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ORIGINAL ARTICLE
Population Science

Long-Term Follow-up Study of Hospitalizations for Acute Coronary Syndrome in Kobe-City and Other Districts Under the Hyogo Smoking Ban Legislation

— A Nationwide Database Study —

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Background: Hyogo Prefecture has managed smoking ban legislation with partial restrictions in public places (Hyogo-L) since 2013. Previous studies have reported a significant decrease in admissions for acute coronary syndrome (ACS) in Kobe-city, but not in other districts of Hyogo Prefecture in the 2 years after Hyogo-L. The aim of the present study was to define the long-term effect of Hyogo-L.

Methods and Results: The JROAD-DPC dataset was used to collect information on the number of hospitalizations for ACS in Hyogo Prefecture, and in Osaka-city without smoking ban legislation, from April 2013 to March 2020. Poisson regression analysis was performed to calculate incident rate ratios (IRRs) and 95% confidence intervals (CIs). ACS records of 3,101 in Kobe-city, 11,375 in areas of Hyogo Prefecture other than Kobe-city and 11,079 in Osaka-city were collected for admissions. The incidence of ACS reduced significantly over time in Kobe-city [IRR (95% CI); 0.96 (0.94–0.97)], but did not reduce in the others. The decrease in Kobe-city was observed in ACS patients without smoking, hypertension, and hyperlipidemia, but not in those with such risk factors.

Conclusions: The long-term ACS reduction or non-reduction under Hyogo-L was determined at the initial period and the same scenario continued, supporting the importance of legislation and compliance with the smoking ban. The lowering effect was remarkable in ACS patients without risk factors such as non-smoking.

Key Words: Acute coronary syndrome; Long-term effects; Nationwide longitudinal study; Smoking ban legislation

Exposure to secondhand smoke causes significant health and economic problems worldwide, including in Japan.[1,2] Government tobacco regulatory policies protecting people from secondhand smoke exposure through legislation banning smoking in public places have powerful evidence of effectiveness and are reported to be linked with reductions in adverse health results;[3] however, they have been implemented with varying levels of success.[4]

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Epidemiological studies have shown that exposure to secondhand smoke has negative effects on cardiovascular health. Meta-analyses have demonstrated that enactment of legislation that imposes smoking bans in public places lowers the incidence of coronary events by 8–17%.[5,6] Locations under legislation with a partial ban have had fewer

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Table 1. Clinical Characterization of ACS Hospitalizations Admitted in Each District

	Hyogo Prefecture			Osaka Prefecture
	Kobe-city	Hanshin area	Other areas	Osaka-city
n	3,101	6,677	4,698	11,079
Age, mean (SD), years	71.9 (11.6)	71.2 (12.3)	70.1 (12.3)	70.9 (12.2)
≥65	2,344 (75.6%)	4,867 (72.9%)	3,305 (70.3%)	8,188 (73.9%)
Sex, male	2,148 (69.3%)	4,662 (69.8%)	3,391 (72.2%)	7,856 (70.9%)
Nonsmoker*	1,862 (67.1%)	3,352 (57.5%)	2,158 (46.8%)	4,635 (49.0%)
Comorbidity				
Hypertension	1,499 (48.3%)	3,307 (49.5%)	2,895 (61.6%)	6,597 (59.5%)
Diabetes mellitus	911 (29.4%)	1,889 (28.3%)	1,537 (32.7%)	3,350 (30.2%)
Hyperlipidemia	1,647 (53.1%)	3,133 (46.9%)	2,938 (62.5%)	6,557 (59.2%)
ACS history	175 (5.6%)	447 (6.7%)	294 (6.3%)	821 (7.4%)
Procedures				
PCI	1,915 (61.8%)	4,464 (66.9%)	3,254 (69.3%)	6,327 (57.1%)
CAG	952 (30.7%)	1,985 (29.7%)	1,195 (25.4%)	3,474 (31.4%)
In-hospital death	161 (5.2%)	485 (7.3%)	270 (5.7%)	465 (4.2%)

Data are expressed as mean (SD) or number (%). *Nonsmoker indicates zero of the Brinkman index. ACS, acute coronary syndrome; CAG, coronary angiography; PCI, percutaneous coronary intervention; SD, standard deviation.

