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Women were noninferior to men in cardiovascular outcomes among patients with ST-segment elevation myocardial infarction treated with primary percutaneous coronary intervention from Taiwan acute coronary syndrome full-spectrum registry

Li-Ping Chou, MD[a,b], Ping Zhao, MD[c], Chieh Kao, MD[d], Yen-Hsun Chen, MD[d], Gwo-Ping Jong, MD, PhD[e,*]

Abstract

This study was conducted to compare the survival rate and the influencing factors between women and men following ST-elevation myocardial infarction (STEMI) treated with primary percutaneous coronary intervention (PCI).

A national-wide Acute Coronary Syndrome Full Spectrum Registry conducted by the Taiwan Society of Cardiology was used for data collection between October 2008 and January 2010. Details of 1621 patients with STEMI treated with primary PCI, including 1350 (83%) men and 271 (17%) women, were collected. Composite outcomes included all-cause death, myocardial reinfarction, and an ischemic stroke. Demographic data, comorbidities, clinical presentations, details of treatment received, and outcomes were recorded at 3-month intervals for 1 year.

No significant difference was observed between men and women in the composite endpoints after STEMI during their hospital stay (5.5% vs 2.5%, $P = .07$). However, women showed significantly higher in-hospital and 1-year mortality rates than those of men (4.1% vs 1.8%, $P = .008$; 11.0% vs 4.1%, $P = .000$, respectively). Compared with men, women presented with higher age (mean age 68.9 vs 58.9 years, $P = .001$), less body weight (58.7 vs 70.9 kg, $P < .001$), more number of risk factors, delayed diagnosis, and more number of inadequate medical treatments. After adjusting for age and cardiovascular risk factors, the difference in mortality ceased to exist between men and women.

Although female patients with STEMI-treated primary PCI had higher in-hospital and 1-year mortality rates than those of males in Taiwan, there was no gender difference after adjusting for age and cardiovascular risk factors.

Abbreviations: ACS = acute coronary syndrome, ECG = electrocardiogram, PCI = primary percutaneous coronary intervention, STEMI = ST-elevation myocardial infarction.

Keywords: cardiovascular outcome, gender difference, mortality, primary PCI, STEMI

1. Introduction

Gender difference has been observed in several diseases in terms of their prevalence and outcomes. Among such diseases, coronary artery disease has been reported to present a delayed onset for 10 years in women, with increased mortality and morbidity rates after acute coronary events compared with the rates among their comparators in many countries.[1]

There is extensive evidence delineating the relationship of gender difference in acute coronary syndrome (ACS).[2,3] However, after adjusting for confounding factors, the gender difference ceased to exist. In general, studies on outcomes have reported higher crude mortality rates in women after ACS, which have been primarily explained by differences in age, management, and comorbidities between men and women. In addition, these studies have identified an age–sex interaction, wherein older age women have a particularly high risk of mortality after ACS even after adjusting for other risk factors.[4–6]

Limited data from the world have also demonstrated that women have worse outcomes after ACS treated with primary percutaneous coronary intervention (PCI)[7,8]; however, to our knowledge, there have been no such reports from Asia. Therefore, we conducted this study to compare the short-term

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[a] Division of Internal Cardiology, Department of Medicine, Sin-Lau Hospital, [b] Department of Health Care Administration, Chang Jung Christian University, Tainan, [c] Department of Ultrasound, Shangluo Central Hospital, Shangluo, Shaanxi Province, [d] Division of Internal Cardiology, Department of Medicine, Sin-Lau Hospital, Tainan, [e] Division of Internal Cardiology, Chung Shan Medical University Hospital and Chung Shan Medical University, Taichung, Taiwan, ROC.

[*] Correspondence: Gwo-Ping Jong, Department of Internal Medicine, Chung Shan Medical University Hospital and Chung Shan Medical University, No. 110, Section 1, Chien-Kuo N. Road, 40201, Taichung, Taiwan, ROC (e-mail: cgp8009@yahoo.com.tw).

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major cardiovascular outcomes and determine the influencing factors between men and women after ST-elevation myocardial infarction (STEMI) treated with primary PCI.

