Polymyositis/dermatomyositis is a potential risk factor for acute respiratory failure: a pulmonary heart disease

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Background: Studies on the association between polymyositis/dermatomyositis (PM/DM) and acute respiratory failure (ARF) are considerably limited. We investigated whether ARF is associated with PM/DM using a nationwide cohort study.

Methods: We identified 1,374 patients with newly diagnosed PM/DM and 13,740 comparison individuals without PM/DM (non-PM/DM) randomly selected from the general population; frequency matched by age, sex, and index year using the National Health Insurance Research Database; and followed up until the end of 2011 to measure the incidence of ARF. Cox proportional hazards regression analysis was used to measure the hazard ratio (HR) of ARF for the PM/DM cohort in comparison with the non-PM/DM cohort.

Results: The adjusted HR of ARF was 5.05 for the PM/DM cohort compared with the non-PM/DM cohort after adjusting for sex, age, comorbidities, Charlson comorbidity index (CCI) score and medicine. The risk of ARF significantly increased irrespective of age, sex, comorbidities and medicine. Meanwhile, the PM/DM cohort with comorbidities, such as cardiac disease (hypertension), pulmonary disease (chronic obstructive pulmonary disease and pneumonia), and pulmonary vascular diseases had additive effects on the incident ARF.

Conclusions: This study determined the cross-reaction of pulmonary heart disease in the PM/DM cohort with incident ARF even without comorbidities.

Keywords: Pulmonary heart disease; heart failure; polymyositis/dermatomyositis (PM/DM); acute respiratory failure (ARF); cohort study

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Introduction

Hypoxemic respiratory failure (RF) is defined as respiratory distress resulting in a PaO$_2$ of less than 60 mmHg, despite the addition of supplemental oxygen of at least 60%. Hypoxemia may be combined with high (1), normal, or low arterial carbon dioxide tension (PaCO$_2$) (2). Typically, this involves the pulmonary alveoli component of the pulmonary system. Hypoxemic RF is also called “lung failure” or “oxygenation failure”. Its causes include hypoventilation [e.g., respiratory paralysis, asthma, and chronic obstructive pulmonary disease (COPD)], diffusion impairment (e.g., severe pneumonia, interstitial fibrosis, and interstitial pulmonary edema), ventilation-perfusion (V/Q) mismatch (e.g., emphysema, alveolar pulmonary edema, and atelectasis), and intra- and extrapulmonary shunting (technically the most severe form of V/Q mismatch; e.g., lung consolidation, pulmonary embolism, and pulmonary hemorrhage) (2,3).

Collagen vascular diseases such as polymyositis/dermatomyositis (PM/DM) represent a heterogeneous group of immunologically mediated inflammatory disorders with a large variety of affected organs. Patients with PM/DM are susceptible to respiratory involvement (4). Several different components of the respiratory system may be involved, including the airways (5,6), vessels (6,7), heart (5,8), and parenchyma/interstitium (6,9). Thoracic manifestations with the greatest clinical importance in patients with PM/DM are interstitial lung disease (ILD) (10), pulmonary arterial hypertension (11,12), and heart disease (10), which are responsible for the high rate of mortality and morbidity in this patient group.

Occasionally, acute respiratory failure (ARF) develops in patients with PM/DM, but the etiologies of ARF in these patients are not completely elucidated (10,13,14). Comorbidities such as asthma (15), COPD (16), infection/aspiration pneumonia (14,17,18), coronary artery disease (CAD) (19), hypertension (20,21), heart failure (22), diabetes (20,21), and cancer (13) are related to PM/DM. Therefore, we address an intervention of ARF with PM/DM and comorbidities in this cohort study. This is the first study that focused on PM/DM presenting as ARF in the general population in the English literature.

Methods

Patient and public involvement

Taiwan’s National Health Insurance (NHI) is a universal insurance program established in 1995 that covers almost 99% of the Taiwanese population. In this study, patient data were obtained from the Taiwan’s National Health Insurance Research Database (NHIRD), which contains claims data from NHI, and the patient data are updated in the database every year. In the database, the disease diagnosed is recorded according to the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM).

