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ORIGINAL RESEARCH

Positive Predictive Value of ICD-10-CM Codes for Myocarditis in Claims Data: A Multi-Institutional Study in Taiwan

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Purpose: The validity of the diagnosis codes to identify myocarditis cases in healthcare databases research remains unclear, and this study aimed to determine the coding accuracy of myocarditis in Taiwan.

Methods: We conducted a cross-sectional study based on Taiwan's largest multi-institutional healthcare system to identify inpatients newly diagnosed with ICD-10-CM myocarditis codes at discharge between January 1st, 2017 and March 31st, 2022. We ascertained the myocarditis diagnosis by a gold standard biopsy or by review of electronic medical records, and the positive predictive values (PPV) with 95% confidence intervals (CI) of the ICD-10-CM codes for myocarditis were determined.

Results: We included a total of 498 inpatients (mean age: 33.8 years old; female: 38.8%) with new myocarditis diagnosis at discharge. Codes I409 (30.1%) and I514 (45.4%) constituted the majority of myocarditis diagnostic codes in any coding position, and the overall PPV of the myocarditis codes was 73.5% (95% CI: 69.6–77.4%). However, the highest PPV (96.6%) for myocarditis diagnosis was noted with code I409 as the primary diagnosis. We found 132 inpatients (26.5%) who were false-positive myocarditis cases, identified by the ICD-10-CM codes, and potential reasons for misclassification included other inflammation diseases (n=35, 26.5%), pre-existing heart failure (n= 25, 18.9%) and acute myocardial infarction (n=16, 12.1%).

Conclusion: The PPV of ICD-10-CM codes for myocarditis in Taiwan was acceptable, but some other inflammation diseases and pre-existing heart diseases may be falsely coded as myocarditis. Our results may serve future secondary database studies as a fundamental reference on the validity of myocarditis diagnosis codes.

Keywords: ICD-CM-10 codes, positive predictive value, myocarditis, multi-institutional study, Chang Gung Research Database

Introduction

Myocarditis, an inflammatory disease of the heart muscle with numerous different etiologies, is a major cause of cardiac death in young adults.[1,2] Myocarditis is mostly caused by viral infection,[3] but other etiologies, such as bacterial, fungal, autoimmune disease and drug origins have been also discussed.[4] The clinical presentation of myocarditis ranges from an asymptomatic status to fatal cardiac arrest. Previously, myocarditis-related mortality has been reported as 19.2%.[5] However, a relatively higher mortality rate after myocarditis caused by COVID-19 infection (51.2%) has been noted.[6] In addition, myocarditis associated with COVID-19 vaccines has been reported worldwide.[7–12] These observations have drawn much medical attention to the epidemiological features of myocarditis in the current pandemic.

Post-immunization myocarditis has been observed in healthcare data, such as claims and electronic medical records data, as a rare but severe complication after COVID-19 vaccinations.[13–16] For example, Wong et al analyzed four large health claims databases in the USA and report that among men aged 18–25 years, the pooled incidence rate was highest after the second dose, at 1.71 per 100,000 person-days for BNT162b2 and 2.17 per 100,000 person-days for mRNA-1273.[17] A recent study analyzing a territory-wide electronic public healthcare database in Hong Kong also found

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a significantly lower rate of mortality among individuals with myocarditis after mRNA COVID-19 vaccination, compared to those with viral infection-related myocarditis.[18]

While healthcare data sources can provide an essential understanding of the epidemiology of myocarditis associated with COVID-19 vaccines, the validity of the diagnostic codes used for myocarditis is rarely investigated.[19] In clinical practice, it is challenging for physicians to accurately diagnose myocarditis due to the heterogeneity of clinical presentations, especially in pediatric patients,[20] and therefore database research using the diagnosis codes to identify myocarditis cases may be vulnerable to misclassification bias. To establish the validity of coding for myocarditis in healthcare data, we compared the accuracy of diagnosis codes from claims data with the corresponding electronic medical records data from Taiwan's largest multicenter routine care database.

Materials and Methods

Study Settings

The data for this study was retrieved from nine hospitals of the Chang Gung Medical Foundation (CGMF) in Taiwan, including branches in Taipei, Keelung, Tucheng, Linkou, Taoyuan, Yunlin, Chiayi, Kaohsiung and Fengshan. CGMF is Taiwan's largest multi-institutional healthcare system covering more than 10% of the entire inpatient population of Taiwan,[21] and data from CGMF has repeatedly provided important real-world evidence for clinical decision making.[22–26] This study has been approved by the Institutional Review Board of CGMF (IRB No: 202200229B0) and was conducted in accordance with the principles laid down in the Declaration of Helsinki. The requirement for informed consent was waived due to the retrospective design.

