Original Research

IJNHS

Predictor of Major Adverse Cardiac Event (MACE) in Acute Coronary Syndrome (ACS) patients: A Scoping Review

Ratna Dewi[1*], Anita Sukarno[2], Utari Yunie Atrie [3], Budi Mulyana[4]

[1-2-4]Esa Unggul University, [3]STIKES Hang Tuah Tanjung Pinang

Article info

Article history:
Received: July 24th, 2022
Revised: August 15th, 2022
Accepted: August 20th, 2022

Coresponden author:
Name: Ratna Dewi
Address: Faculty of Health Sciences, Universitas Esa Unggul. Jl. Arjuna Utara, Kebon Jeruk, Jakarta Barat. Indonesia
E-mail: nsratna@esaunggul.ac.id

International Journal of Nursing and Health Services (IJNHS)
Volume 5, Issue 4, August 20th, 2022
DOI: 10.35654/ijnhs.v5i4.634
E-ISSN: 2654-6310

Abstract

Introduction: Acute Coronary Syndrome (ACS) is a contributor to morbidity and mortality rates every year. The cause of death in ACS is a complication known as a MACE. However, it has not been known what can trigger the occurrence of MACE after post-ACS treatment. **Objective**: This study aimed to review and assess conditions that could predict the occurrence of MACE after treatment of ACS patients. **Method**: We conducted literature on articles between 2016-2021 with four databases: PubMed, Science Direct, CINAHL, and the search engine, namely Google Scholar. The design used is a scoping review. Five independent reviewers analyzed the inclusion and exclusion criteria. The researchers drew data from each article: author, year, region, purpose, design, related factors, and results. Furthermore, the researchers used PRISMA to compile the manuscript. There were 30 articles included in the analysis. One thousand articles were obtained through a basic data search based on the PRISMA flowchart, and after finding the manual, 30 studies were identified. Researchers selected relevant articles, namely predictors associated with MACE after treatment of ACS patients. **Result**: The results found that the predictors associated with MACE in ACS were comorbidities, adherence to hemodynamics medication, clinical parameters, the severity of atherosclerosis, increased cardiac disease assessment scores, and psychosocial disorder.

Keywords: Adult, MACE, ACS, scoping review

INTRODUCTION

Heart and blood vessel disease are contributing to morbidity and mortality. It is estimated that 17 million people die from heart and blood vessel disease every year, mainly from heart attacks and strokes. The most significant contributor to heart and blood vessel disease is ACS (1). ACS is heart disease with typical symptoms of heart chest pain. Pain occurs due to an imbalance of blood supply to the coronary arteries that require oxygen and nutrients in the myocardium. An imbalance in the blood supply can be caused by plaque in the coronary arteries resulting in ischemia. The heart will perform anaerobic metabolism and produce lactic acid, which eventually results in chest pain in the heart (2, 3).

The prevalence of ACS disease globally is around 422.7 million cases with 17.92 million deaths, and it is estimated that the number will increase to 23.3 million by 2030 (1, 3). In 2018, an estimated 1,413,000 patients were treated for ACS. One-third of myocardial infarction patients with ST-segment elevation died within the first 24 hours. Although morbidity and mortality in Unstable Angina Pectoris (UAP) and non-ST elevated myocardial infarction (NSTEMI) were lower, it was still necessary to note that 15% of patients died or experienced recurrent infarction within the first 30 days. In Asia Pacific Region, ACS was the most common coronary heart disease, with a prevalence of death reaching more than 5% (3). Data from the Ministry of Health of the Republic of Indonesia (2016) mentioned that the prevalence of ACS disease in Indonesia in 2015 increased by 15 per 1000 people or about 2,784,064 people and ranks first in cardiovascular problems where DKI Jakarta and West Java became the top 10 provinces with the highest number of sufferers (3, 4). Sample Registration System survey conducted by Basic Health Research (Riskesdas) in 2016 stated that ACS deaths amounted to 12.9% of all deaths in Indonesia (4).

One of the causes of death in ACS is complications known as major adverse cardiac events (MACE). MACE is often defined as a combination of non-fatal stroke, non-fatal myocardial infarction, or cardiovascular death. It is sometimes extended to include heart failure, coronary revascularization, and ischemic cardiovascular events. There are many predictors of MACE in ACS patients, but it has not been known precisely the causes of MACE after treatment of ACS patients.

OBJECTIVE

The study aimed to review and assess MACE-related predictors after treatment of ACS patients.

METHOD

Design

Design used by the authors is a scoping review with an electronic-based search strategy. Endnote X9 was used to select articles in this scoping review.

Data bases and search strategy

The question that guided this scoping review is "After treatment of ACS patients, what predictors influenced or related to MACE?". The design of this study was a scoping review. The data search was conducted from 7 to 12 of July 2021. Three databases, such as PubMed, CINAHL, Science Direct and one search engine, namely Google Scholar, extracted relevant articles. The articles were selected based on inclusion and exclusion criteria followed by Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) to assess each published study. Factors that related to MACE in a patient with ACS was initial search terms in each article title. Several keywords were used to obtain articles relevant to "Predictor or Factors Related to MACE in ACS patient". Published articles related to factors or related to MACE reviewed for data extraction. To obtain comprehensive and relevant published articles, the publication period was limited from 2016 to 2021. The

researchers used the Population-Concept-Context (PCC) format to design the research criteria outlined as follows:

PCC	Mesh	Databases
Population	"ACS" OR "Acute Coronary Syndrome" OR "Cardiac Disease" OR" Infarct Myocardia" OR "Ischemia"	PubMed, CINAHL, Science Direct, Google Scholar
Concept	"Factors Related to MACE" OR "Factors affecting MACE" OR "Prediction of MACE" OR "Factor" OR "Influences" OR "Prediction"	
Context	"MACE" OR "Major Adverse Cardiac Event"	

Eligibility of criteria

These published articles were selected based on inclusion and exclusion criteria followed by the PRISMA framework for assessing each published article. Inclusion criteria include (1) articles published in English and Indonesian from 2016-2021; (2) full-text article; (3) cohort research design, retrospective, RCT, quasi-experimental (4) Under the concept and context of the research; and (5) adult patients with the acute coronary syndrome as population targets. Articles screening were done by all researchers against duplication of articles, headings, abstracts, and full text. All articles must meet the requirements of inclusion. The search and screening strategy follow the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) flowchart pictured in diagram 1. Articles extraction used a table consisting of the researcher's name, year and country, relationship, research design, objectives, and results.

RESULTS

Based on the search and after eliminating duplicate articles, we found as many as 1000 articles. Articles were sourced from 4 databases, namely PubMed (441), Science direct (428), CINAHL (116) and Google scholar (300). Researchers screened and selected articles related to factors to MACE based on the title and abstract of selected articles. After that, researchers re-sorted based on the eligibility criteria (inclusion) we have set, such as the publication period 2016-2021, language, age, suitability of topics and abstracts, availability of full text, and duplicate findings. Of the 1000 articles, 872 were excluded because they did not fit the inclusion criteria.

