excluded after review. Six were included in the final review where 2 207 patients received either high-dose statin treatment (n = 1 111) or placebo/usual care (n = 1 096). The ARMYDA-ACS trial[9] showed that short-term pre-treatment with atorvastatin reduces the incidence of major cardiac events in patients with ACS undergoing elective PCI (odds ratio (OR) = 0.12, confidence interval (CI): 0.05–0.50; p = 0.004). These findings were consistent with the NAPLES II Trial,[13] in which atorvastatin preloading reduced the risk of MI (OR = 0.56, CI: 0.35–0.89). However, the ALPACS[12] trial showed atorvastatin preloading had no significant benefits in reducing post-procedural MI (OR = 0.92, CI: 0.50–1.69) or mortality (OR = 1.06, CI: 0.07–17.01). Three papers reported a significant reduction in post-procedural MI in patients when rosuvastatin was given prior to elective PCI. These were Yun et al.[10] (OR = 0.50, CI: 0.25–0.98), Wang et al.[11] (OR = 0.31, CI: 0.10–0.91), and Cay et al.[14] (OR = 0.05, CI: 0.01–0.41).

CONCLUSIONS

Five studies support the effectiveness of pre-procedural statins in reducing the risk of post-procedural major cardiac events (MACE) in patients undergoing elective PCI, thus supporting routine use of statins in such patients.

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INTRODUCTION

Cardiovascular disease is not only the leading cause of death in the developed world but also an economic concern for the National Health Service, which spent almost £7 billion on cardiovascular disease from 2012–13 alone. This raises a question as to whether a shift to primary prevention is necessary.[1]

One form of cardiovascular disease is acute coronary syndrome (ACS), wherein the heart undergoes an acute ischaemic event due to the rupture of an atheromatous plaque in the wall of a coronary artery, causing variable obstruction to blood flow.[2] The favoured means of cardiac reperfusion is primary percutaneous coronary intervention (PCI).[3] However, this procedure carries the risk of a number of complications such as post-procedural myocardial infarction (MI), embolic stroke, and death.[4] Observational studies show that these risks are greater in patients who were not on statin treatment prior to their procedure.[5–7]

A systematic review conducted by Patti et al. in 2010[8] showed that a course of statins administered prior to PCI resulted in a lower incidence of major adverse cardiac events (MACE), including MI. However, the duration of the statin therapy administered varied between the studies included in the review, some of which were 2 weeks long in duration. The deferral of PCI in order to administer a relatively long course of statins could potentially delay the benefits that the procedure provides and prolongs the time in which the patient's condition remains uncorrected. For this reason, we sought to investigate the effects of statin treatment on post-procedural MI and all-cause mortality when administered within 24 hours of statin-naïve patients undergoing elective PCI. This strategy would minimize the delay in patients receiving PCI.

METHODS

The research question was "what is the efficacy of statin administration prior to elective PCI in reducing the incidence of post-procedural MI or all-cause mortality?" Elective PCI cases were defined as non-emergency interventions i.e. excluding all ST-elevation myocardial infarction (STEMI). Patients who only underwent angiography were not included. To assess the relevant literature available, all four members of the group independently conducted a literature search. We constructed a table from the components of our review question and their synonyms (**Table 1**). We used the terms from this table to form our searches.

Table 1. **A table summarizing the components of our review question and alternative terms**. (MI = myocardial infarction; PCI = percutaneous coronary infusion.)

Population	Intervention	Comparator	Outcome
Elective PCI	Pre-procedural statins	Placebo or no statins	MI
Elective PCI	Statins	Placebo	MI
PCI		No pre-treatment	Heart attack
PCI			Mortality
			Death

Initially, we searched for relevant National Institute for Health and Care Excellence (NICE) guidelines, using the search terms in **Table 1**. We also examined broader categories by browsing for guidelines by topic (e.g. "cardiovascular conditions'") and exploring all the subcategories. We proceeded to search for systematic reviews in the Cochrane Database of Systematic Reviews and then primary papers in Ovid MEDLINE and the Cochrane Central Register of Controlled Trials (CENTRAL). Results were restricted to those published within 10 years from the date we conducted the literature search (between 1 February 2006 and 1 February 2016). We applied this restriction to ensure our data were as up to date as possible. We also restricted searches by study design (systematic reviews and randomized controlled trials). Where possible, we

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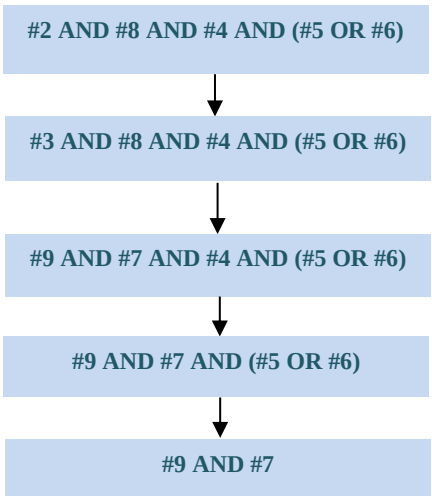
made use of medical subject headings (MeSH) term substitution, namely for "statins", "placebo", and "MI".

