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Clinical Features, Therapeutic Interventions, and Prognostic Outcomes of Plasma Cell-Associated Pericardial Disease in Multiple Myeloma

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Abstract

Extramedullary involvement of multiple myeloma (MM) in the form of plasma cell-associated pericardial disease is a rare, but potentially fatal complication that is often associated with cardiac tamponade or pericardial effusion. Due to its rarity, there was a lack of comprehensive knowledge regarding the clinical presentation, management and prognosis, with just isolated case reports available. In this study, the clinical characteristics, therapeutic choices, and survival of patients with plasma cell-associated pericardial disease were assessed through individual patient data analysis. A retrospective study was performed in 28 patients with known involvement of the pericardium due to MM. Data for demographics, clinical, therapeutic and outcome was extracted and analysed descriptively. The majority of patients had advanced or relapsed/recurrent multiple myeloma and a symptomatic pericardial effusion that required urgent intervention. Pericardiocentesis was the most common procedure performed and systemic chemotherapy and corticosteroids were the most common treatment strategy. Even with multimodal management, prognosis was still poor, and most deaths were due to disease progression. These findings reinforce the aggressive nature of the plasma cell associated pericardial disease and the need for recognition of early disease, rapid pericardial drainage, and multidisciplinary management. More large-scale multi-center studies are needed to develop a standardized diagnosis and treatment protocol and to enhance clinical results.

Keywords: Multiple myeloma, Pericardial disease associated with plasma cells, Pericardial effusion, Tamponade, Extramedullary disease.

1. Introduction

Multiple myeloma is a plasma cell malignancy that is heterogeneous in its nature, associated with a clonal proliferation in the bone marrow, production of monoclonal immunoglobulins, destruction of the bone framework, immune dysfunction, renal failure and diverse systemic complications. Despite the marked improvement in disease control achieved by the use of proteasome inhibitors, immunomodulatory agents, monoclonal antibodies, cellular therapies and transplantation, multiple myeloma remains an incurable disease for the vast majority of patients, due to clonal evolution, space heterogeneity, drug resistance and repeated relapse. The growing prevalence of treatment based on a risk-adapted approach, together with the evaluation of measurable residual disease and rational sequencing of the targeted therapeutic options, is a cornerstone of contemporary management. Technical standardization, limitations of tumor sampling, and interpretation remain a challenge with next generation sequencing, but it has enhanced the sensitivity of residual disease detection and could aid in response adapted treatment decisions (Ferla et al., 2022). The recent treatment algorithms also highlight the importance of personalized therapeutic sequences, especially for those who have been treated with B-cell maturation antigen- and GPRC5D-targeted immunotherapies (Van De Donk et al., 2025). Multiple myeloma's clinical burden is not limited to progression of hematological disease. The patients can suffer from complications of treatment, from orthopaedic morbidity, from inability to function from various organs, from infection and from failure to recover after surgery.

Systemic effects of disease and therapy can be seen in multiple myeloma which has been linked to poor outcomes after large orthopaedic surgeries (Varatharaj et al., 2025). Rare presentations can happen at relapse as well, such as hyperammonemic encephalopathy, which is an aggressive plasma cell biology and which might need quick recognition and treatment (Menakuru et al., 2023). Striking clinical heterogeneity and prognosis, unequal access to therapy, and survival rates between populations also highlight the need for detailed characterization of rare clinical manifestations of these diseases (Elsabah et al., 2024). Extramedullary disease may be one of the most advanced forms of multiple myeloma.

It occurs when abnormal plasma cells leave the bone marrow and spread to soft tissues or organs. This involvement can be at the time of diagnosis or at relapse, and is often associated with treatment resistance, advanced disease, and poor survival. Extramedullary involvement of the central nervous system, orbit, liver, lungs, gastrointestinal tract, skin and other rare anatomical locations may occur. The complexity of diagnosing and treating extramedullary localizations, especially when ruling out systemic disease based on conventional bone marrow-based assessment underestimates the burden of systemic disease (Sammartano et al., 2022), has been emphasized by practical experience. Plasma cell dissemination beyond the marrow compartment is also aggressive as shown by orbital disease that can be associated with various clinical presentations and a poor prognosis (Hu et al., 2022). In the recent reviews, therefore, it is emphasized that imaging, tissue confirmation, assessment of systemic disease, and measurable residual disease (MRD) evaluation should be included in the management of extramedullary myeloma (EMM) (Diaconescu et al., 2025). The involvement of the pericardium is a

very rare type of extramedullary multiple myeloma, but an important one to consider clinically.

