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ABSTRACTS OF THE 10TH INDONESIAN SOCIETY OF INTERVENTIONAL CARDIOLOGY ANNUAL MEETING JAKARTA, 23-25 NOVEMBER 2018

SYSTEMATIC REVIEWS AND META-ANALYSES

THE DIFFERENCES BETWEEN ORAL VITAMIN C AND IV VITAMIN C IN CORONARY HEART DISEASE : A REVIEW LITERATURE

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Background: Some studies have shown that low level of vitamin C has a role on developing coronary heart disease. Chronic insufficiency of vitamin C lead the damage of blood vessel. This damage triggers some biological repair process in which cholesterol-carrying lipoproteins deposit in the arterial wall, lead up atherosclerosis, changes the cells of the artery wall and blood components.The change makes increasing oxidative stress substances, *Reactive Oxygen Species* (ROS), and *Nitric Oxide* (NO) making endothelial dysfunction, plug rupture and becoming acute myocardial infarct.

Objective: This study aims to review the different benefit effect of oral vitamin C and IV vitamin C in coronary heart disease.

Material and methods: Authors were using literature review**.** Published papers from 20 studied were identified for the review based on like PubMed, Cochrane, Google Scholar, Medline. Keyword were “vitamin C” and “coronary” and “cardiovascular”. This method will bring a new knowledge about vitamin C treatment in coronary heart disease.

Result(s): High plasma level vitamin C limiting generation of ROS, and repairing other oxidized scavengers and modulating numerous enzyme reactions, but can also act as a direct radical scavengers. In addition, vitamin C maintain NO mediated endothelial integrity and vasomotor control of coronary vessels. From 5 studies, oral vitamin C shown that no effect for improving outcome coronary heart disease and 2 studies intravenous vitamin C have shown improving myocardial injury on coronary heart disease who undergoing elective PCI.

Conclusion: Intravenous Vitamin C has better result than oral Vitamin C for coronary heart disease. It is reducing micro reperfusion injury on coronary heart disease patient who undergoing elective PCI.

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WHICH ANTITHROMBOTIC(S) SHOULD BE GIVEN TO PATIENT UNDERGOING TRANSCATHETER AORTIC VALVE REPLACEMENT? - A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction

Dual antiplatelet therapy (DAPT) has been used widely in patients undergoing transcatheter aortic valve replacement (TAVR) with uncertain clinical evidence. The aim of this study is to compare the efficacy and safety of DAPT, single antiplatelet therapy (SAPT) with or without oral anticoagulant (OAC).

Methods

Electronic search on PubMed (MEDLINE), EBSCO, EuropePMC, Cochrane Central Database, Clinicaltrials.gov, and Google Scholar was done. Studies comparing the use of DAPT or SAPT with/without OAC in patients undergoing TAVR was included. Meta-analysis directly compared the outcome of DAPT vs SAPT + OAC, DAPT vs SAPT, and indirectly compared SAPT vs SAPT + OAC. There were 13 studies included.

Results

A total of 4 studies (931 patients) that compared DAPT and SAPT + OAC were included. There was no significant difference in mortality, stroke/TIA, and bleeding rate between these groups. An analysis of 5-7 studies (752-1301 patients) comparing DAPT and SAPT yield a non-significant outcome in terms of 30-days all-cause mortality, all-cause mortality, stroke/TIA, and myocardial infarction. However, life-threatening/major bleeding was significantly higher in those who took DAPT [RR = 1.98, 95% CI 1.13-3.45, p=0.02 albeit high heterogeneity] number needed to harm for major/life-threatening bleeding was 12.5. On indirect analysis comparing SAPT vs SAPT + OAC, there was no significant difference in mortality, stroke/TIA, and major bleeding.

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Conclusion

Mortality, stroke/TIA, and myocardial infarction were statistically not significant between groups. However, the number of major/life-threatening bleeding was highest in DAPT. Since DAPT or OAC did not have better efficacy and SAPT having an edge in safety, the latter may suffice in patients undergoing TAVR.

Figure 1. Meta-analysis of all-cause mortality. Comparator: DAPT vs SAPT + OAC

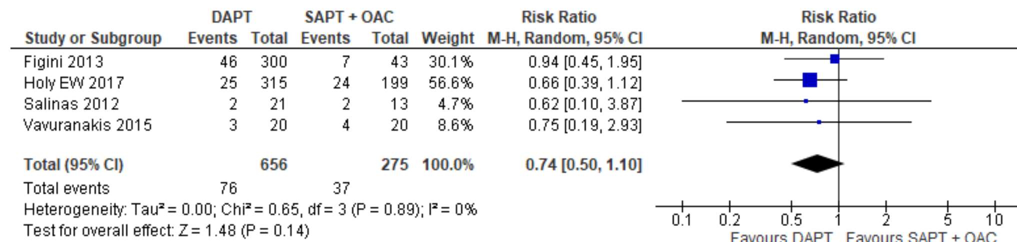

Figure 2. Meta-analysis of Major Bleeding. Comparator: DAPT vs SAPT + OAC

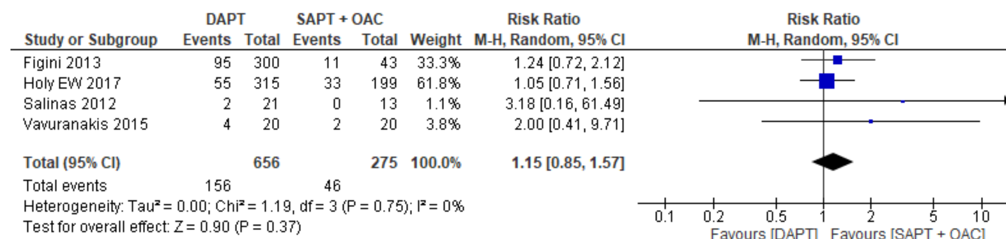

Figure 3. Meta-analysis of all-cause mortality. Comparator: DAPT vs SAPT

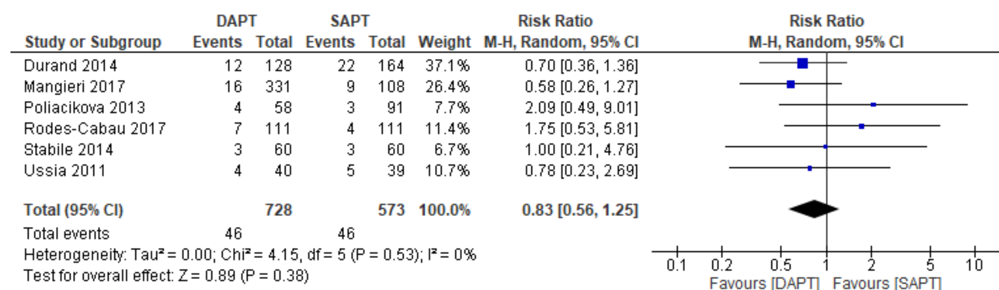

Figure 4. Meta-analysis of Stroke/TIA. Comparator: DAPT vs SAPT

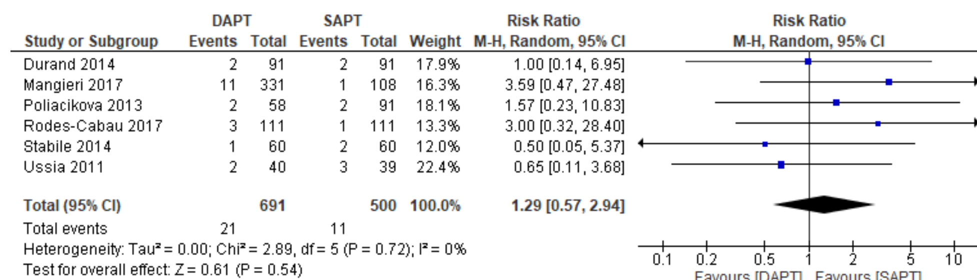

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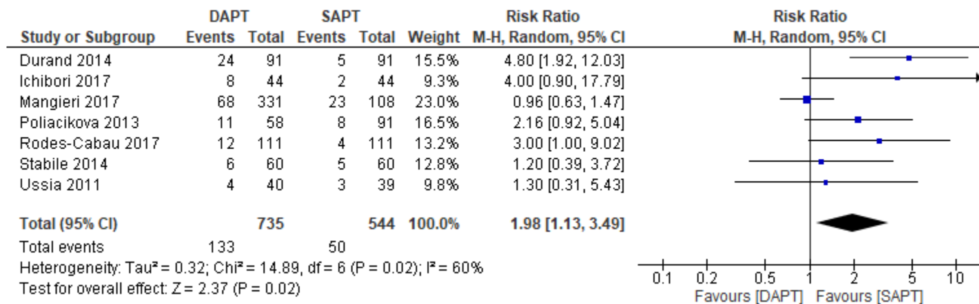
Figure 5. Meta-analysis of major/life-threatening bleeding events. Comparator: DAPT vs SAPT