2. Materials and methods

2.1. Study participants

An ACS Full Spectrum Registry was conducted by the Taiwan Society of Cardiology and implemented between October 2008 and January 2010. A total of 39 tertiary hospitals were included in this registry, all of which have the availability of on-site thrombolytic therapy and on-site cardiac catheterization facility. Details regarding patient recruitment, definition of ACS, and inclusion and exclusion criteria have been previously described.[9]

2.2. Study design

It was mandatory for each hospital to provide data on demographics, clinical characteristics, comorbid conditions, clinical presentations, medical and therapeutic information, and complications or outcomes. Patient details regarding medical interventions and clinical events such as death, myocardial infarction, stroke, and rehospitalization after their discharge were collected and were followed up for 1-year at 3-month intervals through clinical visits. Data collected in this study were entered into a standardized report form, and source documentation and accuracy were monitored in 5% of all case report forms at each recruiting site. The study protocol was approved by the ethics committee of the Sin-Lau Hospital (SL-2012–18) and was performed in accordance with the local regulatory guidelines and the international guidelines for good clinical practice.[10] All the patients provided an informed consent, although it can be waived if they were not willing.

2.3. Cardiovascular outcomes

The endpoint of this study was to assess major adverse cardiac events (MACE) during hospitalization and 1 year after discharge, a composite of all-cause death, myocardial reinfarction, and an ischemic stroke.

2.4. Statistical analysis

Continuous variables were summarized as mean values and standard deviations, whereas categorical variables were summarized as numbers and percentages. Student *t* test was used for comparing continuous variables and Chi-square test was used for comparing categorical variables between males and females. Non-normally distributed continuous variables were summarized using median and interquartile range and were analyzed using the Mann–Whitney test. The association between in-hospital or 1-year outcome and gender after adjusting for various confounders (age, body mass index, diabetes, current smoking status, dyslipidemia, and hypertension) was analyzed using multivariable logistic regression. Finally, time-to-event comparisons among the 2 groups were performed using Kaplan–Meier survival curve analysis. A *P* value of $<.05$ was considered as statistically significant. SAS software version 9.2 (SAS Institute Inc., Cary, NC) was used for performing all statistical analyses.

Table 1

Baseline characteristics of patients enrolled in the registry.

	Total (n = 1621)	Male (n = 1350)	Female (n = 271)	*P*
Age, y, mean ± SD	61.5 ± 13.5	59.9 ± 13.3	68.9 ± 12.2	<.001
BMI, kg/m^2, mean ± SD	25.3 ± 3.8	25.5 ± 3.7	24.6 ± 3.9	.001
Height	164.7 ± 7.6	166.8 ± 6.0	154.4 ± 6.1	<.001
Weight	68.8 ± 12.5	70.9 ± 11.9	58.7 ± 10.4	<.001
Killip class, (%)				<.001
I	60.8	62.5	52.7	
II	20.2	20.3	19.5	
III/IV	19.0	17.2	27.7	
Risk factors, (%)				
Dyslipidemia	33.8	33.6	34.7	.715
Hypertension	58.0	55.6	69.8	<.001
Diabetes	31.0	28.7	42.5	<.001
Current smoker	47.4	54.9	10.7	<.001
Family history	22.6	23.4	18.2	.099
Known CVD, (%)				
CHD	16.1	16.0	16.6	.812
PAOD	1.5	1.4	1.7	.598
CVA	6.4	6.3	6.6	.878

BMI = body mass index; CHD = coronary heart disease; CVA = cerebrovascular attack; PAOD = peripheral artery occlusive disease; SD = standard deviation.

3. Results

3.1. Study participants

Baseline characteristics of the enrolled patients are depicted in Table 1. A total of 1621 patients, including 1350 men and 271 women, were recruited in this study. Mean age of the patients was 62 years, with female patients being 9 years older than male patients ($P < .001$). Female patients also had significantly lower body weight, shorter body height, and lower body mass index than those of male patients. Analysis of disease severity in terms of STEMI presentation revealed that female patients had a higher incidence of Killip III/IV class than that of male patients (27.7% vs 17.2%, $P < .001$). Female patients also had a significantly higher prevalence of hypertension and diabetes mellitus but a lower prevalence of current smoking status. Both genders showed equal prevalence of coronary heart disease, peripheral artery occlusive disease, and cerebrovascular attack.

