Circulation

RESEARCH LETTER

Prevention of Cardiogenic Shock After Acute Myocardial Infarction

Maarten Vanhaverbeke, MD
Kris Bogaerts, PhD
Peter R. Sinnaeve, MD, PhD
Luc Janssens, MD
Paul W. Armstrong, MD
Frans Van de Werf, MD, PhD

Cardiogenic shock (CGS) after an ST-segment elevation acute myocardial infarction has a poor prognosis. Apart from immediate revascularization, no other treatment has improved outcome. A recent large multicenter registry has convincingly shown that the benefit of primary percutaneous intervention (PPCI) is critically dependent on the elapsed time from first medical contact to balloon inflation. For every 10-minute treatment delay, 3.3 additional deaths per 100 PCI-treated patients occur.[1] These data strongly suggest that urgent recanalization of the culprit vessel resulting in reperfusion of the jeopardized myocardium is currently the key treatment to offer patients in CGS after ST-segment elevation acute myocardial infarction. Recent articles on CGS do not mention the option of immediate administration of a fibrinolytic agent as part of a pharmacoinvasive (PhI) strategy to prevent the development of CGS. We report here the results of a meta-analysis assessing the effect of a PhI strategy as compared to PPCI on the incidence of CGS in ST-segment elevation acute myocardial infarction.

We searched the MEDLINE and EMBASE electronic databases for randomized controlled trials from January 2000 to January 2018, containing the MeSH terms fibrinolytic agent and myocardial infarction. In addition, bibliographies of articles were hand searched to identify additional studies without language restriction. Authors were contacted to obtain additional data. Two investigators assessed the eligibility for inclusion of the studies. We included trials comparing PPCI with a PhI strategy with early coronary angiography in ≥80% of the patients and reporting the incidence of CGS or congestive heart failure (CHF) within 30 days after randomization. Facilitated PCI studies were excluded because this reperfusion strategy has not shown benefit over PPCI. A random effect model was used based on the Mantel–Haenszel method using Review Manager 5.3 (Cochrane Collaboration).

The search strategy resulted in 509 publications, of which 476 were excluded based on title and abstract. Including 2 hand-searched references, 35 studies were evaluated on full text, of which 31 were excluded (study design n=1, facilitated PCI n=10, thrombolysis only or absence of data on invasive management n=14, substudies n=3, no 30-day outcome n=1, no data on CHF or CGS after enquiry n=2). Four studies met the inclusion criteria.[2–5] Study design and baseline characteristics were similar, except for a longer symptom onset to reperfusion interval and an upper age limit of 75 years in EARLY-MYO (Early Routine Catheterization After Alteplase Fibrinolysis Versus Primary PCI in Acute ST-Segment-Elevation Myocardial Infarction).[5] Analytic methods and study materials are available on author request.

Patients randomized to a PhI strategy were significantly more likely to have TIMI 2 to 3 flow before PCI (odds ratio [OR], 7.92; 95% CI, 5.67–11.07; $P<0.001$) without a difference in TIMI 2 to 3 flow after PCI (OR, 0.94; 95% CI, 0.21–4.23; $P=0.93$). Patients randomized to a PhI approach had a significantly lower risk of developing CGS (3.76% versus 5.67%; OR, 0.65; 95% CI, 0.46–0.92; $P=0.02$)

Key Words: cardiogenic shock ■ fibrinolysis ■ pharmaco-invasive treatment ■ primary PCI ■ STEMI

