

OBJECTIVES Oxidative stress plays a key role in the occurrence of vascular endothelial dysfunction (ED) and is a common pathophysiological process of various cardiovascular diseases including atherosclerosis (AS). We aim to investigate the role and mechanism of oxidative stress-induced endothelial CaMKII activation in ED.

METHODS Human umbilical vein endothelial cell (HUVECs) were cultured in vitro and H_2O_2 was used to mimic oxidative stress injury. After treated with KN93 (10 μ M, CaMKII inhibitor), KN92 (10 μ M) and DMSO, the level of ROS, cell viability, migration assay and adhesion assay were performed to assess the function of endothelial cells. The mRNA and protein levels of CaMKII, p-CaMKII, ox-CaMKII, notch1, NF-KB-p65, VCAM1 were detected by RT-qPCR and Western Blot respectively. Finally, ApoE-/- mice with high-fat diet were randomly divided into KN93 (10mg/kg/d, IP), KN92 (10mg/kg/d, IP), DMSO (IP) groups. After 12 weeks, body weight was recorded and the level of serum lipid (including TC, TG, LDL, HDL) was detected. Aortic root was prepared for HE staining and entire aorta for oil red staining.

RESULTS We found that ROS level was increased after H_2O_2 treatment, and KN93 improved the cell viability, migration and adhesion of HUVECs compared with KN92. Meanwhile, we detected the down-regulated mRNA levels of notch1, VCAM1 as well as the protein level of p-CaMKII, ox-CaMKII, notch1, NF-KB-p65, VCAM1 in KN93 group compared with KN92. The r-secretase inhibitor (DAPT), which inhibits notch1, showed no effects on CaMKII, p-CaMKII and ox-CaMKII protein levels. In in vivo experiment, the plaque area of aortic root and the entire aorta of mice with KN93 were significantly reduced compared with control and KN92 mice. However, no significant differences of body weight and serum lipid levels were found between KN93 and KN92 groups.

CONCLUSIONS KN93 alleviated ED and postponed the development of AS through CaMKII/notch1/NF-KB-p65/VCAM1 pathway.

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Optimization of Emergency Treatment Process for Patients with STEMI and Assessment of Effects in Chest Pain Center

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OBJECTIVES To discuss the impact of optimizing the emergency treatment process led by nurses on reducing the time delayed in treating patients with ST-Segment Elevated Myocardial Infarction (STEMI) in hospital.

METHODS Chest Pain Center was set up in the ED, and the emergency treatment process for patients with STEMI was optimized and then implemented into clinical practices. The time spent from patient enrollment to the first electrocardiogram recorded, and the specific oral medication administered, and the laboratory test result for cardiac markers come out was recorded.

RESULTS After the implementation of the optimized treatment process, the accomplish rate of recording the first electrocardiogram within 10 min after patient enrollment, and of administering oral medication within 30 min, and of receiving laboratory test results for cardiac markers within 60 min all increased respectively to 96.92%, 92.31%, 84.61%, compared to the accomplish rate before optimization of the emergency treatment process, 91.67%, 77.09%, 77.08%, the difference is significant ($P<0.05$). And percentage of the Door to Balloon (D2B) time within 90 min increased significantly to 93.30% ($P<0.05$). There are significant differences ($P<0.05$) between the average hospitalization time (6.18 ± 3.60 Versus 9.65 ± 4.82) of patients with STEMI before and after the optimization of emergency treatment process, and the mortality rate during hospitalization (3.08% versus 4.17%).

CONCLUSIONS The optimized emergency treatment process led by nurses has a positive impact on reducing the time delayed for treatment of patients with STEMI in hospital.

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Differences in two-year outcomes for patients with non-ST-segment elevation myocardial infarction or unstable angina treated with medication only - findings from the EPICOR Asia study

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OBJECTIVES To evaluate any differences and relationships between medical management strategies used and long-term outcomes in non-ST-segment elevation acute coronary syndrome (NSTEMI-ACS) patients in a real-life setting. Despite marked improvements in real-world outcomes of patients with acute coronary syndrome (ACS) after revascularisation, many are still treated only with medication. There are only few data relating to the management of patients who do not undergo revascularisation, particularly those with NSTEMI-ACS.

METHODS The EPICOR (Long-Term follow-up of antithrombotic management patterns In Acute CORonary Syndrome patients) Asia study (NCT01361386) was a prospective registry study aimed at describing antithrombotic management patterns (AMPs) in a real-life setting for patients with ACS. Patients were enrolled from 219 hospitals across 8 countries/regions in Asia. Final diagnosis, baseline characteristics, AMPs and outcomes data up to 2-year (y) post-discharge were collected. This analysis using EPICOR Asia data compared AMPs used and differences in time to event, including major adverse cardiac events (MACE) and bleeding events, up to 2-y post-discharge between non-revascularised non-ST-elevation myocardial infarction (NSTEMI) and unstable angina (UA) patients.

