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Late Percutaneous Coronary Intervention for the Totally Occluded Infarct-Related Artery: A Meta-Analysis of the Effects on Cardiac Function and Remodeling

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Background: Late percutaneous coronary intervention (PCI) of a totally occluded infarct-related artery (IRA) in stable patients is currently not recommended based on the lack of clear clinical benefits in randomized controlled trials. We sought to perform a systematic review and meta-analysis of randomized controlled trials comparing PCI with optimal medical therapy in patients with IRA occlusion more than 12 hr after onset of acute myocardial infarction (AMI), focusing on left ventricular function and remodeling. Methods and Results: PubMed, CENTRAL, and mRCT were searched for eligible studies. Studies were included in the analysis if they were randomized controlled trials comparing conservative medical management with PCI performed at least 12 hr after the onset of symptoms of AMI, and data on left ventricular ejection fraction (LVEF) at baseline and follow-up were available. Studies were excluded if randomization occurred less than 12 hr after symptom onset, or if patients were hemodynamically unstable. Change in LVEF was the primary outcome of interest, with changes in left ventricular end-diastolic volume index (LVEDVI) and end-systolic volume index (LVESVI) analyzed as secondary endpoints. We retrieved five studies in which baseline and follow up LVEF data were available enrolling a total of 648 patients: 342 patients randomized to PCI and 306 to medical treatment. There was a statistically significant difference in LVEF changes over time favoring PCI (+3.1%, 95% CI +1.0 to +5.2, P = 0.0004). In addition, there were statistically significant differences changes in both LVEDVI (−5.1 ml in favor of PCI, 95% CI of −9.4 to −0.8, P = 0.020) and LVESVI (−5.3 ml in favor in PCI, 95% CI of −8.3 to −2.4, P = 0.0005). Conclusions: This meta-analysis suggests that late revascularization of an occluded IRA may improve left ventricular systolic function and remodeling, supporting the "open artery hypothesis." The reason why these changes have not resulted in clinical benefits in large clinical trials is subject to debate. © 2008 Wiley-Liss, Inc.

Key words: meta-analysis; myocardial infarction; late; revascularization; percutaneous coronary intervention; total occlusion; remodeling

INTRODUCTION

Early reperfusion remains the primary goal in the treatment of acute myocardial infarction (AMI), given the weight of evidence showing a survival advantage in patients with ST-elevation myocardial infarction (STEMI) treated with primary percutaneous coronary intervention (PCI) or thrombolysis, when reperfusion can be achieved within 12 hr of symptom onset [1]. Improvements in survival are thought to derive at least in part from salvage of ischemic myocardium, which in turn leads to preservation of both regional and global left ventricular function [1–3]. Whether a benefit can be derived from reperfusion occurring late (>12 hr) with AMI is, however, controversial. The ''open artery hypothesis'' was derived from observational and experimental data suggesting that in achieving reperfusion in the infarct-related artery (IRA) there may be

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benefits that are necrosis-independent and partially time-independent [2,3]. This hypothesis postulates that late revascularization of the occluded artery prevents unfavorable post-infarction remodeling and long-term unfavorable outcomes [1–4]. However, no single randomized trial to date has shown a clear clinical advantage in performing PCI in this setting. Several small and one large trial have shown inconclusive and conflicting results. The OAT study is the largest and most recent randomized trial designed to test the open artery hypothesis in clinical practice, and showed no significant difference in terms of clinical outcomes between PCI and optimal medical management [5,6]. The recently published SWISSI II trial, on the other hand, showed a survival benefit for patients undergoing PCI of the IRA for residual silent ischemia [7]. An ancillary study from the OAT study, published separately as the TOSCA-2 study, which looked specifically at the effect of PCI on cardiac function and remodeling, showed a nonsignificant trend towards improved cardiac function and remodeling with PCI [8]. Optimal management of stable patients after AMI is therefore controversial. It appears reasonable to consider early angiographic assessment paired with an assessment of ischemia/viability as individual studies (ALKK [9] and SWISSI II [7]) and a recent meta-analysis from our own group [10] show that PCI for subtotal occlusion of the IRA especially in presence of inducible ischemia is associated with a clinically relevant survival benefit. Whether there is any role of PCI of a totally occluded IRA is however unclear. The aim of our study was to perform a systematic review and meta-analysis of the existing RCTs comparing late PCI of a totally occluded IRA to conservative optimal medical management in the setting of stable patients late (>12 hr) in the course of AMI, in order to examine the pooled data with respect to changes in cardiac function and remodeling.

