

Laboratory Analysis and the Pericardiogram in Pericardial Diseases in the Era of Precision Medicine

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Abstract

Pericardial syndromes constitute a heterogeneous group of diseases affecting the pericardium, with varied clinical presentations and multiple etiologies (infectious, autoimmune, traumatic, post-surgical, metabolic, among others). This diversity demands increasingly refined diagnostic approaches, aligned with the principles of precision medicine. A significant transformation has taken place in the understanding of these conditions and their complexity, driven by the development of advanced diagnostic and therapeutic methods.

In the context of precision medicine, the aim is to improve the identification of the causal mechanism, allowing for individualized treatment. Significant advances in pericardiology have been driven by methods including cytopathology, immunohistochemistry, analysis of serum and pericardial biomarkers (including novel tumor markers), and the metagenomic detection of microorganisms.

In parallel, advances in molecular biology and emerging methodologies enable the detailed identification of pathogens and the characterization of multiple phenotypes of pericardial diseases, promoting increasingly accurate and individualized diagnoses. Furthermore, genetic markers have played an important role in elucidating the causes of recurrent pericarditis by identifying genes associated with autoinflammatory diseases and hereditary predispositions.

The objective of this review is to present the state of the art in the diagnosis of pericardial diseases, focusing on techniques that directly assess pericardial fluid and, therefore, effectively assist in the etiological investigation of various pericardial syndromes. A new tool, the “pericardiogram,” is also proposed to organize clinical reasoning and ensure the best use of complementary tests in assisting the investigation of pericardial syndromes.

Keywords

Pericarditis; Cardiac Tamponade; Pericardial Effusion; Precision Medicine

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Introduction

Normal pericardial anatomy, cytology, and physiology

The pericardium consists of two layers, the parietal and the visceral. The parietal layer surrounds the heart externally and is composed of a more superficial layer of fibrous tissue and an inner serous layer, consisting of mesothelial cells, which reflects onto the heart to form the visceral layer.^{1,2} This layer is closely associated with the heart, covering the entire heart and the great vessels.^{1,2} Together, these layers limit expansion of the cardiac chambers.^{3,4}

Regarding innervation, the main nerves involved are the phrenic nerve (sensory innervation) and the vagus nerve (parasympathetic), in addition to sympathetic innervation, which is mainly due to the cardiac nerves. Arterial supply is concentrated in the vessels of the internal thoracic artery and the descending thoracic aorta, whereas venous drainage occurs through the pericardiophrenic and brachiocephalic veins.^{1,5} Pericardial fluid is located in the pericardial cavity, and normal volume ranges from 25 to 50 mL.^{1,2} Its main function, together with the fibrous portion of the pericardial wall, is to reduce the impact during cardiac contractions and minimize friction, in addition to serving as a physical barrier against tumors or infections.^{1,3,4}

Pericardial syndromes and their etiologies

Pericardial diseases have diverse etiologies, which can be divided into infectious or non-infectious, including autoimmune, myopericardial syndromes, post-cardiac injury, traumatic, congenital, metabolic, neoplastic and idiopathic syndromes (Table 1).^{2,6,7} The most common pericardial disease, pericarditis, is an inflammatory process that can be acute or evolve into incessant, chronic, or recurrent forms, with or without effusion.^{2,6,8} Effusion is characterized according to the properties of the accumulated fluid (transudate, exudate, hemorrhagic, and others) as well as by clinical course, and may progress to constrictive pericarditis due to pericardial fibrosis and calcification, with restricted diastolic filling.^{2,6}