Furthermore, the researchers screened by reading more intensively from 128 articles. Finally, we decided that 30 articles were included in this review. In contrast, eight articles were removed because they did not focus on ACS, 40 articles were the review study, and 50 articles did not have full text.

No	Database	Total
1	PubMed	441
2	Science Direct	428
3	CINAHL	116
4	Google Scholar	300

The review was conducted on 30 articles; the study used various designs as observational studies (n=4), cohort (9), retrospective (n=2), interventional quasi-experimental (n=2) and RCT (n=8). The research came from various countries, namely China (n =6), UK (n=4), USA (n=4), Finland (n=2), Indonesia (n=2), Korea, Japan, England, Denmark, Sweden, Brazil, France, Germany, Serbia, Spain, Australia, Egypt. Participants involved in the study were in the age range over 18.

Study design

In this study, the authors found 30 articles. 12 of 30 articles was in the form of a cohort study, 9 of 30 articles was in the form of an observational study, and 9 of 30 articles was in the form of an interventional study.

Comorbid

Seven out of thirty studies described the relationship of diseases that accompany

MACE. Two studies explained the relations of schizophrenia to MACE (5, 6). In addition, this review found that patients with HIV (9), aneurysm rupture (10), kidney disease (AKI) (12), early PCI intervention in diabetic patients (18, 25) with diabetes predicted higher MACE (18, 25).

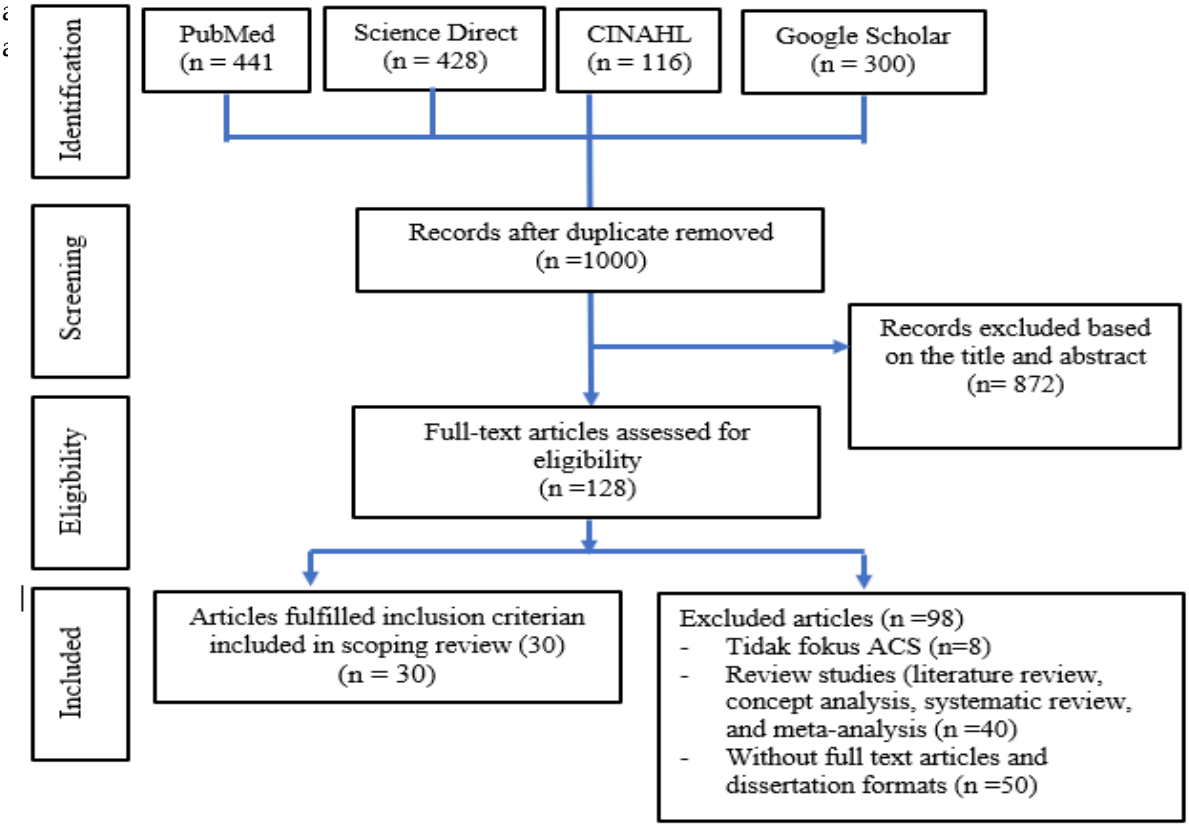

Diagram 1. Diagram of the research selection process based on Prisma flow chart

Antiplatelet

Types of Medicine

Five out of thirty studies explained the relationship of antiplatelet treatment to MACE. The results demonstrated that antiplatelet therapies such as atorvastatin, clopidogrel, and ticagrelor + aspirin were associated with MACE incidence (8, 14, 15, 23, 27).

Treatment Compliance

There was one study that reported a long-term relationship of treatment adherence to a low incidence of MACE (28).

Severity of Atherosclerosis

Two studies explained that PCI intervention in Left Main Coronary Arteries (LMCA) and early PCI in people

Clinical Parameters

Hemodynamics

One study reported a link between high systolic blood pressure (SBP) and HR as risk factors for cardiovascular disease (MACE). High dual product (DP) was associated with MACE for ACS patients treated with PCI (29).

Laboratory Value

Nine out of thirty studies explained the relationship of laboratory examinations in predicting MACE. Blood sugar levels after 2 hours fasting, interleukin-6 (IL-6), fat-rich plaques, low serum albumin, white blood cells, increased leptin, blood homocysteine levels, Cystatin-C (CYS-C) and serial C-Reactive Protein had an association as MACE predictors (11, 13, 16, 19-24, 30).

Increased Score in Heart Disease Risk Assessment

One out of thirty studies explained that an increase in GRACE and TIMI scores could predict MACE higher than RISK-PCI (17).

Psychological and Psychosocial Problems

One out of thirty studies explained that poor sleep, obstructive sleep apnea and night shifts were linked to MACE (7). Two studies linked post-traumatic stress, depression, and anxiety to MACE (7, 31, 32).

DISCUSSION

The cause of death in ACS is a complication known as a major adverse cardiac event (MACE). MACE is often defined as a combination of non-fatal stroke, non-fatal myocardial infarction, or cardiovascular death. It is sometimes extended to include heart failure, coronary revascularization, and ischemic cardiovascular. There are several predictors of MACE occurrence in ACS patients that we have revealed, namely the presence of accompanying diseases, adherence to antiplatelet treatment, clinical parameters, the severity of atherosclerosis, increased heart disease risk assessment scores, and psychosocial conditions.