METHODS

Searching

Three trained investigators (DLA, AA, GBZ) independently searched PubMed, CENTRAL, mRCT, BioMedCentral, Cardiosource, clinicaltrials.gov, and ISI Web of Science using a highly sensitive and specific strategy, as previously described [11]. Search keywords included "randomized," "percutaneous coronary intervention," "PCI," "stent," "angioplasty," "revasc*," "recanaliz*," "acute myocardial infarction," "AMI," "infarct*," "occlusion," "occlu*" (where * denotes a wildcard). Search was updated to October 2007. No language restriction was used.

Selection

Citations initially selected by systematic search were first retrieved as title and/or abstract and preliminarily screened. Potentially relevant reports were then retrieved as complete manuscripts and assessed for compliance to inclusion and exclusion criteria. Inclusion criteria for retrieved studies were as follows: (a) randomized treatment allocation, (b) comparison of late PCI vs optimal medical management, (c) hemodynamic stability of patients, (d) angioplasty for a totally occluded IRA performed late (>12 hr following onset of symptoms) in the course of AMI, (e) availability of measurements of left ventricular ejection fraction (LVEF) (with or without LVESVI and LVEDVI) at baseline and follow-up.

Exclusion criteria includes the following: (a) nonrandomized treatment allocation, (b) enrollment of patients with hemodynamic instability (cardiogenic shock), recurrent symptoms of ischemia, failed fibrinolysis or other indications to early catheterization, (c) duplicate publication, (d) enrolment of patients randomized to PCI within 12 hr of symptom onset, (e) enrolment of patients with subtotal IRA occlusion, (f) lack of baseline or follow up LVEF data, (g) or ongoing studies.

Validity Assessment

Study quality was evaluated according to the established methods of the Cochrane Collaboration. Specifically, we separately estimated the risk of selection, performance, detection and attrition bias, and abstracted additional design features. In addition, allocation concealment was explicitly distinguished as adequate (A), unclear (B), inadequate (C), or not used (D), and methods for generation of randomization sequences and allocation were explicitly abstracted.

Data Abstraction, Study Characteristics, and Imputation

Data extraction was performed on prespecified data forms, including detailed data on populations, interventions, comparisons, and outcomes.

The impact on cardiac function and remodeling was assessed primarily by means of left-ventricular ejection fraction (LVEF). Left ventricular end-systolic volume index (LVESVI) and end-diastolic volume (LVEDVI) measurements were directly abstracted when reported. Otherwise, primary authors were repeatedly contacted to obtain the precise data. Eventually, in case of no or incomplete response, they were imputed using means and standard deviations from baseline and follow-up data according to an unbiased algorithm (available online at http://www.metcardio.org/protocols.html).

Statistical Methods

Statistical analysis was performed using the Review Manager 4.2.4 freeware package and SPSS 11.0 (SPSS, Chicago, IL). Continuous variables were reported as mean (standard deviation) or median (range). Formal Cochran Q chi-square tests and I^2 values were calculated as a measure of heterogeneity. A regression test with the primary end-point as dependent variable and study size as independent variable was used to appraise the presence of small study bias (i.e., publication bias). For the purpose of hypothesis testing, continuous variables were compared using the random effect inverse variance weighting method, which largely accommodates relatively heterogeneous or inconsistent individual study estimates. Reported values were two-tailed and results were considered statistically significant at the 0.05 level.

RESULTS

Search Results and Study Selection

Overall the search permitted the retrieval of 4,435 citations. Several reports were excluded at the title and/or abstract level because these were not pertinent. We identified 20 eligible citations, which were assessed for compliance to inclusion and exclusion criteria. We further excluded 15 studies; 6 were excluded because enrollment was allowed earlier than 12 hr [12–17], 1 study was excluded because it was a non-randomized retrospective analysis [18], 2 were excluded because the randomization process was limited to angiography and not specifically to intervention and only a subgroup of patients were found to have total IRA occlusion and/or underwent PCI [19,20]. Four studies were excluded because LVEF data at baseline and/or follow up were not available [6,9,21,22]. In the case of the TOAT study, the earliest EF data available for comparison, even after contacting the principal investigator, was at 6 weeks after randomization, thus precluding inclusion of the study based on the lack of baseline comparison data [22]. Two additional studies were excluded because various degrees of IRA stenoses were allowed [7,23]. Ultimately, five published studies were selected [8,24–27] (Fig. 1).