Data Sources

Hospitalization claims data reported to Taiwan's National Health Insurance Administration were retrieved from the hospital information system of CGMF hospitals. Information was retrieved on inpatients with a first discharge diagnosis of myocarditis between January 1st, 2017, and March 31st, 2022. The records extracted were identified by the International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) diagnostic codes A381, A3952, B2682, B3320, B3322, B3324, B5881, D8685, I012, I090, I400, I401, I408, I409, I41, I514, J1082 or J1182.

Ascertainment of Myocarditis

We used the findings from endomyocardial biopsy as the gold standard to identify myocarditis based on histological Dallas criteria, however, due to safety concerns, biopsy is rarely conducted in clinical practice.[27] Therefore, we also assessed myocarditis based on the criteria for clinically suspected myocarditis recommended by the European Society of Cardiology, which include the following non-invasive imaging, laboratory data and clinical presentations.[27] Myocarditis is defined by at least one clinical presentation and one diagnostic criterion; two diagnostic criteria are needed for asymptomatic myocarditis. Clinical presentations include acute coronary syndrome-like presentation; despite the absence of coronary artery disease (CAD) and known causes of heart failure, occurrence of 1) new onset or worsening heart failure; 2) chronic heart failure; or 3) life-threatening condition. Diagnostic criteria are based on the results of non-invasive testing such as electrocardiography, myocardiocytolysis markers or cardiac imaging, including echocardiography, coronary angiography and cardiac magnetic resonance imaging (CMR). CMR has also been proven a reliable diagnostic indicator of myocarditis in conjunction with the Lake Louise criteria.[28,29] Thus, positive reports from CMR present in electronic medical records data can also be considered as definite myocarditis diagnosis. In pediatric patients, the clinical presentations of myocarditis suggested by the European Society of Cardiology are less useful; for instance, chest pain is quite common in children older than 10 years old, but rarely heart related.[30] For pediatric myocarditis, we therefore followed the simplified diagnostic guidance proposed by the American Heart Association to confirm the diagnosis,[31] starting with symptoms and signs of incident heart failure and followed by objective examination results.

To confirm the myocarditis diagnosis from the electronic medical records data, we adopted similar algorithms to previous validation studies of ICD-10-CM codes in healthcare databases.[32,33] Two clinical physicians (LYW and SCL) independently reviewed the electronic medical records data from inpatients newly discharged with the ICD-10-CM codes

for myocarditis to judge the definite diagnosis based on drug history, examination reports and cardiac enzyme tests before or during admission. Any disagreement was resolved by discussion to reach a final conclusion (Figure 1).

To understand the reasons for false-positive myocarditis coding, we classified the false-positives into the following groups: 1) tentative diagnoses of myocarditis (eg, symptom mimicking, myocardial infarction, etc) which were later excluded after clinical evaluation and imaging studies; 2) remote history of myocarditis (more than 1 year from this admission); and 3) other pre-existing heart diseases.

Data Analyses

We used descriptive analyses, either mean or proportional statistics, to summarize the patient characteristics of the confirmed myocarditis cases, including age, sex, etiology of myocarditis, treatments for myocarditis (ie, intravenous immunoglobulin, anti-viral drugs or immunosuppressive agents), advanced care (ie, intensive care hospitalization or mechanical circulatory support, such as extracorporeal membrane oxygenation, pacemaker and ventricular assist device) and heart transplant. Length of hospitalization, mortality and relapse of heart failure within six months were also