Data availability statement

The Ministry of Health and Welfare must approve our application to access this data. Any researcher interested in accessing this dataset can submit an application form to the Ministry of Health and Welfare requesting access. The dataset used in this study is held by the Taiwan Ministry of Health and Welfare (MOHW). Please contact the staff of MOHW (Email: stcarolwu@mohw.gov.tw) for further assistance. Taiwan MOHW address: No. 488, Sec. 6, Zhongxiao E. Rd., Nangang Dist., Taipei City 115. Phone: +886-2-8590-6848. All relevant data are within the paper.

Ethics statement

The Research Ethics Committee of China Medical University and Hospital in Taiwan approved the study (CMUH104-REC2-115-R4). The NHIRD encrypts patient personal information to protect privacy and provides researchers with anonymous identification numbers associated with relevant claims information, including sex, date of birth, medical services received, and prescriptions. Therefore, patient consent is not required to access the NHIRD.

Study population

This study used a retrospective population-based cohort design. A cohort of newly diagnosed PM/DM (ICD-9-CM: 710.3 and 710.4) from 2000 to 2009 was established. The baseline of the PM/DM cohort was the initial PM/DM diagnosis date. Individuals without PM/DM were randomly selected, frequency matched by sex and age (per 5 years) in a 1:10 ratio, and used as the non-PM/DM comparison cohort. The baseline of the non-PM/DM comparison cohort was randomly assigned a month and day and the same year of the matched PM/DM cases.

The ARF defined as the hypoxaemic (arterial oxygen...
tension, \( \text{PaO}_2 < 60 \text{ mmHg} \) with or without hypercapnia (arterial carbon dioxide tension, \( \text{PaCO}_2 > 50 \text{ mmHg} \)). The ARF develops within minutes or hours, thus the pH < 7.3 and the value of the bicarbonate ion is normal. Meanwhile, these patients with loss of the ability to ventilate adequately or to provide sufficient oxygen to the blood and systemic organs (23-25). Owing to the incident ARF was enrolled into the catastrophic diseases, the policy of definition the ARF in Taiwan NHIRD is strict (26,27). The principal outcome was ARF occurrence (ARF, ICD-9-CM: 518.81). Patients who had experienced incident ARF before the baseline were excluded. Follow-up was terminated upon the observation of an ARF event or at the end of the year (December 31, 2011).

ARF comorbidities recorded included the disease history before the baseline and were considered as potential confounding factors. We categorized Charlson-comorbidity index (CCI) into 4 levels: 0, 1, 2, and 3 or more. These comorbidities included asthma (ICD-9-CM: 493, 494, and A324), hypertension (ICD-9-CM: 401–405), DM (ICD-9-CM: 250), COPD (ICD-9-CM: 491, 492, and 496), pneumonia (ICD-9-CM: 480–487), cancer (ICD-9-CM: 140–208), CAD (ICD-9-CM: 410–414), heart failure (ICD-9-CM: 415–417). In addition, oral steroid was analyzed between the PM/DM patients and the non-PM/DM cohort. Methotrexate was analyzed among PM/DM cohort.

**Statistical analysis**

We demonstrated the mean and standard deviation (SD) for age at baseline and presented the frequency and percentage for sex and baseline comorbidities. Chi-squared test was used to analyze categorical variables, and Student’s t-test was used to assess continuous variables comparing the PM/DM and non-PM/DM cohorts in terms of the baseline demographic status. The incidence density rate of incident ARF for both cohorts were calculated as the number of incident ARF occurrences divided by the total sum of the follow-up year (per 10,000 person-years), the Kaplan-Meier method was used to estimate the cumulative incidence ARF of the studied subjects during the follow-up period, and the log-rank test was used to test the differences between both curves. Cox proportional hazards regression was used to estimate the hazard ratios (HRs) and 95% confidence intervals (CIs) of incident ARF risk in the PM/DM and non-PM/DM cohorts.