Infiltration of the pericardium by plasma cells can lead to malignant effusion, recurrent effusion, hemodynamic compromise or cardiac tamponade. Given the overlapping signs and symptoms of infection, anemia, renal dysfunction, treatment toxicity, amyloidosis, and other cardiopulmonary disease, these complications are hard to detect. Definitive diagnosis is usually achieved by combining the echocardiographic findings, the cytology and immunophenotyping of the pericardial fluid, imaging and the clinical history of multiple myeloma. This presentation is rare and evidence is from limited case reports and small case series, not prospective cohorts. Therapeutic management is also difficult due to the need to treat both the acute compromise of the pericardium and the underlying plasma cell malignancy. If pericardial effusion is recurrent or persistent, a surgical window may be necessary to give immediate hemodynamic relief, or pericardiocentesis can be done.

Depending on previous exposure, disease status, organ function and availability, systemic therapy may involve the use of corticosteroids, proteasome inhibitors, immunomodulatory agents, monoclonal antibodies, chemotherapy, radiotherapy or transplantation. Regimens that include daratumumab have shown activity in newly diagnosed and relapsed/ refractory multiple myeloma, though results have been variable, depending on the nature of the disease and prior therapies (Hu et al., 2025; Lovas et al., 2025). There are also some consensus statements that emerge on unmet needs in RR disease such as optimal sequencing, resistance management, and treatment of Hr-EM. (Cavo et al., 2026). Therapeutic advances have made prognosis difficult in the patient with plasma cells associated pericardial disease. Conventional prognostic markers such as beta2-microglobulin, renal function, cytogenetic abnormalities, treatment response, and measurable residual disease may also only provide partial information when the disease is mostly extramedullary (Rasheed et al., 2026; Siricharoenthai et al., 2026). Ultimately, real-time genomic monitoring and liquid biopsy could aid in assessing spatially heterogeneous disease, but these are yet to be validated (Rasheed et al., 2026). Guidelines and therapeutic approaches are becoming more personalized and yet few cardiac manifestations are represented in clinical trials and formal guidelines/recommendations (Charliński et al., 2026; Gay et al., 2026). Therefore, a personal patient data analysis can be useful in generating clinically relevant evidence by pooling of scattered observations, discovering recurring presentation patterns, and assessing treatment outcome relationships.

Therefore, the present study is conducted on the individual level data of patients suffering from plasma cell associated pericardial disease in multiple myeloma. The analysis incorporates demographic, clinical, therapeutic and survival data to understand the nature of this rare complication, its management and possible prognostic factors. The objectives of this study are as follows:

1. To characterize the demographic, clinical, and extramedullary features of plasma cell-associated pericardial disease
2. To evaluate systemic and pericardial therapeutic interventions used in affected multiple myeloma patients
3. To assess survival outcomes and identify clinical factors associated with unfavorable

prognosis

2. Materials and Methods

2.1 Study Design

A retrospective individual patient data (IPD) analysis was used to explore the clinical characteristics, treatment and prognosis of plasma cell-associated pericardial disease (PAPD) in multiple myeloma (MM) patients. The records of each patient were collated into a structured analytical patient data set to allow patient-level assessments of disease presentation, treatment strategies and survival. The IPD methodology allowed to capture clinical heterogeneity with the retention of individual patient characteristics. This is a design suitable for rare clinical entities, where much of the evidence that is available comes from published case reports and small case series.

2.2 Data Source and Study Population

A selected set of 28 patients with plasma cell-associated pericardial disease in association with multiple myeloma were analyzed. The information was patient-level data that was abstracted from published clinical reports that included the following data categories: demographics, disease history, immunoglobulin subtype, extramedullary involvement, therapeutic interventions, and survival outcomes. Only cases with adequate clinical and outcome data were analyzed while duplicate cases and reports with missing variables were excluded. The study population included a wide range of clinical presentations and management options that have been reported in the literature.