Study or Subgroup	DAPT Events	DAPT Total	SAPT Events	SAPT Total	Weight	Risk Ratio M-H, Random, 95% CI
Durand 2014	24	91	5	91	15.5%	4.80 [1.92, 12.03]
Ichibori 2017	8	44	2	44	9.3%	4.00 [0.90, 17.79]
Mangieri 2017	68	331	23	108	23.0%	0.96 [0.63, 1.47]
Poliacikova 2013	11	58	8	91	16.5%	2.16 [0.92, 5.04]
Rodes-Cabau 2017	12	111	4	111	13.2%	3.00 [1.00, 9.02]
Stabile 2014	6	60	5	60	12.8%	1.20 [0.39, 3.72]
Ussia 2011	4	40	3	39	9.8%	1.30 [0.31, 5.43]
Total (95% CI)		**735**		**544**	**100.0%**	**1.98 [1.13, 3.49]**
Total events	133		50			

Heterogeneity: Tau² = 0.32; Chi² = 14.89, df = 6 (P = 0.02); I² = 60%
Test for overall effect: Z = 2.37 (P = 0.02)

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PERCUTANEOUS CORONARY INTERVENTION VS CORONARY ARTERY BYPASS GRAFTING IN UNPROTECTED LEFT MAIN ARTERY DISEASE - SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED CONTROLLED TRIAL

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Introduction

Percutaneous coronary intervention (PCI) emerges as a less invasive alternative to the routinely done coronary artery bypass grafting (CABG) for management of unprotected left main coronary artery (ULMCA) disease. This meta-analysis aimed to compare the efficacy of PCI and CABG in the management of ULMCA disease.

Methods

Electronic search on PubMed (MEDLINE), EBSCO, EuropePMC, Cochrane Central Database, Clinicaltrials.gov, and Google Scholar was done. Randomized controlled trials comparing the use of PCI or CABG in patients with ULMCA stenosis were included. Meta-analysis was done to compare the outcome of PCI and CABG. There were 6 studies included. 5 studies exclusively used Drug-Eluting Stent (DES) and 1 study used both Bare Metal Stent (BMS) and DES. The primary outcome of interest was all-cause mortality and secondary was CV death, MACE, myocardial infarction (MI), stroke, and repeat revascularization.

Results

There were a total of 4688 participants from 6 studies. PCI of ULMCA was associated with similar all-cause mortality, CV death, 1-year MACE, MI, and stroke. However, PCI had a higher rate of repeat revascularization [OR 1.78; 95% CI 1.48-2.15; p<0.001] and 3-5-year MACE [OR 1.40; 95% CI 1.21-1.62; p<0.001]. After ousting 1 study that used a mixture of BMS and DES, the result is still significant for repeat revascularization [OR 1.85; 95% CI 1.53-2.23; p<0.001] and 3-5-year MACE [OR 1.40; 95% CI 1.21-1.62; p<0.001].

Conclusion

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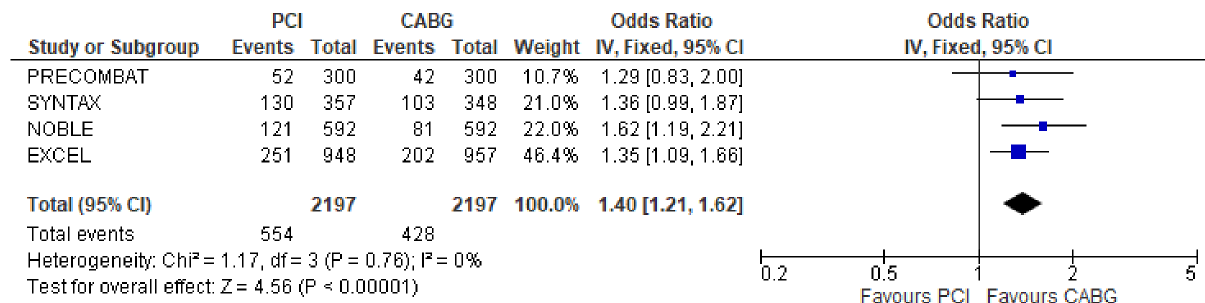
Coronary artery bypass graft still upholds the advantage over PCI in ULMCA revascularization. However, PCI is non-inferior in terms of all-cause mortality, CV death, 1-year MACE, MI, and stroke. Percutaneous coronary intervention can be considered as an acceptable option in inoperable patients.

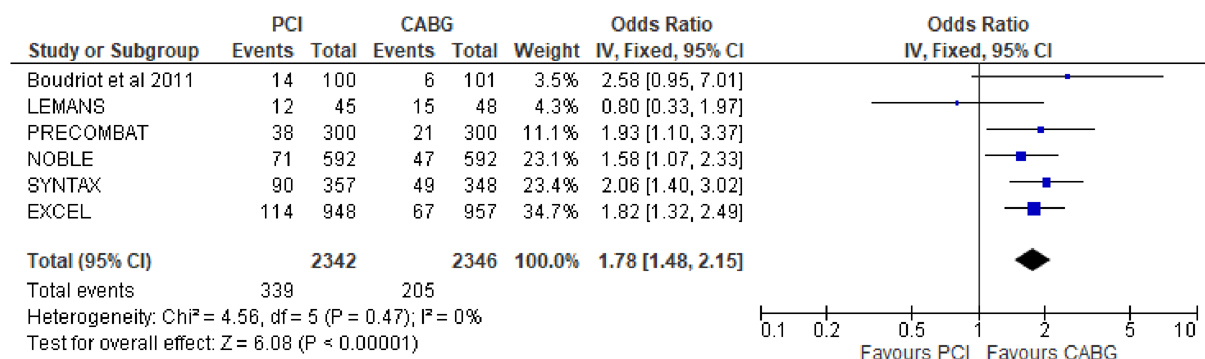
Figure 1. Meta-analysis of 3-5 years Major Adverse Cardiovascular Events. Comparator: PCI vs CABG



Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Odds Ratio IV, Fixed, 95% CI
PRECOMBAT	52	300	42	300	10.7%	1.29 [0.83, 2.00]
SYNTAX	130	357	103	348	21.0%	1.36 [0.99, 1.87]
NOBLE	121	592	81	592	22.0%	1.62 [1.19, 2.21]
EXCEL	251	948	202	957	46.4%	1.35 [1.09, 1.66]
Total (95% CI)		**2197**		**2197**	**100.0%**	**1.40 [1.21, 1.62]**
Total events	554		428			

Heterogeneity: Chi² = 1.17, df = 3 (P = 0.76); I² = 0%
Test for overall effect: Z = 4.56 (P < 0.00001)

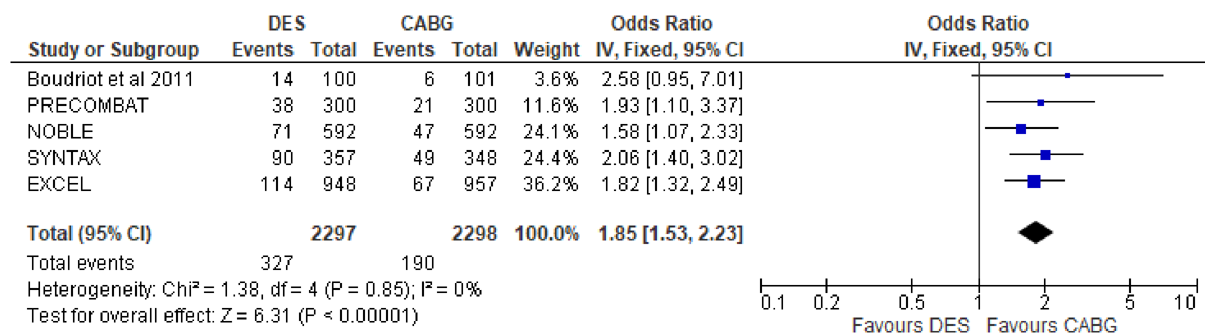
Figure 2. Meta-analysis of Repeat Revascularization. Comparator: PCI vs CABG