reductions in hospital admissions for acute coronary syndrome (ACS: acute myocardial infarction [AMI] and unstable angina pectoris [UAP]) compared with areas that have implemented comprehensive smoking ban legislation. We recently reported a significant reduction in the number of hospital admissions for ACS in Kobe-city during a 2-year observation after the implementation of the Hyogo smoking ban legislation with a partial ban in public places (Hyogo-L) in 2013. (The details of this smoking ban are described in a previous study.[7]) However, this lowering effect was not observed in other districts in Hyogo Prefecture and the difference was linked to significantly higher rates of recognition and compliance with the smoking ban among residents of Kobe-city where a prefectural government office is located.[8] However, most of the previous studies were on the short-term effects (i.e., within 3 years after the enactment of smoking ban legislation in public places) and the long-term effect has not been established. Therefore, this research was designed as a long-term follow-up of ACS hospitalizations under Hyogo-L from 2013 to 2019 using a large real-world administrative database to define whether the ACS reduction in Kobe-city and non-reduction in other areas has continued and whether the reducing effect in Kobe-city is different for patients with and without ACS risk factors such as smoking.

Methods

Study Population

The Japanese Registry Of All cardiac and vascular Disease-diagnosis procedure combination (JROAD-DPC) was used to obtain a longitudinal dataset of insurance claims developed by the Japanese Circulation Society. The JROAD-DPC dataset has been explained elsewhere.[9,10] In brief, the dataset contains the unique hospital identifier, age, sex, main diagnosis, comorbidities, length of hospital stay, in-hospital medications, in-hospital cost, and discharge status of patients with records of cardiovascular or cerebrovascular diseases in any diagnosis category.

Patients admitted to hospital with ACS between April 2013 and March 2020, or April 2012 and March 2016 were identified using the ICD-10 codes recorded in the DPC system. Entries codes as I200, I21 or I22 in the main diagnosis, admission-precipitating diagnosis, most resource-consuming diagnosis, or second resource-consuming diagnosis were considered to be ACS. Entries codes as I200 in the diagnosis were considered as UAP and entries codes as I21 or I22 in the diagnosis were considered as AMI. Also, comorbidity was defined as the presence of index ICD-10 codes in the diagnostic category of comorbidity: hypertension as I1, diabetes as E10, E11, E12, E13, and E14, hyperlipidemia as E78. Smoking was defined as >0 of the Brickman index, which calculates at admission and cannot distinguish between past and current smoker in the DPC dataset. The dataset was restricted to hospitals that submitted DPC data in all 7 or 4 consecutive years to observe longitudinal changes in the number of hospitalizations over the study periods. Data were compared among the 4 districts defined by the Ministry of Internal Affairs and Communications municipal code: Kobe-city (urban area with Hyogo-L), Hanshin area (urban area with Hyogo-L between Osaka-city and Kobe-city, which includes Amagasaki-city, Nishinomiya-city, Ashiya-city, Itami-city, Takarazuka-city, Kawanishi-city, Sanda-city and Inagawa-town), other areas of Hyogo Prefecture aside from Kobe-city and Hanshin area (urban and rural areas with Hyogo-L), and Osaka-city (urban area with no smoking ban legislation) of Osaka Prefecture, next to Hyogo Prefecture. In 2019, the population was 1.51 million in Kobe-city, 1.71 million in the Hanshin area, 2.25 million in the rest of Hyogo Prefecture, and 2.74 million in Osaka-city.

Ethics Statement

The present study was conducted in accordance with the 1964 Declaration of Helsinki and its later amendments and was approved by the Hyogo Prefecture Amagasaki General Medical Center ethics committee (authorization no. 3-39).

Statistical Analysis

Data are expressed as the mean and standard deviation for continuous variables and number with percentage (%) for