2.3 Study Variables

Variables were subdivided into the demographic, clinical, therapeutic, and prognostic categories. Demographic variables were age and sex. The clinical variables included were disease duration, the immunoglobulin subclass, and known extramedullary organ involvement such as pulmonary, hepatic, renal, pancreatic, breast, and pericardial disease. Various therapies were used, such as chemotherapy, corticosteroid therapy, radiotherapy, stem cell transplantation, pericardiocentesis, creation of surgical pericardial window, and interventions within the pericardial cavity. Survival time, patient status at the follow-up visit and the reported cause of death were used as prognostic variables. These variables were chosen to capture a comprehensive picture of clinical presentation, management of the disease, and clinical outcomes.

2.4 Processing/Quality Assessment of Data

The data was systematically checked for the integrity and consistency of the data set. All variable names were uniformized and categorical responses were given uniform coding for accurate analysis. Continuous variables were checked for plausibility, consistency and categorical variables were checked for completeness and logical consistency on patient records. Records have been duplicated and eliminated, if applicable. The missing information was left at "No information" and because of the retrospective nature of the data and limited sample size, it was decided not to impute this information.

The finalized dataset was then ready for descriptive and survival analyses.

2.5 Statistical Analysis

Data was analyzed using python. The mean and standard deviation or the median and interquartile range were used to summarize continuous variables, depending on the distribution, and frequencies and percentages were used for categorical variables. Demographic data, clinical manifestations, treatment, and outcomes were reported descriptively. The overall survival was calculated by the reported follow-up duration for each patient, and when appropriate, Kaplan–Meier survival analysis was used. Throughout the analysis a two-sided p value < 0.05 was considered statistically significant.

3. Results

3.1 Baseline Demographic and Disease Characteristics

Twenty-eight patients with plasma cell-associated pericardial disease secondary to multiple myeloma were analyzed. The mean age of the study population was approximately 61 years and the number of male vs female patients was almost equal. Pericardial involvement followed a diagnosis of multiple myeloma in most people. Systemic chemotherapy was documented in most cases and smaller proportions had received hematopoietic stem cell transplantation or radiotherapy. Baseline characteristics showed that plasma cell associated pericardial disease was more common in patients with advanced or previous multiple myeloma (Table 1).

Table 1: Baseline Demographic and Disease Characteristics of the Study Population (N = 28)

Characteristic	Category	Value
Age (years)	Mean ± SD	61.5 ± 14.7
Sex	Male	15 (53.6%)
	Female	13 (46.4%)
Previous chemotherapy	Yes	24 (85.7%)
	No	4 (14.3%)
Hematopoietic stem cell transplantation	Yes	5 (17.9%)
	No	23 (82.1%)
Previous radiotherapy	Yes	5 (17.9%)
	No	23 (82.1%)

3.2 Clinical Presentation and Extramedullary Disease

Clinical presentation was very different in different patients. The most common cardiac finding was pericardial effusion, which often had symptoms that demanded immediate assessment. In addition to pericardial involvement, several patients had extramedullary disease with involvement of lungs, liver, kidneys, pancreas and breast, suggesting systemic dissemination of plasma cell disease. However, a large number of patients had an aggressive disease phenotype, as indicated by the presence of several

extramedullary sites. Variability was also observed for immunoglobulin subtypes, which corresponds to the heterogeneity of the biological features of the multiple myelomas associated with pericardial disease (Table 2) (Figure 1).

Table 2: Clinical Presentation and Extramedullary Organ Involvement

Clinical Variable	Category	n	%
Pericardial involvement	Present	10	35.7
Lung involvement	Present	2	7.1
Pancreatic involvement	Present	2	7.1
Liver involvement	Present	1	3.6
Kidney involvement	Present	1	3.6
Breast involvement	Present	1	3.6

