e-Figure 1

4,837 DILD patients with ICD-10 codes: J702, J703, J704 (after excluding patients who were diagnosed as ILD or DILD at admission)

2,343 DILD cases who required either
- High dose corticosteroids: ≥ 500 mg, ≥ 3 days
- Moderate dose corticosteroids: 200-500 mg, ≥ 3 days
- Low dose corticosteroids: 30-200 mg, ≥ 7 days

41,771,128 hospitalized patients were candidates for the controls

1 to 4 case-control matching

Same primary diagnosis (the first three digits of the patients’ ICD-10 codes at admission)
Same sex
Within 10-year age difference
Hospitalised within the adjacent fiscal year
The same hospital

Example scheme

Admission to onset

Case 1
- Control 1-1
- Control 1-2
- Control 1-3
- Control 1-4

Case 2
- Control 2-1
- Control 2-2
- Control 2-3

Length of stay

2,050 DILD cases
7,581 controls

A total of 2,413 case-control patients which case patients started corticosteroid treatment on the day of admission were omitted

1,541 DILD cases
5,677 controls

A flow diagram of DILD case and controls. Case patients were 1 to 4 matched to control patients. As shown in the example scheme, case patients were matched to control patients with length of stay longer than admission to onset in case patients. Case patients can be chosen as control. Case 2 is chosen as Control (Control 1-4) for Case 1 in the example scheme. Case patient were not necessarily matched to four patients if not possible as shown in Case 2.

DILD: drug-induced interstitial lung disease

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e-Figure 2

75 drug categories based on package inserts from the PMDA

A total of 33 drug categories were omitted for not having referred to in the five review articles and one population based study of DILD.

42 drug categories with potential risk

Another 23 drug categories were omitted for having less than five patients prescribed in either the case or the control after selecting drugs with potential risk prescribed before corticosteroid therapy.

19 drug categories with potential risk

Two drug categories were omitted for having less than 5 patients prescribed in either the case or the control after excluding drugs prescribed after three days before discharge from drugs with potential risk.

17 drug categories with potential risk

Seven drug categories did not show significant difference in univariate analysis and were not included in the conditional multivariable logistic regression analysis.

10 drug categories with potential risk

The use of three drug categories were not significantly different and one drug category showed lower incidence of DILD after adjustment with conditional multivariable logistic regression analysis.

Six drug categories with potential risk

A flow diagram of causative drugs for drug-induced interstitial lung disease.

PMDA: the Pharmaceuticals and Medical Devices Agency