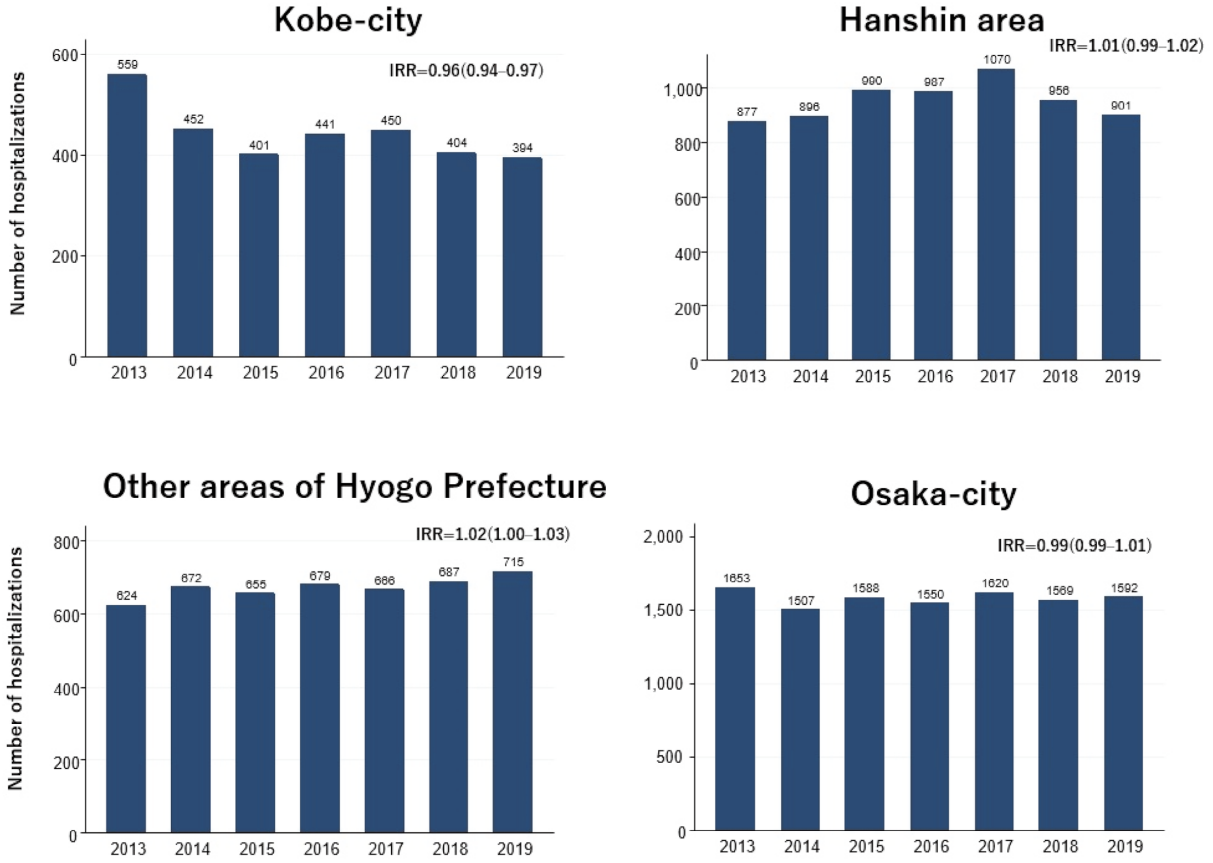

Figure. Annual number of ACS hospitalizations and IRR for each district. The number of ACS hospitalizations significantly reduced in Kobe-city and did not reduce in the Hanshin area and other areas of Hyogo Prefecture. Over the study period, there was no change in the number of ACS hospitalizations in Osaka-city. ACS, acute coronary syndrome; IRR, incident rate ratio.

categorical variables. The total number of ACS hospitalizations was summarized for each year as a discrete variable. The annual change in the number of ACS hospitalizations was determined using univariate Poisson regression analysis, treating "study period" as a continuous variable. This indicated the time trend of the yearly change during 7 or 4 years. Incident rate ratios (IRRs) and 95% confidence intervals (CIs) were calculated for the study period. An IRR <1 indicated a decrease in the number of ACS hospitalizations during the study period and IRR ≥1 indicated an increase. When the CI contained 1.0, the ACS number was not statistically changed over the study period. IRR was also calculated for the time trend of AMI or UAP hospitalizations. Furthermore, in order to investigate relevant factors of reducing ACS hospitalization, stratified analysis was performed with variables such as age, sex, smoking, hypertension, diabetes mellitus, hyperlipidemia, and ACS history. The stratified dataset was created by extracting the specific category and then the number of ACS hospitalizations by year was summarized as a discrete variable. Statistical analysis was performed using Stata, version 16 (College Station, TX, USA).

Results

Table 1 shows the clinical characteristics of the total ACS patients admitted to hospitals in each of the 4 districts from 2013 to 2019.