RESULTS NSTEMI-ACS patients treated with medication only in EPICOR Asia ($n=2289$) were classified as NSTEMI ($n=996$, 44%) or with UA ($n=1293$, 56%). NSTEMI patients comprised more patients >75 y than UA (20.0% vs 14.2%, $p<0.001$), more had diabetes (33.5% vs 27.5%, $p<0.01$) and more were current smokers (26.6% vs 18.7%, $p<0.0001$). MACE incidence increased with time post-discharge, and in NSTEMI 2-y post-discharge was twice that for UA (NSTEMI vs UA: 19.9% vs 10.1%; unadjusted hazard ratio [HR] [95% confidence interval (CI)] 2.12, 1.70–2.65, $p<0.0001$). The rate of bleeding by 1-y post-discharge was slightly lower in UA compared with NSTEMI but markedly increased in UA at 2-y post-discharge (NSTEMI vs UA: 7.3% vs 4.1%, unadjusted HR [95% CI] 0.59, 0.41–0.84, $p<0.01$). More UA than NSTEMI patients took only 1 antiplatelet (48.0% vs 35.0%) but more NSTEMI than UA patients (56.2% vs 38.4%) took at least 2 antiplatelets during follow-up. For UA patients treated with single or dual antiplatelet therapy, the incidence of MACE or bleeding was similar.

CONCLUSIONS 2-y MACE and bleeding events post-discharge show clear differences between NSTEMI and UA patients treated only with medication. To improve prognosis, the factors underlying these differences eg, bleeding in UA, and any relationship with antithrombotic strategies need to be further identified.

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Comparison of Dual Antiplatelet Therapy with Clopidogrel and Ticagrelor in Patients with Acute Coronary Syndrome at High Risk of Bleeding

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OBJECTIVES Optimal management of dual antiplatelet therapy (DAPT) of aspirin and P2Y₁₂ receptor antagonists is not well studied in patients with acute coronary syndrome (ACS) at high risk of bleeding. This review and meta-analysis aimed to survey patients with ACS reported in primary literature to compare differences in bleeding outcomes between DAPT with clopidogrel and ticagrelor.

METHODS A systematic literature review of studies on ACS patients treated with clopidogrel or ticagrelor in combination with aspirin was conducted. Databases included MEDLINE®, Embase and Cochrane Central Register of Controlled Trials from 2010 to 2017. Abstracts presented at relevant congresses from 2012 to 2017 were also reviewed. Patients at high risk of bleeding, as defined by study authors, were included in this review. Bayesian network meta-analysis

(NMA) and direct meta-analysis were performed to compare the therapies.

RESULTS Five observational studies and one randomized controlled trial with 7,454 patients were included. Patients were treated with clopidogrel and aspirin (n=4,116), ticagrelor and aspirin (n=629) or aspirin monotherapy (n=2,709) according to study protocol. For all-cause mortality, there was a trend in favor of DAPT with clopidogrel compared to ticagrelor, but the effect was not statistically significant (risk ratio 0.87 [95% CI 0.54-1.5]). The risk of major bleeding was also found to be not statistically significant between the clopidogrel and ticagrelor combinations (1.1 [95% CI 0.78-1.6]). The results of direct meta-analysis found a statistically significant effect favoring DAPT with clopidogrel compared to ticagrelor for overall bleeding (0.62 [95% CI 0.47-0.82]) and minor bleeding (0.51 [95% CI 0.31-0.84]). No difference was observed for life-threatening bleeding (0.95 [95% CI 0.78-1.15]).

CONCLUSIONS In patients at high risk of bleeding, DAPT with clopidogrel yields reduced overall bleeding and minor bleeding events, with similar all-cause mortality compared to ticagrelor. There is limited data for ticagrelor in patients with high bleeding risk and a lack of standard techniques for risk stratification in the setting of ACS. Further evidence is needed to establish reliable guidance for prescribers when selecting optimal DAPT strategies in these patients.

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Clinical Outcomes Associated with Medical Management versus Coronary Intervention in Patients with Acute Coronary Syndrome



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OBJECTIVES An invasive management strategy with percutaneous coronary intervention (PCI) is recommended in patients with acute coronary syndrome (ACS), with or without ST-segment elevation, who are eligible for revascularization. However, there is still wide variation observed in the real-life use of coronary interventions across hospitals. There is need to understand the benefits and risks of management choices in everyday clinical practice. The aim of this review and meta-analysis was to examine the relative efficacy and safety of medical management versus invasive management with PCI for the treatment of ACS in the real-world.