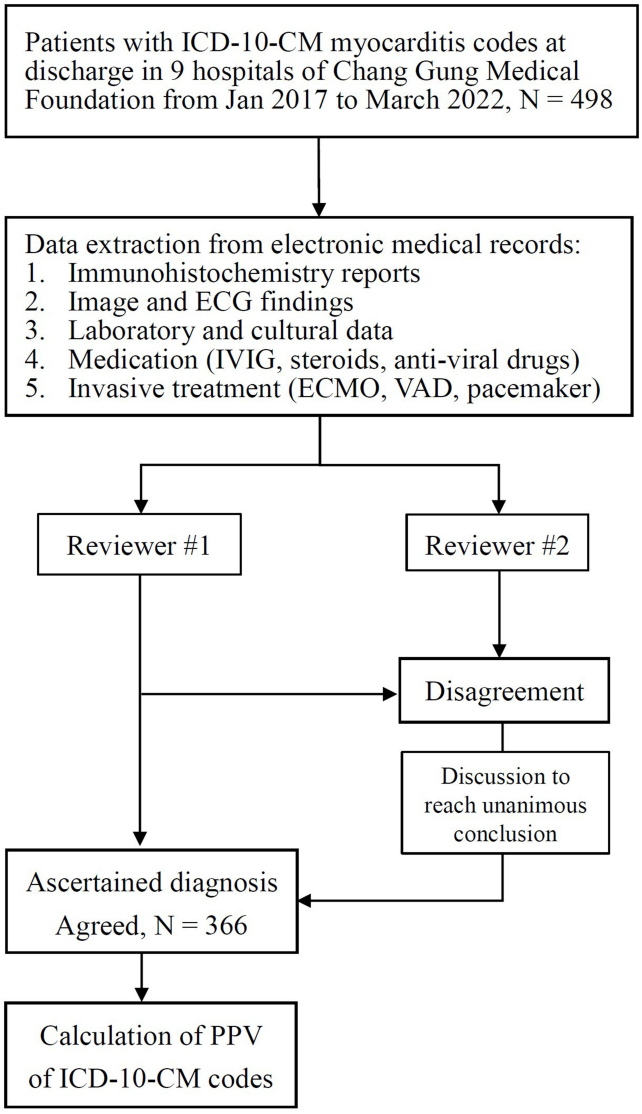

Figure 1 Process of case ascertainment.

Abbreviations: ECG, Electrocardiography; ECMO, Extracorporeal Membrane Oxygenation; ICD-10-CM, International Classification of Diseases, Tenth Revision, Clinical Modification; IVIG, Intravenous immunoglobulin; PPV, Positive predictive value; VAD, Ventricular assist device.

analyzed.[34,35] The positive predictive value (PPV) was calculated as the percentage of myocarditis cases confirmed from chart reviews out of the total myocarditis cases identified by ICD-10-CM codes, and the 95% confidence interval (CI) of the PPV was estimated using the Clopper-Pearson exact method. Data analyses were performed using SAS Enterprise Guide 7.13 (SAS Institute, Inc., Cary, NC, USA).

Results

We included a total of 498 inpatients with ICD-10-CM myocarditis codes of A381, A3952, B2682, B3320, B3322, B3324, B5881, D8685, I012, I090, I400, I401, I408, I409, I41, I514, J1082 or J1182 in their discharge diagnosis during the study period. We found 9 inpatients had been coded with more than one of these ICD-10-CM myocarditis codes. Initially, the reviewing physicians reached agreement on their myocarditis judgments in 447/498 inpatients (89.4%) after independent reviews of the electronic medical records data. In the case of discrepancies, the two physicians made their final myocarditis judgments after full, case-by-case discussion (Figure 1).

The overall PPV for ICD-10-CM myocarditis codes was 73.5% (95% CI: 69.6–77.4%), and we present the number of true-positive myocarditis cases and PPV for each diagnostic code separately in Table 1. Code I409 in the primary diagnosis position constituted the majority of true-positive cases (23.5%) and yielded the highest PPV (96.6%) among the different ICD-10-CM myocarditis codes and diagnosis positions. However, after expanding the case definition to the