Initially, our searches were as specific to our review questions as possible; however, we consistently became more general to collate as many relevant papers as possible. Our search strategy is detailed in **Figure 1**.



#1	MeSH descriptor: [Percutaneous Coronary Intervention] explode all trees
#2	Elective percutaneous coronary intervention
#3	Elective PCI
#4	Placebo
#5	All-cause mortality
#6	MeSH descriptor: [Myocardial Infarction] explode all trees
#7	MeSH descriptor: [Hydroxymethylglutaryl-CoA Reductase Inhibitors] explode all trees
#8	Pre-procedural statin
#9	Before PCI

Figure 1. Flowchart detailing the search strategy we adopted when searching for systematic reviews and randomized controlled trials

Initially, we selected elective PCI for NSTEMI-ACS and expanded this to include stable angina, to involve the NAPLES II and Cay et al. trials. Furthermore, we searched the citations of the papers we found to discover other relevant papers.

After each researcher had completed the literature searches, we collaborated and established a compilation of potential papers. Papers were screened against pre-specified exclusion criteria by two sets of two researches. These exclusion criteria included: previous statin therapy; statin administration outside 24 hours pre-PCI; unsuitable outcomes measured; papers not available in full (NB: no attempts were made to contact authors for papers that were not available in full); and non-randomized trials. Papers that met these exclusion criteria were excluded and the remaining papers were deemed suitable for review. Data relevant to our primary outcomes were extracted: post-procedural MI and all-cause mortality to be presented as odds ratio (OR), accompanied by the p value and confidence interval (CI). We planned to evaluate the papers by appraising them against a Critical Appraisal Skills Programme (CASP) checklist (available at http://www.casp-uk.net/#!casp-tools-checklists/c18f8) to review their quality and risk of bias and summarize their main results.

RESULTS

No NICE guidance pertinent to our review topic was found. We proceeded to search for systematic reviews and then primary papers in databases. These literature searches yielded three systematic reviews and 83 randomized controlled trials (61 discounting 22 duplicates). After screening these papers against our exclusion criteria, all three systematic reviews were excluded,[8,16,17] as none of them reviewed studies which administered statins pre-PCI. This left six remaining RCTs. Most papers were excluded for not administering statin treatment within 24 hours prior to PCI. A summary of this exclusion process can be seen in **Figure 2**. The papers evaluated in this review are summarized in **Table 2**. The OR of all the papers are summarized in the form of a Forest plot in **Figure 3**.