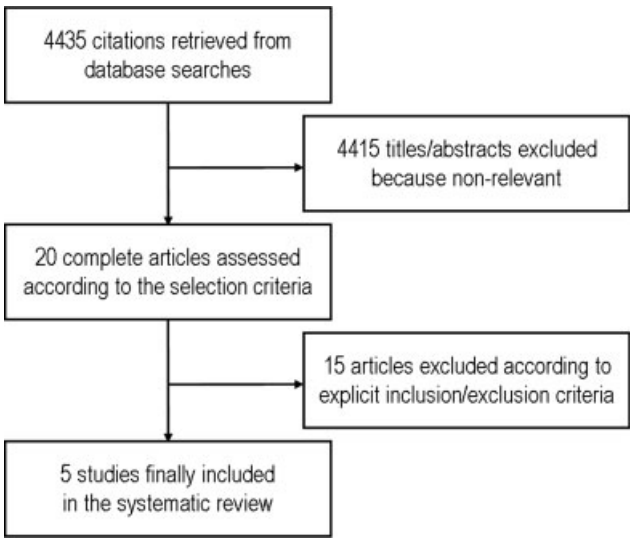

Fig. 1. Reviewing process.

Baseline Characteristics

The five studies included in the final analysis randomized 648 patients; 342 randomized to PCI and 306 to medical therapy only (see Tables I, II & III). Three studies were multicenter trials [8,24,26], the remaining were single centers trials [25,27]. The mean age was 58 years. On average, men accounted for 81% of subjects. The average value for the median time from MI to intervention was 8 days. The latest time for enrollment was 6 weeks [26]. Follow up duration ranged from 6 weeks to 5 years. The average baseline LVEF was 48%. LVEF at baseline and follow-up was measured by left-ventriculography in three studies [8,24,27], cardiac MRI in one study [25], and either radionuclide scanning or left-ventriculography in one study [26]. All studies report blinding of physicians participating in the study to randomization with regard to LVEF assessment except in one study [25], where blinding was not specifically reported. Three studies

TABLE I. Baseline Characteristics of Patients in the Included Studies

	Year of publication	Number of patients	Number randomized to interventional arm	Number randomized to control arm	Mean age (years)	Percentage of male patients	Time from symptom onset to PCI (days)	Thrombolytics prior to PCI
Dzavik [26] TOMIIS	1994	44	25	19	58	70	11	No
Dzavik [8] TOSCA-2	2006	381	195	186	58	83	10	No
Horie [27]	1998	83	44	39	62	76	8	No
Silva [25]	2005	36	18	12	55	64	8	No
Steg [24] DECOPI	2004	212	109	103	57	85	8	No

PCI indicates percutaneous coronary intervention.

TABLE II. Additional Clinical Characteristics and Details of the Included Studies

	Totally occluded IRA at time of randomization	Angiographic success (final TIMI grade 3 following PCI) (%)	Routine or provisional use of stents	Routine or provisional use of GP IIb/IIIa inhibitors in PCI group	Routine or provisional use of clopidogrel or ticlopidine	Crossover from control arm to intervention arm	Midterm follow-up	Long-term follow-up	Method used to calculate LVEF	Blinded assessment of LVEF
Dzavik [26] TOMIIS	Yes	72	No	No	Not stated	No	4 months	–	Radionuclide (n = 31), Angiogram (n = 6)	Yes
Dzavik [8] TOSCA-2	Yes	85.1	Yes (91%)	Yes (81%)	Yes (PCI 92.8%, controls 30.6%)	Yes (8%)	–	12 months	Left ventriculogram	Yes
Horie [7]	Yes	86	No	No	Not stated	No	6 months	–	Left ventriculogram	Yes
Silva [5]	Yes	100	Yes (100%)	Yes (22%)	Yes (all PCI patients for 30 days)	No	6 months	–	Cardiac MRI	Not stated
Steg [4] DECOPI	Yes	82.2	Yes (80.4%)	Yes (9%)	Yes (if stent placed, $\geq$ 30 days)	Yes (9%)	–	35 months	Left Ventriculogram	Yes

IRA, indicates infarct-related artery; TIMI, thrombolysis in myocardial infarction; PCI, percutaneous coronary intervention; GP, glycoprotein; LVEF, left ventricular ejection fraction.