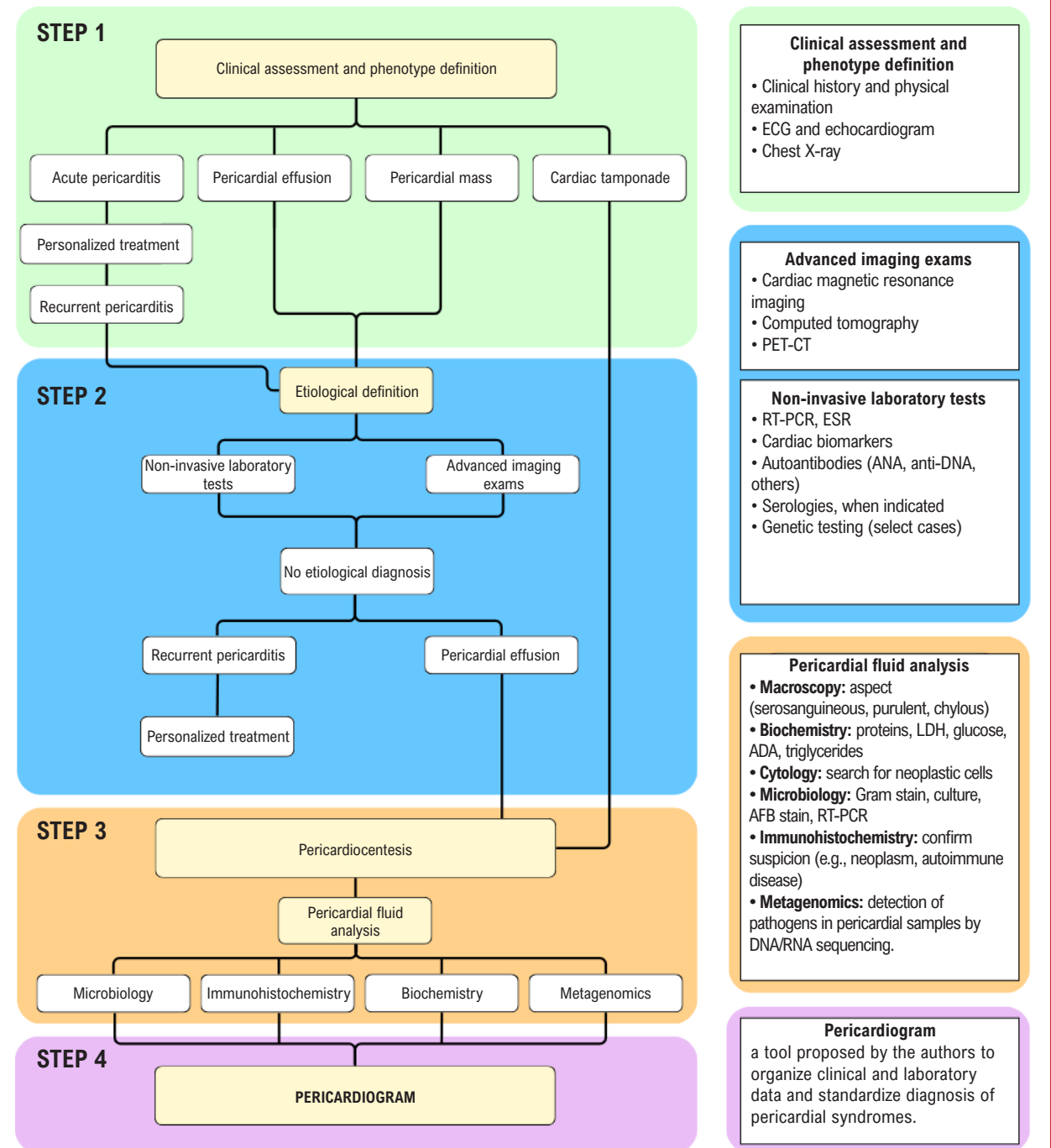
From an epidemiological perspective, the prevalence of different etiologies varies according to geographic location, age range, and clinical and family history. In high-income countries, acute idiopathic inflammatory pericarditis predominates, whereas in low- and middle-income countries, especially Brazil, Sub-Saharan Africa, and India, tuberculosis accounts for approximately 70% of cases.⁹

In clinical practice, information is often fragmented, and inadequate management or inappropriate disposal

Central Illustration: Laboratory Analysis and the Pericardiogram in Pericardial Diseases in the Era of Precision Medicine



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Steps for diagnosis and management of pericardial syndromes, from clinical assessment to etiological definition and pericardial fluid analysis, according to the 2025 European Society of Cardiology recommendations (steps 1 to 3). Stage 4 proposes a new tool for institutional standardization of clinical and laboratory data of patients diagnosed with pericardial syndromes. ADA: adenosine deaminase; ANA: antinuclear antibody; AFB: acid-fast bacilli; ECG: electrocardiogram; ESR: erythrocyte sedimentation rate; LDH: lactate dehydrogenase; PET-CT: positron emission tomography and computed tomography; RT-PCR: reverse transcription polymerase chain reaction.