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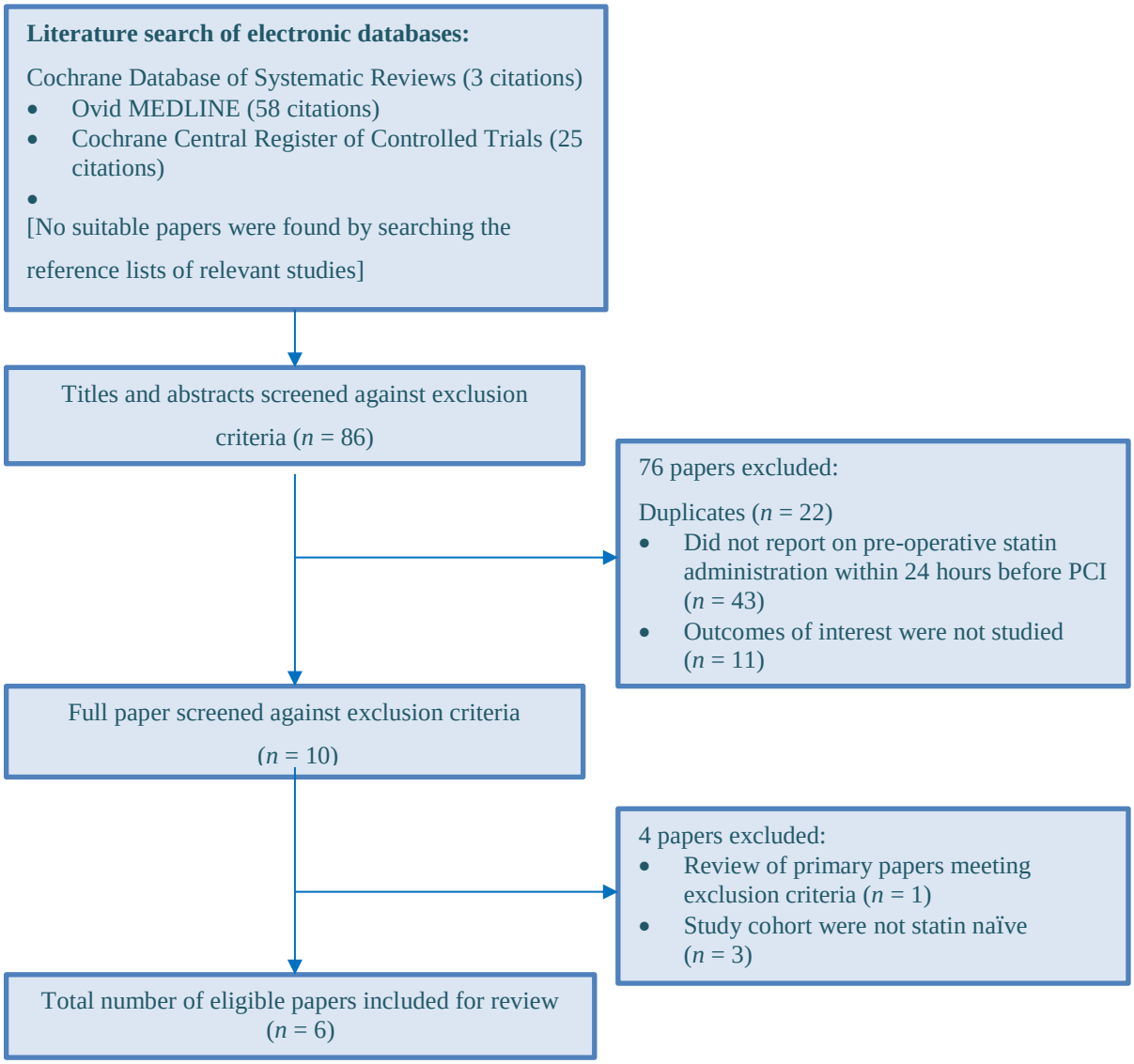

Figure 2. Results of literature search and exclusion screening

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Table 2: A table summarizing the main descriptors of the six papers included in this review

Study authors and year	Study design	Participant number	Intervention	Comparator	Primary outcome	Main result
Patti G *et al.* 2007	Randomized, double-blind, placebo-controlled trial	171	**Atorvastatin**: 80 mg at 12 hours; 40 mg 2 hours before PCI	Placebo	30-day mortality	Preloading atorvastatin showed a better event-free survival from post-procedural MI and death at 30 days after elective PCI (OR = 0.12, CI 0.05–0.50; p = 0.004)
Yun KH *et al.* 2009	Randomized, open-label, controlled trial	445	**Rosuvastatin**: 40 mg 16 hours before PCI	No statin administration	Post-procedural MI	Pretreatment rosuvastatin showed a lower incidence of post-procedural MI and death (OR = 0.44, CI: 0.22–0.85, p = 0.035)
Wang Z *et al.* 2013	Randomized, double-blind, placebo-controlled trial	125	**Rosuvastatin** : 20 mg 2–4 hours before PCI	Placebo	30-day incidence of major adverse cardiac events	When calculating the OR from raw data, high-dose rosuvastatin may reduce MI in ACS patients (OR = 0.31, CI: 0.10–0.91, p = 0.034)
Jang Y *et al.* 2014	Randomized Open-label, controlled trial	499	**Atorvastatin**: 80 mg 12 hours and 40 mg 2 hours before PCI	No statin administration	30-day incidence of major adverse cardiac events	Preloading with atorvastatin was not statistically significant in reducing MI incidence (OR = 0.92, CI: 0.50–1.69) or mortality (OR = 1.06, CI: 0.07–17.01)
Briguori *et al.* 2009	Randomized, open-label controlled trial	668	**Atorvastatin**: 80 mg within 24 hours before PCI	No statin administration	Post-procedural MI	Preloading with atorvastatin reduced the risk of MI (OR = 0.56, CI: 0.35–0.89, p < 0.001)
Cay S *et al.* 2010	Randomized, open-label, controlled trial	299	**Rosuvastatin**: 40 mg within 24 hours before PCI	No statin administration	Post-procedural MI and myocardial necrosis	Pretreatment rosuvastatin showed a lower incidence of an MI, defined by rise in CK-MB (OR = 0.05, CI: 0.01–0.41, p < 0.001)