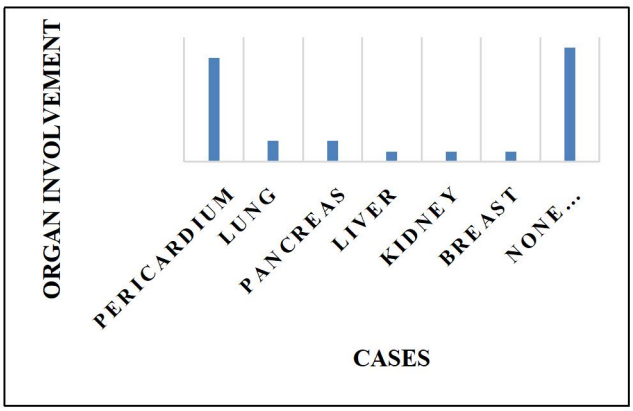

Figure 1: Distribution of Extramedullary Organ Involvement

3.3 Therapeutic Interventions

Management was with emergency pericardial procedures and systemic anti-myeloma therapy. Pericardiocentesis was the most common procedure performed and the first procedure performed in most patients with symptomatic pericardial effusion or cardiac tamponade. Selected cases of recurrent and persistent effusions had a surgical window created in the pericardium. After diagnosis, chemotherapy was administered in combination with corticosteroids as the most common systemic treatment; in a smaller group of patients, only corticosteroid or radiotherapy, or even therapeutic interventions in the pericardium, were administered. The choice of treatment seemed to be influenced by severity of the disease, previous treatment, and clinical condition (Table 3) (Figure 2).

Table 3: Therapeutic Interventions Performed

Treatment Modality	Patients (n)	Percentage (%)
Pericardiocentesis	25	89.3

Pericardial window	6	21.4
Intrapericardial therapy	6	21.4
Chemotherapy + corticosteroids	14	50.0
Corticosteroids alone	4	14.3
Radiotherapy	1	3.6

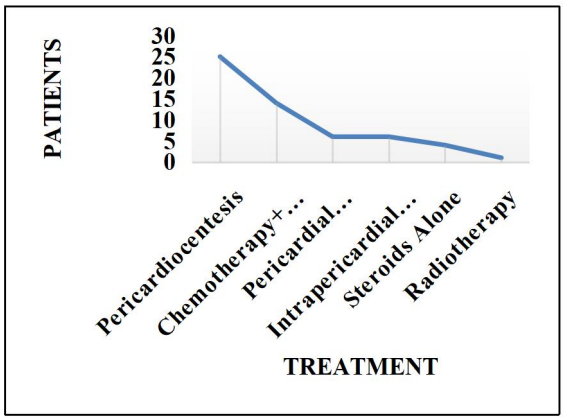

Figure 2: Distribution of Therapeutic Interventions

3.4 Survival Outcomes and Mortality

The clinical findings showed that the plasma cell-associated pericardial disease had a poor prognosis. Subsequent data revealed significant variation in survival time, with the proportion of patients with known survival still being high. Systemic disease proved to be the most aggressive cause of death, with progression to multiple myeloma the chief cause of death. In spite of this, in selected patients the early treatment with combined local pericardial drainage and systemic anti-myeloma therapy resulted in long-term survival (Table 4), which indicates that early intervention may be helpful in these patients (Figure 3).

Table 4: Survival Outcomes and Mortality of Patients with Plasma Cell-Associated Pericardial Disease (N = 28)

Outcome Variable	Category	Value	Percentage (%)
Patient status at follow-up	Alive	8	28.6
	Deceased	20	71.4
Cause of death	Progressive multiple myeloma	15	53.6
	Cardiac complications	3	10.7
	Infection/Other causes	2	7.1
Survival duration (weeks)	Median (Range)	6 (2–152)	100.0
Patients surviving >24 weeks	Yes	6	21.4
	No	22	78.6

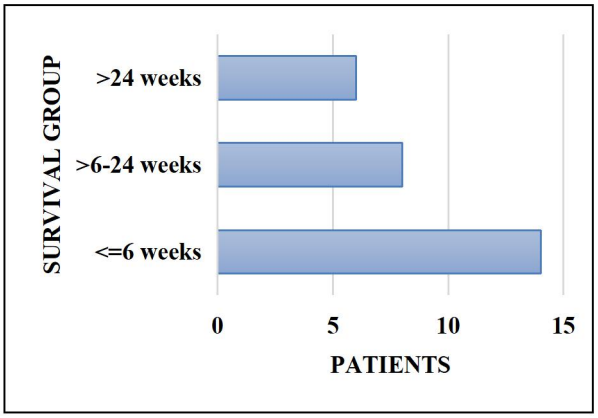

Figure 3: Distribution of Survival Duration Categories

3.5 Association Between Clinical Characteristics and Patient Outcomes

Patients with large extramedullary disease had more unfavorable clinical responses as revealed by comparative evaluation, compared with those with isolated pericardial involvement. More than one invasive procedure (such as repeated pericardiocentesis or creation of a surgical pericardial window) was often associated with more advanced disease course. In most patients, previous chemotherapy and hematopoietic stem cell transplantation (HSCT) indicated the presence of relapsed and/or refractory multiple myeloma (r/r MM). Patients with early pericardial drainage followed by systemic therapy, however, showed an advantage in obtaining temporary clinical stabilization, with a guarded prognosis in the long term (Figure 4).