TABLE III. LVEF, LVEDV, and LVESV Data from Individual Studies

	Number with available baseline/follow up EF data (control group)	Number with available baseline/follow up EF data (PCI group)	Paired data	LVEF change (control group) (mean% [stdev] or [IR])	LVEF change (PCI group) (mean% [stdev] or [IR])	LVEDVI change (control group) (mean [stdev] or [IR])	LVEDVI change (PCI group) (mean [stdev] or [IR])	LVESVI change (control group) (mean [stdev] or [IR])	LVESVI change (PCI group) (mean [stdev] or [IR])
Dzavik [26] TOMIIS	16	21	Yes	+4.1 [±8.2]	+5.3 [±9.7]	–	–	–	–
Dzavik [8] TOSCA-2	136	150	Yes	+3.5 [±8.2]	+4.2 [±8]	+5.3 [−4.6, +23.2]	+3.2 [−9.3, 5.0]	+1.0 [−5.7, +7.3]	−1.7 [−30.3, +14.9]
Horie [27]	17/39	32/44	No	+1.6[a]	+5.6[a]	+9.0[a,b]	−0.3[a,b]	+3.8[a,b]	−3.5[a,b]
Silva [25]	12	18	Yes	−0.8 [±6.6]	+5.0 [±5.1]	+7.2 [±14.9]	+2.0 [±13.6]	+5.0 [±12.7]	−1.4 [±8.3]
Steg [24] DECOPI	103/79	109/87	No[a]	+4.0[a]	+8.0[a]	–	–	–	–

LVEF, left ventricular ejection fraction; PCI, percutaneous coronary intervention; LVEDV, left-ventricular end-diastolic volume; LVESV, left-ventricular end-systolic volume.
[a]Values represent differences in mean values rather than mean difference; standard deviation not computed.
[b]Values represent mean differences in LVEDV and LVESV, rather than LVEDVI and LVESVI.

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TABLE IV. Medication Use in Control and PCI Groups for Each Study

	ACEI or ARB		Beta-blockers		Statins		Antiplatelet (ASA ± clopidogrel or ticlopidine)	
	Control (%)	PCI (%)	Control (%)	PCI (%)	Control (%)	PCI (%)	Control (%)	PCI
Dzavik [26] TOMIIS	82	62	94	79	n/a		100	100
Dzavik [8][a] TOSCA-2	90	87	93	85	90	88	98	96
Horie [27]	23	11	28	27	n/a		47[b]	64[b]
Silva [25]	100	100	83	100	25	39	100	100
Steg [24] DECOPI	57[c]		81[c]		82[c]		83[c]	

PCI, percutaneous coronary intervention; ACEI, angiotensin converting enzyme inhibitor; ASA, acetyl-salicylic acid.
[a]Values stated are at 1 year from randomization.
[b]All were given aspirin at randomization according to protocol, but actual rate not given, value in table represents antiplatelet agent at baseline not further defined in text
[c]Values stated apply to entire cohort with no breakdown of figures according to arm of study; text states that values were similar or the same in each group