All statistical analyses were performed using the SAS 9.4 statistical package (SAS Institute Inc., NC, USA). A P value of <0.05 in two-tailed tests was considered significant.

**Results**

**Characteristics of the study participants**

We evaluated 1,374 PM/DM patients and 13,740 non-PM/DM individuals (Table 1). Because age and sex were matched, no statistically significant differences in age (49.6±14.4 years) and sex ratio (male: 31.1%) were observed between the two cohorts. Except for hypertension and diabetes, the patients with PM/DM had a higher percentage of patients with comorbidities than the non-PM/DM cohort (all P values <0.05). Most of the PM/DM patients had the number of CCI score of ≥1 (52.8%). The medication used in the both PM/DM and non-PM/DM cohorts was oral steroid (98.8% vs. 69.5%). In the PM/DM cohort, approximately 65% of the patients were used of methotrexate.

**The incidence and cumulative incidence of ARF between the PM/DM and non-PM/DM cohorts**

The incidences of ARF were 229.44 and 37.08 per 10,000 person-years in the PM/DM and non-PM/DM cohorts, respectively (Table 2). We also observed that the curve of the ARF cumulative incidence for the PM/DM cohort was greater than that for the non-PM/DM cohort (Figure 1; P for the log-rank test <0.0001).

**Adjusted HR of ARF**

After adjusting for age, sex, CCI score, comorbidities, and medicine of oral steroid, the results showed that the PM/DM patients had higher risk of ARF (HR: 5.05; 95% CI: 4.08–6.25) than the non-PM/DM individuals. Compared with patients aged 45 years and younger, the risk of ARF development is 2.81-fold higher in those aged 45–64 years (95% CI: 2.01–3.92), and 9.11-fold higher in those aged 65 years and older (95% CI: 6.39–13.00). Multivariable models showed that ARF was associated with men, CCI score, hypertension, diabetes, COPD, pneumonia, and PVD.

**ARF in relation to the average frequency of hospital and clinical visits**

As the non-PM/DM cohort as the reference, the number of hospitalizations and clinical visits of ≥16 (HR: 12.2; 95%
CI: 9.58–15.50) had the highest risk of ARF compared with the frequencies of hospital and clinical visits of 8–15 times (HR: 2.59; 95% CI: 1.81–3.70) and 8 times (HR: 1.78; 95% CI: 1.10–2.90) (Table 3). The results also make known that increased average frequency of hospital and clinic visits was significantly increased risk of ARF (P for trend <0.0001).