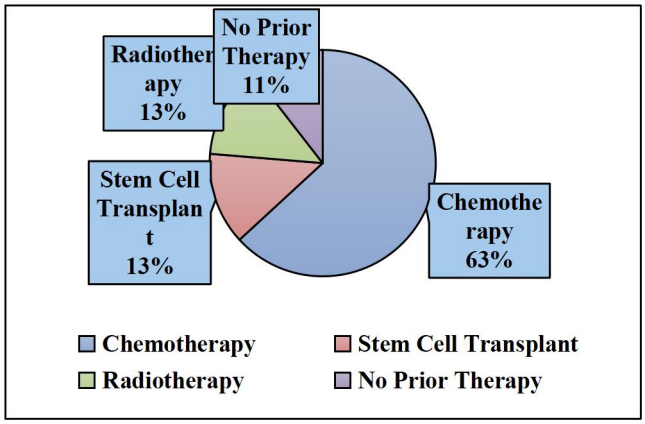

Figure 4: Previous Treatment Exposure Among Patients

4. Discussion

Plasma cell-associated pericardial disease as a rare but clinically aggressive disease of multiple myeloma. The most important findings were that most patients with affected lesions had received treatment for disease or had had advanced disease, that most patients had required urgent pericardial drainage, and that there was significant mortality despite combined local and systemic therapy. Pericardiocentesis was the most common procedural treatment while systemic treatment with steroids was the most common systemic treatment. Survival was variable but overall, involvement of the pericardium was associated with a poor disease course that was typically one of relapse,

extramedullary dissemination, treatment resistance or progressive myeloma.

The disease profile of this cohort is advanced as is reflected in more recent evidence which indicates that extramedullary multiple myeloma is a disease entity separate from disease in the bone marrow. Extramedullary lesions are the result of the capacity of malignant plasma cells to grow outside the marrow environment and invade the visceral or soft tissue. More recent studies of modern disease have shown that patients with extramedullary disease often present with high-risk disease features and poor outcomes compared to patients without extramedullary disease (Broughton et al., 2025). Rare visceral presentations such as gastric plasmacytoma also occur in the relapsed setting, and can be a sign of aggressive clonal evolution (Dirican et al., 2025). Pericardial infiltration thus seems to be part of the spectrum of more advanced extramedullary dissemination and not a separate cardiovascular complication.

Limited effectiveness of follow-up therapy in heavily pretreated patients could also be responsible for the poor outcomes observed in the present analysis. However, the complexity of the treatment choice after multiple relapses (Dimopoulos et al., 2021; Charliński et al., 2026) is increasing even with the addition of proteasome inhibitors, immunomodulatory agents, anti-CD38 antibodies, autologous transplantation, and bispecific antibodies and cellular therapies. Despite the success of B-cell maturation antigen (BCMA) targeting chimeric antigen receptor T-cell (CAR T) therapy, the results of its post-progression effects are not always positive in patients with extramedullary or paramedullary disease (Abuhelwa et al., 2025). The observations indicate that pericardial disease can be a clue to an active systemic biology that is resistant, especially when it occurs following chemotherapy, radiotherapy, or transplantation.

In patients analyzed, the most commonly used intervention was pericardiocentesis, which is the procedure of choice for the emergency management of large pericardial effusions and cardiac tamponade. Modern procedural guidance has found echocardiographic guidance for pericardiocentesis to be a useful tool for immediate decompression, symptom resolution, hemodynamic stabilization, and sampling for fluid analysis for diagnostic purposes (Luis et al., 2020). Pericardial fluid examination is particularly valuable in the diagnosis of multiple myeloma because effusions are usually caused by infiltration of the pericardium by plasma cells and not by infection, inflammatory reaction associated with treatment, renal failure, amyloidosis, or hemorrhage. This may, therefore, be a valuable confirmation of the direct involvement of plasma cells by cytological and immunophenotypic evaluation.