The study found that patients with ACS accompanied by schizophrenia had a greater increased incidence of MACE, mortality, and stroke (5). The same study by Attar et al. (2020) re-investigated that in addition to the high risk of mace incidence, patients with AMI disease accompanied by schizophrenia also had a higher risk of heart failure than AMI patients without schizophrenia (6). Other diseases such as HIV infection, ruptured aneurysm, extended operating times, acute kidney failure (GGA), and hyperglycemia also increased the incidence of MACE. According to Boccara et al. (2020), although the overall risk of MACE incidence was not statistically significant between HIV-infected with ACS and ACS patients without HIV infection, HIV infection had a chance of repeated occurrences of ACS (9).

Similarly, the condition of a ruptured aneurysm and a long-time surgical procedure was associated with a significant increase in MACE (10). In addition, Acute Kidney Injury (AKI) was identified as a significant increase in MACE in emergency departments when ACS patients accompanied by AKI came to the emergency department (12). Then the condition of hyperglycemia in ACS patients also affects MACE; the higher the blood sugar concentration of ACS patients when admission, the higher the risk and the faster MACE occurred during treatment (33).

Recovery from or progression of Mets (metabolic syndrome status) in a population was also associated with an altered risk for MACE. The Mets recovery group had a significantly lower risk of MACE compared to the chronic Mets group. The Mets-developed group had a significantly higher MACE risk than the Mets-free group. Among the Mets components, changes in hypertension were associated with the most significant difference in MACE risk. Recovery from Mets was significantly associated with a reduced risk of MACE, whereas the development of Mets was associated with an increased risk (34).

This review also found an association between antiplatelet medication and the risk of developing MACE. One study reported that ticagrelor plus low-dose aspirin for up to 1 year was associated with lower rates of major bleeding events and lower incidence of MACE (CV death, myocardial infarction, stroke) in ACS patients. The overall safety profile of ticagrelor in this population aligns with current prescribing information (14). This is in line with a subsequent study reported that treatment with the PCSK9 inhibitor alirocumab was associated with a lower incidence of MACE in patients with ACS (23).

Meanwhile, early discontinuation of P2Y12 antagonists after percutaneous coronary intervention therapy (clopidogrel) was predicted to be a significant factor in bleeding and was associated with increased MACE (15). In addition, loading doses of atorvastatin before PCI has not been shown to reduce MACE at 30 days, so the findings do not support the routine use of this therapy (8).

Yang et al. (2021) reported a clearer correlation between the different timing of DAPT initiation in the Emergency Department (ED) and outcome in patients with NSTEMI. Patients who received DAPT within 6 hours had a low risk of developing MACE. Still, on the other hand, the risk of MACE was more significant in patients who had a history of DAPT treatment more than 6 hours at the time of initiation to the ED. This suggested that, among patients with NSTEMI required PCI. It was associated with atherosclerotic plaque rupture, ulceration, fissuring, erosion, or dissection with intraluminal thrombus in one or more of the coronary arteries. it caused decreased myocardial blood flow or distal platelet embolism. Thereby results in myocyte necrosis. Patients who received DAPT more than 6 hours after arriving at the ED had a 2-fold higher in-hospital MACE rate than those who received DAPT within 6 hours (27).

DAPT with aspirin and P2Y12 receptor blockers may reduce the risk of ischemic events. The outcome in patients with NSTEMI was affected by the timing of PCI and the duration of DAPT after PCI. However, the relationship between patient outcome and pre-treatment DAPT, meaning DAPT before PCI, remains controversial. It was logical to assume that early administration of DAPT before coronary angiography (referred to as upstream therapy or pre-treatment) and PCI should provide a more significant benefit. However, pre-treatment DAPT in NSTEMI patients were still debated. The advantages of early DAPT before PCI suggest that achieving maximal platelet inhibition early in the clinical presentation may be beneficial in reducing the fractional size and decrease the risk of stent thrombosis for patients undergoing percutaneous revascularization, thereby preventing downstream morbidity. Several guideline recommendations have been suggested for the administration of DAPT early in the hospital course. However, inhibiting platelets before invasive procedures may increase the risk of bleeding (27)

Furthermore, research conducted by (Bansilal et al., (2016) reported a relationship between medication adherence and the incidence of MACE. Full adherence to guideline-recommended therapy was associated with predicted lower MACE rates and cost savings, with a threshold effect on adherence >80% in the post-MI population; at least a 40% long-term compliance rate needs to be maintained to continue to benefit. A new approach to improve adherence can significantly reduce cardiovascular.

In terms of clinical parameters, high systolic blood pressure (SBP) was a risk factor for cardiovascular disease. Several studies have shown that heart rate (HR) was also a risk factor for cardiovascular mortality and morbidity in ACS patients. Recently, a meta-analysis concluded that increased HR might increase mortality in ACS patients in the era of PCI. The dual product (DP), which included SBP and HR values, was initially calculated to assess myocardial oxygen uptake indirectly during stress testing. DP has been shown as a predictive parameter to evaluate the prognosis in acute myocardium treated with thrombolytic agents. However, in the general population, one study found that DP had no value in predicting mortality other than SBP and HR. until this date, there is little information on the predictive value of DP for ACS patients treated with PCI. This study reported that high DP was associated with MACE for ACS patients treated with PCI. In our analysis, low DP admission was a protective factor for two-year MACE (29).

Furthermore, laboratory values can be a predictor of MACE occurrence. 2-hour postprandial blood glucose test improved prognostic prediction in ACS patients (11). In patients after ACS, IL-6 concentrations were associated with MACE regardless of established risk predictors and biomarkers. These findings supported the concept of IL-6 as a potential therapeutic target in patients with unstable ischemic heart disease (13). Arteriosclerosis presence (fat-rich plaque) in other vessels after ACS has a low predictor of future MACE (16). Low serum albumin elevated white blood cells, high leptin levels, blood homocysteine levels, PCSK9 inhibitor Alirocumab, Cystatin-C (CYS-C), and serial C-Reactive Protein can also be predictors of MACE.

Regarding the severity of ACS, it was stated that the location of the blood vessels in which ACS occurred also determined the severity of the disease and predicts the level of MACE risk. In research conducted by Jia et al. (2020), patients with ACS who underwent LMCA PCI were at greater risk of developing MACE when compared to ACS patients who underwent non-LMCA PCI. The main findings of this study suggested that (1) in patients with ACS, LMCA-targeted PCI was associated with a higher 2-year risk of cardiac death, myocardial infarction, in-stent thrombosis, and stroke. (2) Compared with non-LMCA PCI, LMCA-targeted PCI was an independent risk factor for 2-year MI.