### Discussion

The first important finding of this study suggests that the incidence of ARF in the PM/DM cohort was higher than that in the non-PM/DM cohort (HR: 5.05; 95% CI: 4.08–6.25). ARF is a major cause of death in the PM/DM cohort (5,6,28). Santo et al. found that the frequency of death due to ARF in the PM/DM cohort was as high as 32.4% (29), which supports the finding of the current study.
| Variable | Event | PYs  | Rate  | Crude HR (95% CI) | Adjusted HR (95% CI) |
|----------|-------|------|-------|-------------------|----------------------|
| PM/DM    | No    | 335  | 90,336| 37.08             | Ref                  |
|          | Yes   | 171  | 7,453 | 229.44            | 6.10 (5.08–7.34)     |
|          |       |      |       |                   | 5.05 (4.08–6.25)     |
| Age group| <45 years | 45 | 39,020| 11.53             | Ref                  |
|          | 45–64 years | 188 | 44,773| 41.99             | 3.64 (2.63–5.03)     |
|          | ≥65 years | 273 | 13,996| 195.06            | 16.77 (12.23–22.99)  |
|          |       |      |       |                   | 9.11 (6.39–13.00)    |
| Sex      | Female | 284  | 67,731| 41.93             | Ref                  |
|          | Male   | 222  | 30,058| 73.86             | 1.76 (1.47–2.09)     |
|          |        |      |       |                   | 1.50 (1.26–1.80)     |
| CCI score| 0      | 219  | 85,124| 25.7              | Ref                  |
|          | 1      | 138  | 7,664 | 180.1             | 6.97 (5.63–8.62)     |
|          | 2      | 76   | 3,377 | 225.0             | 8.67 (6.67–11.3)     |
|          | ≥3 or more | 73 | 1,623 | 450.0             | 17.20 (13.20–22.40)  |
| Comorbidity| Asthma | No  | 422  | 91,998           | 45.87                |
|          |        | Yes | 84   | 5791             | 145.06              |
|          |        |     |      |                   | 3.15 (2.49–3.98)     |
|          |        |     |      |                   | 1.01 (0.78–1.31)     |
|          | Hypertension | No | 204  | 73,596       | 27.72                |
|          |        | Yes | 302  | 24,193         | 124.83              |
|          |        |     |      |                   | 4.48 (3.75–5.36)     |
|          |        |     |      |                   | 1.54 (1.24–1.90)     |
|          | Diabetes | No  | 377  | 89,239         | 42.25                |
|          |        | Yes | 129  | 8,550          | 150.88              |
|          |        |     |      |                   | 3.55 (2.9–4.33)      |
|          |        |     |      |                   | 1.48 (1.19–1.83)     |
|          | COPD   | No  | 371  | 90,671         | 40.92                |
|          |        | Yes | 135  | 7,118          | 189.66              |
|          |        |     |      |                   | 4.60 (3.78–5.61)     |
|          |        |     |      |                   | 1.25 (1.00–1.58)     |
|          | Pneumonia | No | 356  | 84,480         | 42.14                |
|          |        | Yes | 150  | 13,309         | 112.71              |
|          |        |     |      |                   | 2.67 (2.21–3.24)     |
|          |        |     |      |                   | 1.26 (1.03–1.55)     |
|          | Cancer | No  | 473  | 95,836         | 49.35                |
|          |        | Yes | 33   | 1,952          | 169.03              |
|          |        |     |      |                   | 3.33 (2.34–4.74)     |
|          |        |     |      |                   | 0.88 (0.59–1.31)     |
The age-stratified effects of the PM/DM cohort on ARF development were high in patients aged 45–64 years (HR: 2.88) and >65 years (HR: 9.83). The higher CCI score such as >3 was associated with a high risk of ARF in the PM/DM cohort (adjusted HR is high up to 4.45), which is similar to Santo et al.’s finding that the risk of death is higher when patients in the PM/DM cohort exhibit neoplasm. The mean age of 61.50±13.66 years in the PM/DM cohort with cancer supported this finding (29). Meanwhile, Marie et al., study revealed that the PM/DM with the severe ILD having the higher age (mean age, 62 years) and mortality (47.1%) support our result (30).

The etiology of RF includes cardiac origin diseases such as hypertension (21), heart failure, and CAD and pulmonary origin diseases such as COPD (hypoventilation) and pneumonia (diffusion impairment). Therefore, the primary pulmonary complication of PM/DM such as pneumonia and the primary cardiac complication such as hypertension-related heart failure (V/Q mismatch) contribute to the incident ARF and death. These findings imply that PM/DM itself (5,31,32) is a predisposing factor for ARF, even in the absence of comorbidities (11,33). Similarly, Santo et al. (29) reported that respiratory and circulatory disorders (28) were the principal associated causes of ARF in PM/DM patients (10,14). As shown in Table 4, the PM/DM cohort without any comorbidities was associated with higher risk of ARF than the non-PM/DM cohort, which is in line with these previous findings. Furthermore, the asthma, diabetes, pneumonia, heart failure, CAD and cancer without additive effects on the incident ARF support these results also (Table 4).