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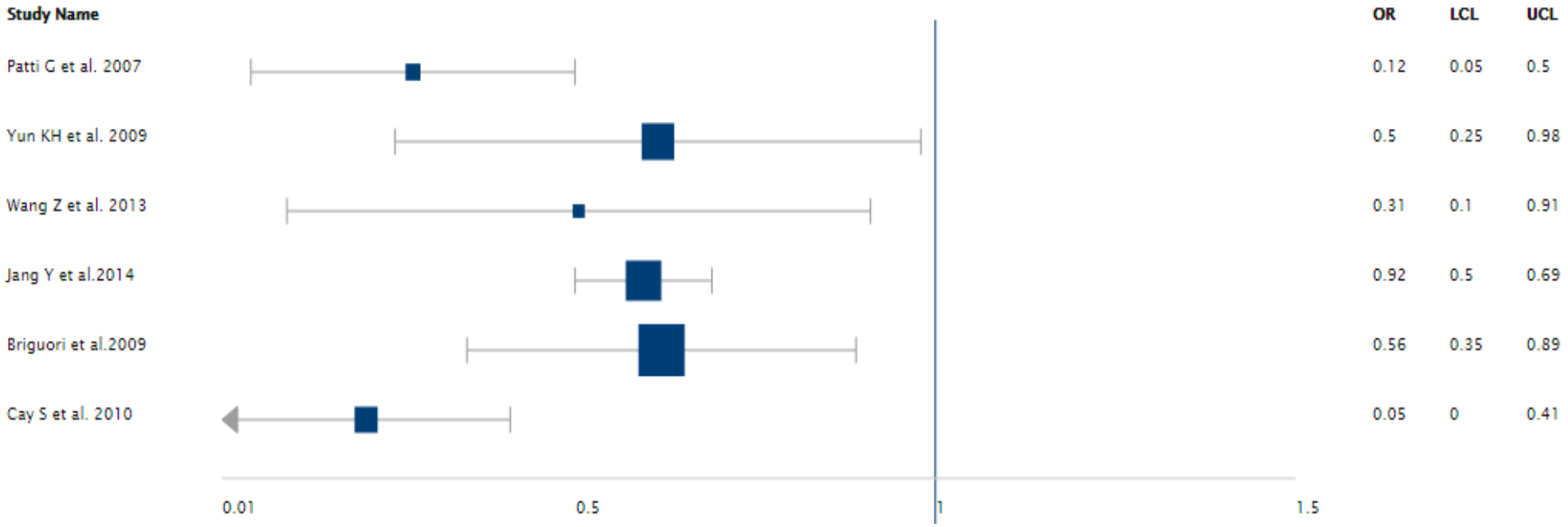

Figure 3. A Forest plot of the odds ratios for post-procedural MI incidence

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LITERATURE APPRAISAL

Depending on findings at coronary angiography, the decision to proceed to PCI during the same procedure was based on the operating clinician's discretion. These methods were declared as baseline characteristics by all studies (except the ALPACS trial) and the variation between arms is probably due to chance. All studies excluded patients who did not have PCI (i.e. had medical therapy or coronary artery bypass grafting), except Cay et al. where all patients had confirmed de novo lesions as an entry requirement.

Patti et al.[9] conducted the ARMYDA-ACS trial, a multi-centre, randomized, double-blinded trial of atorvastatin given pre-treatment in patients with non-ST elevation ACS undergoing PCI. Using an electronic spread sheet, 171 patients were randomized to receive either two loading doses of atorvastatin (80 mg and 40 mg) or placebo. Patients and physicians performing the procedure and the follow-up assessments were blinded. The demographics and baseline clinical features between the two arms were similar and the management of intervention and control group patients was the same, with all patients receiving aspirin and clopidogrel. The decision on the use of glycoprotein IIb/IIIa inhibitors in 23 atorvastatin and 18 placebo patients was left to the discretion of the blinded operator. Follow-up was 100% without any crossover. The primary endpoint of the trial was any occurrence of MACE from the procedure up to 30 days, including: death; MI (measured by an increase in creatine kinase-MB (CK-MB) of more than two-fold above the upper limit of normal); and target vessel revascularization (defined as repeat PCI or surgery on the target vessels). The study did not mention blinding of data analysis (triple blinding), which may affect the reliability of the results given the pressures to publish studies with positive findings, especially those with pharmaceutical funding. The trial methods were robust following the CASP checklist. The study had a clearly defined question with study arms that had equal methods and follow-up was complete. Overall, the study has a low risk of bias. Pre-treatment with atorvastatin compared with placebo group had an OR event-free survival at 30 days of 0.12 (CI: 0.05–0.50, p = 0.004).

