学 位 論 文 の 要 旨

氏名　　安田　優

学　位　論　文　名　Incidence of Mid-Term Prognostic Events in Patients With Acute Coronary Syndrome During the Late 2010s in 2 Tertiary Hospitals in a Rural Area of Japan – A Temporal Comparison –

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著　　者　　名　Yu Yasuda, Hironori Ishiguchi, Madoka Yamaguchi, Kei Murakami, Natsu Kinoshita, Takayoshi Kato, Masaaki Yoshida, Koji Imoto, Kazuhiko Sonoyama, Tetsuya Kawabata, Takayuki Okamura, Akihiro Endo, Shigeki Kobayashi, Masafumi Yano, Tsuyoshi Oda and Kazuaki Tanabe

論 文 内 容 の 要 旨

INTRODUCTION

Cardiovascular diseases are a universal healthcare issue because they are the leading cause of death worldwide. Acute myocardial infarction (AMI) accounts for the major burden of all cardiovascular diseases. With the development of guidelines, evidence-based therapeutic strategies for AMI, such as early primary percutaneous coronary intervention (PCI) and optimal medical therapy, have been implemented mainly in Western countries since the 2000s. Because of this, significant improvements in the prognosis of AMI during the acute and chronic periods have been observed in some countries. However, most reports compared data from the 1990s, when guideline-based management had not been developed, with date from the 2000s, when management prevailed. Hence, the prognostic information for AMI in the 2010s, when an evidence-based therapeutic strategy was established, remains to be elucidated. In particular, data from the late 2010s are limited. To address this issue, we compared the mid-term prognosis of acute coronary syndrome (ACS) between the late 2010s and prior periods by analyzing the incidence of mid-term clinical events in patients who developed ACS between 2009 and 2018 in a rural area of Japan.

MATERIALS AND METHODS

In this study, we retrospectively included and collected data for 889 patients with ACS (ST-elevation myocardial infarction [STEMI]/non-ST-elevation ACS [NSTE-ACS]) discharged

alive from 2 tertiary hospitals in Izumo City, in rural Japan, between August 2009 and July 2018. Patients were divided into 3 time groups according to admission date (T1: August 2009-July 2012; T2: August 2012-July 2015; T3: August 2015-July 2018).

ACS was diagnosed based on ischemic symptoms with electrocardiographic changes and/or abnormal myocardial wall motion determined using echocardiography. ACS comprised ST-elevation myocardial infarction (STEMI) and non-ST-elevation ACS (NSTE-ACS). NSTE-ACS was subdivided into non-STEMI (NSTEMI) and unstable angina pectoris. STEMI/NSTEMI was diagnosed when cardiac troponin or high-sensitivity cardiac troponin were above the 99th percentile. Planned coronary revascularization for the target lesion or revascularization for asymptomatic patients was not considered for clinical events. Stroke was diagnosed as a neurological symptom, with plausible abnormal findings obtained using imaging modalities. Major bleeding events were defined as bleeding with a severity of ≥3 according to the Bleeding Academic Research Consortium criteria.

The primary endpoint of the study was the cumulative incidence of MACE within 2 years of discharge. MACE included all-cause death, recurrence of ACS, and stroke. Secondary endpoints were the cumulative incidence of major bleeding and hospitalization for heart failure within 2 years of discharge.

The study was performed in accordance with the Declaration of Helsinki and the ethical standards of The Institutional Review Boards of Shimane Prefectural Central Hospital and Shimane University Hospital approved this study.

RESULTS AND DISCUSSION

The patient demographics of the total population were comparable among the 3 temporal groups. Parameters associated with therapeutic strategy, the proportion of PCI, coronary artery bypass grafting (CABG), and conservative therapy were also comparable among the 3 groups. The use of new-generation drug-eluting stent (DES) increased significantly over time, along with a decrease in the use of bare-metal stent (BMS). The use of conventional guideline-recommended agents was consistently high among the groups. The proportion of STEMI among all patients with ACS was consistently high in the 3 temporal groups.

The incidence of freedom from MACE was significantly higher in the T3 group than in the T1 and T2 groups (93 [95% confidence interval {CI} 90-96%] vs. 86% [95% CI 83-90] and 89% [95% CI 90-96], respectively; P=0.03). In terms of the clinical events that comprised MACE, freedom from all-cause death was higher in the T3 than T1 and T2 groups (96% [95% CI 94–98%] vs. 93% [95% CI 91–96%] and 92% [95% CI 89–95%], respectively; P=0.07).

There was a tendency for a higher incidence of STEMI among patients in T3 (P=0.057). Freedom from all-cause death tended to be higher in the T3 than T1 and T2 groups (98

[96–100%] vs. 94% [91–98] and 93% [90–97], respectively; P=0.09). The incidence of NSTE-ACS was comparable among the 3 groups (P=0.31). In the total ACS population and in each of the subgroups, the incidence of major bleeding and hospitalization for heart failure was comparable among the groups.

This is the first study to conduct a temporal comparison of the incidence of mid-term prognostic events in patients who developed ACS between the late 2010s and prior periods in Japan. Previous studies comparing the incidence of clinical events between the mid-2000s and the early 2010s reported that the prognosis of patients with STEMI was unchanged or scarcely improved. Compared with this previous population, our late 2010s population had a higher proportion of the use of conventional guideline-recommended agents, relatively new devices for PCI, and newly approved therapeutic agents. Our data suggest that implementing guideline-directed management of ACS in current clinical settings could help to further improve the incidence of prognostic events in patients with STEMI. We did not find an improvement in the incidence of clinical events in patients with NSTE-ACS in the late-2010s. Our data imply that further studies regarding the management of patients with NSTE-ACS are warranted to improve the incidence of prognostic events.

Our study has several limitations. First, our data were collected from only 2 institutions in the same medical area. Hence, it remains unclear whether our data can be extrapolated to other medical areas in Japan and other countries. Second, because our data were collected retrospectively, unmeasured factors could have been missed. Third, therapeutic management of AMI continues to progress, even in contemporary clinical settings. Fourth, our data show that in-hospital mortality was slightly higher and all-cause mortality after discharge was lower than in a previous study. That is, the data could imply that patients with a severe status tend to die during hospitalization, which may make the mortality after discharge appear lower in our medical area. Finally, most part of our study period was before the COVID-19 pandemic.

CONCLUSION

Our findings suggest that the incidence of mid-term MACE in patients who developed ACS during the late 2010s (2015–2018) was lower than that in prior periods (2009–2015). The difference originates from an improvement in the incidence of patients with STEMI.