Longitudinal changes in the number of ACS hospitalizations are shown in the **Figure**. The incidence of ACS in Kobe-city decreased significantly over the study period (IRR, 0.96; 95% CI, 0.94–0.97), but did not decrease in the Hanshin area and other areas of Hyogo Prefecture (IRR, 1.01; 95% CI, 0.99–1.02 and IRR, 1.02; 95% CI, 1.00–1.03, respectively). No significant changes were observed in the number of ACS hospitalizations in Osaka-city (IRR, 0.99; 95% CI, 0.99–1.01). In addition, when we included the data for the pre-Hyogo-L year and analyzed the time trend from 2012 to 2015, Kobe-city still showed a significant decrease in the total number (IRR, 0.93; 95% CI, 0.88–0.99), whereas the other areas showed significant increases (**Supplementary Table 1**).

As shown in **Table 2** and **Table 3**, the number of ACS hospitalizations in Kobe-city from 2013 to 2019 decreased significantly in both male and female patients, as well as patients aged ≥65 years and <65 years. Furthermore, a significant reduction was observed in each patient group without smoking, hypertension or hyperlipidemia. However, the number of ACS hospitalizations in smokers and each group with hypertension, and hyperlipidemia did not change significantly over the 7 years. Furthermore, for AMI, only Kobe-city showed no change in hospitalization

Table 2. IRR for the Number of ACS Hospitalizations During the Study Period by Age and Sex Groups

	Hyogo Prefecture						Osaka Prefecture	
	Kobe-city		Hanshin area		Other areas		Osaka-city	
	IRR (95% CI)	P value	IRR (95% CI)	P value	IRR (95% CI)	P value	IRR (95% CI)	P value
Sex								
Male	0.96 (0.94–0.98)	0.001	1.01 (0.99–1.02)	0.160	1.02 (1.00–1.04)	0.023	1.00 (0.99–1.01)	0.600
Female	0.94 (0.91–0.97)	<0.001	1.01 (0.99–1.03)	0.373	1.01 (0.98–1.04)	0.498	1.01 (0.99–1.02)	0.561
Age, years								
<65	0.93 (0.90–0.97)	<0.001	0.98 (0.95–1.00)	0.050	0.99 (0.97–1.02)	0.547	0.99 (0.97–1.01)	0.184
≥65	0.96 (0.95–0.98)	<0.001	1.02 (1.01–1.04)	0.002	1.03 (1.01–1.05)	0.002	1.00 (0.99–1.01)	0.522

ACS, acute coronary syndrome; CI, confidence interval; IRR, incident rate ratio.

Table 3. IRR for the Number of ACS Hospitalizations in Kobe-city

		Kobe-city		
		IRR (95% CI)	P value	Interaction
Smoking	Yes	1.03 (0.99–1.06)	0.132	<0.001
	No	0.92 (0.90–0.95)	<0.001	
Hypertension	Yes	0.98 (0.95–1.00)	0.104	0.001
	No	0.94 (0.91–0.96)	<0.001	
Diabetes mellitus	Yes	1.00 (0.97–1.04)	0.766	0.246
	No	0.94 (0.92–0.96)	<0.001	
Hyperlipidemia	Yes	1.02 (0.99–1.05)	0.063	<0.001
	No	0.89 (0.86–0.91)	<0.001	
ACS history	Yes	0.92 (0.86–0.99)	0.038	0.536
	No	0.96 (0.94–0.98)	<0.001	

ACS, acute coronary syndrome; CI, confidence interval; IRR, incident rate ratio.

numbers (IRR, 1.02; 95% CI, 0.99–1.05), but all other areas showed a significant increase from 2013 to 2019 (**Supplementary Table 2**). In contrast, all areas except the other areas of Hyogo Prefecture showed a significant decrease in UAP (**Supplementary Table 3**), although Kobe-city still showed a significantly decreased trend (IRR, 0.91; 95% CI, 0.89–0.94).

Discussion

Growing evidence suggests that legislation for smoking bans in public places shows rapid and short-term (within 3 years) reduction in ACS incidence, particularly if a comprehensive smoking ban is implemented.[11–13] Our previous short-term study demonstrated that under Hyogo-L, the ACS lowering effect was observed in Kobe-city, but not in other districts.[7] However, the long-term effect is yet to be determined. Abreu et al reported a continuous decline in ACS admissions during 6 years under a comprehensive smoking ban.[14] A meta-analysis suggested that the passage of strong smoke-free legislation produces rapid and substantial benefits in terms of AMI reduction, and these benefits grow with time.[12] Also, studies with longer data collection following legislation showed greater estimates of risk reduction in univariate random effects meta-regression analysis.[15] The present study showed that the reduction in Kobe-city and non-reduction in the other districts persisted up to 7 years after Hyogo-L with partial restriction. Kobe-city showed that the early and late phases after the enforcement of ordinances are likely to be affected differently. A substantial decrease in ACS incidence was observed in the first year following the implementation of Hyogo-L, but the incidence of ACS seems to have plateaued thereafter, which may indicate that the presence or absence of a decline in ACS admissions is determined mainly in the initial period and the same situation continues in the long term. Further long-term analysis following legislation is necessary.