Yun et al.[10] investigated the benefits of high-dose rosuvastatin preloading in patients with ACS undergoing PCI. A total of 445 patients were randomly allocated to rosuvastatin loading before PCI (n = 225) or no statin treatment (n = 220). The randomization method was not described in the paper and allocation of patients was not concealed from researchers. Patients were not blinded as no placebo was administered. The baseline characteristics between the arms were similar and all patients received the same post-procedural treatment. There was no loss to follow-up or patient crossover between groups. There are several limitations to this trial. It is an open trial and had a broad exclusion criteria, thus introducing omission bias and thus making the results less generalizable. Therefore, this trial has a high risk of bias. The primary outcome measured was peri-procedural MI defined by post-procedural increase of CK-MB over two-fold higher than the upper limit of normal. The use of CK-MB levels was justified by the authors because a normal CK-MB followed by an abnormal result after angioplasty is evidence for new myocardial ischemia. Secondary endpoints included MACE during the first month (death, Q-wave MI, target vessel revascularization, ischaemic stroke). The study results showed that the high-dose rosuvastatin group had a lower incidence of death and post-procedural MI at 30 days (OR = 0.44, CI: 0.22–0.85, p = 0.02) compared with the control group. The OR specifically for the incidence of post-procedural MI was 0.50 (CI: 0.25–0.98, p = 0.04).

In the 2009 NAPLES II Trial "Novel Approaches for Preventing or Limiting Events", conducted by Briguori et al.,[13] 668 statin-naïve patients who were scheduled for PCI were randomized to receive either 80 mg atorvastatin before the procedure (n = 338) or receive usual care only (n = 330). The primary outcome assessed was post-procedural MI defined as an elevation of CK-MB over three-fold the normal upper limit, measured at 6 and 12 hours post-procedure. The

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allocations were not blinded and no placebo was administered to the control group. Furthermore, follow-up was only performed for 24 hours. These factors limit the full generalizability of these results. There was no significant difference between the baseline characteristics of the trial arms. The paper specifically analysed patients who received stenting, for which the decision was made after statin administration by non-blinded individuals. This accounted for loss of 49% and 50% of the intervention/control group respectively. Less than 1% was subsequently lost to follow-up. The results show an OR of 0.56 (CI: 0.35–0.89, $p < 0.001$) for the incidence of MI within 12 hours of PCI. The reduction was most pronounced in the subgroup that had raised C-reactive protein (CRP), lending support to atorvastatin's anti-inflammatory properties over lipid lowering as the biochemical mechanism. Subsequent stabilization of the plaque reduced future thrombotic events. This statistically significant result gives evidence for the claim that atorvastatin is able to reduce myocardial tissue death post-PCI and prevent biochemically defined MI.

Wang et al.[11] investigated the effects of rosuvastatin pre-treatment compared with placebo on post-procedural outcomes, such as death and MI, in 125 patients with ACS undergoing PCI. They defined MI based on both normal and raised pre-PCI cardiac marker levels, i.e. CK-MB and cardiac troponin I (cTnl). The former was defined by post-PCI levels of CK-MB/cTnI reaching 300% of the upper limit of normal. In patients whose pre-PCI levels were above the normal ranges, MI was defined by a post-PCI level of CK-MB/cTnI reaching 300% of the pre-PCI baseline level. Participants were randomized to a rosuvastatin or a placebo group and the experiment was double-blinded from the investigators; however, there was no mention of whether there was any allocation concealment. The patients' baseline characteristics were similar between both groups before the start of the trial. Both groups underwent the same treatment of coronary intervention with stenting if indicated. All patients who underwent PCI (both with and without rosuvastatin) completed the trial. The results showed those in the intervention group had a lower rate of MI (8.1% vs 22.2%) and there were no deaths in either group at 30 days. For these primary outcomes, OR = 0.31 CI: 0.10–0.91, $p = 0.034$. Inflammatory marker levels (CRP, IL-6 and monocyte chemoattractant protein-1 [MCP-1]) also demonstrated a statistically significant reduction in the rosuvastatin group before and after PCI (at 6, 24 and 72 hours). This trial indicates that the use of rosuvastatin pre-PCI reduces the incidence of post-procedural MI.