3.2. Evaluation and diagnostic procedure in emergent department

During presentation in the emergency room, female patients showed a significantly lower diastolic blood pressure. Male patients comprised a significantly higher proportion than female patients in undergoing the first electrocardiogram (ECG) within 10 minutes (57.4% vs 48.8%, $P = .013$). No statistical difference was observed between men and women in terms of culprit arteries, severity of TIMI flow in the culprit arteries, and left ventricular (LV) systolic function (Table 2).

3.3. Reperfusion in STEMI patients

Table 3 summarizes the details of comparison of reperfusion therapy in patients with STEMI between the 2 genders. The probability of undergoing primary PCI was higher among both genders, although female patients comprised a significantly lower proportion than that of male patients in this context (95.2%

Table 2

Evaluation in the ED, diagnostic, and angiographic procedures.

	Total	Male	Female	P*
SBP, mm Hg, mean ± SD	135.95 ± 33.0	135.4 ± 33.0	138.8 ± 32.9	.110
DBP, mm Hg, mean ± SD	81.59 ± 21.40	82.2 ± 21.3	78.9 ± 21.5	.017
HR, beats/min	79.77 ± 21.8	79.4 ± 21.5	81.6 ± 23.3	.145
Examinations				
First ECG < 10 min (%)		57.4	48.8	.013
Cardiac angiography				
Median time to hours		9.0	11	.08
Culprit artery (%)				
LM		2.2	2.4	.226
LAD		51.3	46.2	.204
LCx		14.0	13.1	.796
RCA		38.4	36.6	.563
Artery flow (%)				.271
TIMI 0/1		69.1	64.8	
TIMI 2		17.1	17.6	
TIMI 3		13.8	17.6	
Median ejection fraction, mean ± SD		53.8 ± 12.2	54.1 ± 13.1	.705

DBP = diastolic blood pressure; ECG = electrocardiogram; HR = heart rate; LAD = left anterior descending; LCx = left circumflex; LM = left main; RCA = right coronary artery; SBP = systolic pressure; SD = standard deviation; TIMI = thrombolysis in myocardial infarction.

vs 98.2%, $P = .014$). Female patients had a longer door-to-balloon time than that of male patients (103 vs 92 minutes, $P = .049$). Guideline-derived door-to-balloon time was less among female patients within 60 or 90 minutes compared with that in male patients (18.6% vs 25.9%, $P = .029$; 43.8% vs 49.4%, $P = .148$, respectively).

3.4. Pharmacological management of STEMI for acute use and at discharge

No significant gender differences were observed in medication for acute use (within the first 24 hours of admission) of aspirin, clopidogrel, GP IIb/IIIa inhibitors, heparin, beta-blockers, angiotensin-converting enzyme inhibitors (ACEIs), and angiotensin receptor blockers (ARBs). The proportion of acute use of statins was significantly less in women than that in men (45.5% vs 52.5%, $P = .030$). Furthermore, compared with male patients, female patients received significantly less medications at discharge such as clopidogrel (88.7% vs 79.0%, $P = .000$), aspirin + clopidogrel (81.7% vs 74.1%, $P = .003$), beta-blockers (57.2% vs 50.0%, $P = .027$), statins (64.2% vs 55.2%, $P = .004$), and ACEIs/ARBs (68.6% vs 61.7%, $P = .006$) (Table 4).

3.5. In-hospital and 1-year cardiovascular outcomes

Table 5 summarizes the details of in-hospital and 1-year follow-up cardiovascular outcomes. There was no significant difference in composite endpoints (males 2.5% vs females 5.5%, $P = .07$); however, compared with male patients, females had significantly higher rates of total mortality (1.7% vs 4.1%, $P = .004$) and cardiac mortality (1.4% vs 3.1%, $P = .027$) among the in-hospital cardiovascular outcomes. No difference was observed between both genders in terms of TIMI major or minor bleeding, new onset of cardiogenic shock, ventricular arrhythmia, atrial fibrillation, and acute renal failure.

After STEMI, a lower mortality rate that persisted till 1 year was observed in male patients [hazard ratio: 0.36%, 95% confidence interval (95% CI): 0.23–0.55] (Fig. 1). The gender difference in terms of in-hospital and 1-year cardiac mortality after STEMI was still existent; however, after adjusting for sex and age (model 1) or by age, sex, and other cardiovascular risk factors (model 2), the difference became nonsignificant (Table 6).