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Table 1 – Main etiologies of pericarditis, their causes, and typical clinical findings

Etiology	Causes/examples	Clinical findings
Viral	CMV, ADV, B19, HIV	Pleuritic chest pain, pericardial friction rub, diffuse ECG changes, low-grade fever
Tuberculosis	<i>Mycobacterium tuberculosis</i>	Prolonged fever, night sweats, pericardial effusion
Bacterial	<i>Pneumococcus</i> , <i>Staphylococcus aureus</i>	High fever, chills, toxemia, purulent effusion
Fungal	<i>Histoplasma</i> , <i>Aspergillus</i>	Fever, respiratory symptoms, effusion refractory to antibiotics
Autoimmune	Systemic lupus erythematosus, rheumatoid arthritis, Behçet disease	Chest pain, pericardial friction rub, effusion, systemic manifestations of underlying disease
Neoplastic	Lung/breast/lymphoma metastases	Hemorrhagic or malignant effusion, signs of primary tumor
Trauma/post-surgical	Postoperative or traumatic	Chest pain, effusion, possible tamponade
Drug-induced	Procainamide, hydralazine, chemotherapy	Symptoms after medication use, resolving after discontinuation of the drug
Post-cardiac injury	Post-infarction, revascularization	Chest pain, fever, pericardial friction rub, mild effusion

Clinical findings are suggestive and may vary depending on disease severity and patient comorbidities. Identification of the etiology should be confirmed by laboratory tests, imaging, and, when necessary, analysis of pericardial fluid or biopsy. Source: European Society of Cardiology 2025 guideline for the management of myocarditis and pericarditis.⁸ Adapted by the authors. ADV: adenovirus; B19: parvovirus B19; CMV: cytomegalovirus; ECG: electrocardiogram; HIV: human immunodeficiency virus.

of pericardial fluid frequently compromises etiological investigation. Within this context, this article proposes a new systematic tool: the “pericardiogram.” Modeled after a complete blood count, this standardization aims to organize clinical reasoning and ensure the structured collection of data, maximizing diagnostic accuracy, as subsequently discussed.

Recurrent pericarditis

Recurrent pericarditis is characterized by the return of symptoms after clinical resolution of the initial event, usually weeks to months after the acute episode. Its pathophysiology involves a persistent or reactivated inflammatory response, frequently with an underlying autoimmune component.⁸

Pericardial effusion

Pericardial effusion is diagnosed when the volume of pericardial fluid exceeds 50 mL. This usually results from dysregulation of drainage mechanisms, either due to interruption or excessive exudate production in an inflammatory or non-inflammatory context.¹⁰

Regarding size, the effusion is classified, according to echocardiography, as trivial, when it is less than 1 cm and is not visible throughout the cardiac cycle; small, when it measures less than 1 cm; moderate, when it measures between 1 and 2 cm; large, when it is between 2 and 2.5 cm; and very large when it exceeds 2.5 cm.^{10,11} Furthermore, pericardial effusions can be categorized according to their anatomical distribution, duration, and biochemical composition, as shown in Table 2.^{10,12}

Cardiac tamponade

Cardiac tamponade is characterized by a large increase and equalization of intracardiac pressures at the end of diastole, due to the rapid and excessive accumulation of blood or other fluids in the pericardium. A diastolic restriction then develops, preventing proper filling of the cardiac chambers, resulting in decreased cardiac output. This condition constitutes a cardiac emergency requiring immediate intervention.^{10,13,14}