Also, in the analysis of UAP and AMI admissions, the effect of the smoking ban legislation in Kobe-city was explicitly observed compared with other areas in both cases. Previous studies showed reductions of ACS and AMI admissions and the present study findings suggested that it is effective not only for AMI, but also UAP hospitalizations.

Our findings suggest that the long-term reduction in ACS under smoke-free public spaces with partial restrictions is remarkable in non-smoking, non-hypertensive, and non-hyperlipidemic patients than in the patients with such risk factors. The data on smokers and non-smokers back up the report that the short-term ACS lowering effect of Scotland's comprehensive smoking ban legislation was stronger in non-smokers than in smokers.[16] This effect can be explained by the degree of decrease in exposure to sec-

ondhand smoke under smoking ban legislation being greater in non-smokers than in smokers. However, there are few reports regarding the association between secondhand smoke and risk factors of coronary artery disease such as hypertension and dyslipidemia in the development of ACS. On the ACS reducing effect in non-hypertensive and non-hyperlipidemic patients, one possible mechanism is that each group of non-hypertensive and non-hyperlipidemic patients may include relatively more non-smokers, compared with the patients with hypertension and hyperlipidemia, respectively. However, the patient numbers in Kobe-city in the present study were too small to verify this problem. Another possible mechanism is that patients without coronary risk factors would be relatively health-minded and may be more sensitive to Hyogo-L and compliance, compared with patients with coronary risk factors. Further studies including questionnaire surveys are required to investigate the differences between ACS patients with and without risk factors.

The relative effectiveness of smoking bans in urban and rural areas remains controversial.[17,18] In the present study, the long-term lowering effect of ACS admissions was observed in Kobe-city, which is an urban area, but not in the Hanshin area as an urban area, or in the other urban and rural area. Furthermore, the smoking prevalence in Hyogo Prefecture and Kobe-city were comparable in 2013 and 2019 (19.2% and 15.7% in Hyogo Prefecture and 18.9% and 14.6% in Kobe-city, respectively).[19] This suggests that the factors of urban or rural area and smoking prevalence have no bearing on the difference in the ACS reducing effect between Kobe-city and other districts of Hyogo Prefecture. Previous studies using questionnaires revealed that adherence and recognition to Hyogo-L in bars and restaurants were higher in Kobe-city than in Amagasaki-city in the Hanshin district with a significant difference.[8] As a result, the higher compliance with Hyogo-L in Kobe-city may have contributed to the long-term differences between Kobe-city and other districts. Also, this shows the significance of compliance and recognition among residents of smoking ban legislation with partial restrictions.

Study Limitations

First, the DPC dataset lacks detailed information on smoking habits such as smoking prevalence or secondhand smoke exposure. The DPC dataset only includes Brickman index values and provides information on whether patients were smokers or not at admission. Second, because the dataset was limited to hospitals that submitted DPC data for all 7 consecutive years and was extracted only by ICD10 code, the present results may not fully reflect the studied districts. Lastly, due to the limited number of cases in this DPC database, we examined the changes since the start of the smoking ban legislation in 2013. As in the previous report,[7] it is desirable to analyze the changes from before the ban legislation. However, although the observation period was shortened, the similar effects of the smoking ban legislation were observed in all the districts between 2012 and 2015 (**Supplementary Table 1**).

Conclusions

The long-term ACS reduction or non-reduction under the Hyogo smoking ban legislation in public spaces with partial restrictions was determined at the outset and the same situation was maintained over time, which supports the importance of the legislation and compliance. The reducing effect was remarkable in the patients without the ACS risk factors such as non-smokers.

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Conflicts of Interest

None.

Disclosures

T.A. is a member of *Circulation Journal*'s Editorial Team.

IRB Information

The present study was conducted following the 1964 Declaration of Helsinki and its later amendments and was approved by the Hyogo Prefecture Amagasaki General Medical Center ethics committee (authorization number, 3–39).

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Supplementary Files

Please find supplementary file(s);
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