4. Discussion

From this study, we found that gender disparities exist in terms of age, comorbidities, medication management, primary PCI, and

Table 3

Reperfusion status in patients diagnosed with STEMI at the time of admission.

	Total (n = 1621)	Male (n = 1350)	Female (n = 271)	P*
Reperfusion therapy performed (%)				
Primary PCI	98.2	98.2	95.2	.014
Fibrinolysis + Primary PCI	1.8	1.8	4.8	.285
Fibrinolysis				
Median door-to-needle time, min	65	65	95	.355
Door-to-needle within 30 min, n/N (%)	6/45 (13.3)	6/38 (15.8)	0/7 (0.0)	.569
Primary angioplasty				
Median door-to-balloon time, min	93	92	103	.049
Door-to- balloon within 60 min, (%)	24.8	25.9	18.6	.029
Door-to- balloon within 90 min (%)	28.6	49.4	43.8	.148

PCI = percutaneous coronary intervention.

Table 4

Medication prescription for acute use and at patient discharge.

	Total (n = 1716)	Male (n = 1426)	Female (n = 290)	P*
Medication, acute use, (%)				
Aspirin	95.2	95.4	94.5	.518
Clopidogrel	96.9	97.0	96.2	.489
Aspirin + clopidogrel	93.1	93.3	92.4	.600
GP IIb/IIIa inhibitor	23.3	22.9	25.2	.396
Any heparin	95.5	95.6	94.8	.574
Beta-blocker	47.3	47.6	45.5	.514
Statin	51.3	52.5	45.5	.030
ACE inhibitor/ARB	64.0	64.1	63.1	.202
Medication, at discharge, n/N (%)				
Aspirin	85.0	85.7	81.7	.084
Clopidogrel	86.6	88.0	79.7	.000
Aspirin + clopidogrel	80.4	81.7	74.1	.003
Beta-blocker	56.0	57.2	50.0	.024
Statin	62.7	64.2	55.2	.004
ACE inhibitor/ARB	67.5	68.6	61.7	.006

ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker; GP = glycoprotein.

in-hospital and 1-year mortality rates among patients with STEMI. However, after adjusting for age and cardiovascular risk factors, there was no gender difference in the in-hospital and 1-year mortality rates among patients with STEMI.

This study on the role of gender in patients with STEMI treated with primary PCI in Taiwan has demonstrated inconsistent results compared with those of previous studies.[4,5,11–14] Female patients with STEMI were older and had a higher prevalence of hypertension and diabetes mellitus than those of male patients, which is consistent with the results of previous studies[15–18] and might also explain the poorer prognosis. The time to first ECG at the emergency department was longer among women, which might delay receiving appropriate treatment for STEMI. A possible delay for performing ECG in women could be attributed to a lack of STEMI symptoms and atypical angina presentation when symptoms occur. [15] Our data also revealed a significant underutilization of dual antiplatelet therapy and statins when women are discharged from the hospital. These results are in accordance with previous studies that found a consistent lower utilization rate of medications in women.[15,19] A study based on a large Canadian registry found that women had lower chances of receiving lipid-lowering agents, even after adjustment for all relevant variables.[20] Moreover, similar results with lower rates of treatment with aspirin and statins were reported in a study based on the American College of Cardiology-National Cardiovascular Data Registry.[21] Underutilization of antiplatelet therapy could be justified by higher rates of nonobstructive coronary artery disease in women. This notion is supported by a

Table 5

In-hospital and at discharge outcomes according to gender.

N (%)	Total (n = 1716)	Male (n = 1426)	Female (n = 290)	P*
In-hospital				
Death	36 (2.1)	24 (1.7)	12 (4.1)	.008*
Cardiac	29 (82.9)	20 (87.0)	9 (75.0)	.391
Composite of death or MI or stroke	52 (3)	36 (2.5)	16 (5.5)	.007*
Re-MI	10 (0.6)	9 (0.6)	1 (0.3)	1
Stroke	6 (0.3)	3 (0.2)	3 (1.0)	.064
TIMI bleeding				
major	9 (0.5)	7 (0.5)	2 (0.7)	.654
Minor	23 (1.3)	18 (1.3)	5 (1.7)	.573
New onset				
Cardiogenic shock	84 (4.9)	73 (5.1)	11 (3.8)	.340
Ventricular arrhythmia	101 (5.9)	82 (5.8)	19 (6.6)	.597
Atrial fibrillation	44 (2.6)	33 (2.3)	11 (3.8)	.146
Acute renal failure	33 (1.9)	24 (1.7)	9 (3.1)	.108
1-y follow-up				
Death	91 (5.3)	59 (4.1)	32 (11.0)	.000‡
Cardiac	47 (2.7)	32 (2.2)	15 (5.2)	.008†
Noncardiac	22 (1.3)	15 (1.1)	7 (2.4)	.063
Composite of death or MI or stroke	170 (10.0)	127 (8.9)	43 (14.8)	.012*
Stroke	29 (1.7)	23 (1.6)	6 (2.1)	.686
Re-MI	70 (4.1)	62 (4.3)	8 (2.8)	.450