Study or Subgroup	PCI Events	PCI Total	CABG Events	CABG Total	Weight	Odds Ratio IV, Fixed, 95% CI
Boudriot et al 2011	14	100	6	101	3.5%	2.58 [0.95, 7.01]
LEMANS	12	45	15	48	4.3%	0.80 [0.33, 1.97]
PRECOMBAT	38	300	21	300	11.1%	1.93 [1.10, 3.37]
NOBLE	71	592	47	592	23.1%	1.58 [1.07, 2.33]
SYNTAX	90	357	49	348	23.4%	2.06 [1.40, 3.02]
EXCEL	114	948	67	957	34.7%	1.82 [1.32, 2.49]
Total (95% CI)		**2342**		**2346**	**100.0%**	**1.78 [1.48, 2.15]**
Total events	339		205			

Heterogeneity: Chi² = 4.56, df = 5 (P = 0.47); I² = 0%
Test for overall effect: Z = 6.08 (P < 0.00001)

Figure 3. Meta-analysis of Repeat Revascularization. Comparator: DES vs CABG



Study or Subgroup	DES Events	DES Total	CABG Events	CABG Total	Weight	Odds Ratio IV, Fixed, 95% CI
Boudriot et al 2011	14	100	6	101	3.6%	2.58 [0.95, 7.01]
PRECOMBAT	38	300	21	300	11.6%	1.93 [1.10, 3.37]
NOBLE	71	592	47	592	24.1%	1.58 [1.07, 2.33]
SYNTAX	90	357	49	348	24.4%	2.06 [1.40, 3.02]
EXCEL	114	948	67	957	36.2%	1.82 [1.32, 2.49]
Total (95% CI)		**2297**		**2298**	**100.0%**	**1.85 [1.53, 2.23]**
Total events	327		190			

Heterogeneity: Chi² = 1.38, df = 4 (P = 0.85); I² = 0%
Test for overall effect: Z = 6.31 (P < 0.00001)

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IS FOLATE BENEFICIAL OR HARMFUL IN POST-PERCUTANEOUS CORONARY INTERVENTION PATIENTS? - A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

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Introduction

Elevated homocysteine level was found to be an independent predictor of cardiovascular and all-cause mortality. Folic acid was shown to be able to reduce the homocysteine level. However, folic acid/folate was found to induce restenosis in post-percutaneous coronary intervention (PCI) patients according to one double-blind randomized controlled trial (RCT). Our aim is to investigate whether folate is harmful in post-PCI patients.

Methods

Search on [(folate) OR (folic acid) AND (restenosis)] and its synonyms were conducted through PubMed, EuropePMC, EBSCOhost and snowballing. The primary outcome was restenosis. Two authors independently extracted and assessed the risk of bias. Only double-blind RCT in the English language were included. A total of 242 results were found, 4 were relevant titles/abstract. 4 studies were included. We used the Inverse Variance method with a fixed-effect model for meta-analysis.

Results

There were a total of 1594 post-PCI patients from 4 double-blind RCT.[3-6] Three studies that measured homocysteine levels demonstrated a significant reduction in homocysteine levels at follow-up. The results on minimal lumen diameter (MLD) was conflicting in two studies. Folate regimen caused restenosis in a study involving 636 patients but other studies showed either reduction or no effect on restenosis. One of the studies that showed no effect on restenosis used a folate only regiment without pyridoxine/B6/B12. Target vessel revascularization (TVR) was not significant in one study, reduced in two, and increased in a study (however, 95% CI of RR crossed 1). MACE was reduced in two studies and increased in one. A meta-analysis was done the only outcome affected was homocysteine level despite high heterogeneity level (MD -3.07 [-3.45 to -

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2.69]; I^2= 91%; p <0.001). There was no significant effect on MLD, restenosis, TVR, MACE, or death.

Conclusion

This study showed that folate regiment can reduce homocysteine level significantly. However, the successful reduction in homocysteine through folate regiment translate to neither clinically beneficial nor harmful outcome.

Figure 1. Effect of folate on homocysteine levels

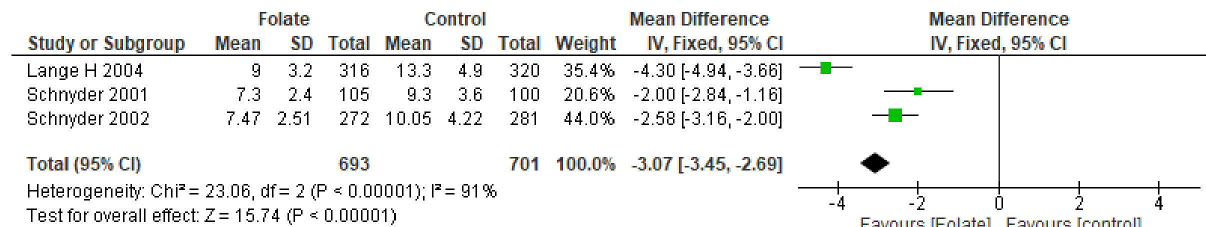

Figure 2. Effect of folate on minimal lumen diameter

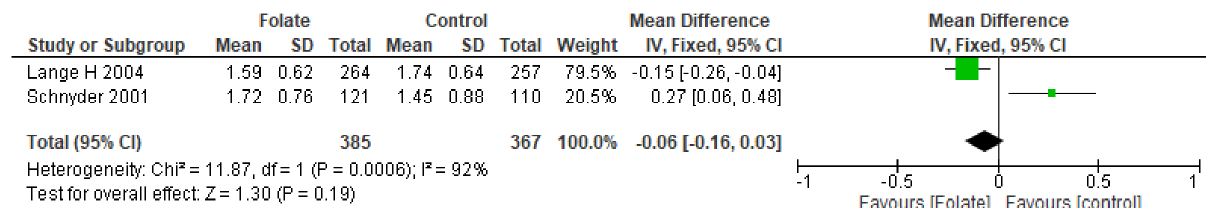

Figure 3. Effect of folate on restenosis

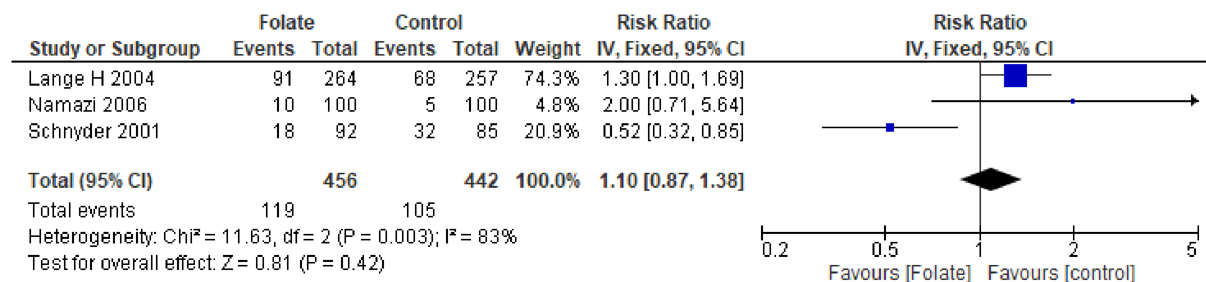

Figure 4. Effect of folate on target-vessel revascularization

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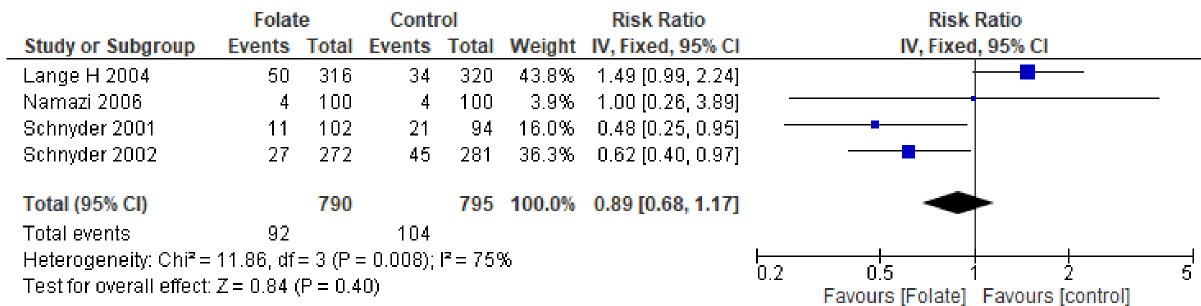
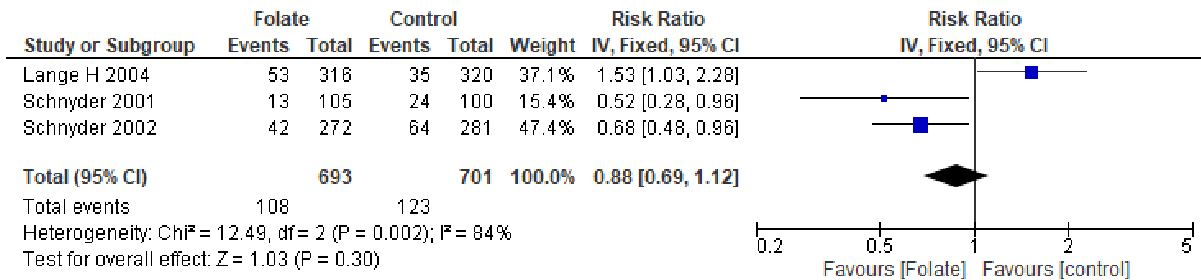