Table 1 Accuracy of Different Case Definitions to Identify Myocarditis

Case Definitions (ICD-10-CM Codes)		TP, n	FP, n	PPV, %	95% CI
I409	Acute myocarditis, unspecified				
	1st position diagnosis	86	3	96.6	90.5–99.3
	2nd position diagnosis	29	6	82.9	66.4–93.4
	3rd position diagnosis	11	4	73.3	44.9–92.2
	Any position diagnosis	131	19	87.3	80.9–92.2
I408	Other acute myocarditis				
	1st position diagnosis	16	1	94.1	71.3–99.9
	2nd position diagnosis	9	1	90.0	55.5–99.8
	3rd position diagnosis	0	1	0.0	0.0–97.5
	Any position diagnosis	30	4	88.2	72.6–96.7
I514	Myocarditis, unspecified				
	1st position diagnosis	61	7	89.7	79.9–95.8
	2nd position diagnosis	33	28	54.1	40.9–66.9
	3rd position diagnosis	27	25	51.9	37.6–66.0
	Any position diagnosis	139	87	61.5	54.8–67.9
J1182	Influenza due to unidentified influenza virus with myocarditis				
	1st position diagnosis	8	1	88.9	51.8–99.7
	2nd position diagnosis	1	0	100.0	2.5–100
	3rd position diagnosis	1	0	100.0	2.5–100
	Any position diagnosis	10	1	90.9	58.7–99.8
I400	Infective myocarditis				
	1st position diagnosis	16	2	88.9	65.3–98.6
	2nd position diagnosis	11	1	91.7	61.5–99.8
	3rd position diagnosis	6	3	66.7	29.9–92.5
	Any position diagnosis	40	7	85.1	71.7–93.8
J1082	Influenza due to other identified influenza virus with myocarditis				
	1st position diagnosis	15	3	83.3	58.6–96.4
	2nd position diagnosis	2	1	66.7	9.4–99.2
	3rd position diagnosis	4	2	66.7	22.3–95.7
	Any position diagnosis	23	6	79.3	60.3–92.0

(*Continued*)

Table 1 (Continued).

Case Definitions (ICD-10-CM Codes)		TP, n	FP, n	PPV, %	95% CI
I41	Myocarditis in diseases classified elsewhere				
	1st position diagnosis	0	0	N/A	N/A
	2nd position diagnosis	0	1	0.0	0.0–97.5
	3rd position diagnosis	0	1	0.0	0.0–97.5
	Any position diagnosis	0	2	0.0	0.0–84.2
B3322	Viral myocarditis				
	1st position diagnosis	0	0	N/A	N/A
	2nd position diagnosis	1	1	50.0	1.3–98.7
	3rd position diagnosis	0	0	N/A	N/A
	Any position diagnosis	2	2	50.0	6.8–93.2
I401	Isolated myocarditis				
	1st position diagnosis	0	0	N/A	N/A
	2nd position diagnosis	0	0	N/A	N/A
	3rd position diagnosis	0	0	N/A	N/A
	Any position diagnosis	0	1	0.0	0.0–97.5
I090	Rheumatic myocarditis				
	1st position diagnosis	0	0	N/A	N/A
	2nd position diagnosis	0	1	0.0	0.0–97.5
	3rd position diagnosis	0	1	0.0	0.0–97.5
	Any position diagnosis	0	3	0.0	0.0–70.8

Abbreviations: CI: confidence interval; FP: false positive; TP: true positive; N/A: not available.

secondary, tertiary, or any position of diagnosis, the PPVs of most ICD-10-CM codes decreased, while the number of identified myocarditis cases increased. With regard to the 132 false-positive cases with ICD-10-CM myocarditis codes, 35 cases (26.5%) involved other inflammation diseases, 25 cases (18.9%) involved pre-existing heart failure and 16 cases (12.1%) involved acute myocardial infarction (Table 2).

Table 2 False-Positive Myocarditis Cases (N=132)

Classifications	Reasons	N (%)	
Reasons for acute troponin elevation	Acute myocardial infarction	16	(12.1)
	Tachyarrhythmias	3	(2.3)
	Hypotension/Shock	7	(5.3)
	Heart failure	25	(18.9)
	Other cardiac inflammation		
	Endocarditis	1	(0.8)
	Pericarditis	2	(1.5)
	Cardiac procedures	3	(2.3)
	Acute respiratory distress syndrome	9	(6.8)
	Sepsis	12	(9.1)
	Stroke	1	(0.8)
	Chronic kidney disease	1	(0.8)
	Hyperthyroidism	2	(1.5)
	Strenuous exercise	5	(3.8)
	Sympathomimetic drug intoxication	1	(0.8)
Symptoms similar to myocarditis	Other inflammation diseases	35	(26.5)
	Adverse drug reactions	4	(3.0)
	Tako-tsubo cardiomyopathy	1	(0.8)

(*Continued*)

Table 2 (Continued).