Cay et al.[14] studied the effect of a single 40 mg loading dose of rosuvastatin 24 hours before undergoing PCI on post-procedural MI and myocardial necrosis in 299 statin-naïve patients with stable angina, compared with no statin administration. The primary outcomes of the study were post-procedural myocardial necrosis and MI, the latter defined as a cardiac biomarker level increase greater than three-fold the 99th percentile upper limit of normal. The results of two cardiac biomarkers, measured 12 hours after PCI, are given: CK-MB and cTnI. The paper gives no detail on the method of randomization, the extent of concealment, or on the extent of blinding. However, as the intervention is a statin tablet and the control group did not receive a placebo, it is likely that neither the patients nor the health workers were blinded, introducing the risk of bias. Other weaknesses of the study include a small sample size, which limits the generalizability of the study. The paper also fails to specify where these patients were recruited from, referring only to "study centres". Finally, the patients were followed up for 12 hours, whereas other studies demonstrated benefit from stating therapy over the following month. There were no significant differences in baseline characteristics or management of patients between the study arms. The study proceeded to completion without participant attrition or crossover of patients between the study arms. The authors reported that the OR between the rosuvastatin group and the control group for the incidence of an MI-defining rise in cTnI was 0.22 (CI: 0.12–0.42, $p < 0.001$) and in CK-MB was 0.05 (CI: 0.00–0.41, $p < 0.001$). On

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closer examination of the CI of the latter result, it was discovered that the authors had made a rounding error: on repeat calculation, the CI was found to be 0.01–0.41 for OR of 0.05. Nonetheless, these results show evidence of a statistically significant reductive effect of rosuvastatin pre-loading on biochemically-defined MI.

In the 2013 ALPACS study, conducted by Jang et al.,[12] 499 adults were randomized, with 247 given 80 mg atorvastatin at 12 hours and 40 mg at 2 hours before PCI. They were compared with patients who received usual care only. We extracted the raw data for incidence of death and MI from the primary outcome of MACE at 30 days. There was no evidence of systematic differences in baseline characteristics. All patients were analysed based on their random allocation. The method of randomization was not declared. There was significant loss to follow-up of 34% and 32% in the intervention and control group, respectively. The study did not detail methods of follow-up or explain the attrition levels. The study was funded by Pfizer and conflicts of interest were declared. Preloading with atorvastatin was not statistically significant for MI (OR = 0.92, CI: 0.50–1.69) or mortality (OR = 1.06 CI: 0.07–17.01). Although the authors calculated that their study had sufficient power to observe the effect of their intervention, the study would have benefitted from a larger a sample size and closer follow-up to strengthen the results.

DISCUSSION

This review focused on six studies that investigated the use of varying dosages and frequency of atorvastatin or rosuvastatin given pre-procedurally up to 24 hours prior to PCI. There was significant diversity in the study populations investigated. Out of the six trials reviewed, two were Western European, three were Asian, and one was Middle Eastern. The age of patients was similar between the trials with mean ages between 60 and 65 years. Other measures were more varied, e.g. average diabetes rate ranged from 18% to 38%. A meta-analysis across the studies, which is beyond the scope of this review, could provide statistical quantification of a treatment effect.

The trials followed different outcomes, broadly split in to MACE over 30 days and biochemical MI within 48 hours of PCI. We selected the raw data for MI and mortality. Troponin is the current preferred biomarker for confirming ACS in new patients, however alternative biomarkers were used in some studies. Nonetheless, as baseline biomarkers were taken post-procedurally and then repeated, the biomarkers are appropriate in monitoring subsequent cardiac cell death through enzyme release. The inconsistency between studies in how post-procedural MI was defined would make direct comparison via meta-analysis challenging. Furthermore, there were different lengths of follow-up between the papers, contributing to the heterogeneity. All the papers in this review, except for the NAPLES II trial,[13] reported that the administration of glycoprotein IIb/IIIa inhibitors was at the operators' discretion. However, the lack of specific indications or criteria for their administration, could potentially introduce performance bias.

The usual care provided was otherwise consistent between all papers, consisting of aspirin, clopidogrel, and intravenous heparin. Not all the papers reviewed described their methods in detail, which could mask further procedural variation between the trials.

The ALPACS trial, conducted by Jang et al.,[12] showed results that did not reach statistical significance in demonstrating the benefits of preloading with statins, despite being similar to the robust ARMYDA-ACS trial conducted by Patti et al.[9] There is little difference in the baseline characteristics, study methods, intervention, or outcome measured to explain the differing results. The difference may be a result of reduced trial quality, with ALPACS[12] being open label with a 34% loss of follow up. There is no significant correlation between dose and effect across the studies. In the ARMYDA-ACS[9] trial, atorvastatin at high dose

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showed the greatest effect; in the ALPACS[12] trial, the same dosage showed no effect. In the NAPLES-II[13] trial, significant effect at was shown at lower dosage, but patients were only followed-up for 24 hours. With rosuvastatin, Cay et al.[14] showed the most pronounced effect with 40 mg doses, followed by 20 mg doses in Wang et al.11 and 40 mg in Yun et al.[10] All papers showed an effect for rosuvastatin, but a dose-response relationship cannot be established due to the different outcome definitions used.