Several randomized controlled studies have compared the long-term clinical outcomes of LMCA disease patients undergoing different revascularization procedures in recent years. Some studies showed similar rates of long-term side effects between patients undergoing LMCA PCI or CABG, while other trial findings suggested that CABG may still be a better option for these patients. However, little is known about the long-term effects of PCI in ACS patients with significant LMCA disease. The presence of unprotected LMCA occlusion in patients undergoing primary PCI was an independent predictor of 30-day and 3-year all-cause mortality. Because the LMCA supplies blood perfusion to a large part of the left ventricular myocardium regardless of the predominance of a coronary artery, acute LMCA infarcts result in a large area. Most AMI patients with LMCA involvement develop cardiogenic shock, at increased risk of in-hospital and short-term death 25

Type 1 diabetes significantly reduced life expectancy mainly due to complications of cardiovascular disease (CVD). PCI, which is part of standard procedures in the treatment of STEMI, plays an important role and contributes to the incidence of MACE. A study conducted by Karjalainen et al., 2016 reported that early PCI in diabetic patients had poorer long-term outcomes than non-diabetics, mainly driven by more frequent cardiac death (18).

Another finding was that the results of a risk factor assessment with a high score on cardiovascular disease can predict the incidence of MACE. Several assessment scores can be used to predict 30-day MACE and ACS mortality, such as GRACE, TIMI and Risk-PCI. According to (17), RISK-PCI is the only scoring system to predict recurrent ischemia. In addition, psychosocial conditions can also increase the incidence of MACE in ACS patients. Patients who had a habit of insufficient sleep duration, obstructive sleep apnea, night shift work, post-traumatic stress, and anxiety are predictors of a significant MACE occurrence in the future. In (7) study, patients who reported sleeping <6 hours per night had a 29% higher MACE risk than those who slept longer. Patients positively screened for obstructive sleep apnea had a 12% higher MACE risk than those not screened positive. Night shift work (3-night shifts/week for one year) was associated with a 15% higher MACE risk. A gradual increase in cardiovascular risk was observed for individuals with more than one risk factor. People with all three risk factors have a twofold higher risk of MACE (7). According to Sari et al. (2018),

anxiety in ACS patients is an independent predictor of the occurrence of MACE within seven days and increases the risk of developing MACE for seven days (32).

CONCLUSION

An effort to reduce mortality due to complications in ACS patients is to reduce the incidence of MACE. Many factors can relate to and affect MACE. Knowing these factors can be included in the nursing plan so that it can reduce MACE. Some recommendations that can be given are: 1) improve patient compliance by scheduling visits and taking medication; 2) increase alertness for the patient with comorbidities in providing education regarding signs and symptoms of comorbid diseases ; 3)Teach self-monitoring (HR, blood pressure, blood sugar, temperature); 4)Teach stress management (calm yourself, increase worship, gather with family and relatives); 5) Advise routine control after hospitalization by making reminders by nurses to patients; and 6) Provide health education related to lifestyle changes

REFERENCES

1. World Health Organization (WHO). Cardiovascular Diseases (CVDs) Geneva, Switzerland: WHO; 2020 [Available from: https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds).
2. Black JM, Hawks JH. Keperawatan Medikal Bedah : Manajemen Klinis untuk Hasil yang Diharapkan. 8 E, editor. Singapure: Elsevier; 2014.
3. Pangestika DD, Trisyani Y, Nur'aeni A. The Effect of Dhikr Therapy on the Cardiac Chest Pain of Acute Coronary Syndrome (ACS) Patients. Nurse Media Jurnal of Nursing. 2020;Volume 10 Nomor 2.
4. KEMENKES. Riset Kesehatan Dasar Tahun 2016 Jakarta: KEMENKES RI; 2016 [Available from: https://kesmas.kemkes.go.id/assets/upload/dir_519d41d8cd98f00/files/Hasil-riskesdas-2018_1274.pdf.
5. Attar R, Valentin JB, Freeman P, Andell P, Aagaard J, Jensen SE. The effect of schizophrenia on major adverse cardiac events, length of hospital stay, and prevalence of somatic comorbidities following acute coronary syndrome. European heart journal Quality of care & clinical outcomes. 2019;5(2):121-6.
6. Attar R, Wester A, Koul S, Eggert S, Polcwiartek C, Jernberg T, et al. Higher risk of major adverse cardiac events after acute myocardial infarction in patients with schizophrenia. Open heart. 2020;7(2).
7. Barger LK, Rajaratnam SMW, Cannon CP, Lukas MA, Im K, Goodrich EL, et al. Short Sleep Duration, Obstructive Sleep Apnea, Shiftwork, and the Risk of Adverse Cardiovascular Events in Patients After an Acute Coronary Syndrome. J Am Heart Assoc. 2017;6(10).
8. Berwanger O, Santucci EV, de Barros ESPGM, Jesuíno IA, Damiani LP, Barbosa LM, et al. Effect of Loading Dose of Atorvastatin Prior to Planned Percutaneous Coronary Intervention on Major Adverse Cardiovascular Events in Acute Coronary Syndrome: The SECURE-PCI Randomized Clinical Trial. Jama. 2018;319(13):1331-40.
9. Boccara F, Mary-Krause M, Potard V, Teiger E, Lang S, Hammoudi N, et al. HIV Infection and Long-Term Residual Cardiovascular Risk After Acute Coronary Syndrome. J Am Heart Assoc. 2020;9(17):e017578.
10. Bosiers MJ, Tran K, Lee JT, Donas KP, Veith FJ, Torsello G, et al. Incidence and prognostic factors related to major adverse cerebrovascular events in patients with complex aortic diseases treated by the chimney technique. Journal of vascular surgery. 2018;67(5):1372-9.