https://www.ahajournals.org/journal/circ

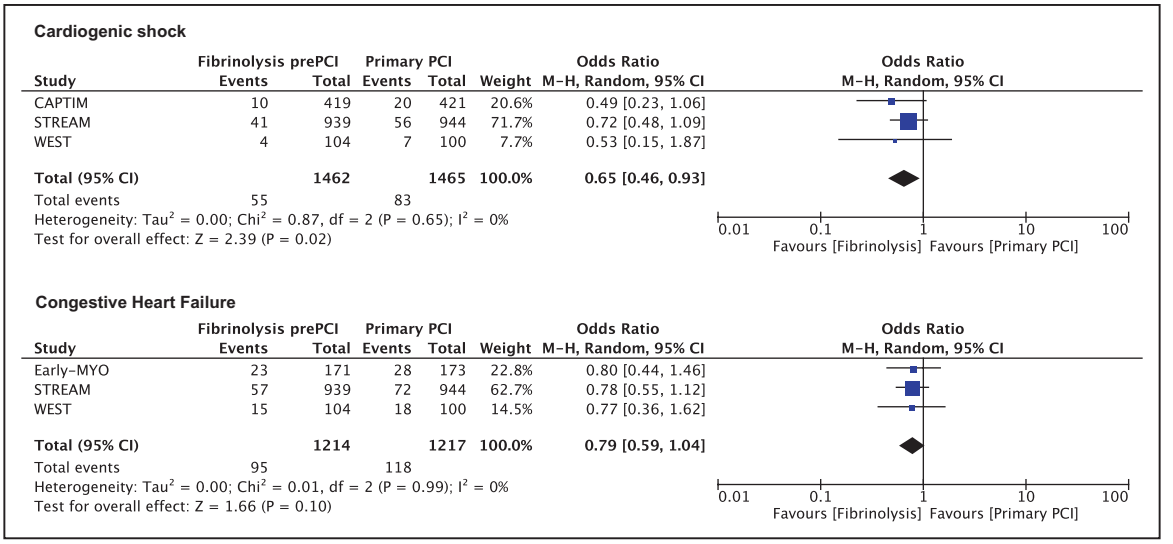

Figure. Comparison of the incidence of cardiogenic shock and congestive heart failure in studies that have compared a pharmacoinvasive treatment (fibrinolysis before PCI) with primary PCI.
PCI indicates percutaneous coronary intervention.

(Figure). There was also a trend toward a reduced incidence of CHF in the PhI group (7.83% versus 9.70%; OR, 0.79; 95% CI, 0.59–1.04; *P*=0.10) (Figure). The risk of intracranial hemorrhage (ICH) was significantly higher in the PhI group (0.68% versus 0.12%; OR, 4.66; 95% CI, 1.18–18.35; *P*=0.02), without a significant difference in major nonintracranial bleeding (3.92% versus 3.30%; OR, 1.01; 95% CI, 0.27–3.47; *P*=0.99) or all-cause death (3.74% versus 3.96%; OR, 0.94; 95% CI, 0.66–1.35; *P*=0.75). When excluding the 379 patients from the STREAM trial (Strategic Reperfusion Early After Myocardial Infarction) before amending the dose of tenecteplase by half in patients ≥75 years of age (because of excess ICH), differences in CGS remained significant (OR, 0.61; 95% CI, 0.42–0.90; *P*=0.01), whereas rates of ICH were reduced (0.42% versus 0.14%) and no longer significantly different (OR, 2.52; 95% CI, 0.57–11.11; *P*=0.22). Faster reperfusion of the jeopardized myocardium in a large proportion of patients in the PhI group seems to be the most likely explanation for the observed lower risk of CGS. The reduced incidence of CHF at 30 days further supports this hypothesis. Better tissue reperfusion, as observed in the EARLY-MYO trial, may also have played a role.[5] ICH is an infrequent but major drawback of fibrinolysis as apparent in this analysis. Reducing the dose of the lytic agent in elderly patients had a positive effect on the risk of ICH in STREAM.[2] Half-dose tenecteplase is now recommended in patients ≥75 years of age.

Our results should be interpreted with caution. The total number of patients is relatively small, and individual patient data were not available. In 3 studies, patients were included only if PPCI within 60 or 90 minutes was unavailable.[3–5] There was no central adjudication of CGS or CHF. Nevertheless, these data suggest that a PhI strategy may help to prevent the development of CGS in patients with ST-segment elevation acute myocardial infarction who cannot get immediate PPCI. This observation is hypothesis-generating and needs validation in a large randomized study. Such a study should randomize patients who are at high risk of developing CGS (eg, based on risk scores) and are unable to get to a PCI hospital, PPCI, or a PhI treatment in time, including a safer fibrinolytic dosing in elderly.