Constrictive pericarditis

Constrictive pericarditis represents the progression of a pericardial syndrome, with tuberculosis being one of its most frequently associated causes.^{10,15} It is characterized by thickening, fibrosis, adhesions, and calcification of the pericardium, resulting in loss of its elasticity and consequent restriction of diastolic filling.^{10,15,16}

Diagnostic approach

Non-invasive approach

The initial approach to diagnosing pericardial diseases should include a detailed medical history, physical examination, and targeted complementary tests according to clinical suspicion.¹⁰ Based on current criteria for the diagnosis and management of pericarditis,^{10,17,18} diagnosis requires chest pain associated with at least one of the following findings: pericardial friction rub, typical electrocardiographic changes (diffuse ST-segment elevation and/or PR interval depression), elevated inflammatory markers, pericardial effusion on imaging, or signs of pericardial inflammation detected on imaging.¹⁰

Table 2 – Classification of pericardial effusions

Criteria	Classification	Examples/observations
Distribution	Localized	Restricted to a region of the pericardium
	Circumferential	Involves the entire pericardial space
Time of occurrence	Acute	< 1 week
	Subacute	1 week to 3 months
	Chronic	> 3 months
Composition	Transudate	Low in proteins (e.g., heart failure, uremia)
	Exudate	High in proteins (e.g., infection, neoplasm, autoimmune)

Biomarkers play an essential role in the diagnosis and management of pericardial diseases. In acute pericarditis, C-reactive protein stands out as a marker of inflammation that is useful for both diagnostic confirmation and therapeutic monitoring, although normal values do not exclude the disease.^{8,19}

Troponin levels assess myocardial involvement, whereas B-type natriuretic peptide (BNP), N-terminal B-type natriuretic peptide (NT-proBNP), and soluble tumorigenicity suppressor 2 (sST2) assist in the stratification of myopericarditis.¹⁸ Inflammatory cytokines such as TNF- α , IL-1 β , IL-6, and IL-17A can aid in etiological investigation.⁸

Andreis et al. (2024) described a complementary innovative tool for the diagnosis of pericarditis: the INFLA-score. This index includes parameters such as total leukocyte count, platelet count, neutrophil-to-lymphocyte ratio, and C-reactive protein levels, generating a score ranging from –16 to +16. Values above zero suggest low-grade inflammation, with high sensitivity (86%) and specificity (64%) for the inflammatory phenotype, contributing to confirmation of pericarditis.²⁰

Moreover, genetic factors can influence severity and recurrence. Genes such as MEFV, NLRP3, and TNFRSF1A are associated with inflammation; SCN5A and KCNQ1 with electrical conduction; and TTN and LMNA with cardiac structure, contributing to individualized stratification.^{21–23} In idiopathic recurrent pericarditis, autoantibodies reinforce the autoimmune component: antinuclear antibodies are positive in approximately 43% of cases, with high titers associated with recurrence, whereas anti-histone antibody is related to higher rates of relapses and hospitalizations, reinforcing the role of the autoimmune response in the pathophysiology of the disease.²⁴

Invasive approach

In cases of cardiac tamponade or when diagnostic clarification is needed, especially regarding suspected infection, pericardial drainage is indicated as a diagnostic and therapeutic procedure²⁵ (Figure 1). The main methods include pericardiocentesis, pericardioscopy, and pericardial window. Pericardiocentesis should be guided by fluoroscopy and/or echocardiography to improve accuracy and prevention of complications. The subxiphoid approach is the most frequently used when fluoroscopy is available.^{17,26,27}

A pericardial window is indicated in recurrent effusions after pericardiocentesis, with resection of part of the pericardium for drainage into the mediastinum or pleural cavity.^{12,17,28} Labbé et al. (2015) demonstrated a higher success rate with the window (94.7%) compared to pericardiocentesis (64%), in spite of their similar diagnostic capacity and complication rate. Thus, although it is more invasive, pericardial window offers better recurrence control. Accordingly, the decision should be individualized according to clinical profile and risk-benefit ratio.²⁹