METHODS A comprehensive literature search was conducted in MEDLINE and Embase databases from 2007 onward to identify observational studies that compared patients with ACS who were treated medically or had undergone PCI. A pairwise meta-analysis using a random effects model was performed to estimate odds ratios with 95% confidence intervals. The primary efficacy endpoints included all-cause mortality, cardiovascular mortality, and major adverse cardiovascular events (MACE), defined as the composite of death, reinfarction, recurrent revascularization, heart failure, cardiac arrest, cardiac shock, and stroke. The primary safety endpoint was major bleeding, defined as fatal or life-threatening, intracranial, associated with a 15% decrease in hematocrit, at least a 3-5 g/dL fall in hemoglobin, needing transfusion or surgical intervention.

RESULTS A total of 15 studies reporting data for 43,927 patients were included in this analysis. Management with PCI showed statistically significant reduction in the odds of mortality in-hospital (OR 0.28 [95% CI 0.23-0.35]; $p < 0.0001$), at 4 weeks (OR 0.28 [95% CI: 0.14-0.57]; $p < 0.001$), and at 1 year (OR 0.27 [95% CI: 0.18-0.41]; $p < 0.0001$). In subgroup analyses, the in-hospital mortality remained significantly lower with PCI in ST-elevation myocardial infarction (STEMI) patients (OR 0.30 [95% CI 0.26-0.35]) and non-STEMI or unstable angina patients (OR 0.30 [95% CI 0.26-0.35]). The risk of in-hospital

cardiovascular mortality (OR 0.34 [95% CI: 0.27-0.44]; $p < 0.0001$) and MACE (OR 0.36 [95% CI: 0.32-0.41]; $p < 0.0001$) were lower with PCI than with medical management. In-hospital major bleeding was similar in the two groups (OR 1.05 [95% CI 0.63-1.53]; $p = 0.81$).

CONCLUSIONS An invasive management strategy with PCI is associated with significant reductions in the risk of in-hospital mortality and cardiovascular events compared to medical therapy only. A significant reduction mortality with PCI was also observed at 4 weeks and 1-year follow-up. The results of this analysis found greater clinical benefit with PCI on mortality and cardiovascular endpoints without increased risk of major bleeding complications compared to medical management. These findings underscore the importance of adherence to guideline-recommended management strategies and increasing patient access to PCI-capable facilities.

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Endpoints in patients with myocardial infarction

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OBJECTIVES Study of endpoints in patients with myocardial infarction.

METHODS The study included 76 male patients with primary Q-wave MI, not older than 10 days between the ages of 29 to 60 years. According to the study the final analysis included data of patients who within one year from the start of them to develop meaningful clinical outcomes: death, recurrent nonfatal MI; occurrence or progression of heart failure or coronary artery disease destabilization that required hospitalization.

RESULTS We have evaluated the forecast in the studied groups of patients. The analysis showed that in 1 years of follow-noted development reinfarction in 14 (18.4%) cases, including 5(6.6%) fatal and nonfatal - 9 (11.8%), and 6 (7.9%) cases of sudden death. Depending on the development of reinfarction analysis on various factors showed that recurrent MI was significantly more likely to develop at the rear location of the primary IM ($\chi^2 = 13.25$; $P = 0.001$), and the statistical significance of this distribution is preserved as in the case of a fatal ($\chi^2 = 20.1$; $P = 0.0001$), and nonfatal MI ($\chi^2 = 18.366$; $P = 0.001$).

Availability initially cardiac arrhythmia also significantly influences the development of reinfarction: in the group with cardiac arrhythmia in 10.5% of cases developed reinfarction ($P < 0.001$). Analysis of prognostic parameters showed that patients who developed adverse outcomes for extended surveillance had a greater number of heart rate, lower left ventricular ejection fraction less than 40%.

CONCLUSIONS Determination of early predictors of poor prognosis in patients with myocardial infarction identifies patients at high cardiovascular risk.

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Prognostic value of fractalkine/CX3CL1 concentration in patients with acute myocardial infarction treated with primary percutaneous coronary intervention

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OBJECTIVES This study aimed to investigate the prognostic value of circulating fractalkine (FKN) in patients with ST-elevated acute myocardial infarction (STEMI) after primary PCI.

METHODS We enrolled ninety consecutive STEMI patients and investigated the association of circulating FKN with myocardial salvage and the occurrence of major adverse cardiac events (MACE) after PCI.

RESULTS During a median follow-up of 387 days, total 15 MACE (16.67%) were registered in the study population. Patients with MACE were more likely to be occurred in elderly patients with 3-vessel disease. Correlation analysis demonstrated the level of FKN at day 1 after PCI (FKN@day-1) not only significantly correlated with the levels of hs-TnT at day 7 after PCI ($R^2 = 0.06$; $p = 0.02$) but inversely correlated with the measurements of LVEF at 1-month observation ($R^2 = 0.10$; $p < 0.001$). Kaplan-Meier survival analyses further revealed that patients with the level of FKN@day-1 above the median had a higher