Multimodal imaging can also enhance the diagnostic impression by providing a better assessment of effusion size and degree of chamber compression, pericardial thickening, associated masses and extracardiac disease. Echocardiography is the main imaging tool for identification of tamponade physiology, while computed tomography and cardiac magnetic resonance imaging can provide other anatomical and tissue characterization. The increasing importance of integrated imaging is of special interest when dealing with malignant effusions, where the severity of the hemodynamic changes may not correspond directly with the amount of effusion and/or where infiltrative lesions are harder to

recognize with only one technique (Gajjar et al., 2026). Imaging should thus be used in conjunction with clinical examination and pericardial fluid analysis if the plasma cell-associated pericardial disease is suspected.

The recurrence is a great concern after the drainage of malignant pericardial effusion. From larger cancer populations, it has been found that the type of cancer, extent of disease, characteristics of the fluid collected and further oncological treatment all affect the rate of recurrence and survival after pericardiocentesis (Ahmed et al., 2022). Some patients in the present cohort were treated with surgical formation of a window in the pericardium, likely as a consequence of persistent, recurrent or clinically significant effusion. Surgical window procedures can be used to achieve more persistent drainage in certain patients, and modified pleuropericardial techniques have been suggested to decrease recurrence (Hemead et al., 2022). But performance status, prognosis, coagulopathy, thrombocytopenia, previous treatment and intent of treatment should be taken into account in procedural selection.

This is especially important in patients with multiple myeloma who may be thrombocytopenic, have received anticoagulant therapy, renal impairment, or be susceptible to bleeding as a result of the therapy. Well-executed pericardiocentesis appears to be feasible in patients on antithrombotic agents, provided proper imaging guidance and procedural precautions are employed, as per available evidence (Zhu et al., 2022). However, a risk stratification for each patient is required, particularly in cases of severe cytopenias or rapidly progressive disease.

The findings are supportive of a multidisciplinary approach to management, adopting a team approach comprising hematology, cardiology, cardio-oncology, imaging specialists, cytopathology, and cardiothoracic surgery. The need for immediate drainage and the likelihood of failure with local intervention alone in the absence of effective systemic treatment if the patient is experiencing acute hemodynamic compromise. So treatments should be directed towards the plasma cell malignancy as well as the pericardial emergency. The best systemic therapy is not yet clear since there is significant variation in prior therapy use, resistance, organ function, and availability of sophisticated immunotherapies in patients.

The limitations of this study include its patient-level retrospective design, the small number of patients enrolled, lack of completeness in reporting, heterogeneous follow-up, and publication bias for severe or unusual cases. Comparisons of treatment response should thus be viewed with caution because treatment was not uniform and the potential for confounding due to severity of the disease was not avoided. Despite the fact that there are limitations, the analysis brings together scattered information regarding a rare clinical disease and shows common themes in advanced disease, emergency surgical procedures, and poor outcome. Standardized reporting and prospective registry should be established to better define the diagnostic pathway, recurrence risk, therapeutic efficacy, and survival outcomes in plasma cell-associated pericardial disease.

5. Conclusion

Pericardial disease associated with plasma cells is a rare but life-threatening extramedullary form of multiple myeloma and is often associated with the advanced disease and systemic dissemination and

poor prognosis. In this individual patient data analysis, the majority of affected patients had previously been treated for myeloma and many needed urgent interventions to the pericaridum, especially pericardiocentesis, to treat symptomatic cardiac tamponade and/or PE. Multimodal treatment with local drainage procedure and systemic treatment was often used, but prognosis remained poor, reflective of the aggressive biological behaviour of extramedullary plasma cell disease. The results also underscore the wide variability in clinical characteristics, treatment, and prognosis, which underscores the need for personalized patient care. Early diagnosis of cardiac involvement with timely imaging, cytological diagnosis and multidisciplinary assessment can help to ensure timely intervention and clinical stabilization in the short term. However, long-term disease control remains dependent on effective systemic chemotherapy that is able to treat the underlying hematological malignancy. Although there were some limitations due to the retrospective design, small number of papers, and a lack of uniformity of the published reports, this study gathered the existing patient-level data and offered clinically relevant information regarding the presentation, management, and prognosis of this rare complication. Additional multicenter registries and prospective collaborative studies are required to define a standard approach to diagnosis, fine-tune therapeutic decision making, and help to improve long-term outcome of plasma cell associated pericardial disease in multiple myeloma.

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