Study or Subgroup	Folate Events	Folate Total	Control Events	Control Total	Weight	Risk Ratio IV, Fixed, 95% CI
Lange H 2004	50	316	34	320	43.8%	1.49 [0.99, 2.24]
Namazi 2006	4	100	4	100	3.9%	1.00 [0.26, 3.89]
Schnyder 2001	11	102	21	94	16.0%	0.48 [0.25, 0.95]
Schnyder 2002	27	272	45	281	36.3%	0.62 [0.40, 0.97]
Total (95% CI)		**790**		**795**	**100.0%**	**0.89 [0.68, 1.17]**
Total events	92		104			

Heterogeneity: Chi² = 11.86, df = 3 (P = 0.008); I² = 75%
Test for overall effect: Z = 0.84 (P = 0.40)

Figure 5. Effect of folate on major adverse cardiac events



Study or Subgroup	Folate Events	Folate Total	Control Events	Control Total	Weight	Risk Ratio IV, Fixed, 95% CI
Lange H 2004	53	316	35	320	37.1%	1.53 [1.03, 2.28]
Schnyder 2001	13	105	24	100	15.4%	0.52 [0.28, 0.96]
Schnyder 2002	42	272	64	281	47.4%	0.68 [0.48, 0.96]
Total (95% CI)		**693**		**701**	**100.0%**	**0.88 [0.69, 1.12]**
Total events	108		123			

Heterogeneity: Chi² = 12.49, df = 2 (P = 0.002); I² = 84%
Test for overall effect: Z = 1.03 (P = 0.30)

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EFFICACY OF PHARMACOLOGICAL THERAPIES FOR MYOCARDIAL ISCHEMIA/REPERFUSION INJURY: A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED CLINICAL TRIALS

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Objective. Aim of this study is to compare the efficacy of various pharmacological therapies (drugs targeting nitric oxide/cyclic guanosine monophosphate signaling pathway; drugs targeting mitochondrial function; drugs with indirect or unspecified target) in patients with STEMI undergoing PCI. The primary outcome is cardiovascular mortality, and the secondary outcomes are left ventricular ejection fraction, recurrent myocardial infarction, hospital readmission for heart failure and all-cause mortality.

Methods. We performed a meta-analysis according to PRISMA guideline. Articles were searched in following databases: PubMed, EMBASE, Web of Science, and Google Scholar. Using random-effects meta-regression model, data was pooled to determine relative risk (RR) of primary and secondary outcomes. The meta-analysis was conducted using RevMan v.5.3 software.

Result. Total of 28 trials, comprising of 7,173 patients, met our inclusion criteria. Our pooled analysis showed that the pharmacological therapies were associated with significant reduction in cardiovascular mortality and recurrent MI (RR 0.80, 95%CI 0.65-0.99 and RR 0.62, 95%CI 0.42-0.90, respectively). Pharmacological therapies were not associated with significant improvement of LVEF (MD 0.62, 95%CI: -0.16-1.40), reduction in hospital readmission for HF (RR 0.89, 95%CI: 0.76-1.06), and all-cause mortality (RR 1.02, 95%CI 0.77-1.36). After subgroup analysis according to each drugs' mechanism of action, only drugs targeting NO/cGMP signaling pathway showed consistent results in reducing cardiovascular mortality and recurrent MI (RR 0.75, 95%CI: 0.57-0.97 and RR 0.56, 95%CI: 0.33-0.96, respectively). Subgroup analysis for drugs with indirect or unspecified target also showed significant improvement of LVEF and reduction in hospital readmission for HF (MD 1.40, 95%CI: 0.09-2.71 and RR 0.89, 95%CI: 0.28-0.84, respectively).

Conclusion. Administration of drugs targeting NO/cGMP signaling pathway in STEMI patients undergoing primary PCI appear to have effect on reducing cardiovascular mortality and recurrent MI. The drugs with a broad-spectrum mechanism of action seem to be more effective in increasing LVEF and reducing hospital readmission for HF.

Keywords: myocardial infarction; percutaneous coronary intervention; reperfusion injury

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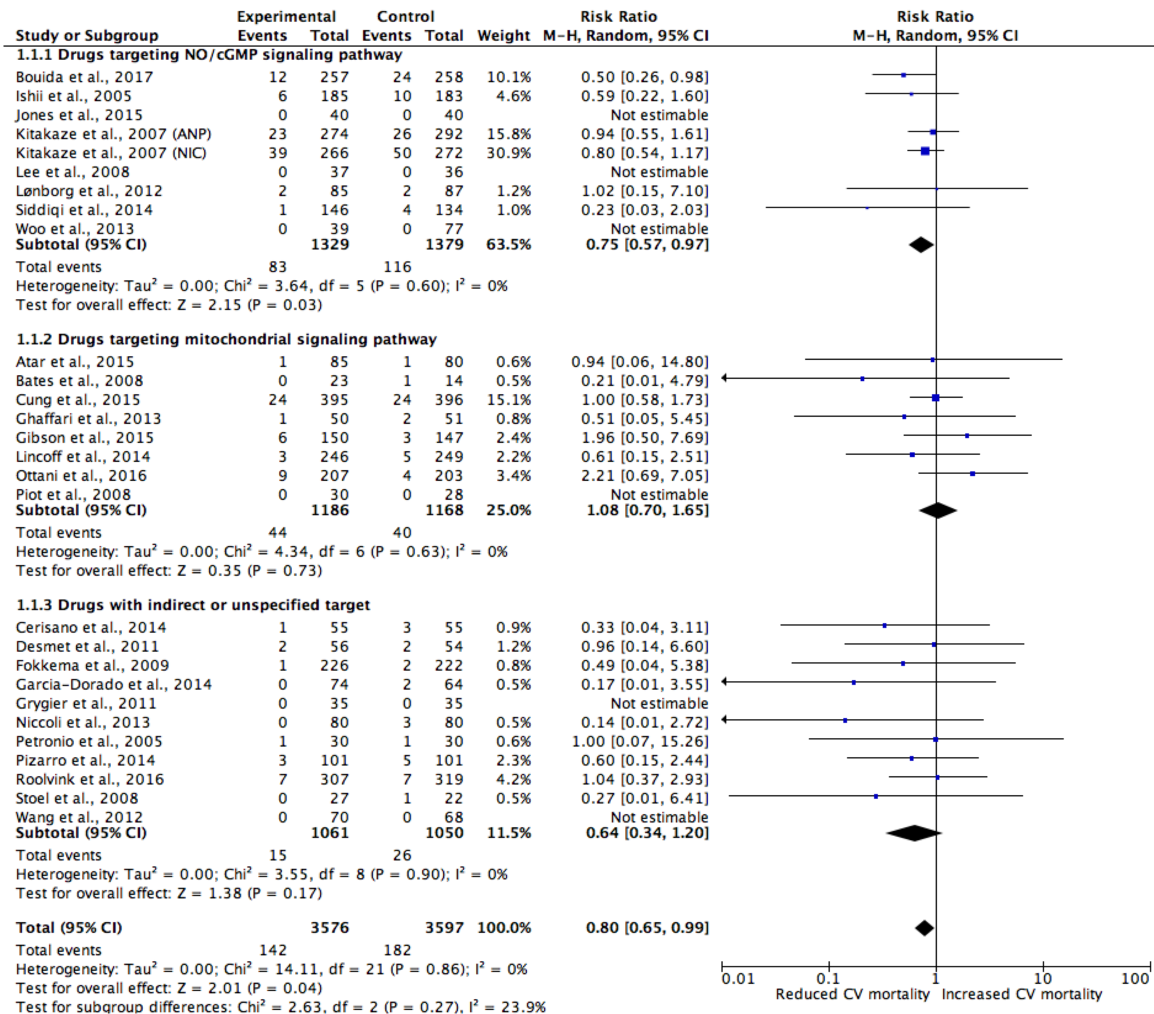