The mechanism of ACS involves plaque rupture as a key step in new thrombus formation.[18,19] The link between the use of statins and the reduction in cardiac events may be explained by their possible function in stabilizing atherosclerotic plaques. This may be induced via various mechanisms, such as the increase in the inhibition of metalloproteinase-1.[20] It may also be due to the composition of the plaque itself, where statin administration increases smooth muscle cell content while decreasing collagen degradation.[21] Together, these may point to a viable mechanism by which statins reduce the risk of plaques destabilizing.

Our review includes international studies across diverse demographics. However, this heterogeneity limits direct comparison of the studies. Due to the specific nature of our research question, our search yielded only six papers, which limits the credibility of any conclusions drawn. Nevertheless, our review supports the administration of high-dose statin within 24-hours prior to PCI, and this time window for introducing a statin intervention could potentially be further expanded. Furthermore, the cardio-protection conferred by statins could potentially be harnessed in cases of ACS and/or stable angina that are medically managed (i.e. not requiring PCI or coronary artery bypass grafting). Finally, the lack of side effects reported in these studies, even with relatively high doses of statins, lends support to future studies with more aggressive dosing strategies.

CONCLUSION

This review has highlighted the presence of five studies that support the efficacy of pre-procedural statins in reducing the risk of MI or mortality after elective PCI. A meta-analysis would provide statistical quantification of the treatment effect that we have observed across these studies. A large multi-centre triple-blinded placebo-controlled randomized trial on statin-naïve patients would provide greater insight, especially if patients were followed up for more than 30 days. Such a study may provide evidence for testing the hypothesis that reducing mild tissue necrosis post-PCI could also confer long-term clinical benefit.

This review has given medical students the opportunity to search, select and review an interesting range of scientific papers. We have developed our skills of working collaboratively and developing a group view that we have put forward. Statins, which are widely used, have a key role for physicians in treating ACS and maximizing health outcomes.

Competing Interest and Funding

Nothing to declare

Keywords:
Statins; Hydroxymethylglutaryl-CoA Reductase Inhibitors; Percutaneous Coronary Intervention; Percutaneous Coronary Revascularisation; Myocardial Infarction;

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What is known already:

- Patients undergoing elective PCI are at risk of post-procedural MI and death. Observational studies show that patients who are statin naïve experience these complications at a higher rate than patients on previous statin therapy.
- A systematic review conducted by Patti et al. in 2010 showed that patients who received a course of statins prior to undergoing PCI experienced a lower rate of post-procedural complications.
- However, the studies evaluated in the systematic review covered a wide range of statin therapies, with some necessitating a 2-week period of treatment prior to PCI. As such, there may have been some delay to PCI, in order to receive this treatment beforehand.

What this study adds:

- This review evaluated six studies that investigate the effect of high-dose statin on post-procedural MI and mortality when administered within 24 hours before PCI.
- We found that five of the six papers reviewed supported the benefits of this treatment strategy.
- The benefit of statin treatment administered shortly before PCI provides grounds to investigate the use of emergency pre-procedural statin administration prior to PCI in patients requiring urgent non-elective PCI.

REFERENCES

1. Bhatnagar P, Wickramasinghe K, Williams J, Rayner M, Townsend N. The epidemiology of cardiovascular disease in the UK 2014. Heart. 2015;101(15):1182–9. DOI: 10.1136/heartjnl-2015-307516.

2. Timmis A. Acute coronary syndromes. BMJ. 2015;351:h5153. DOI: 10.1136/bmj.h5153.

3. National Institute for Health and Care Excellence. Acute Coronary Syndromes in Adults (QS68). London, UK: National Institute for Health and Care Excellence; 2014.

4. Grech ED. Percutaneous coronary intervention. II: The procedure. BMJ. 2003;326(7399):1137–40. DOI: 10.1136/bmj.326.7399.1137.

5. Spencer FA, Allegrone J, Goldberg RJ, Gore JM, Fox KA, Granger CB, et al. Association of statin therapy with outcomes of acute coronary syndromes:the GRACE Study. Ann Intern Med. 2004;140(11):857–66. DOI: 10.7326/0003-4819-140-11-200406010-00006.

6. Chan AW, Bhatt DL, Chew DP, Quinn MJ, Moliterno DJ, Topol EJ, et al. Early and sustained survival benefit associated with statin therapy at the time of percutaneous coronary intervention. Circulation. 2002;105(6):691–6. DOI: 10.1161/hc0602.103586.

7. Yun KH, Shin IS, Shin SN, Choi JH, Kim SH, Rhee SJ, et al. Effect of previous statin therapy in patients with acute coronary syndrome and percutaneous coronary intervention. Korean Circ J. 2011;41(8):458–63. DOI: 10.4070/kcj.2011.41.8.458.