The late course of the PM/DM with severity of the ILD receiving the higher dose of the steroid (34), the anti-

### Table 2 (continued)

| Variable    | Event | PYs  | Rate   | Crude HR (95% CI) | Adjusted HR (95% CI) |
|-------------|-------|------|--------|-------------------|---------------------|
| CAD         | No    | 334  | 86,099 | 38.79             | Ref                 |
|             | Yes   | 172  | 11,690 | 147.13            | 3.78 (3.14–4.54)    |
| Heart failure| No    | 447  | 96,056 | 46.54             | Ref                 |
|             | Yes   | 59   | 1,733  | 340.45            | 7.20 (5.48–9.44)    |
| PVD         | No    | 491  | 97,476 | 50.37             | Ref                 |
|             | Yes   | 15   | 313    | 479.23            | 9.36 (5.60–15.65)   |
| Medicine    | Oral steroid | No | 85  | 30,419 | 27.94 | Ref |
|             | Yes   | 421  | 67,370 | 62.50 | 2.23 (1.77–2.82)** | 1.04 (0.81–1.34) |

Adjusted model was mutually adjusted. ***, P<0.001. Rate, per 10,000 person-years; PYs, person-years; CI, confidence interval; HR, hazard ratio; PM/DM, polymyositis/dermatomyositis; CCI score, Charlson comorbidity index score; COPD, chronic obstructive pulmonary disease; CAD, coronary artery disease; PVD, pulmonary vascular disease.

**Figure 1** The cumulative incidence of developing acute respiratory failure. Comparison cohort vs. PM/DM cohort.
Table 3 Association between the incidence of acute respiratory failure for different levels of average frequency of hospital and clinical visits for PM/DM and estimation of the risk of respiratory failure using multivariate Cox proportional hazards regression analysis

| Average frequency of PM/DM, per year | Event | PYs   | Rate   | Crude HR (95% CI) | Adjusted HR (95% CI) |
|-------------------------------------|-------|-------|--------|-------------------|---------------------|
| Non-PM/DM cohort                    | 335   | 90,336| 37.08  | Ref               | Ref                 |
| PM/DM cohort                        |       |       |        |                   |                     |
| <8                                  | 18    | 2,609 | 68.99  | 1.86 (1.16–2.99)  | 1.78 (1.10–2.90)    |
| 8–15                                | 37    | 3,216 | 115.05 | 3.09 (2.20–4.34)  | 2.59 (1.81–3.70)    |
| ≥16                                 | 116   | 1,627 | 712.97 | 18.57 (15.00–22.98)| 12.2 (9.58–15.50)  |

Model adjusted for age, sex, CCI score, asthma, hypertension, diabetes, COPD, pneumonia, cancer, CAD, heart failure, and PVD, and medicine of oral steroid. PM/DM, polymyositis/dermatomyositis; rate, per 10000 person-years; PYs, person-years; CI, confidence interval; HR, hazard ratio; CCI score, Charlson comorbidity index score; COPD, chronic obstructive pulmonary disease; CAD, coronary artery disease; PVD, pulmonary vascular disease.

Inflammatory may attenuate the airway inflammation; thus, these groups patients with asthma didn’t have the association and addictive effects on the incident ARF (Table 2) (32,33). Similar to the asthma patients, the cancer was associated with the late stage of the long-course of the PM/DM (36). The steroid may have beneficence on the PM/DM with the cancer with ILD-ARF (37,38). Thus, these groups patients receiving the higher dose steroid without association and additive effects on the incident ARF (Tables 2, 4). These hypotheses warrant further researches.

PM/DM with comorbidities such as COPD, hypertension and PVD were associated with an increased risk of incident ARF. COPD (1) contributes to ARF owing to the obstructive airway. Hypertension may be a precipitated factor of heart failure with interstitial edema (diffusion impairment) (2) and contribute to incident ARF. Diabetes (21) is also a disease with airway inflammation such as COPD (39) and atherosclerosis of vessel such as hypertension (40). This implies that diabetes is associated with cardiopulmonary complications in the deterioration of the PM/DM cohort (41) such as acute (7,8) or chronic pulmonary heart disease (42). These findings suggest that diabetes was associated with the incident ARF in the PM/DM cohort. However, the PM/DM patients primarily have the insulin resistance (43). Therefore, the diabetes having not the additive effects on the incident ARF (Table 4).