11. Chattopadhyay S, George A, John J, Sathyapalan T. Adjustment of the GRACE score by 2-hour post-load glucose improves prediction of long-term major adverse cardiac events in acute coronary syndrome in patients without known diabetes. Eur Heart J. 2018;39(29):2740-5.
12. Dieter BP, Daratha KB, McPherson SM, Short R, Alicic RZ, Tuttle KR. Association of Acute Kidney Injury with Cardiovascular Events and Death in Systolic Blood Pressure Intervention Trial. American journal of nephrology. 2019;49(5):359-67.
13. Fanola CL, Morrow DA, Cannon CP, Jarolim P, Lukas MA, Bode C, et al. Interleukin-6 and the Risk of Adverse Outcomes in Patients After an Acute Coronary Syndrome: Observations From the SOLID-TIMI 52 (Stabilization of Plaque Using Darapladib-Thrombolysis in Myocardial Infarction 52) Trial. J Am Heart Assoc. 2017;6(10).
14. Gao R, Wu Y, Liu H, Su G, Yuan Z, Zhang A, et al. Safety and Incidence of Cardiovascular Events in Chinese Patients with Acute Coronary Syndrome Treated with Ticagrelor: the 12-Month, Phase IV, Multicenter, Single-Arm DAYU Study. Cardiovascular drugs and therapy. 2018;32(1):47-56.
15. Harris DE, Lacey A, Akbari A, Obaid DR, Smith DA, Jenkins GH, et al. Early Discontinuation of P2Y(12) Antagonists and Adverse Clinical Events Post-Percutaneous Coronary Intervention: A Hospital and Primary Care Linked Cohort. J Am Heart Assoc. 2019;8(21):e012812.
16. Hoshino M, Yonetsu T, Usui E, Kanaji Y, Ohya H, Sumino Y, et al. Clinical Significance of the Presence or Absence of Lipid-Rich Plaque Underneath Intact Fibrous Cap Plaque in Acute Coronary Syndrome. J Am Heart Assoc. 2019;8(9):e011820.
17. Jakimov T, Mrdović I, Filipović B, Zdravković M, Djoković A, Hinić S, et al. Comparison of RISK-PCI, GRACE, TIMI risk scores for prediction of major adverse cardiac events in patients with acute coronary syndrome. Croatian medical journal. 2017;58(6):406-15.
18. Karjalainen PP, Airaksinen JK, de Belder A, Romppanen H, Kervinen K, Sia J, et al. Long-term outcome of early percutaneous coronary intervention in diabetic patients with acute coronary syndrome: insights from the BASE ACS trial. Annals of medicine. 2016;48(5):376-83.
19. Wang W, Wang CS, Ren D, Li T, Yao HC, Ma SJ. Low serum prealbumin levels on admission can independently predict in-hospital adverse cardiac events in patients with acute coronary syndrome. Medicine. 2018;97(30):e11740.
20. Shah B, Baber U, Pocock SJ, Krucoff MW, Ariti C, Gibson CM, et al. White Blood Cell Count and Major Adverse Cardiovascular Events After Percutaneous Coronary Intervention in the Contemporary Era: Insights From the PARIS Study (Patterns of Non-Adherence to Anti-Platelet Regimens in Stented Patients Registry). Circulation Cardiovascular interventions. 2017;10(9).
21. Puurunen VP, Kiviniemi A, Lepojärvi S, Piira OP, Hedberg P, Junttila J, et al. Leptin predicts short-term major adverse cardiac events in patients with coronary artery disease. Annals of medicine. 2017;49(5):448-54.
22. Liu J, Quan J, Li Y, Wu Y, Yang L. Blood homocysteine levels could predict major adverse cardiac events in patients with acute coronary syndrome: A STROBE-compliant observational study. Medicine. 2018;97(40):e12626.
23. Tuñón J, Steg PG, Bhatt DL, Bittner VA, Díaz R, Goodman SG, et al. Effect of alirocumab on major adverse cardiovascular events according to renal function in patients with a recent

acute coronary syndrome: prespecified analysis from the ODYSSEY OUTCOMES randomized clinical trial. Eur Heart J. 2020;41(42):4114-23.
24. Mani P, Puri R, Schwartz GG, Nissen SE, Shao M, Kastelein JJP, et al. Association of Initial and Serial C-Reactive Protein Levels With Adverse Cardiovascular Events and Death After Acute Coronary Syndrome: A Secondary Analysis of the VISTA-16 Trial. JAMA cardiology. 2019;4(4):314-20.
25. Jia S-D, Yao Y, Song Y, Tang X-F, Zhao X-Y, Gao R-L, et al. Two-Year Outcomes after Left Main Coronary Artery Percutaneous Coronary Intervention in Patients Presenting with Acute Coronary Syndrome. Journal of Interventional Cardiology. 2020:1-8.
26. Park S, Lee S, Kim Y, Lee Y, Kang MW, Han K, et al. Altered Risk for Cardiovascular Events With Changes in the Metabolic Syndrome Status: A Nationwide Population-Based Study of Approximately 10 Million Persons. Annals of Internal Medicine. 2019;171(12):875-84.
27. Yang J-H, Shih H-M, Pan Y-C, Chang S-S, Li C-Y, Yu S-H. Early Dual-Antiplatelet Therapy at the Emergency Department Is Associated with Lower In-Hospital Major Adverse Cardiac Event Risk among Patients with Non-ST-Elevation Myocardial Infarction. Cardiology Research & Practice. 2021:1-7.
28. Bansilal S, Castellano JM, Garrido E, Wei HG, Freeman A, Spettell C, et al. Assessing the Impact of Medication Adherence on Long-Term Cardiovascular Outcomes. Journal of the American College of Cardiology (JACC). 2016;68(8):789-801.
29. Tan X, Youqin Z, Nan L, Zhuoqiao H, Xi S, Xuerui T, et al. Double product reflects the association of heart rate with MACEs in acute coronary syndrome patients treated with percutaneous coronary intervention. BMC Cardiovascular Disorders. 2017;17:1-7.
30. Tayeh O, Rizk A, Mowafy A, Salah S, Gabr K. Cystatin-C as a predictor for major adverse cardiac events in patients with acute coronary syndrome. The Egyptian Heart Journal. 2012;64(3):87-95.
31. Edmondson D, Rieckmann N, Shaffer JA, Schwartz JE, Burg MM, Davidson KW, et al. Posttraumatic stress due to an acute coronary syndrome increases risk of 42-month major adverse cardiac events and all-cause mortality. Journal of Psychiatric Research. 2011;45(12):1621-6.
32. Sari DP, Mudjaddid E, Ginanjar E, Muhadi. Relationship between Symptoms of Depression and Anxiety with Major Adverse Cardiac Event in 7 days in Patients with Acute Coronary Syndrome in Cipto Mangunkusumo Hospital. Jurnal Penyakit Dalam Indonesia. 2018;5.
33. Martalena D, Nasution SA, Purnamasari D, Harimurtin K. The Effect of Hyperglycemia on Admission on Survival of Major Adverse Cardiac Events during Hospitalization in Patients with Acute Coronary Syndrome in Coronary Care Unit Cipto Mangunkusumo Hospital, Jakarta. EJKI. 2013;1.
34. Park KH, Jeong MH, Hong YJ, Ahn Y, Kim HK, Koh YY, et al. Effectiveness and Safety of Biolimus A9™-Eluting stEnt in Patients with AcUTe Coronary sYndrome; A Multicenter, Observational Study (BEAUTY Study). Yonsei medical journal. 2018;59(1):72-9.