Classifications	Reasons	N (%)	
Miscoding		1	(0.8)
Remote myocarditis		3	(2.3)

Table 3 Patient Characteristics of Confirmed Myocarditis Cases

	All		<18 Years Old		18–65 Years Old		>65 Years Old	
Age, mean (SD)	33.8	(23.1)	9.3	(5.8)	39.6	(7.8)	75.0	(14.0)
Male, n (%)	224	(61.2)	40	(34.5)	170	(78.7)	14	(41.2)
Etiology, n (%)								
Virus	91	(24.9)	35	(30.2)	45	(20.8)	11	(32.4)
Bacteria	44	(12.0)	15	(12.9)	24	(11.1)	5	(14.7)
Vaccine	34	(9.3)	17	(14.7)	16	(7.4)	1	(2.9)
Autoimmune	14	(3.8)	3	(2.6)	9	(4.2)	2	(5.9)
Unknown	182	(49.7)	46	(39.7)	121	(56.0)	15	(44.1)
Advanced care, n (%)								
ICU	248	(67.8)	92	(79.3)	134	(62.0)	22	(64.7)
ECMO	55	(15.0)	12	(10.3)	37	(17.1)	6	(17.6)
Heart transplant	3	(0.8)	0	(0.0)	3	(1.4)	0	(0.0)
Treatment, n (%)								
Anti-viral drugs	65	(17.8)	24	(20.7)	31	(14.4)	10	(29.4)
IVIG	26	(7.1)	22	(55.0)	3	(1.8)	1	(7.1)
Pacemaker	26	(7.1)	4	(3.4)	17	(7.9)	5	(14.7)
VAD	12	(3.3)	2	(1.7)	10	(4.6)	0	(0.0)
Length of hospitalization, Mean days (SD)	12.3	(14.6)	10.8	(12.5)	12.1	(14.3)	18.4	(18.9)
Mortality, n (%)	41	(11.2)	8	(6.9)	27	(12.5)	6	(17.6)
HF complication, n (%)								
At discharge	110	(30.1)	14	(12.1)	81	(37.5)	15	(44.1)
Recovered after 6-month follow-up	96	(87.3)	14	(100.0)	68	(84.0)	14	(93.3)

Abbreviations: ECMO, extracorporeal membrane oxygenation; HF, heart failure; ICU, intensive care unit; IVIG, intravenous immunoglobulin; VAD, ventricular assist device.

Of the 366 true myocarditis cases coded by ICD-10-CM codes in any position, most (n=216, 59.0%) were 18–59 years old and male (n=224, 61.2%). Despite the advanced care (intensive care unit, ICU: 67.8%; Extracorporeal Membrane Oxygenation, ECMO: 15.0%) provided to most of these patients, 11.2% of the true myocarditis cases died. During the 6-month follow-up after discharge, patients with incident heart failure caused by myocarditis mostly recovered (87.3%) and children with cardiac impairment caused by myocarditis all recovered (100.0%). Other important characteristics of the confirmed myocarditis cases are listed in Table 3.

Discussion

This study from the largest multi-center healthcare system in Taiwan found that ICD-10-CM codes I409 and I514 accounted for 75% of the diagnostic codes for myocarditis in any coding position with an overall PPV for myocarditis diagnosis of 73.5%. However, the PPV increased to 96.6% for the ICD-10-CM myocarditis code I409 if it was coded as the primary diagnosis, with the trade-off that such a narrow definition might cause a loss of true cases of myocarditis with ICD-10-CM codes in a position other than the primary position of the discharge diagnosis. More importantly, we found the potential reasons for misclassification in the 132 false-positive ICD-10-CM myocarditis cases included other inflammation diseases, acute myocardial ischemia and pre-existing heart failure. Taking together these findings, we

considered the ICD-10-CM codes in routine care data in Taiwan to be acceptable for the identification of myocarditis cases.

In contrast to other cardiovascular diseases, such as acute coronary syndrome or cardiac arrest,[36–40] the PPV of ICD-10-CM codes for myocarditis is not well understood. To the best of our knowledge, there has been only one validation study, conducted in the Danish National Patient Registry, which reported the PPV of myocarditis (I40, I41, I090, I514) to be 80% as primary diagnosis, and 36% as secondary diagnosis.[41] Consistent with this, our overall PPV of ICD-10-CM myocarditis codes was 73.5%, and higher in the primary diagnosis position (92.3%), but lower in other diagnosis positions. However, the ICD-10-CM codes in the Danish study only included commonly coded types of myocarditis such as I514 (myocarditis, unspecified), so the coding validity of other myocarditis types remains unclear. In our present and comprehensive study, we determined the validity of a broad range of ICD-10-CM codes related to myocarditis. For example, the ICD-10-CM codes J1082 and J1182 (influenza-related myocarditis) were not validated in the Danish study, but attained a high PPV as primary diagnosis in our ascertained myocarditis cases (83.3% and 88.9%). Hence, our findings may be more generalizable to the performance of various myocarditis diagnosis codes.