Fig. 1 Forest Plot for Cardiovascular Mortality

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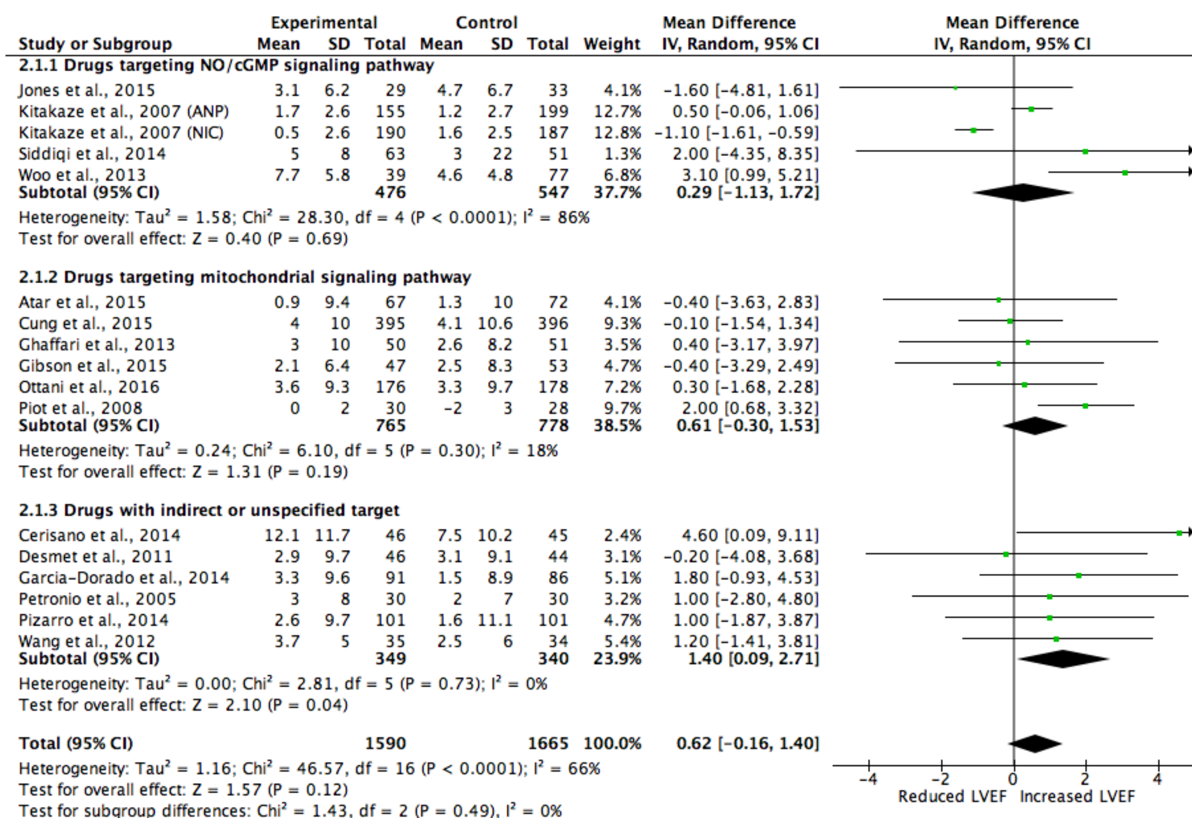

Study or Subgroup	Experimental Mean	Experimental SD	Experimental Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Random, 95% CI
2.1.1 Drugs targeting NO/cGMP signaling pathway								
Jones et al., 2015	3.1	6.2	29	4.7	6.7	33	4.1%	-1.60 [-4.81, 1.61]
Kitakaze et al., 2007 (ANP)	1.7	2.6	155	1.2	2.7	199	12.7%	0.50 [-0.06, 1.06]
Kitakaze et al., 2007 (NIC)	0.5	2.6	190	1.6	2.5	187	12.8%	-1.10 [-1.61, -0.59]
Siddiqi et al., 2014	5	8	63	3	22	51	1.3%	2.00 [-4.35, 8.35]
Woo et al., 2013	7.7	5.8	39	4.6	4.8	77	6.8%	3.10 [0.99, 5.21]
Subtotal (95% CI)			**476**			**547**	**37.7%**	**0.29 [-1.13, 1.72]**
Heterogeneity: Tau² = 1.58; Chi² = 28.30, df = 4 (P < 0.0001); I² = 86%								
Test for overall effect: Z = 0.40 (P = 0.69)								
2.1.2 Drugs targeting mitochondrial signaling pathway								
Atar et al., 2015	0.9	9.4	67	1.3	10	72	4.1%	-0.40 [-3.63, 2.83]
Cung et al., 2015	4	10	395	4.1	10.6	396	9.3%	-0.10 [-1.54, 1.34]
Ghaffari et al., 2013	3	10	50	2.6	8.2	51	3.5%	0.40 [-3.17, 3.97]
Gibson et al., 2015	2.1	6.4	47	2.5	8.3	53	4.7%	-0.40 [-3.29, 2.49]
Ottani et al., 2016	3.6	9.3	176	3.3	9.7	178	7.2%	0.30 [-1.68, 2.28]
Piot et al., 2008	0	2	30	-2	3	28	9.7%	2.00 [0.68, 3.32]
Subtotal (95% CI)			**765**			**778**	**38.5%**	**0.61 [-0.30, 1.53]**
Heterogeneity: Tau² = 0.24; Chi² = 6.10, df = 5 (P = 0.30); I² = 18%								
Test for overall effect: Z = 1.31 (P = 0.19)								
2.1.3 Drugs with indirect or unspecified target								
Cerisano et al., 2014	12.1	11.7	46	7.5	10.2	45	2.4%	4.60 [0.09, 9.11]
Desmet et al., 2011	2.9	9.7	46	3.1	9.1	44	3.1%	-0.20 [-4.08, 3.68]
Garcia-Dorado et al., 2014	3.3	9.6	91	1.5	8.9	86	5.1%	1.80 [-0.93, 4.53]
Petronio et al., 2005	3	8	30	2	7	30	3.2%	1.00 [-2.80, 4.80]
Pizarro et al., 2014	2.6	9.7	101	1.6	11.1	101	4.7%	1.00 [-1.87, 3.87]
Wang et al., 2012	3.7	5	35	2.5	6	34	5.4%	1.20 [-1.41, 3.81]
Subtotal (95% CI)			**349**			**340**	**23.9%**	**1.40 [0.09, 2.71]**
Heterogeneity: Tau² = 0.00; Chi² = 2.81, df = 5 (P = 0.73); I² = 0%								
Test for overall effect: Z = 2.10 (P = 0.04)								
Total (95% CI)			**1590**			**1665**	**100.0%**	**0.62 [-0.16, 1.40]**
Heterogeneity: Tau² = 1.16; Chi² = 46.57, df = 16 (P < 0.0001); I² = 66%								
Test for overall effect: Z = 1.57 (P = 0.12)								
Test for subgroup differences: Chi² = 1.43, df = 2 (P = 0.49), I² = 0%								

Fig.2 Forest Plot for Left Ventricular Ejection Fraction (LVEF)