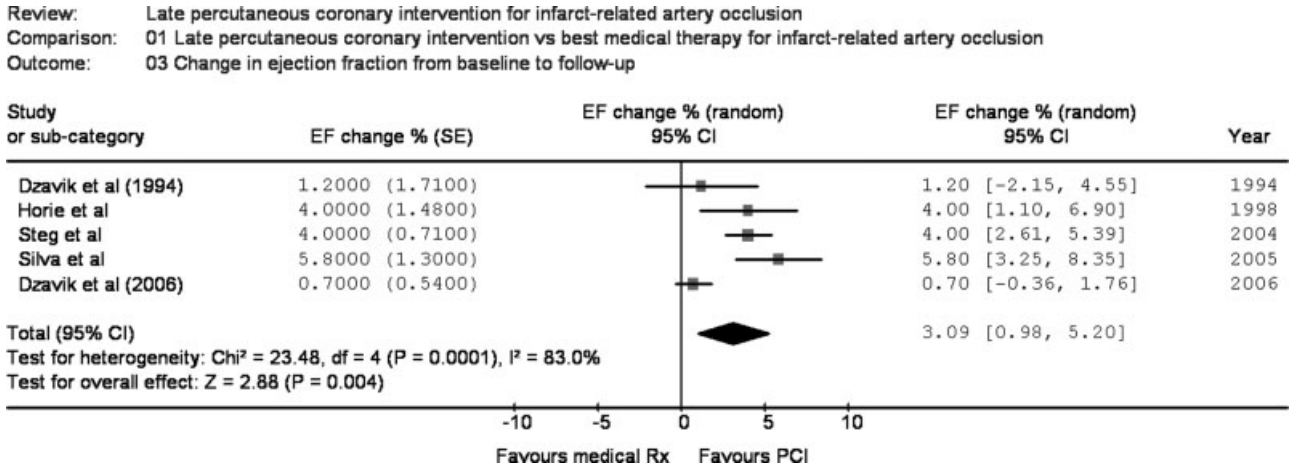

Fig. 2. Forest plot for change in left ventricular ejection fraction (EF). CI = confidence interval; df = degrees of freedom; PCI = percutaneous coronary intervention; SE = standard error.

presented paired data at baseline and follow up for a total of 353 patients (189 patients in the PCI group and 164 patients in the medical therapy only group) [8,25,26]. The remaining two studies presented unpaired data for LVEF at baseline and follow up [24,27].

Angiographic PCI success ranged from 72% [26] to 100% [25], with a median success rate across studies of 85%. Intracoronary stents were not used in two studies [26,27], while in the remaining three studies the rate of stenting ranged from 80 to 100%, with drug-eluting stents implanted in only one study [8]. Glycoprotein IIb/IIIa inhibitors were used in the TOSCA-2, where they were used routinely (86% of patients), [8] in the DECOPI study, where their use was left at physicians' discretion (9% of patients), [24] and by Silva et al [25] in 22% of PCI patients. No cross-over occurred in three studies [25–27], while in the remaining studies cross-over rates ranged from 8 to 11%. With regard to medical therapy, use of anti-platelet agents, beta-blockers, ACE-inhibitors, and lipid-lowering agents were similar between control and PCI groups within each study, although rates did vary across studies. (Table IV) Furthermore, the impact of PCI on changes in LVEF appeared to be unrelated to variations in medical therapy between studies.

Quantitative Data Synthesis

Considering the primary endpoint, late PCI of a totally occluded IRA in stable patients after AMI was associated with a significant difference in change in LVEF over time favoring PCI versus medical therapy alone, with an LVEF difference of +3.1% (95% CI +1.0 to +5.2, $P = 0.0004$) (Fig. 2). With regard to the secondary endpoints of change in LVESVI and LVEDVI, only three studies presented both baseline and follow-up data. The difference in LVEDVI changes between the PCI group and controls was −5.1 ml

