Real-World Clinical Characteristics and Recurrence Burden of Patients Diagnosed with Recurrent Pericarditis in the United States

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INTRODUCTION

- Pericarditis is inflammation of the pericardial sac. It is the most common manifestation of pericardial disease worldwide and often presents as a chest pain that is sharp and pleuritic along with pericardial rub[1,2]
- Clinicians diagnose pericarditis as idiopathic, which is most often presumed to be viral, or non-idiopathic, which is most frequently caused by autoimmune disorders, cancer, metabolic disorders, bacterial infections, and certain cardiovascular conditions, such as post-pericardiotomy syndrome[1,2]
- Viral or immune-mediated idiopathic pericarditis comprises the vast majority of diagnoses, which leads to challenges when attempting to target medical therapy at the disease etiology[3]
- Patients diagnosed with acute pericarditis (AP) may subsequently develop recurrent pericarditis (RP), which is characterized by the recurrence of clinical features of AP following a symptom-free period of 4-6 weeks[4]
- RP affects ~15–30% of AP patients and leads to a diminished quality of life due to the direct symptoms of the disease and secondarily from the side effects associated with conventional treatments[5]
- Persistent recurrence and inadequate response to treatment presumably increase disease burden

STUDY OBJECTIVE

To use real-world data to describe the clinical characteristics (e.g., pericarditis etiology, comorbidities) and recurrence burden (e.g., time to first recurrence, mean number of recurrences per patient) of patients suffering from RP in the United States (US)

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 (i.e., employees, spouses, dependents, and retirees) from Fortune 500 companies with information on plan enrollment and duration of eligibility
- Information pertaining to the patients' demographics, as well as medical procedure and diagnosis (reported with International Classification of Diseases [ICD]) and prescription drugs, is available

Study Design

A retrospective cohort design was used to address the study objective

- AP episode of care was defined by an AP claim for an emergency department (ED) visit, hospitalization, or outpatient visit, and encompassed all AP claims occurring within 4 weeks of the previous claim. The end of the episode of care was defined as the date of the last AP claim within the episode
- Recurrence was defined as an episode of care occurring more than 4 weeks after the end of the previous episode of care
- The index date was defined as the date of the first recurrence
- The observation period spanned from the index date until the time of health plan disenrollment, or lack of available follow-up data, whichever occurred first

Study Population

Inclusion Criteria

- ≥1 ED, hospitalization, or outpatient claim with a diagnosis of AP
- ≥1 pericarditis recurrence during the observation period
- Aged ≥18 years at the index date
- ≥12 months of continuous enrollment in the database pre-index

Exclusion Criteria

- Health maintenance organization or Medicare coverage (patients may have incomplete information)
- AP with non-idiopathic etiology
  - Non-idiopathic conditions 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
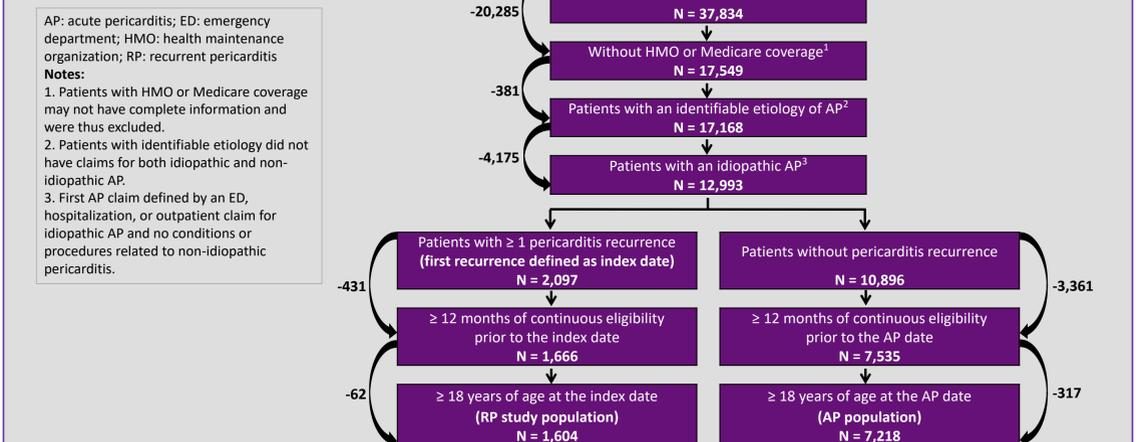
Statistical Analysis