Laboratory analysis

Subsequently, laboratory tests of pericardial fluid are essential for complementing etiological investigation, including biochemical, cytological, and immunohistochemical analyses (Central Illustration). The pericardial fluid, an ultrafiltrate of plasma produced by mesothelial cells, is serous and cytologically rich in nucleated cells, especially mesothelial cells and lymphocytes.³⁰ Reference values for glucose, cholesterol, complement proteins, albumin, fluid/serum protein ratio, total hemolytic complement, and lactate dehydrogenase (LDH) are described in Table 3.³⁰

Cytopathological methods include cell block, which concentrates the material in a paraffin block after fixation in 10% formalin for approximately 24 hours and preserves cell morphology and nucleic acids, enabling histological sections. This technique allows for specific staining, genetic testing, and immunohistochemistry with higher diagnostic quality, especially in neoplasms,^{31,32} and it is more sensitive than smear because it offers better structural visualization.³³ Test requests should be individualized according to the etiological suspicion.

Microbiological analyses

For suspected bacterial infections in pericardial effusion, cultures of the fluid in aerobic and anaerobic environments are indicated due to their level of evidence. Blood culture aids in the detection of systemic infection and identification of the agent. Gram staining provides rapid results using dyes such as crystal violet and safranin, identifying Gram-positive and Gram-negative bacteria.³⁴ For suspected viral infections, reverse transcription polymerase chain reaction (RT-PCR) for cardiotropic viruses in pericardial fluid is essential to identify viral genetic material.³⁴ Additional tests may be necessary, depending on the clinical suspicion.