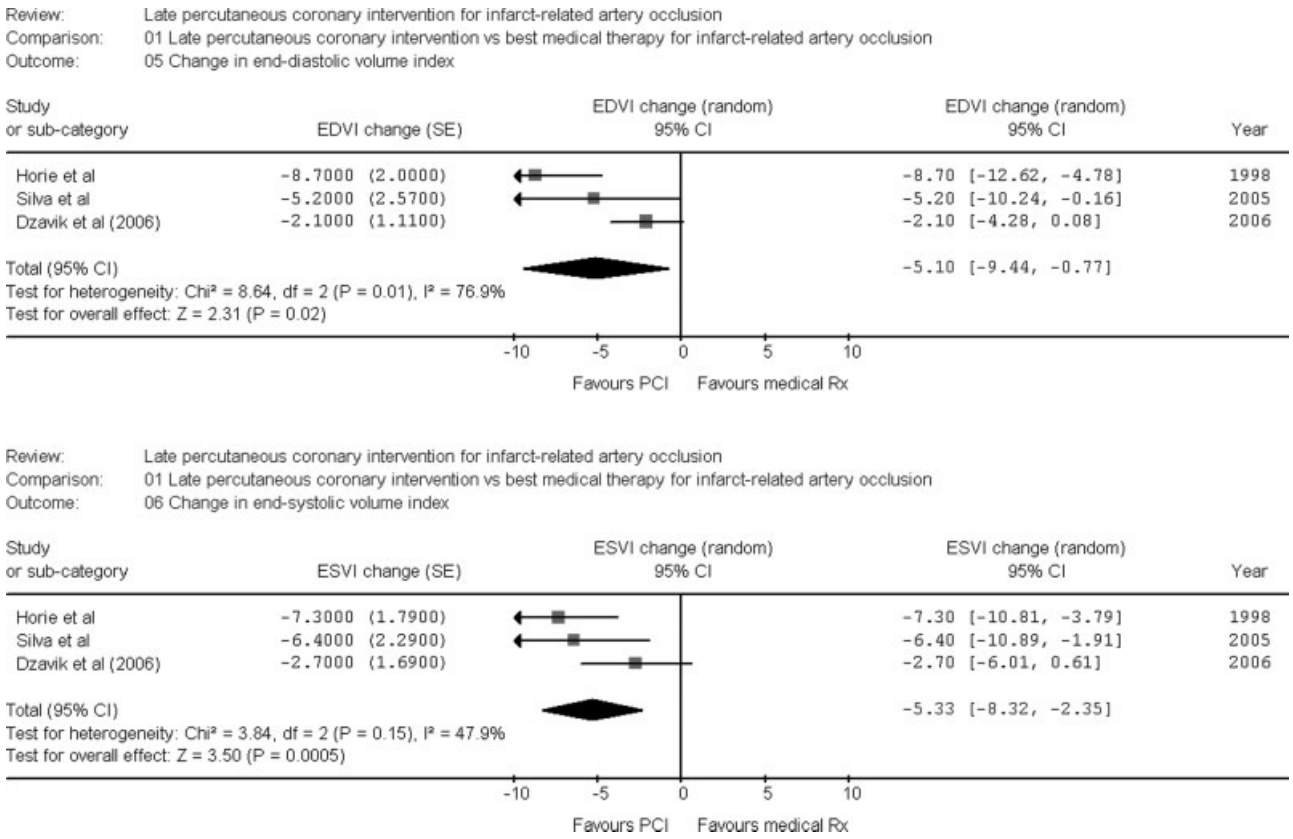

Fig. 3. Forest plot for change in left ventricular end-diastolic volume index (EDVI). CI = confidence interval; df = degrees of freedom; PCI = percutaneous coronary intervention; SE = standard error.

(95% CI of −9.4 to −0.8, $P = 0.020$), in favor of PCI (Fig. 3). The difference in changes in LVESVI between the PCI group and controls was −5.3 ml (95% CI of −8.3 to −2.4, $P = 0.0005$) also in favor of PCI (Fig. 3).

Of some concern when considering the variations in study parameters was the fact there was also some inconsistency in the methods used to calculate LVEF in the TOMIIS study [26]. With this in mind, we elected to perform a separate analysis of our primary endpoint (change in LVEF) excluding the TOMIIS study [26]. The result was a change in LVEF of +3.5 (95% CI of 1.0 to 5.9, $P = 0.005$) in favor of PCI, thus retaining a statistically significant functional improvement despite the elimination of the aforementioned study. Testing for publication bias by means of visual inspection of scatter or regression analysis assessing for a correlation between sample size and effect size did not disclose evidence of small study bias ($P = 0.44$) (Fig. 4). Finally, sensitivity analyses conducted after exclusion of every study confirmed in both direction and magnitude of statistical significance the findings of the overall analysis (all $P < 0.05$).

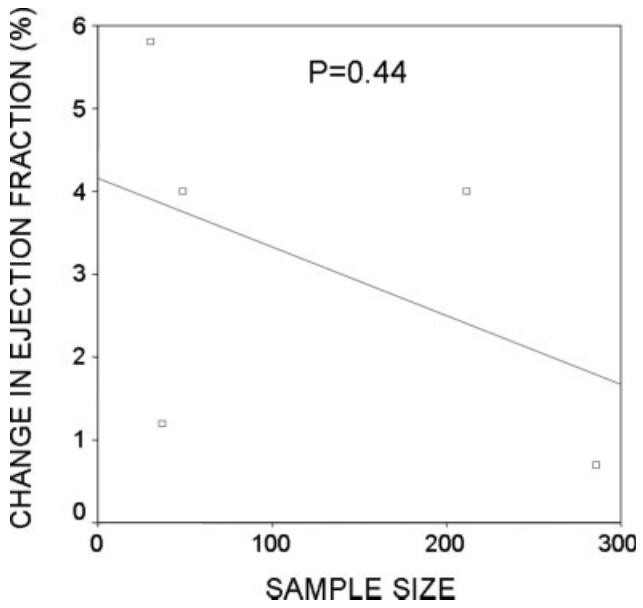

Fig. 4. Forest plot for change in left ventricular end-systolic volume index (ESVI). CI = confidence interval; df = degrees of freedom; PCI = percutaneous coronary intervention; SE = standard error.