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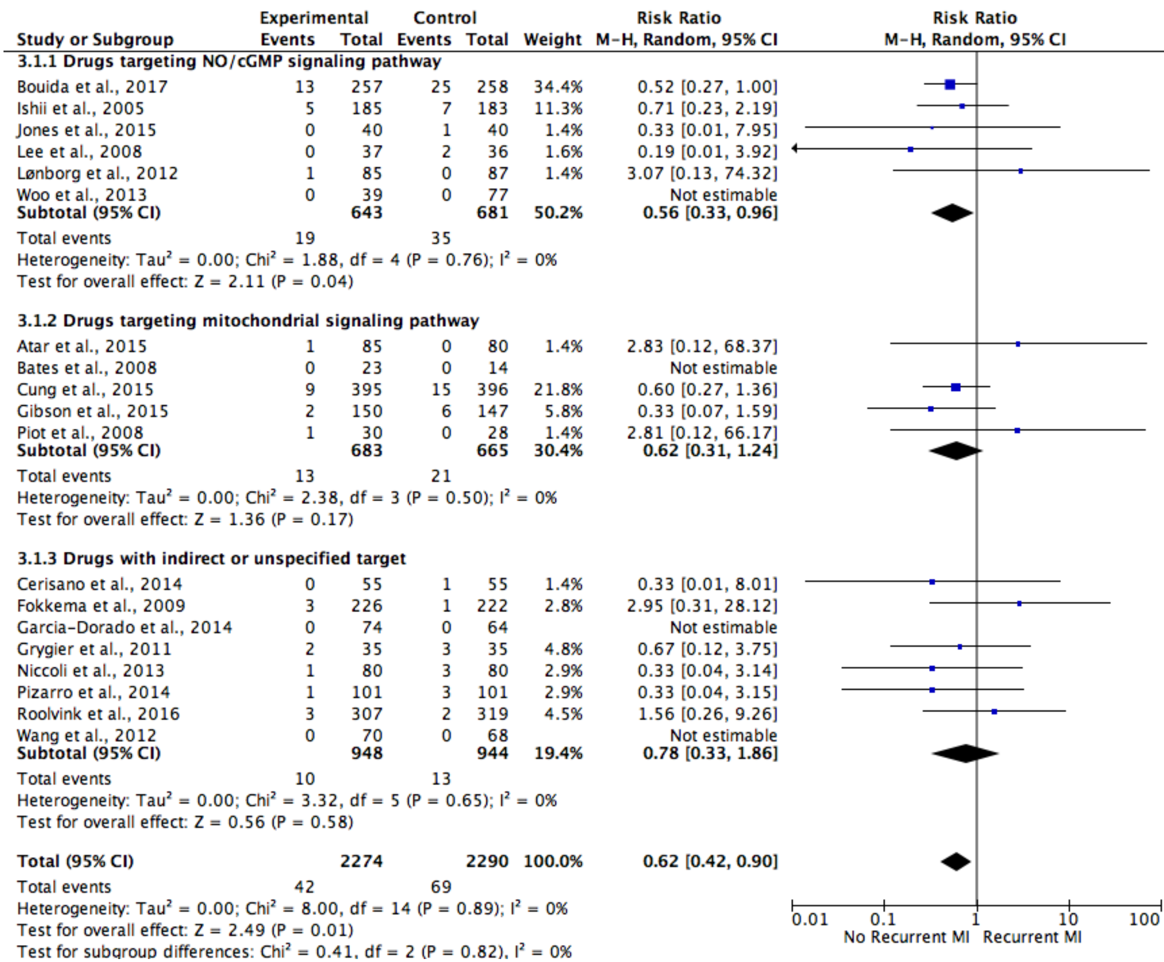

Fig.3 Forest Plot for Recurrent Myocardial Infarction (MI)

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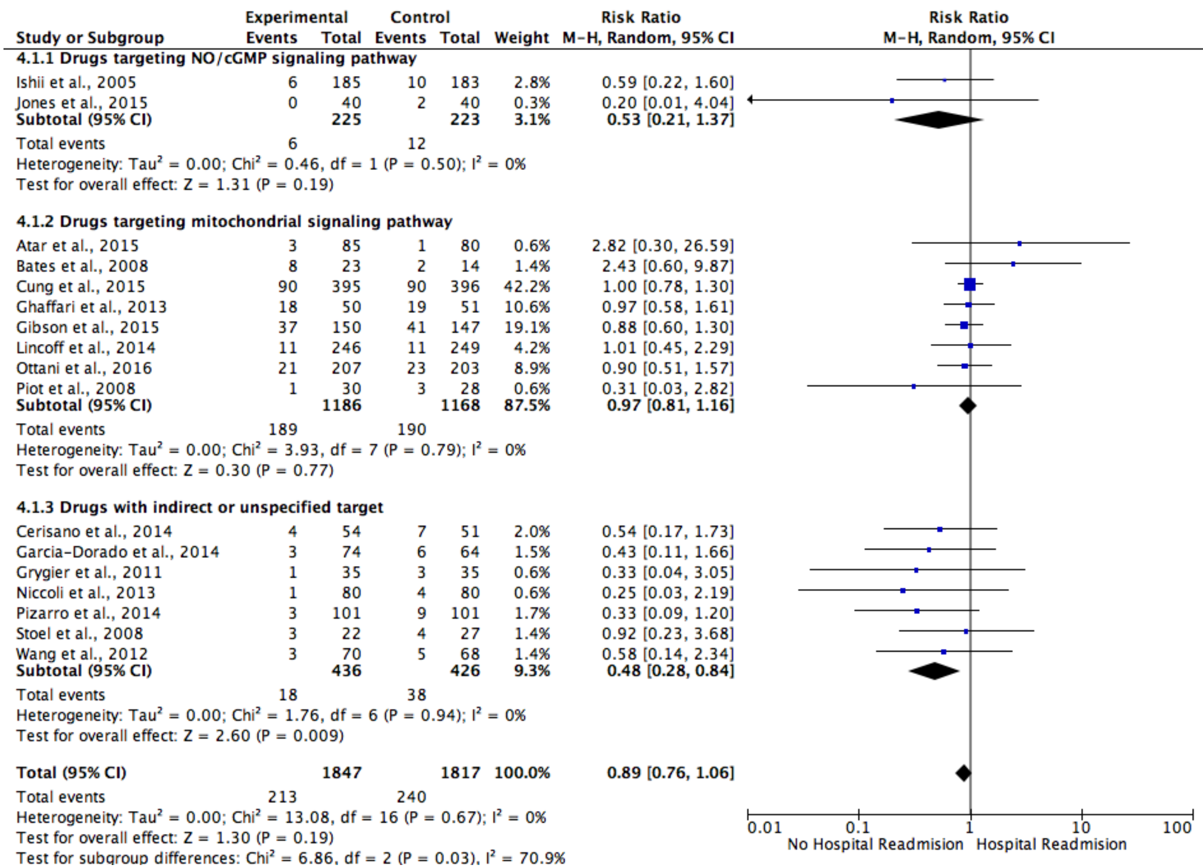

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
4.1.1 Drugs targeting NO/cGMP signaling pathway						
Ishii et al., 2005	6	185	10	183	2.8%	0.59 [0.22, 1.60]
Jones et al., 2015	0	40	2	40	0.3%	0.20 [0.01, 4.04]
Subtotal (95% CI)		**225**		**223**	**3.1%**	**0.53 [0.21, 1.37]**
Total events	6		12			
Heterogeneity: Tau² = 0.00; Chi² = 0.46, df = 1 (P = 0.50); I² = 0%						
Test for overall effect: Z = 1.31 (P = 0.19)						
4.1.2 Drugs targeting mitochondrial signaling pathway						
Atar et al., 2015	3	85	1	80	0.6%	2.82 [0.30, 26.59]
Bates et al., 2008	8	23	2	14	1.4%	2.43 [0.60, 9.87]
Cung et al., 2015	90	395	90	396	42.2%	1.00 [0.78, 1.30]
Ghaffari et al., 2013	18	50	19	51	10.6%	0.97 [0.58, 1.61]
Gibson et al., 2015	37	150	41	147	19.1%	0.88 [0.60, 1.30]
Lincoff et al., 2014	11	246	11	249	4.2%	1.01 [0.45, 2.29]
Ottani et al., 2016	21	207	23	203	8.9%	0.90 [0.51, 1.57]
Piot et al., 2008	1	30	3	28	0.6%	0.31 [0.03, 2.82]
Subtotal (95% CI)		**1186**		**1168**	**87.5%**	**0.97 [0.81, 1.16]**
Total events	189		190			
Heterogeneity: Tau² = 0.00; Chi² = 3.93, df = 7 (P = 0.79); I² = 0%						
Test for overall effect: Z = 0.30 (P = 0.77)						
4.1.3 Drugs with indirect or unspecified target						
Cerisano et al., 2014	4	54	7	51	2.0%	0.54 [0.17, 1.73]
Garcia-Dorado et al., 2014	3	74	6	64	1.5%	0.43 [0.11, 1.66]
Grygier et al., 2011	1	35	3	35	0.6%	0.33 [0.04, 3.05]
Niccoli et al., 2013	1	80	4	80	0.6%	0.25 [0.03, 2.19]
Pizarro et al., 2014	3	101	9	101	1.7%	0.33 [0.09, 1.20]
Stoel et al., 2008	3	22	4	27	1.4%	0.92 [0.23, 3.68]
Wang et al., 2012	3	70	5	68	1.4%	0.58 [0.14, 2.34]
Subtotal (95% CI)		**436**		**426**	**9.3%**	**0.48 [0.28, 0.84]**
Total events	18		38			
Heterogeneity: Tau² = 0.00; Chi² = 1.76, df = 6 (P = 0.94); I² = 0%						
Test for overall effect: Z = 2.60 (P = 0.009)						
Total (95% CI)		**1847**		**1817**	**100.0%**	**0.89 [0.76, 1.06]**
Total events	213		240			
Heterogeneity: Tau² = 0.00; Chi² = 13.08, df = 16 (P = 0.67); I² = 0%						
Test for overall effect: Z = 1.30 (P = 0.19)						
Test for subgroup differences: Chi² = 6.86, df = 2 (P = 0.03), I² = 70.9%						

