Recurrence Burden in Recurrent Pericarditis: A US-Based Retrospective Study of Administrative Healthcare Claims

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INTRODUCTION

- Acute pericarditis (AP) is the most common form of pericardial disease encountered in clinical practice.[1,2] The majority of diagnoses are idiopathic, which poses considerable therapeutic challenges.[3]
- Recurrence occurs when a subsequent episode follows a symptom-free period of at least 4 weeks and affects up to 30% of patients within 18 months following the initial episode of AP[2,4]
- Recurrent pericarditis (RP) is associated with a high burden of disease:[2,5]
  - Substantial impacts on health-related quality of life and debilitating chest pain that limits physical activity
  - Potentially life-threatening complications, including cardiac tamponade and constrictive pericarditis
  - Limited efficacy data, side effects of conventional therapeutic options (NSAIDS, aspirin) and corticosteroids with the most severe cases requiring invasive and high risk surgical procedures (i.e., pericardiectomy)
- A subset of RP patients experience frequent recurrences (i.e., two or more) due to persistent underlying disease and inadequate treatment response to conventional therapy and corticosteroids[6,7]
- Recurrence burden (e.g., frequency, length and patterns of recurrences, residual pain, disease duration) remains poorly characterized in the literature. An improved understanding of recurrence burden is critical for disease management and treatment, and successful patient outcomes.

STUDY OBJECTIVE

- To use real-world claims data to describe recurrence burden among patients with RP in the United States

METHODS

Data Source

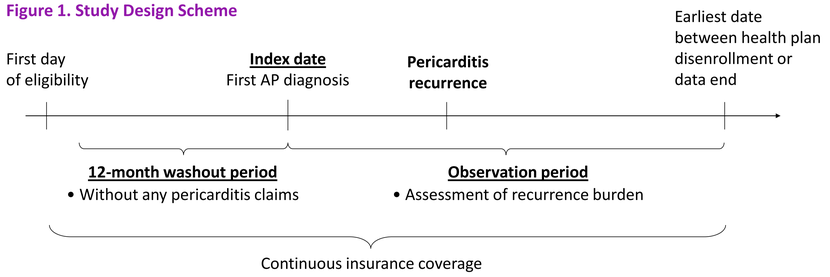
- OptumHealth Care Solutions, Inc. Reporting and Insights employer claims database from January 1, 2007 to March 31, 2017 was used
- Contains administrative claims for over 19.1 million privately insured individuals from Fortune 500 companies with information on plan enrollment and duration of eligibility
- Includes patients' demographics, medical diagnoses (reported with International Classification of Disease [ICD] codes), procedures, and prescription drug dispensing

Study Design

A retrospective longitudinal cohort design was used with the following definitions (**Figure 1**):

- *Index date:* the first AP diagnosis date
- *Episodes of care (EOC):* all AP claims (hospitalization, emergency department [ED], or outpatient) occurring in sequence without a gap of 4 weeks
- *Recurrence:* a subsequent EOC occurring >4 weeks after the end of the previous EOC
- *Observation period:* the index date until the time of confirmed health plan disenrollment or data end date, whichever occurred first
- *Disease duration:* the time from the first AP diagnosis to the end of the last recurrence and free of a subsequent AP diagnosis for at least 1.5 years. Patients who did not reach the end of disease duration prior to the 1.5-year AP-free period were censored.
- Recurrence frequency and time between recurrences were evaluated in a subset of patients with ≥3 years of disease duration to ensure a sufficient longitudinality

Figure 1. Study Design Scheme



Study Population

Inclusion Criteria

- Aged ≥18 years
- ≥1 hospitalization, ED, or outpatient claim with a diagnosis of AP
- ≥12 months of continuous eligibility prior to the index date and ≥18-month observation period
- ≥1 pericarditis recurrence during the observation period

Exclusion Criteria

- Health maintenance organization or Medicare coverage (patients may have incomplete information)
- AP with attributable etiology other than post-viral
  - Potential causes were evaluated in the 90 days prior to or on the first AP claim, except traumatic and cardiac syndromes or procedures, for which a period of 30 days was used
  - AP patients who did not fit the aforementioned criteria were categorized with idiopathic etiology

Statistical Analysis

- Conducted using SAS Enterprise Guide Version 7.15 (SAS Institute Inc., Cary, NC)
- Disease duration was evaluated using Kaplan-Meier analysis, accounting for right censoring
- Recurrence burden (i.e., likelihood, frequency, and time between recurrences) was evaluated using descriptive statistics, including means (± standard deviations [SDs]) and medians for continuous variables, and frequencies and proportions for categorical variables

RESULTS

Patient Characteristics

- Among a total of 5,146 selected patients with AP, 944 (18.3%) patients had ≥1 recurrence and 375 (7.3%) had ≥2 recurrences
- Among patients with ≥1 recurrence, the mean age was 51.57 years and 51.0% were female (**Table 1**)
- The mean Quan-Charlson comorbidity index score was 1.24, with the most common comorbidities being hypertension (43.8%), cardiac arrhythmias (32.9%), and valvular disease (25.7%; **Table 1**)