1. Research Data

No	Researcher, Year and Country	Title	Design	Factor(s)	Aims	Result
1	Attar, Valentin (5), Denmark	The effect of schizophrenia on major adverse cardiac events, length of hospital stays, and prevalence of somatic comorbidities following acute coronary syndrome	Observational	Schizophrenia	Identified MACE in schizophrenic populations with ACS	Patients with schizophrenia have an increased risk of MACE [hazard ratio (HR) 1.62, 95% confidence interval (CI) 1.45–1.81], death (HR 2.54, 95% CI 2.22–2.90), dan stroke (HR 1.51, 95% CI 1.15–1.99)
2	Attar, Wester (6), Sweden	Higher risk of major adverse cardiac events after acute myocardial infarction in patients with schizophrenia	Observational	Schizophrenia	Identified Patients with and without schizophrenia who have an acute myocardial infarction (AMI) are associated with MACE within five years	AMI patients with schizophrenia have a higher risk of MACE (aHR=2.05, 95% CI 1.63 to 2.58), death (aHR=2.38, 95% CI 1.84 to 3.09) and hospitalization due to heart failure (aHR=1.39, 95% CI 1.04 to 1.86) compared to AMI patients without schizophrenia
3	Barger, Rajaratnam (7), United State	Short Sleep Duration, Obstructive Sleep Apnea, Shiftwork, and the Risk of Adverse Cardiovascular Events in Patients After an Acute Coronary Syndrome	Multinational, double-blind, placebo-controlled trial	Short Sleep Duration, Obstructive Sleep Apnea, Overnight Shiftwork	Is short sleep duration, obstructive sleep apnea and overnight shift work associated with repeated risk of MACE after ACS	Patients who reported a night's sleep <6 hours/night had a 29% higher risk of MACE (adjusted hazard ratio, 1.29; 95% confidence interval, 1.12–1.49; P<0.001) than people who sleep longer. Patients screened positive for obstructive sleep apnea had a 12% higher MACE (1.12; 1.00–1.24; P=0.04) Than without obstructive sleep apnea. Night shift (≥3-night shifts/week for ≥one year) associated with 15% higher MACE (1.15; 1.03–1.29; P=0.01). A gradual increase in cardiovascular risk was observed for individuals with more than one sleep-related risk factor. Individuals with all three sleep-related risk factors have a two times higher risk of MACE. (2.01; 1.49–2.71; P<0.0001).

No	Researcher, Year and Country	Title	Design	Factor(s)	Aims	Result
4	Berwanger, Santucci (8), Brazil	Effect of Loading Dose of Atorvastatin before Planned Percutaneous Coronary Intervention on Major Adverse Cardiovascular Events in Acute Coronary Syndrome: The SECURE-PCI Randomized Clinical Trial	Multicenter, double-blind, placebo-controlled, randomized clinical trial	Loading Dose of Atorvastatin before PCI	Identified whether periprocedural loading doses of atorvastatin can reduce 30-day MACE in ACS patients on invasive management.	Among patients with ACS and planned invasive management with PCI, periprocedural atorvastatin did not reduce MACE levels at 30 days. These findings do not support the routine use of atorvastatin doses among ACS patients.
5	Boccara, Mary-Krause (9), France	HIV Infection and Long-Term Residual Cardiovascular Risk After Acute Coronary Syndrome	Consecutive PLHIV and matched HIV− patients Patients were matched for age, sex, and ACS type	HIV Infection	Compared MACE after the first diagnosis of ACS between people with HIV and non-HIV and to identify differences in cardiovascular prognoses.	Although the overall risk of MACE was not statistically significant between HIV and non-HIV, HIV patients have a greater chance of recurrent ACS.
6	Bosiers, Tran (10), Germany	Incidence and prognostic factors related to major adverse cerebrovascular events in patients with complex aortic diseases treated by the chimney technique	an international, retrospective multicenter study	Aneurysm rupture & prolonged operation time	Evaluate the occurrence and risk factors associated with cerebrovascular	aneurysm rupture (OR, 5.33; 95% CI, 1.74-16.33) and long duration of surgery (>290 minutes; OR, 1.005; 95% CI, 1.001-1.008) associated with a significantly increased risk of MACE.
7	Chattopadhyay, George (11), UK	Adjustment of the GRACE score by 2-hour post-load glucose improves prediction of long-term major adverse cardiac events in acute coronary syndrome in patients without known diabetes	A retrospective cohort study	2-hour post-load glucose	We identified whether 2 hours post-load plasma glucose (2h-PG) could increase GRS based on predictive models of ACS patients without known DM.	Two-hour Plasma Glucose (PG), but not Fasting Plasma Glucose (FPG), was an independent predictor of adverse outcomes after ACS even after adjusting for GRS. Two-hour PG, but not FPG, improve the predictability of prognostic models containing GRS.
8	Dieter, Daratha (12), USA	Association of Acute Kidney Injury with Cardiovascular Events and Death in Systolic Blood Pressure Intervention Trial	Post hoc analysis of a multicenter, randomized, controlled, open-label clinical trial.	Acute Kidney Injury	In the Systolic Blood Pressure Intervention Trial, the possible association between Acute Kidney Injury (AKI) and the risk of major cardiovascular events and death was unknown.	Episodes of AKI were identified as having a significant adverse effect on MACE. Based on AKI status, the Cox proportional hazards models assess risk for primary (MACE) and secondary (death) outcomes.

No	Researcher, Year and Country	Title	Design	Factor(s)	Aims	Result
9	Fanola, Morrow (13), USA	Interleukin-6 and the Risk of Adverse Outcomes in Patients After an Acute Coronary Syndrome: Observations From the SOLID-TIMI 52 (Stabilization of Plaque Using Darapladib-Thrombolysis in Myocardial Infarction 52) Trial	a randomized trial of darapladib	Interleukin-6 (IL-6)	Interleukin-6 (IL-6) is an inflammatory cytokine involved in plaque instability in acute coronary syndrome (ACS), aimed to evaluate the prognostic implications of IL-6 post-ACS.	In patients after ACS, IL-6 concentrations are associated with adverse cardiovascular outcomes regardless of established risk predictors and biomarkers. These findings support the concept of IL-6 as a potential therapeutic target in patients with unstable ischemic heart disease.
10	Gao, Wu (14), China	Safety and Incidence of Cardiovascular Events in Chinese Patients with Acute Coronary Syndrome Treated with Ticagrelor: the 12-Month, Phase IV, Multicenter, Single-Arm DAYU Study	an interventional, open-label, multicenter, single-arm	Ticagrelor plus low-dose aspirin for up to 1 year	Assessed safety and incidence of cardiovascular (CV) events with ticagrelor in Chinese patients with the acute coronary syndrome (ACS).	Ticagrelor added with low-dose aspirin for up to 1 year was associated with lower rates of major bleeding events and lower major cardiovascular events (CV death, myocardial infarction, stroke) in Chinese patients with ACS. The overall safety profile of ticagrelor in this population is in line with current prescribing information.
11	Harris, Lacey (15), USA	Early Discontinuation of P2Y (12) Antagonists and Adverse Clinical Events Post-Percutaneous Coronary Intervention: A Hospital and Primary Care Linked Cohort	a retrospective observational population cohort	Early discontinuation of Clopidogrel	(1) analyzed the rate of early discontinuation of P2Y12 antagonists following the percutaneous coronary intervention, (2) explored the factors associated with early discontinuation, and (3) analyzed the risk of major adverse cardiovascular events (death, acute coronary syndrome, revascularization, or stroke) associated with discontinuation of prescribed prescribing instructions for one year.	Discontinuation earlier than the intended duration was associated with an increased rate of side effects, especially in those with bleeding.