- Descriptive statistics included means (± standard deviations [SDs]) and medians for continuous variables, and frequencies and proportions for categorical variables

RESULTS

Pericarditis Etiology and Patient Characteristics

- Of 17,168 AP patients, 12,993 (75.7%) had idiopathic, and 4,175 (24.3%) had non-idiopathic etiology (**Figure 1**)

Figure 1. Patient Disposition

AP: acute pericarditis; ED: emergency department; HMO: health maintenance organization; RP: recurrent pericarditis
Notes:
1. Patients with HMO or Medicare coverage may not have complete information and were thus excluded.
2. Patients with identifiable etiology did not have claims for both idiopathic and non-idiopathic AP.
3. First AP claim defined by an ED, hospitalization, or outpatient claim for idiopathic AP and no conditions or procedures related to non-idiopathic pericarditis.

- The most common non-idiopathic etiologies included metastatic neoplasm (6.6%) and autoimmune disease (6.5%; **Table 1**)
- Application of exclusion criteria left 8,822 idiopathic AP patients, of whom 1,604 (18.2%) had at least one recurrence (**Table 2**)
- Among idiopathic RP patients, 633 (39.5%) were hospitalized for their initial AP episode, with a mean (±SD) length of stay of 6.6 (±8.2) days (**Table 2**)
- The mean observation period for RP patients was 29 months; patients were aged 50.7 years (mean) and 51.6% female (**Table 2**)
- Most common comorbidities were hypertension (42.3%), cardiac arrhythmia (33.8%), valvular disease (24.5%), coronary artery disease (23.8%), and chronic pulmonary disease (20.9%; **Table 2**)

Table 1. Disease Etiology in AP Patients

Etiology	AP patients (N = 17,168)
Idiopathic, n (%)	12,993 (75.7)
Non-idiopathic,[1,2] n (%)	4,175 (24.3)
Metastatic neoplasm	1,141 (6.6)
Autoimmune	1,109 (6.5)
Systemic lupus erythematosus	343 (2.0)
Rheumatoid arthritis	273 (1.6)
Ulcerative colitis	107 (0.6)
Crohn's disease	90 (0.5)
Still's disease	12 (0.0)
Cardiac syndromes/procedures	853 (5.0)
Post-pericardiotomy syndrome	81 (0.5)
Metabolic	361 (2.1)
Bacterial	360 (2.1)
Traumatic	298 (1.7)
Fungal	235 (1.4)
Parasitic	7 (0.0)
Other[2]	229 (1.3)

AP: acute pericarditis
Notes for Table 1:
1. Patients may have more than one condition related to non-idiopathic pericarditis.
2. Includes patients with a non-specific non-idiopathic diagnosis.

Table 2. Baseline Demographics and Clinical Characteristics

Characteristics	RP patients (N = 1,604)
Observation period, months, mean [median] (SD)	29.4 [25] (23.2)
Site of care of initial pericarditis visit, n (%)	
Hospitalization	633 (39.5)
Length of stay, days, mean [median] (SD)	6.6 [4] (8.2)
ED	168 (10.5)
Outpatient	803 (50.1)
Age[1], years, mean [median] (SD)	50.7 [53] (14.1)
Female[1], n (%)	828 (51.6)
Quan-CCI, mean [median] (SD)	1.34 [0] (1.88)
Comorbidities of interest, n (%)	
Coronary artery disease	382 (23.8)
Hypercholesterolemia	187 (11.7)
Myocardial infarction	117 (7.3)
Elixhauser's comorbidities with a prevalence >10%, n (%)	
Hypertension	679 (42.3)
Cardiac arrhythmias	542 (33.8)
Valvular disease	393 (24.5)
Chronic pulmonary disease	335 (20.9)
Congestive heart failure	277 (17.3)
Diabetes without chronic complications	233 (14.5)
Hypothyroidism	225 (14.0)
Depression	194 (12.1)
Solid tumor without metastasis	194 (12.1)
Fluid and electrolyte disorders	194 (12.1)

ED: emergency department; Quan-CCI: Quan-Charlson comorbidity index; RP: recurrent pericarditis; SD: standard deviation
Notes for Table 2:
1. Evaluated at the index date (i.e., the date of the first recurrence).