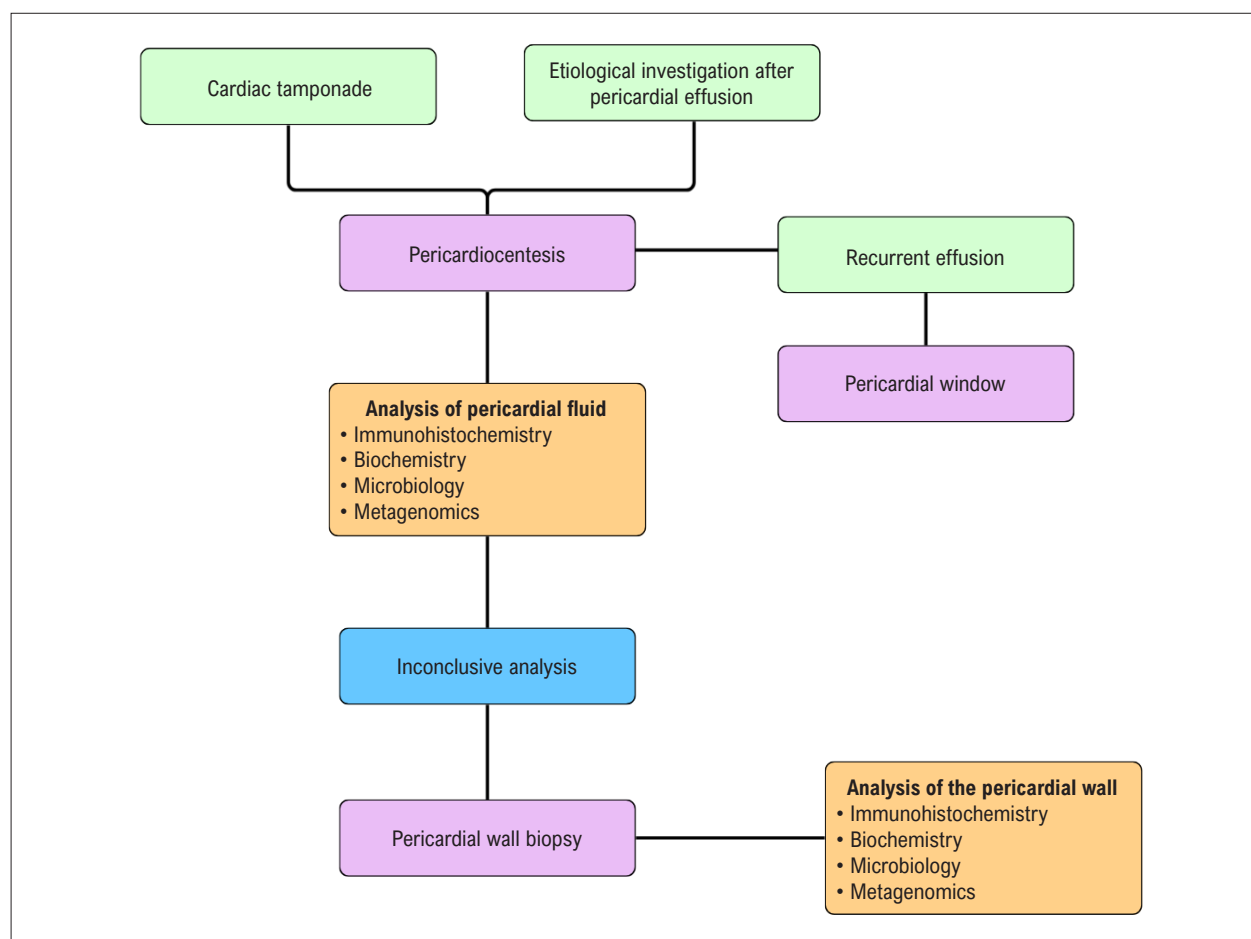


Figure 1 – Flowchart illustrating diagnostic management of pericardial effusion, highlighting drainage procedures, laboratory analysis, and complementary tests in cases of cardiac tamponade or recurrent effusion.

Table 3 – Reference values for pericardial fluid

Parameter	Reference value
Glucose	80–134 mg/dL
Cholesterol	12–69 mg/dL
Complement protein C3	35–127 mg/dL
Complement protein C4	6.3–23 mg/dL
Albumin	1.19–3.06 g/dL
Fluid/serum protein ratio	> 0.5
Total hemolytic complement	1.9–9.1 units
Lactate dehydrogenase	141–2613 U/L

Metagenomics

Metagenomics is a valuable analytical tool, using material collected directly from the clinical environment, such as pericardial fluid, blood, or tissues, to simultaneously evaluate a wide variety of microorganisms. Collection must

follow strict aseptic and preservation protocols to avoid contamination, allowing assessment of both the taxonomic composition and functional potential of the ecosystem present in the sample.^{35,36}

To this end, all DNA is extracted and can be sequenced by amplification, with selection of specific genetic markers, or by shotgun sequencing, which reads all the DNA, offering a comprehensive view of the taxonomic and functional profile.^{37–39} Subsequently, the data are processed and compared with pre-established databases, allowing precise identification of microorganisms and their functions. In pericardial diagnosis, metagenomics can accelerate and increase etiological accuracy, reducing idiopathic cases and guiding treatment.^{35,36,38}

- Biochemical analyses associated with infection

Glucose, leukocytes, and LDH should be evaluated. Glucose levels below 60 mg/dL and/or fluid/serum ratio < 0.3 suggest purulent effusion. Furthermore, high white blood cell counts and LDH above 200 U/L are typical of exudate, contributing to diagnosis of bacterial infection.³⁴

Proper collection of pericardial fluid

Pericardial fluid collection must follow standardized protocols to ensure that samples are suitable for different types of analysis. The material must be obtained aseptically, and the correct choice of container and storage conditions is essential to preserve sample quality and the reliability of results.