ARTICLE INFORMATION

Data sharing: The analysis will be made available on request.

Correspondence

Frans Van de Werf, MD, PhD, Department of Cardiovascular Sciences, KU Leuven, Herestraat 49, 3000 Leuven, Belgium. Email frans.vandewerf@kuleuven.be

Affiliations

Department of Cardiovascular Sciences (M.V., P.R.S., F.V.d.W.), I-BioStat (K.B.), KU Leuven, Belgium. I-BioStat, UHasselt, Belgium (K.B.). Department of Cardiology, Imelda Hospital, Bonheiden, Belgium (L.J.). Canadian VIGOUR Centre, University of Alberta, Edmonton, Canada (P.W.A.).

Disclosures

Dr Van de Werf has received grants (via institution) from Boehringer Ingelheim, Genentech Inc, and Sanofi. Dr Sinnaeve reports grants (via institution) from Astra-Zeneca, Bayer, Bristol-Myers Squibb, Boehringer Ingelheim, Daiichi Sankyo, and Pfizer. Dr Bogaerts reports receiving consulting fees (via institution) from Boehringer Ingelheim. Dr Armstrong has received grants from Boehringer Ingelheim. The other authors report no conflicts of interest.

REFERENCES

1. Scholz KH, Maier SKG, Maier LS, Lengenfelder B, Jacobshagen C, Jung J, Fleischmann C, Werner GS, Olbrich HG, Ott R, Mudra H, Seidl K, Schulze PC, Weiss C, Haimerl J, Friede T, Meyer T. Impact of treatment delay on mortality in ST-segment elevation myocardial infarction (STEMI) patients presenting with and without haemodynamic instability: results from the German prospective, multicentre FITT-STEMI trial. *Eur Heart J*. 2018;39:1065–1074. doi: 10.1093/eurheartj/ehy004

2. Bonnefoy E, Lapostolle F, Leizorovicz A, Steg G, McFadden EP, Dubien PY, Cattan S, Boullenger E, Machecourt J, Lacroute JM, Cassagnes J, Dissait F, Touboul P; Comparison of Angioplasty and Prehospital Thromboysis in Acute Myocardial Infarction study group. Primary angioplasty versus prehospital fibrinolysis in acute myocardial infarction: a randomised study. *Lancet*. 2002;360:825–829. doi: 10.1016/S0140-6736(02)09963-4
3. Armstrong PW; WEST Steering Committee. A comparison of pharmacologic therapy with/without timely coronary intervention vs. primary percutaneous intervention early after ST-elevation myocardial infarction: the WEST (Which Early ST-elevation myocardial infarction Therapy) study. *Eur Heart J*. 2006;27:1530–1538. doi: 10.1093/eurheartj/ehl088
4. Armstrong PW, Gershlick AH, Goldstein P, Wilcox R, Danays T, Lambert Y, Sulimov V, Rosell Ortiz F, Ostojic M, Welsh RC, Carvalho AC, Nanas J, Arntz HR, Halvorsen S, Huber K, Grajek S, Fresco C, Bluhmki E, Regelin A, Vandenberghe K, Bogaerts K, Van de Werf F; STREAM Investigative Team. Fibrinolysis or primary PCI in ST-segment elevation myocardial infarction. *N Engl J Med*. 2013;368:1379–1387. doi: 10.1056/NEJMoa1301092
5. Pu J, Ding S, Ge H, Han Y, Guo J, Lin R, Su X, Zhang H, Chen L, He B; EARLY-MYO Investigators. Efficacy and safety of a pharmaco-invasive strategy with half-dose alteplase versus primary angioplasty in ST-segment-elevation myocardial infarction: EARLY-MYO Trial (Early Routine Catheterization After Alteplase Fibrinolysis Versus Primary PCI in Acute ST-Segment-Elevation Myocardial Infarction). *Circulation*. 2017;136:1462–1473. doi: 10.1161/CIRCULATIONAHA.117.030582