No	Researcher, Year and Country	Title	Design	Factor(s)	Aims	Result
12	Hoshino, Yonetsu (16), Japan	Clinical Significance of the Presence or Absence of Lipid-Rich Plaque Underneath Intact Fibrous Cap Plaque in Acute Coronary Syndrome	Observational Study	Presence or Absence of Lipid-Rich Plaque underneath IFC	Investigated the clinical significance of IFC concerning the presence or absence of LRP observed via optical coherence tomography in lesions causing acute coronary syndromes.	The absence of LRP under IFC-causing lesions in acute coronary syndromes may predict a lower future risk of MACE.
13	Jakimov, Mrdović (17), Serbia	Comparison of RISK-PCI, GRACE, TIMI risk scores for prediction of major adverse cardiac events in patients with acute coronary syndrome	single-centre retrospective study	Grace, TIMI &Risk-PCI	Compares the prognostic performance of three major risk assessment systems, including the global registry for acute coronary events (GRACE), thrombolysis in myocardial infarction (TIMI), and prediction of 30-day major adverse cardiovascular events after primary percutaneous coronary intervention (RISK-PCI).	Compared with the GRACE and TIMI scores, the RISK-PCI scores indicate a non-inferior ability to predict 30-day MACE and mortality in ACS patients. In addition, RISK-PCI is the only scoring system that can predict recurrent ischemia requiring TVR.
14	Karjalainen, Airaksinen (18), Finland	Long-term outcome of early percutaneous coronary intervention in diabetic patients with acute coronary syndrome: insights from the BASE ACS trial	RCT	early PCI in diabetic patients	It was knowing the comparative outcome of BAS versus EES in diabetic patients with ACS.	Diabetic patients treated with early percutaneous coronary intervention for ACS had poorer long-term outcomes than non-diabetics, primarily driven by more frequent cardiac deaths. The long-term effect of BAS is comparable to that of EES in people with diabetes.

No	Researcher, Year and Country	Title	Design	Factor(s)	Aims	Result
15	Wang, Wang (19), China	Low serum albumin levels on admission can independently predict in-hospital adverse cardiac events in patients with acute coronary syndrome	a cohort study	Low serum albumin	We evaluate prealbumin levels at admission and predict subsequent adverse cardiac events in hospitalized patients with acute coronary syndromes (ACS).	Lower serum albumin levels at admission could independently predict subsequent adverse cardiac events in hospitals in patients with ACS.
16	Shah, Baber (20), USA	White Blood Cell Count and Major Adverse Cardiovascular Events After Percutaneous Coronary Intervention in the Contemporary Era: Insights from the PARIS Study (Patterns of Non-Adherence to Anti-Platelet Regimens in Stented Patients Registry)	multicenter, prospective, observational PARIS study	WBC		Elevated WBC is an independent predictor of MACE after percutaneous coronary intervention.
17	Puurunen, Kiviniemi (21), Finlad	Leptin predicts short-term major adverse cardiac events in patients with coronary artery disease	Prospective cohort	Leptin	We have examined whether leptin predicts major adverse cardiac events (MACE) in coronary artery disease (CAD) patients.	High plasma leptin levels predict the occurrence of CHF or short-term cardiac death and ACS or stroke in patients with CAD independently of the established risk factors. The possible harmful effects of leptin should be thoroughly investigated.
18	Liu, Quan (22), China	Blood homocysteine levels could predict major adverse cardiac events in patients with acute coronary syndrome: A STROBE-compliant observational study	single-centre observational study	Blood Homocysteine levels	Evaluating plasma homocysteine levels in addition to the GRACE score increases the predictive value for MACE in patients with acute coronary syndromes (ACS).	Blood homocysteine levels are significantly associated with the GRACE risk score. Using both parameters can further improve risk stratification in patients with acute coronary syndromes.
19	Tuñón, Steg (23), Spain	Effect of alirocumab on major adverse cardiovascular events according to renal function in patients with a recent acute coronary syndrome: prespecified analysis from the ODYSSEY OUTCOMES randomized clinical trial.	a randomized, double-blind, placebo-controlled	PCSK9 Inhibitor Alirocumab	Determining the effect of the PCSK9 inhibitor alirocumab on reducing the incidence of cardiovascular death after ACS is influenced by renal function	In patients with recent ACS, alirocumab was associated with fewer cardiovascular occurrences and mortality across the renal function range studied, with a more significant relative risk reduction in those with eGFR >60 mL/min/1.73 m2.

No	Researcher, Year and Country	Title	Design	Factor(s)	Aims	Result
20	Mani, Puri (24), Australia	Association of Initial and Serial C-Reactive Protein Levels with Adverse Cardiovascular Events and Death After Acute Coronary Syndrome: A Secondary Analysis of the VISTA-16 Trial	double-blind, multicenter, randomized clinical	Serial C-Reactive Protein Levels	Assessing the longitudinal increase in hsCRP measurements over 16 weeks after ACS independently associated with a greater risk of a major adverse cardiac event (MACE), all-cause mortality, and cardiovascular death.	An early increase in hs-CRP levels for 16 weeks after ACS is associated with a greater risk of combined MACE, cardiovascular death, and all-cause mortality despite established therapy. Serial measurements of hsCRP after ACS can help identify patients at higher risk of death and morbidity.
21	Osama Tayeh et al. (2012), Mesir		non-randomized controlled trial	Cystatin-C (CYS-C)	We evaluated the predictive value of CYS-C levels for major adverse cardiac events (MACE), including mortality and morbidity during a hospital stay and three months.	CYS-C was an independent predictor of MACE and heart failure complications either in the hospital or during follow-up ($P < 0.05$).
22	Donald Edmondson et al. (2011), UK		observational cohort study	Post-traumatic stress		Post-traumatic symptoms are a strong and independent predictor of an increased risk of MACE and should be considered in risk stratification of ACS patients.
23	Diah Pravita Sari et al (2018), Indonesia		cohort prospective	Depression dan Anxiety	Determined the relationship between depression and anxiety with a major adverse cardiac event (MACE) in 7 days in ACS patients	Anxiety in ACS patients is an independent predictor of the occurrence of MACE within seven days and increases the risk of developing MACE at seven days. There was no association between depression and MACE at seven days in ACS patients.
24	Dewi Martalena et al (2013), Indonesia		cohort retrospective	Hyperglycemia	To examine the role of admission hyperglycemia as a predictor of Major Adverse Cardiac Event (MACE) and determine	There were differences in survival in the admission hyperglycemia group in the occurrence of MACE. The higher the blood glucose concentration of ACS patients at admission, the higher the risk and the faster MACE occurs during treatment.