DISCUSSION

The findings of this meta-analysis of five randomized trials enrolling 648 patients comparing late PCI with optimal medical management more than 12 hr after an AMI in stable patients with total IRA occlusion show a statistically significant beneficial effect of PCI on left ventricular function and remodeling when compared to medical management supporting the pathophysiologic basis of the "open artery hypothesis," which proposes that recanalization of a totally occluded IRA, even late in the course of an AMI, has a favorable effect on left ventricular function and remodeling, as potentially viable or hibernating myocardium is thought to be salvaged through reperfusion [2–4]. The largest and most recent study in this cohort was the recently published TOSCA-2 study [8]. The parent study (OAT) of the TOSCA-2 found no significant effect on the primary combined endpoint of death, recurrent MI or hospitalization for class IV congestive heart failure [6]. While the TOSCA-2 data showed no significant difference in LVEF changes over time, the pooled data in this meta-analysis, which includes the TOSCA-2 data, showed a significantly greater increase in LVEF with PCI as compared to medical management alone. Of note the TOSCA-2 study found a statistically significant association between patency of the IRA at follow-up with greater increase in LVEF, regardless of treatment allocation, supporting the potential value of the "open artery hypothesis."

The "open artery hypothesis" postulates that restoration of antegrade blood flow to the peri-infarct area is beneficial to the myocardium even late and beyond the time limit set for salvage from myocardial necrosis. The finding of a beneficial effect of late recanalization found in this meta-analysis supports the general premise of the open-artery hypothesis. Myocardial salvage due to interruption of ischemia-driven apoptosis may be a plausible explanation for this effect [4,28–31]. Reperfusion, even late in the course of AMI, may favorably affect the apoptotic cascade [4,28–31]. The viability of stunned myocardium has indeed been demonstrated days to weeks following AMI, suggesting that revascularization could potentially prevent the transition of hibernating myocardium to necrotic or apoptotic myocardium [32–35]. Ischemia itself stimulates formation of collateral circulation, which in the setting of AMI can serve to preserve some degree of retrograde perfusion, potentially prolonging viability of myocardium at risk [36].

As with any meta-analysis, there are inherent difficulties in using data from multiple studies of a similar nature to derive conclusions about an overall effect of a particular intervention. It needs to be also noted that this meta-analysis includes two older studies in which PCI involved balloon-only angioplasty (without stent placement) [26,27] and without the use of newer antiplatelet therapies such as glycoprotein IIb/IIIa inhibitors, along with as newer studies where these therapies were utilized. Evidence shows that the use of stents along with adjuvant anti-platelet therapy such as the glycoprotein IIb/IIIa inhibitors at the time of primary PCI following AMI leads to improved morbidity and mortality [37–39]. The result of including older studies could potentially serve to underestimate the positive effect of the current standard of care in PCI.

In terms of methodology, the meta-analysis is potentially limited by several factors. First, only five of the many screened studies had available baseline and follow up LVEF data. Second, paired LVEF data were only available in three of the five studies [8,25,26]. Third, the difference in techniques used to measure LVEF, with some studies using left-ventriculography [8,24,27], one using cardiac MRI [25], and one study using a combination of radionuclide scans and left-ventriculography [26]. Nevertheless, our assessment was based on the relative change in LVEF over time, rather than absolute values of LVEF, which would be more dependent on the technique used. Figure 2 shows that the trend towards a greater improvement LVEF with PCI was evident in all studies. One study [25] did not specifically state whether the investigators measuring LVEF were blinded to randomization, leading to potential bias in that study. Differences in inclusion and exclusion criteria must also be considered when interpreting these data. Therapy prior to randomization also differed between studies in some instances. In the TOMIIS study [26] patients were excluded if they had received thrombolytic therapy prior to randomization. There is also considerable variability in time to randomization from onset of symptoms between the studies, with median time from symptom onset to randomization ranging from 5 to 12 days, with the earliest time of enrollment in most studies being >3 days following MI. We have deliberately excluded studies enrolling patients treated within12 hr of symptom onset, to reduce the possibility that limitation of infarct size would be a confounding factor. No data were available for treatment between 12 and 72 hr since the only randomized controlled trial enrolling these patients (BRAVE-2) [21], while showing a clinical benefit associated with PCI, did not provide data on cardiac function.