As regards the false-positive myocarditis cases, we found that 26.5% were miscoded due to mimicked myocarditis symptoms and signs. Moreover, 94.3% of these cases were children. This may be because physicians often give a tentative diagnosis of myocarditis in pediatric cases with tachypnea and tachycardia together with fever and viral or bacterial infection. Also, pre-existing heart failure accounted for 18.9% of the false-positive myocarditis cases because these patients usually have cardiac enzyme elevation with corresponding symptoms, such as dyspnea, comparable with diagnostic criteria of myocarditis. Our findings suggested that personal medical history should be considered before making the diagnosis of myocarditis.

The patients' characteristics of the confirmed myocarditis cases in this present study show 61.2% were male with a median age of 30.4 years. Our results were compatible with the epidemiology of myocarditis in previous studies.[3,42,43] Our reported mortality rate of 11.2% among the included myocarditis cases was similar to that of previous reports (4–15%).[3,44,45] These comparisons, together with our findings, confirm the internal and external validity of the myocarditis definitions. However, we found a lower myocarditis mortality in children (0–18 years old: 6.9%), compared to adults (18–65 years old: 12.5%; >65 years old: 17.6%). One possible explanation may lie in the different treatment patterns for myocarditis across various age groups, whereby the pediatric group (0–18 years old) may receive more advanced care (such as admission to ICU and receipt of intravenous immunoglobulin treatment) as the initial management. Future studies should aim to determine factors prognostic of mortality in myocarditis within different age groups.

Our study has several limitations. First, this study did not include a control group of inpatients without ICD-10-CM myocarditis codes, and therefore we failed to determine the negative predictive value, sensitivity, and specificity of ICD-10-CM myocarditis codes. However, it is worth emphasizing the value of determining the PPV of ICD-10-CM myocarditis codes in healthcare database research, because it enables researchers to evaluate the accuracy with which patients in a given cohort can be assumed to be true cases of myocarditis. For example, if researchers aim to create a cohort of patients with myocarditis to investigate the disease's epidemiological features, we recommend the case definition of "code I409 as primary diagnosis", which yields the highest PPV (96.6%), ensuring that patients in this cohort are nearly all true cases of myocarditis. Second, despite endomyocardial biopsy being recognized as the gold standard for identifying myocarditis based on histological Dallas criteria, we found only 1.4% (7/498) of the cases included in this study had endomyocardial biopsy reports. As an alternative, we therefore reviewed the electronic medical records to judge the diagnosis of myocarditis, based on non-invasive imaging, laboratory data and clinical presentation, as recommended by the European Society of Cardiology and the American Heart Association, whereby the consistency of judgment between our two independent reviewers was high (89.4%). Third, our findings were derived from the largest multi-institutional healthcare system with several academic medical centers and regional and district hospitals in Taiwan, so the results might be representative of the inpatient population in Taiwan. However, the generalizability of our findings to other healthcare databases remains unclear.

Conclusion

The overall PPV of ICD-10-CM myocarditis codes was 73.5% in routine care data in Taiwan, whereby some misclassification may occur in patients with other inflammation diseases, acute myocardial ischemia or pre-existing heart failure. Future studies based on other secondary data sources worldwide are suggested to confirm our observations.

Data Sharing Statement

This study analyzed the electronic medical records data from the Chang Gung Memorial Hospitals (CGMF) in Taiwan. The access to the analyzed data needs the official approval from the CGMF. Also, all analyses should be conducted at the CGMF on site, and any individual-level data were not allowed to be taken out for data privacy and safety concerns. However, the analytical codes of SAS software in this study are available from corresponding author upon reasonable request.

Ethics Approval

This study has been approved by the Institutional Review Board of CGMF (IRB No: 202200229B0) and was conducted in accordance with the principles laid down in the Declaration of Helsinki. The requirement for informed consent was waived due to the retrospective design. All accessed data complied with relevant data protection and privacy regulations from CGMF.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest in this work.

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