Fig.4 Forest Plot for Hospital Readmission for Heart Failure (HF)

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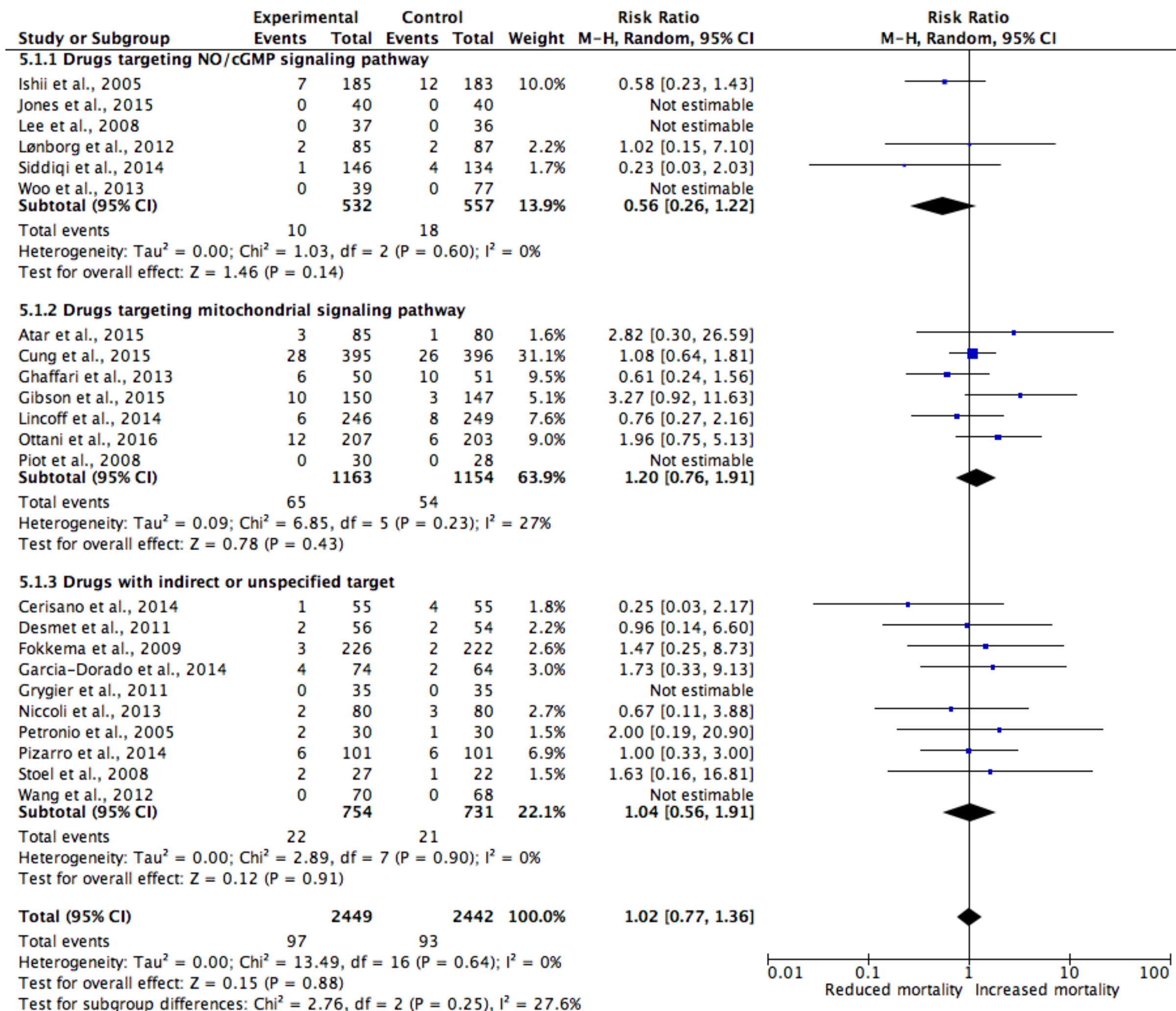

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
5.1.1 Drugs targeting NO/cGMP signaling pathway						
Ishii et al., 2005	7	185	12	183	10.0%	0.58 [0.23, 1.43]
Jones et al., 2015	0	40	0	40		Not estimable
Lee et al., 2008	0	37	0	36		Not estimable
Lønborg et al., 2012	2	85	2	87	2.2%	1.02 [0.15, 7.10]
Siddiqi et al., 2014	1	146	4	134	1.7%	0.23 [0.03, 2.03]
Woo et al., 2013	0	39	0	77		Not estimable
Subtotal (95% CI)		**532**		**557**	**13.9%**	**0.56 [0.26, 1.22]**
Total events	10		18			
Heterogeneity: Tau² = 0.00; Chi² = 1.03, df = 2 (P = 0.60); I² = 0%						
Test for overall effect: Z = 1.46 (P = 0.14)						
5.1.2 Drugs targeting mitochondrial signaling pathway						
Atar et al., 2015	3	85	1	80	1.6%	2.82 [0.30, 26.59]
Cung et al., 2015	28	395	26	396	31.1%	1.08 [0.64, 1.81]
Ghaffari et al., 2013	6	50	10	51	9.5%	0.61 [0.24, 1.56]
Gibson et al., 2015	10	150	3	147	5.1%	3.27 [0.92, 11.63]
Lincoff et al., 2014	6	246	8	249	7.6%	0.76 [0.27, 2.16]
Ottani et al., 2016	12	207	6	203	9.0%	1.96 [0.75, 5.13]
Piot et al., 2008	0	30	0	28		Not estimable
Subtotal (95% CI)		**1163**		**1154**	**63.9%**	**1.20 [0.76, 1.91]**
Total events	65		54			
Heterogeneity: Tau² = 0.09; Chi² = 6.85, df = 5 (P = 0.23); I² = 27%						
Test for overall effect: Z = 0.78 (P = 0.43)						
5.1.3 Drugs with indirect or unspecified target						
Cerisano et al., 2014	1	55	4	55	1.8%	0.25 [0.03, 2.17]
Desmet et al., 2011	2	56	2	54	2.2%	0.96 [0.14, 6.60]
Fokkema et al., 2009	3	226	2	222	2.6%	1.47 [0.25, 8.73]
Garcia-Dorado et al., 2014	4	74	2	64	3.0%	1.73 [0.33, 9.13]
Grygier et al., 2011	0	35	0	35		Not estimable
Niccoli et al., 2013	2	80	3	80	2.7%	0.67 [0.11, 3.88]
Petronio et al., 2005	2	30	1	30	1.5%	2.00 [0.19, 20.90]
Pizarro et al., 2014	6	101	6	101	6.9%	1.00 [0.33, 3.00]
Stoel et al., 2008	2	27	1	22	1.5%	1.63 [0.16, 16.81]
Wang et al., 2012	0	70	0	68		Not estimable
Subtotal (95% CI)		**754**		**731**	**22.1%**	**1.04 [0.56, 1.91]**
Total events	22		21			
Heterogeneity: Tau² = 0.00; Chi² = 2.89, df = 7 (P = 0.90); I² = 0%						
Test for overall effect: Z = 0.12 (P = 0.91)						
Total (95% CI)		**2449**		**2442**	**100.0%**	**1.02 [0.77, 1.36]**
Total events	97		93			
Heterogeneity: Tau² = 0.00; Chi² = 13.49, df = 16 (P = 0.64); I² = 0%						
Test for overall effect: Z = 0.15 (P = 0.88)						
Test for subgroup differences: Chi² = 2.76, df = 2 (P = 0.25), I² = 27.6%						

Fig.5 Forest Plot for All-Cause Mortality

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MICROVASCULAR OBSTRUCTION AND REPERFUSION STRATEGY IN ACUTE ST-ELEVATION MYOCARDIAL INFARCTION: A META-ANALYSIS OF MULTICENTER RANDOMIZED CONTROLLED TRIAL

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Background. Primary percutaneous coronary intervention (PPCI) is the gold standard in restoring reperfusion, but fibrinolysis combined with rescue PCI or routine early PCI strategy, called pharmacoinvasive (PhI) strategy, can be considered when optimal door to needle time is not feasible. Recent meta-analysis showed that PPCI have better outcomes in reduction of thirty-day ischemia incidence and thirty-day re-infarction incidence than PhI strategy. But, in this study, microvascular obstruction (MVO) is not assessed. Microvascular obstruction (MVO) is the major independent predictors of long-term mortality and heart failure in survivors of STEMI.