The finding of a statistically significant improvement in LVEF in the absence of a proven survival advantage with PCI, as demonstrated in the recent OAT study is an important finding that requires careful analysis. Ejection fraction following MI is known to be an independent predictor of survival following MI [40,41].

The lack of a survival advantage despite improved LVEF in this setting would seem counterintuitive and suggests that one or more competing adverse events are negating the beneficial effect on remodeling in this group of patients. The OAT study showed an excess of recurrent AMI after PCI, which may, at least in part, explain the lack of clinical benefit. However, there is some debate on whether the OAT study is representative of real life treatment scenarios [42]. Recruitment in the study was indeed difficult and interrupted early. Only 2 patients per year per center were enrolled on average representing a very small minority of patients [5,6,42] Moreover, real long-term follow up data of the OAT study are still lacking. Only 44% of patients had a follow-up that extended more than 2 years, and survival curves at 4 years were constructed using estimates, which may have overestimated event rate in the intervention arm due to early attrition and underestimated late effects of intervention which may become apparent only several years later [6,42].

The exclusion of the TOAT study also deserves specific discussion [22]. The TOAT study [22] is a randomized trial including 66 patients randomized to late revascularization of the IRA (mean time after MI 26 days) or medical therapy alone. Patients enrolled in the TOAT underwent a first assessment of cardiac function 6 weeks after AMI ($\sim$2 weeks after randomization), and a second assessment at 12 months. No effects of PCI on LVEF were found and, actually, a less favorable remodeling pattern in patients undergoing PCI was found, which was, however, at odds with the improved functional capacity and quality of life in patients undergoing PCI [22]. The reasons why no changes in LVEF were found in the TOAT study are unclear. Lack of true baseline data may be associated with undisclosed differences in baseline characteristics. A potential difference in the LVEF recovery between the 2 groups occurring early and before the 6-week assessment is also possible. On the hand, the difference may depend on the time from AMI to PCI which was substantially longer in the TOAT [22].

By showing an overall beneficial impact on accepted surrogate endpoints such as left ventricular size and function, this meta-analysis confirms the potential benefits described in the "open artery hypothesis." While current evidence from randomized trials has not shown any advantage in survival or any other "hard" endpoint for PCI overall, it is possible that there may be settings or subgroups of patients in which benefit from reperfusion may outweigh risks of the procedure. Selection of the patients more likely to benefit from late PCI is clinically challenging but necessary. Patients with evidence of myocardial viability as determined by objective viability scans following an MI may preferentially benefit from reperfusion [20]. On the other hand, it is necessary to identify the reasons why such beneficial effects in function and remodeling are not translated in clinical benefits, and further studies may be needed. The OAT trial [6] showed a tendency towards more frequent recurrent AMI in the PCI group. This illustrates the inherent limitations and long-term complications of PCI as a means of achieving sustained reperfusion, and highlights the need for further refinement in stent technology and other novel agents designed to improve the longevity of IRA patency following stent placement.

CONCLUSIONS

This review presents a meta-analysis of data from five randomized controlled trials in which patients treated late (>3 days) during the course of AMI were randomized to PCI of the totally occluded IRA versus conservative management and shows a statistically significant improvement in cardiac function and a reduction in adverse remodeling, as measured by LVEF, LVEDVI, and LVESVI, supporting the pathophysiologic value of the "open artery hypothesis." These favorable changes did not translate in a clinically relevant benefit in the largest clinical trial specifically addressing this question [6]. In conclusion while treatment of the IRA in case of a subtotal occlusion and/or evidence of ischemia/viability appears to be warranted according to two independent RCTs [7,9] and a recent meta-analysis [10], the translation of changes in cardiac remodeling and function to clinical endpoints in the setting of total IRA occlusions is not established.

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