8. Patti G, Cannon CP, Murphy SA, Mega S, Pasceri V, Briguori C, et al. Clinical benefit of statin pretreatment in patients undergoing percutaneous coronary intervention: a collaborative patient-level meta-analysis of 13 randomized studies. Circulation. 2011;123(15):1622–32. DOI: 10.1161/CIRCULATIONAHA.110.002451.

9. Patti G, Pasceri V, Colonna G, Miglionico M, Fischetti D, Sardella G, et al. Atorvastatin pretreatment improves outcomes in patients with acute coronary syndromes undergoing early percutaneous coronary

doi:10.2218/resmedica.v24i1.1487

intervention: results of the ARMYDA-ACS randomized trial. J Am Coll Cardiol. 2007;49(12):1272–8. DOI: 10.1016/j.jacc.2007.02.025.

10. Yun KH, Jeong MH, Oh SK, Rhee SJ, Park EM, Lee EM, et al. The beneficial effect of high loading dose of rosuvastatin before percutaneous coronary intervention in patients with acute coronary syndrome. Int J Cardiol. 2009;137(3):246–51. DOI: 10.1016/j.ijcard.2008.06.055.

11. Wang Z, Dai H, Xing M, Yu Z, Lin X, Wang S, et al. Effect of a single high loading dose of rosuvastatin on percutaneous coronary intervention for acute coronary syndromes. J Cardiovasc Pharmacol Ther. 2013;18(4):327–33. DOI: 10.1177/1074248412474346.

12. Jang Y, Zhu J, Ge J, Kim YJ, Ji C, Lam W. Preloading with atorvastatin before percutaneous coronary intervention in statin-naïve Asian patients with non-ST elevation acute coronary syndromes: a randomized study. J Cardiol. 2014;63(5):335–43. DOI: 10.1016/j.jjcc.2013.09.012.

13. Briguori C, Visconti G, Focaccio A, Golia B, Chieffo A, Castelli A, et al. Novel approaches for preventing or limiting events (NAPLES) II trial: impact of a single high loading dose of atorvastatin on periprocedural myocardial infarction. J Am Coll Cardiol. 2009;54(23):2157–63. DOI: 10.1016/j.jacc.2009.07.005.

14. Cay S, Cagirci G, Sen N, Balbay Y, Durmaz T, Aydogdu S. Prevention of peri-procedural myocardial injury using a single high loading dose of rosuvastatin. Cardiovasc Drugs Ther. 2010;24(1):41–7. DOI: 10.1007/s10557-010-6224-1.

15. Ge J, Kim YJ, Jang YS, Zhu J, Marschner IC, Lam W. Design and rationale of a study in Asia of atorvastatin pretreatment in patients undergoing percutaneous coronary intervention for non-ST elevation acute coronary syndromes. J Cardiol. 2010;55(3):303–8. DOI: 10.1016/j.jjcc.2009.12.002.

16. Vale N, Nordmann AJ, Schwartz GG, de Lemos J, Colivicchi F, den Hartog F, et al. Statins for acute coronary syndrome. Cochrane Database Syst Rev. 2014;(9):CD006870. DOI: 10.1002/14651858.CD006870.pub3.

17. Adams SP, Tsang M, Wright JM. Lipid-lowering efficacy of atorvastatin. Cochrane Database Syst. Rev. 2015;(3):CD008226. DOI: 10.1002/14651858.CD008226.pub3.

18. Dave T, Ezhilan J, Vasnawala H, Somani V. Plaque regression and plaque stabilisation in cardiovascular diseases. Indian J Endocrinol Metab. 2013;17(6):983–89. DOI: 10.4103/2230-8210.122604.

19. Schartl M, Bocksch W, Koschyk DH, Voelker W, Karsch KR, Kreuzer J, et al. Use of intravascular ultrasound to compare effects of different strategies of lipid-lowering therapy on plaque volume and composition in patients with coronary artery disease. Circulation. 2001;104(4):387–92. DOI: 10.1161/hc2901.093188.

20. Aikawa M, Rabkin E, Okada Y, Voglic SJ, Clinton SK, Brinckerhoff CE, et al. Lipid lowering by diet reduces matrix metalloproteinase activity and increases collagen content of rabbit atheroma: a potential mechanism of lesion stabilization. Circulation. 1998;97(24):2433–44. DOI: 10.1161/01.CIR.97.24.2433.

21. de Lorenzo F, Feher M, Martin J, Collot-Teixeira S, Dotsenko O, McGregor JL. Statin therapy—. evidence beyond lipid lowering contributing to plaque stability. Curr Med Chem. 2006;13(28):3385–93. DOI: 10.2174/092986706779010324