MI = myocardial infarction; TIMI = thrombolysis in myocardial infarction.

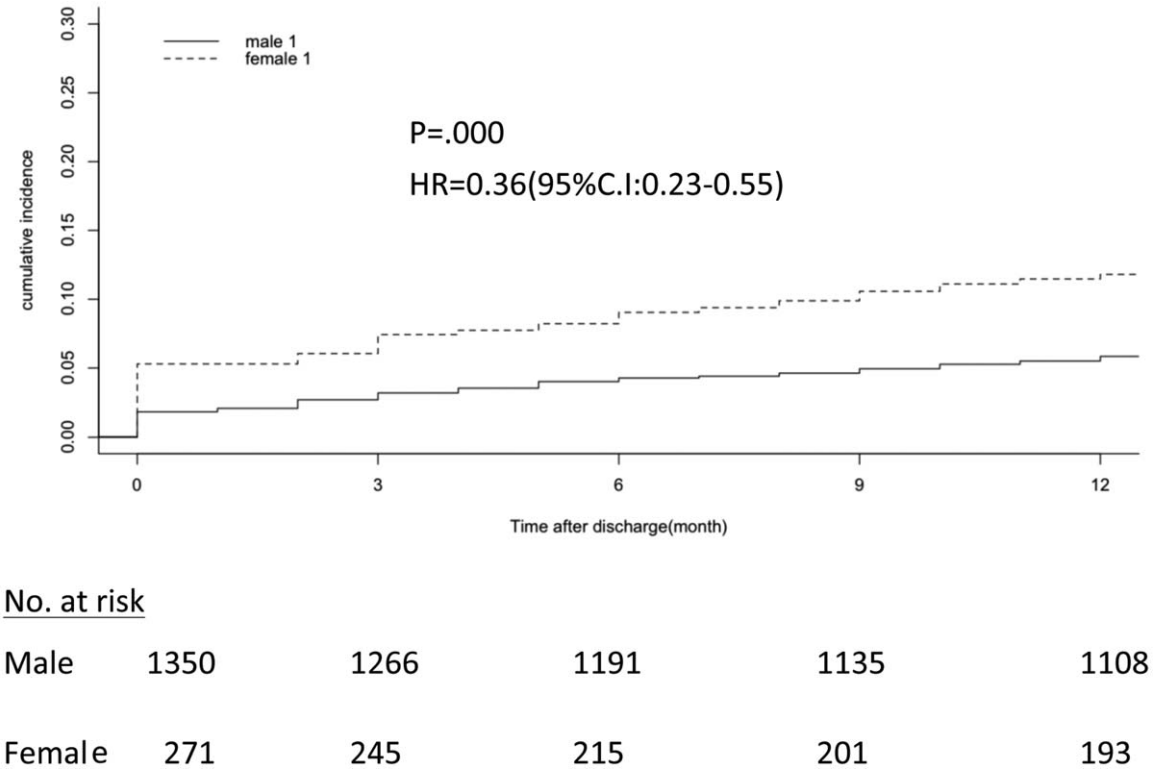

Figure 1. Comparison 1-year mortality rate by Kaplan–Meir method between males and females after STEMI.

previous study based on the 2004 to 2010 ACSIS surveys that showed underutilization of evidence-based medications in patients with nonobstructive coronary artery disease.[22]

Women were also less likely to undergo primary PCI, had longer door-to-balloon time, and a higher Killip class (3 and 4) compared with those among men. Our results are consistent with those of several previous studies.[5,11,14,23,24] and can be explained by the observation that women of older age and having more number of comorbidities are probably at a higher risk for undergoing primary PCI. The fact that women experienced a longer median time to have a coronary angiography than men could be related to the fact that women are less likely to experience symptoms of STEMI, and when they develop such symptoms, they are often present as atypical angina, which complicates the STEMI diagnosis. [15,19–21]

Table 6

Multivariable-adjusted odds ratios for the association between gender and outcome.