Table 1. Demographics and Clinical Characteristics at First Recurrence

Characteristics	RP Patients (N = 944)
Observation period, years, mean [median] (SD)	3.92 [3.58] (2.67)
Type of visit at the index date, n (%)	
Hospitalization	382 (40.5)
Length of stay, days, mean [median] (SD)	5.87 [4] (6.40)
ED	108 (11.4)
Outpatient	454 (48.1)
Age, years, mean [median] (SD)	51.57 [54] (13.73)
Female, n (%)	481 (51.0)
Geographical region, n (%)	
South	243 (25.7)
Northeast	297 (31.5)
Midwest	232 (24.6)
West	102 (10.8)
Unknown	70 (7.4)
Quan-CCI[1], mean [median] (SD)	1.24 [0] (1.69)
Comorbidities[1], n (%)	
Coronary artery disease	242 (25.6)
Hypercholesterolemia	118 (12.5)
Myocardial infarction	69 (7.3)
Elixhauser comorbidities[1], n (%)	
Hypertension	413 (43.8)
Cardiac arrhythmias	311 (32.9)
Valvular disease	243 (25.7)
Chronic pulmonary disease	200 (21.2)
Congestive heart failure	171 (18.1)
Diabetes without chronic complications	149 (15.8)

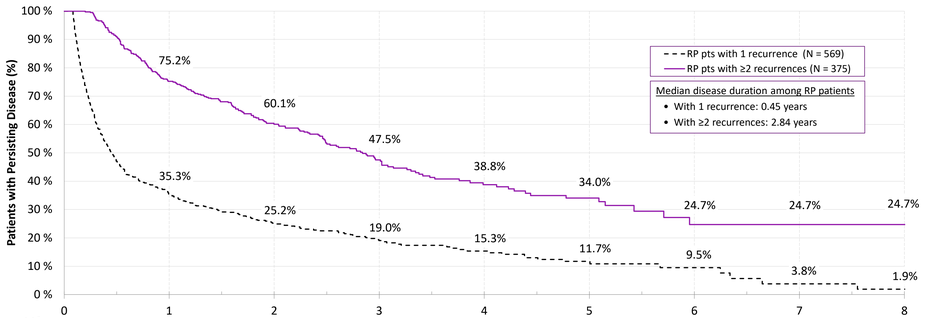
Note: 1. Evaluated in the 12-month period prior to the first recurrence.

RESULTS

Disease Duration among RP Patients, Stratified by Number of Recurrences

- Among the 944 RP patients, 375 (39.7%) had ≥2 recurrences
- Median RP duration was 0.45 years and 2.84 years among patients with 1 and ≥2 recurrences, respectively (**Figure 2**). Patients with ≥2 recurrences experienced 2.39 additional years of disease burden and duration.

Figure 2. Kaplan-Meier Disease Duration[1] among RP Patients, Stratified by Number of Recurrences



No. of patients at risk[2]

With 1 recurrence	569	201	101	51	28	13	6	2	1
With ≥2 recurrences	375	282	182	99	54	28	10	6	2

Notes:
1. Disease duration was defined as the time from the first AP diagnosis to the end of the last recurrence and free of a subsequent AP diagnosis for at least 1.5 years. Patients who did not reach the end of disease duration prior to the 1.5-year AP-free period were censored.
2. Number of patients still observed at the specific point in time.

Recurrence Burden Among the Subset of Complicated/High-Risk RP Patients with ≥2 Recurrences and ≥3 Years of Disease Duration

- Among these 99 (10.5%) high-risk patients, the time (mean ± SD) between the first two AP episodes was 1.06 ± 1.30 years, and was 0.97 ± 1.00 years between the second and third recurrence; subsequent recurrences were 0.61 ± 0.58 years apart
- Of the high-risk patients, 46.4% had ≥ 5 pericarditis episodes (**Table 2**)

Table 2. Frequency of Recurrences over Disease Duration[1] among the Subset of Complicated/High-Risk RP Patients

Frequency of recurrences, n (%)	With ≥2 Recurrences (N = 99)
2 recurrences	28 (28.3)
3 recurrences	25 (25.3)
≥4 recurrences	46 (46.4)

Note: 1. With ≥2 recurrences and ≥3 years of disease duration. Disease duration is defined in Figure 2, Note 1 (see above).

LIMITATIONS

- Follow-up duration limits and pericarditis episodes not resulting in a healthcare encounter likely underreport recurrence burden
- Some of the ICD codes are not specific to pericarditis potentially resulting in an over-representation of patients with one episode
- The minimum of 18 months of continuous health plan enrollment was imposed to ensure a sufficient follow-up period. This may introduce selection bias.
- Findings were obtained in commercially-insured patients and may, therefore, not be generalizable to the entire RP population

SUMMARY OF CONCLUSIONS

- **In this US real-world setting, there is a subset of pericarditis patients that suffer from a high recurrence burden and prolonged disease duration, despite currently available conventional, off-label therapies**
- **Approximately 40% of RP patients, and over 7% of all pericarditis patients, suffer from ≥2 recurrences**
- **Among patients with ≥2 recurrences, median disease duration was 3 years, experiencing disease for approximately 2.4 years after the first recurrence**
- **Patients with high recurrence burden would potentially derive benefit from a treatment that could rapidly resolve pericarditis signs and symptoms and prevent future episodes**

DISCLOSURES

This study was sponsored by Kiniksa Pharmaceuticals Ltd. DL and CM have nothing to report. MM and JFP are employees of Kiniksa. FL, DL, MD, MM, and MSD are employees of Analysis Group, Inc. a consulting company that has received research grants from Kiniksa.

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