Objective. To assess the effect of PhI strategy and PPCI reperfusion strategy on MVO in patients with acute STEMI.

Method. We systematically searched Pubmed and Cochrane Database-Registry up to September 2018 for randomized-controlled-trial evaluating the effect of PhI strategy and PPCI reperfusion strategy on MVO in patients with acute STEMI. The primary endpoint was MVO. The secondary endpoints were incidence of heart failure, left ventricular ejection fraction (LVEF), major bleeding, mortality, and re-infarction.

Result. Eight high quality of multicenter RCT (n=2.352 patients) were included. There is no significantly different effect between PhI strategy and PPCI in the incidence of MVO (RR 0.87, 95% CI 0.62 to 1.24), the incidence of heart failure (RR 0.83, 95% CI 0.56 to 1.23), LVEF (MD -2.00, 95% CI -7.78 to 3.77), major non-intracranial bleeding (RR 1.20, 95% CI 0.71 to 2.03), intracranial bleeding (RR 1.85, 95% CI 0.51 to 6.74), and re-infarction (RR 1.81, 95% CI 0.96 to 3.40). But, the PhI strategy have higher incidence of mortality than PPCI (RR 1.54, 95% CI 1.01 to 2.32).

Conclusion. PhI strategy and PPCI had same outcome in the incidence of MVO and other outcomes, except incidence of mortality. PPCI is remain the gold standard in restoring reperfusion in STEMI.

Keywords: Microvascular obstruction, pharmacoinvasive strategy, primary percutaneous coronary intervention, ST-elevation myocardial infarction

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Appendix

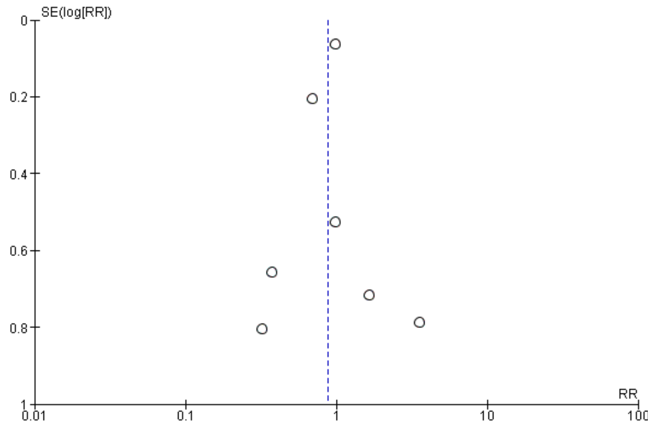

Figure 1. Funnel Plot of Included Studies

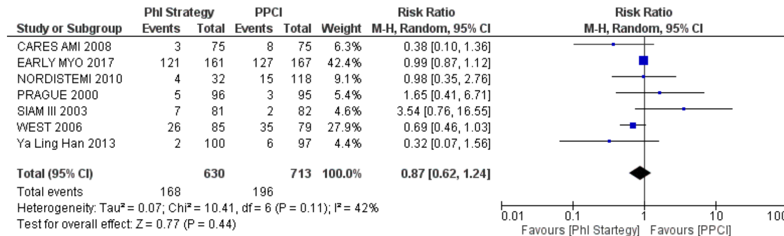

Figure 2. Forrest Plot of Comparison: PhI Strategy vs PPCI, outcome: MVO

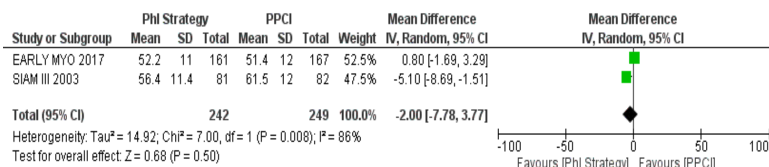

Figure 3. Forrest Plot of Comparison: PhI Strategy vs PPCI, outcome: LVEF

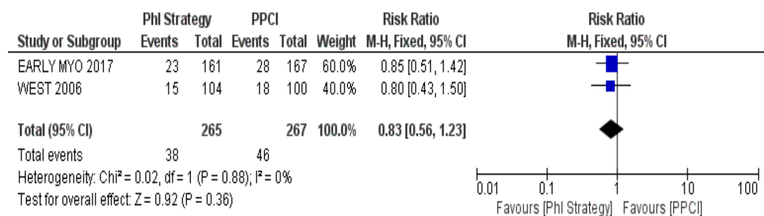

Figure 4. Forrest Plot of Comparison: PhI Strategy vs PPCI, outcome: Heart Failure

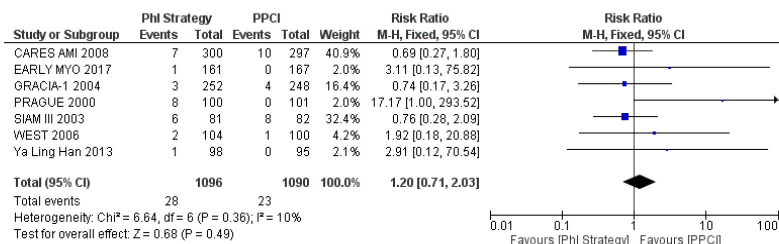

Figure 5. Forrest Plot of Comparison: PhI Strategy vs PPCI, outcome: Major Non-Intracranial Bleeding

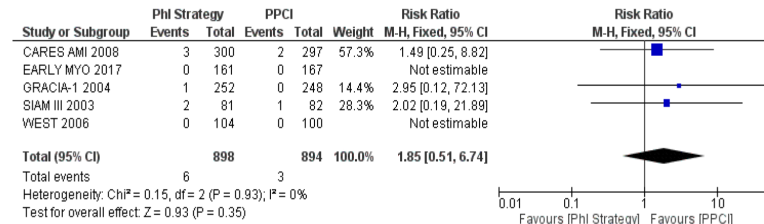

Figure 6. Forrest Plot of Comparison: PhI Strategy vs PPCI, outcome: Intracranial Bleeding

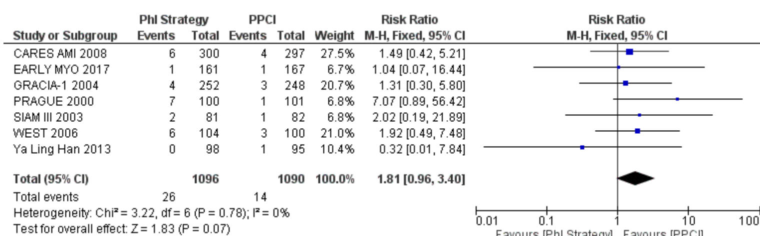

Figure 7. Forrest Plot of Comparison: PhI Strategy vs PPCI, outcome: Re-infarction

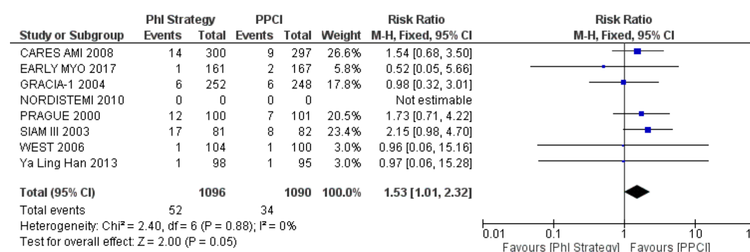

Figure 8. Forrest Plot of Comparison: PhI Strategy vs PPCI, outcome: Mortality