	Unadjusted	Model I	Model II
Death			
In-hospital	2.52 (1.25–5.10)*	1.49 (0.64–3.52)	1.38 (0.57–3.32)
12-mo	2.87 (1.83–4.50)*	1.65 (0.98–2.78)	1.48 (0.87–2.54)
Death or re-MI or ischemic stroke			
In-hospital	2.25 (1.23–4.12)*	1.30 (0.62–2.72)	1.30 (0.60–2.81)
12-mo	1.89 (1.30–2.76)*	1.14 (0.74–1.77)	1.13 (0.72–1.78)

Model I = adjust age, BMI.

Model II = adjust age, BMI, hypertension, diabetes, current smoker, dyslipidemia, concurrent medications.

BMI = body mass index; MI = myocardial infarction.

* $P < .05$.

Finally, although female patients had higher in-hospital and 1-year mortality rates than those of males, no gender difference was observed after adjusting for age and cardiovascular risk factors. Although previous studies have shown that women tend to develop worse outcomes, the role of gender in mortality has been controversial in several studies.[3,10,11,21,25,26] Our study has shown that women tend to have higher in-hospital and 1-year mortality rates, which is consistent with the results of most of the previous studies.[27–30] This poorer cardiovascular outcome in females could most probably be related to the higher age of females and the higher incidence rates of coronary risk factors such as diabetes mellitus and hypertension, as well as the higher incidence rates of Killip class 3 and cardiogenic shock. However, after adjusting for age and cardiovascular risk factors, the difference in mortality between both genders became nonsignificant, which is consistent with the result of previous studies[15–18] and further suggests the significance of age and cardiovascular risk factors in this context.

There are 3 limitations in this study. First, it is a nonrandomized and an observational study, which thus makes it difficult to determine the cause-and-effect relationships between cardiovascular outcomes and STEMI. However, the results of this study provide valuable real-world data regarding the current clinical practices across the full spectrum of STEMI, which could help improve the management of STEMI in Taiwan. Second, unmeasured sex-specific differences may also exist. The database lacks details of family history and unmeasured confounders. Therefore, caution must be exercised while interpreting our data. Third, all the patient details in this study were collected from 39 general hospitals equipped with catheterization rooms in

Taiwan; therefore, it is unclear how our findings can be generalized to patients in different areas.

Despite some limitations, this study has 2 aspects of strength. First, the data used in this study represent > 90% of the hospitals equipped with catheterization rooms in Taiwan. This study also provides valuable real-world data regarding the current clinical practices in Taiwan. Second, the collected data are prospective and allow better observation of the results over a 1-year follow-up period in this study.

5. Conclusion

Gender disparities exist in terms of age, comorbidities, medication management, primary PCI, and in-hospital and 1-year mortality rates among patients with STEMI in Taiwan. However, after adjusting for age and cardiovascular risk factors, there was no gender difference in the in-hospital and 1-year mortality rates among patients with STEMI in Taiwan. With potential prognostic importance, these findings call for more work to evaluate the role of gender among patients with STEMI treated with primary PCI to reduce gender difference in contemporary care.

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Author contributions

Conceptualization: Li-Ping Chou, Ping Zhao, Gwo-Ping Jong.
Funding acquisition: Li-Ping Chou, Gwo-Ping Jong.
Investigation: Li-Ping Chou, Yen-Hsun Chen.
Methodology: Li-Ping Chou, Ping Zhao, Gwo-Ping Jong.
Project administration: Li-Ping Chou, Gwo-Ping Jong.
Resources: Li-Ping Chou, Chieh Kao, Yen-Hsun Chen.
Supervision: Gwo-Ping Jong.
Visualization: Li-Ping Chou, Ping Zhao.
Writing – original draft: Li-Ping Chou, Gwo-Ping Jong.
Writing – review & editing: Li-Ping Chou, Gwo-Ping Jong.
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