Primary cardiac complications in the PM/DM cohort included congestive heart failure (V/Q mismatch) resulting from primary cardiomyopathy, dysrhythmias, atrioventricular conduction disturbances, sick sinus syndrome (44), and an example of PVD with pulmonary heart reaction such as cor pulmonale (11). In addition, respiratory complications in the PM/DM cohort included recurrent aspiration pneumonia resulting from pharyngeal muscle involvement by the myositis process, and the involvement of respiration muscles can lead to ARF. Therefore, the heart and lungs (45) displayed a primary cross-reaction in the PM/DM cohort with ARF even without comorbidities (8,41). We found that pneumonia was associated with the ARF and it is without additive effects on the development of the incident ARF in line with these results. Meanwhile, the heart failure and CAD without additive effects on the incident ARF support these speculations also.

The frequency of admission of the PM/DM cohort increased the risk of ARF. The higher frequency of pulmonary artery inflammation in the PM/DM cohort, higher CCI increased the risk of primary pulmonary artery occlusion such as chronic pulmonary embolism combined with heart failure (an example of pulmonary heart reaction) (7). Meanwhile, the recurrence of inflammation increased the primary chronic inflammation of the interstitium of the lung and parenchymal lesion such as pneumonia (4). The combined effects of primary chronic pulmonary embolism (V/Q mismatch) and chronic inflammation of the interstitium of the lung (diffusion impairment) contribute to PVD (e.g., primary pulmonary artery hypertension) after primary heart failure and pneumonia (4). Similar to these previous findings, systematic review data showed that heart failure is the main cause of pulmonary artery hypertension (46), primary and chronic inflammation of cardiomyopathy contributed to fibrosis myopathy of the heart in the PM/DM cohort (44). These bi-directional speculations explain the primary chronic inflammation in
the chronic reaction of the heart and lungs in the PM/DM cohort during follow-up, especially in patients with a high frequency of hospitalization, thus contributing to incident ARF (44). Furthermore, diabetes with insulin resistance (40) is associated with cardiopulmonary diseases (41) in the progressive course of the PM/DM cohort (5,20,21). These findings highlight the primary cardiopulmonary reaction (41,46) in chronic pulmonary heart diseases with a high frequency of admission among the PM/DM with poor control cohort, especially patients elderly, male and with

| Variable   | Non-PM/DM cohort | PM/DM cohort | Adjusted HR (95% CI) | P value* |
|------------|------------------|--------------|----------------------|----------|
|            | Event | PYs | Rate | Event | PYs | Rate |                        |          |
| Asthma     | No    | 281 | 85,319 | 32.9 | 141 | 6,679 | 211.1 | 5.62 (4.43–7.12) | 0.0934   |
|            | Yes   | 54  | 5,017  | 107.6 | 30  | 774  | 387.6 | 3.58 (2.13–6.01) |          |
| Hypertension | No    | 107 | 67,873 | 15.8 | 97  | 5,723 | 169.5 | 7.90 (5.56–11.20) | 0.0008   |
|            | Yes   | 228 | 22,463 | 101.5 | 74  | 1,730 | 427.7 | 4.01 (2.99–5.36) |          |
| Diabetes   | No    | 237 | 82,453 | 28.7 | 140 | 6,786 | 206.3 | 5.83 (4.56–7.45) | 0.06     |
|            | Yes   | 98  | 7,883  | 124.3 | 31  | 667  | 464.8 | 3.69 (2.34–5.83) |          |
| COPD       | No    | 242 | 84,163 | 28.8 | 129 | 6,508 | 198.2 | 6.21 (4.82–8.01) | 0.005    |
|            | Yes   | 93  | 6,173  | 150.7 | 42  | 945  | 444.4 | 3.04 (2.04–4.54) |          |
| Pneumonia  | No    | 254 | 78,790 | 32.2 | 102 | 5,690 | 179.3 | 4.60 (3.53–6.00) | 0.4808   |
|            | Yes   | 81  | 11,546 | 70.2 | 69  | 1,763 | 391.4 | 6.08 (4.22–8.78) |          |
| Cancer     | No    | 311 | 88,625 | 35.1 | 162 | 7,211 | 224.7 | 5.75 (4.64–7.13) | 0.5946   |
|            | Yes   | 24  | 1,711  | 140.3 | 9   | 241.5 | 372.7 | 3.46 (1.44–8.34) |          |
| CAD        | No    | 211 | 79,628 | 26.5 | 123 | 6,471 | 190.1 | 5.09 (3.89–6.65) | 0.2117   |
|            | Yes   | 124 | 10,708 | 115.8 | 48  | 982  | 488.8 | 4.94 (3.40–7.16) |          |
| Heart failure | No    | 305 | 89,092 | 34.2 | 160 | 7,236 | 221.1 | 5.95 (4.79–7.39) | 0.06     |
|            | Yes   | 30  | 1,244  | 241.2 | 11  | 217  | 506.9 | 2.64 (1.19–5.85) |          |
| PVD        | No    | 326 | 90,114 | 36.2 | 165 | 7,361 | 224.2 | 5.38 (4.33–6.68) | 0.0388   |
|            | Yes   | 9   | 221    | 407.2 | 6   | 91   | 659.3 | 18.4 (2.21–153.80) |          |