Pericarditis Recurrence

- Mean (±SD) time from initial AP diagnosis to first recurrence was 8.7 (±12.1) months and the mean (±SD) number of recurrences was 1.7 (±1.3) per patient
- A total of 512 RP patients had ≥4 years of follow-up after the initial AP diagnosis
  - Within 4 years of the initial AP diagnosis, 184 (35.9%) had ≥2 recurrences, 93 (18.2%) had ≥3 recurrences, and 50 (9.8%) had ≥4 recurrences (**Table 3**)

**Table 3. Recurrence Episodes[1] among RP Patients with ≥4 Years of Follow-up**

Outcomes	RP patients (N = 512)
Recurrences within 4 years of the initial AP diagnosis, n (%)	
≥1 recurrence	476 (93.0)
≥2 recurrences	184 (35.9)
≥3 recurrences	93 (18.2)
≥4 recurrences	50 (9.8)

AP: acute pericarditis; ED: emergency department; RP: recurrent pericarditis; SD: standard deviation
Notes:
1. Each recurrence was defined by an AP claim for an ED visit or hospitalization (based on primary or secondary diagnosis) or an outpatient visit (based on primary diagnosis) occurring more than 4 weeks after the last AP claim in the previous episode of care. An episode of care was defined as any ED, hospitalization, or outpatient AP claim following the prior recurrence with no gap between claims greater than 4 weeks.

- The proportion of patients with ≥1 recurrences in the 4 years after the first AP diagnosis went from 62.3% during the first year to 14.8% during the fourth year (**Figure 2**)

Figure 2. Proportion of Patients with Recurrence in Each Year After the Initial AP Diagnosis in RP Patients with ≥4 Years of Follow-up (N = 512)
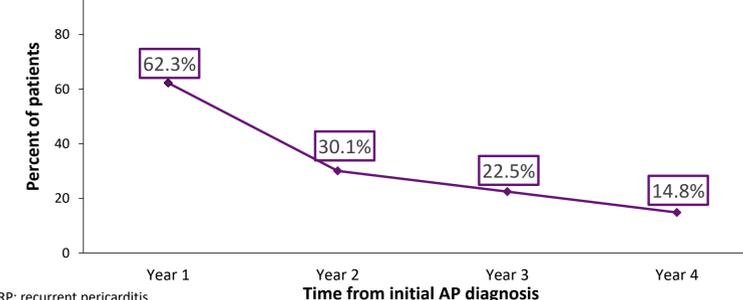
AP: acute pericarditis; RP: recurrent pericarditis

LIMITATIONS

- Enrollment of individuals in this administrative database is on average 29 months, it is likely that some patients with recurrences were not identified due to right censoring of the data
- Use of claims data to infer etiology may explain the lower rates of idiopathic etiology reported here (75.7%) compared to prior studies (~80-90%)[6]
- Due to the nature of claims databases, coding inaccuracies or omissions in procedures and diagnoses could have occurred

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SUMMARY OF CONCLUSIONS

Despite advances in the understanding of pericarditis, over 18% of US patients still experience recurrence. Among patients who experience RP, almost 10% will experience five or more episodes within four years of the initial diagnosis

- A large proportion of AP patients have idiopathic etiology, and cardiovascular disease and other associated comorbidities are common among patients with RP. It is not clear if pericarditis is associated with these comorbid conditions or serves as a potential warning sign of other health issues. This question warrants further research
- Persistent recurrence and overall clinical complexity in a subset of patients with pericarditis suggest a high clinical burden of illness. These patients would likely benefit from treatment approaches that can reduce the risk of recurrence
- Due to a lack of follow-up, some recurrences may not have been identified, leading to an underestimation of the proportion of patients with RP. Future investigations taking into account right censoring will need to be considered