No	Researcher, Year and Country	Title	Design	Factor(s)	Aims	Result
					its effect on the rate of occurrence of MACE in Acute Coronary Syndrome (ACS).	
25	Elena Tessitore et al (2021), USA		an observational, monocentric cohort study	Covid-19	Investigated whether patients with previous CVD have increased risk of death and major adverse cardiovascular event (MACE) when hospitalized for COVID-19	History of CVD is associated with higher in-hospital mortality and MACE in hospitalized patients with COVID-19. Other factors associated with higher in-hospital mortality are older age, male sex and elevated CRP on admission
26	Yang et al. (2021), Cina	Early Dual-Antiplatelet Therapy at the Emergency Department is Associated with Lower In-Hospital Major Adverse Cardiac Event Risk among Patients with Non-ST-Elevation Myocardial Infarction	Retrospective	DAPT	Shows a correlation between different times of DAPT initiation in the ED and outcome in patients with NSTEMI	A total of 938 NSTEMI patients with PCI were enrolled. Patients who received DAPT more than 6 hours were relatively old (65.70 ± 14.13 versus 63.16 ± 13.31, p = 0.014) and had relatively more comorbidities and higher Killip scores than those who received DAPT. Receive DAPT within 6 hours. The group receiving DAPT within 6 hours had lower rates of in-hospital MACE (3.52% versus 8.37%, p = 0.009). Multivariate logistic regression showed the group beyond 6 hours was independently associated with a higher risk for in-hospital MACE rates (OR: 2.09, 95% CI 1.07-4.07, p = 0.030).
27	Jia et al. (2020), Cina	Two-Year Outcomes after Left Main Coronary Artery Percutaneous Coronary Intervention in Patients Presenting with Acute Coronary Syndrome	Cohort study two years.	PCI pada kelompok LMCA dan non-LMCA	Evaluating long-term outcome after percutaneous coronary intervention (PCI) left main coronary artery (LMCA) in patients with the acute coronary syndrome (ACS).	155 (2.4%) patients had target lesions in the LMCA, whereas 6274 (97.6%) patients belonged to the non-LMCA group. Compared with non-LMCA patients, LMCA patients generally have more comorbidities and poorer baseline conditions. Two-year follow-up revealed that LMCA patients had a significantly higher rate of cardiac death (2.6% vs 0.7%, p = 0.034),

No	Researcher, Year and Country	Title	Design	Factor(s)	Aims	Result
						myocardial infarction (7.1% vs 1.8%, p < 0.001), in-stent thrombosis (4.5% vs 0.8%, p < 0.001), and stroke (7.1% vs 6.4%, p = 0.025). After adjusting for confounding factors, LMCA remained independently associated with a higher 2-year myocardial infarction rate (HR = 2.585, 95% CI = 1.243-5,347, p = 0.011).
28	Park et al. (2019) Korea	Altered Risk for Cardiovascular Events with Changes in the Metabolic Syndrome Status: A Nationwide Population-Based Study of Approximately 10 Million Persons	Cohort study	Metabolic Syndrome Status	We are investigating recovery from or progression of MetS (metabolic syndrome status) in a population associated with an altered risk for MACE.	At a median follow-up of 3.54 years, the Mets recovery group (incidence rate, 4.55 per 1000 person-years) had a significantly lower risk of MACE (adjusted IRR, 0.85 [95% CI, 0.83 to 0,87]) compared with the chronic MetS group (incidence rate, 8.52 per 1000 person-years). The Mets-developed group (incidence rate, 6.05 per 1000 person-years) had a significantly higher MACE risk (adjusted IRR, 1.36 [CI, 1.33 to 1.39]) than the Mets-free group (incidence rate, 1.92 per 1000 person-years). Among the MetS components, changes in hypertension were associated with the most significant difference in MACE risk. Recovery from MetS was significantly associated with a reduced risk of MACE, whereas the development of MetS was associated with an increased risk.

No	Researcher, Year and Country	Title	Design	Factor(s)	Aims	Result
29	Tan et al. (2017). Cina	Double product reflects the association of heart rate with MACEs in acute coronary syndrome patients treated with percutaneous coronary intervention	Retrospective study	Double product reflects	We have investigated whether DP reflects the predictive power of heart rate (HR) or systolic blood pressure (SBP) in PCI-treated ACS patients. The duration of follow-up was two years. Major cardiovascular adverse events (MACEs) include all-cause death, recurrent myocardial infarction, and stroke.	The incidence rate of MACE was 2.94%. MACE occurred in 94 (2.45%) patients with DP < 9657 and 129 (3.43%) patients with DP > 9657. The high DP group noted significantly higher MACE levels (relative risk 1.41, 95% CI 1.08 to 1.83, p = 0.012). However, in the full adjustment model, after including HR and SBP, the predicted value of DP was not significant (0.86 relative risks, 95% CI 0.55 to 1.33, p = 0.499). The HR predictive value for MACE was statistically significant (relative risk 1.74, 95% CI 1.33-2.28, p < 0.001). It should be noted that a history of hypertension was strongly associated with MACE (relative risk 1.53, 95% CI 1.11-2.11, p = 0.009).
30	Bansilal et al. (2016)	Assessing the Impact of Medication Adherence on Long-Term Cardiovascular Outcomes	Cohort study	Medication Adherence on Long-Term	We have determined the relationship between treatment adherence and long-term MACE in patients.	The fully adherent group had significantly lower MACE levels than the non-adherent (18.9% vs. 26.3%; hazard ratio [HR]: 0.73; p = 0.0004) and partially adherent (18.9 % vs 24.7%; HR: 0.81; p = 0.02) group at 2 years. The fully adherent group reduced ADM costs per patient for MI hospitalizations by $369 and $440 compared with the partially adherent and non-adherent groups. In the ATH cohort, the fully adherent group had significantly lower MACE levels than the non-adherent (8.42% vs. 17.17%; HR: 0.56; p < 0.0001) and the partially adherent (8.42 % vs 12.18%; HR: 0.76; p < 0.0001) group at 2 years. The fully adherent group had reduced ADM costs per patient for MI hospitalizations by $371 and $907 compared to the partially adherent and non-adherent groups.