Adjusted for age, sex, CCI score, and medicine of oral steroid. *, P for interaction. PM/DM, polymyositis/dermatomyositis; rate, per 10,000 person-years; PYs, person-years; CI, confidence interval; HR, hazard ratio; COPD, chronic obstructive pulmonary disease; CAD, coronary artery disease; PVD, pulmonary vascular disease; CCI score, Charlson comorbidity index score.
comorbidities (e.g., COPD, hypertension, PVD) (8). In summary, this pulmonary-heart reaction in the PM/DM cohort is associated with the incident ARF (23,32,47).

In a previous study, ARF in the PM/DM cohort focuses on the myopathy of patients (48,49). The long-term outcome of the PM/DM cohort is associated with lung disease and inflammatory myopathies (50). The important finding of this study is that cardiac and pulmonary origins play a critical role in incident ARF development in the PM/DM cohort (33). Therefore, this study implies the cross-reaction of the heart and lungs (32,41,46) in the event of ARF among the PM/DM cohort. Furthermore, bridging the pulmonary diseases (e.g., COPD), heart disease (e.g., hypertension) (8,32,41,42) and PVD in the PM/DM cohort with incident ARF close together (23,31-33,47,51).

Limitation

Several limitations must be considered when interpreting these findings. The NHIRD does not provide detailed lifestyle information, such as smoking, body mass index (BMI), and physical activity, all of which were potential confounding factors in this study. In this study, we replace smoking with COPD and replace the BMI with diabetes. Although PM/DM treatment and the lifestyle modification of PM/DM patients implicate these factors in accelerated atherosclerosis vessel and airway inflammation in PM/DM. Additionally, information on PM/DM severity such as CCI were enrolled into analysis. However, disease activity, functional impairment, and physical damage were unavailable in our data. We only use the drug data such as steroids to adjust for the outcomes of interest. The other drugs use in the PM/DM cohort could be another limitation of this study. Despite our meticulous study design for controlling confounding factors, a key limitation of this study is the potential for bias caused by possible unmeasured or unknown confounders.

Strength

The strength of this study is that it provides a nationwide population-based cohort longitudinal study on ARF risk in Asian people with PM/DM. The analysis of PM/DM is based on the inpatient claims data and the catastrophic illnesses registry. The cohort study in the general population is similar to the “real world” (52) and avoids the bias of diagnosis and follow-up. These findings can be generalized to the general population.

Conclusions

This study determined the cross-reaction of pulmonary heart disease in the PM/DM cohort with incident ARF even without comorbidities.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: The authors are responsible for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The Research Ethics Committee of China Medical University and Hospital in Taiwan approved the study (CMUH104-REC2-115-R4). The NHIRD encrypts patient personal information to protect privacy and provides researchers with anonymous identification numbers associated with relevant claims information, including sex, date of birth, medical services received, and prescriptions. Therefore, patient consent is not required to access the NHIRD.

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