- Microbiological and biochemical analyses

Collection should be done in a sterile container, without anticoagulants, with an ideal volume of 30 to 50 mL to allow for multiple tests. The material can remain at room temperature for up to two hours; if processing takes longer, it should be refrigerated between 2 and 8 °C.^{35,36} At room temperature, stability is short, and refrigeration for up to 2 hours is recommended. For bacterial, fungal, and mycobacterial cultures, the material should not be frozen. Thus, prior contact with the laboratory is essential to define the appropriate container and optimize the diagnosis.³⁶

- Metagenomics

Collection should be performed directly into sterile containers and kept refrigerated between 2 and 8 °C to remain stable for 24 hours. If processing takes more than 24 hours, continuous freezing at -20 to -80 °C is recommended.³⁶

- Immunohistochemical analyses

The material should preferably be collected directly into a dry or EDTA-containing sterile container, or collected with a sterile syringe and transferred to this container. If a secondary container is necessary, a sterile container can be used. In this way, the cells remain intact until processing. It is recommended to prepare one or two direct smears on clean slides to preserve cell morphology for later analysis. The remaining fluid should be stored at a temperature of 2 to 8 °C and rapidly sent to the laboratory.⁴⁰

Pericardial wall biopsy

When analysis of the pericardial fluid is inconclusive and symptoms persist, a biopsy of the pericardial wall is indicated, especially when infection or neoplasia is suspected (Central Illustration). The main techniques include fluoroscopy-guided biopsy, pericardioscopy with standard sampling, and pericardioscopy with extended sampling.^{8,41}

Fluoroscopy-guided biopsy collects 3 to 6 fragments of the parietal pericardium, but without direct visualization, which reduces its accuracy and increases the risk of false negatives.⁴¹

On the other hand, pericardioscopy is indicated when the etiology remains uncertain, in suspected malignant effusion, purulent pericarditis, tuberculosis, or in situations where pericardiocentesis is not feasible.^{8,42} This procedure is minimally invasive and uses endoscopy to visualize the pericardial cavity, thus allowing macroscopic visualization of the pericardium.^{17,41,43}

Tuberculous pericarditis

Tuberculous pericarditis is a rare and potentially serious form of extrapulmonary tuberculosis caused by *Mycobacterium tuberculosis*. Although it represents only 1% to 2% of pulmonary tuberculosis cases, it is considered the main cause of pericarditis in countries with a low human development index. The clinical presentation is usually nonspecific, especially in the early stages; symptoms include fever, cough, chest pain, and dyspnea, making early diagnosis difficult.^{9,44} An uncommon presentation of tuberculous pericarditis consists of the presence of multiple floating masses in pericardial fluid, possibly formed by caseous material, fibrin, and inflammatory debris, which may resemble tumors, potentially confounding the diagnosis.

Laboratory analysis

Diagnostic confirmation of tuberculous pericarditis ideally depends on the direct detection of *M. tuberculosis* by techniques such as PCR, culture, or genetic sequencing. However, these approaches may have low sensitivity in the early stages of the disease. Therefore, the use of complementary laboratory methods becomes essential, such as the T-SPOT.TB test, tuberculin test (PPD) with a strongly reactive result, in addition to excluding other etiologies through serologies and negative tumor markers.⁹ Given this scenario, the investigation of pericardial fluid should involve different types of analysis in order to increase diagnostic accuracy:

- Microbiological analyses

M. tuberculosis can be directly detected by various methods:^{45,46}

Acid-fast bacilli staining allows identification of the bacillus through retention of the dye in its cell wall.

Mycobacterial culture in a specific medium is considered the most sensitive method, although it is time-consuming, which may delay the start of treatment.

RT-PCR for *M. tuberculosis* directly detects bacillus DNA by genetic amplification, providing a rapid result that is useful even when the culture is negative.

- Histochemical analyses

Certain biochemical parameters in pericardial fluid are useful as indirect markers of tuberculous infection. These include:^{44,45}

Elevated adenosine deaminase (ADA) enzyme, especially when ADA > 40 U/L;

Increased presence of pericardial lysozyme.

These parameters, although not specific, are suggestive of tuberculosis and indicate the need for further investigation.

- Cytological analyses

Even in the absence of microbiological confirmation, morphological analysis of the tissue can provide important evidence. It is essential to observe the following:⁴⁷

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The presence of caseous granulomas;

Hyperplastic granulation tissue mixed with caseous material;

Caseous necrosis in the pericardial tissue.

These findings constitute strong histopathological evidence of pericardial tuberculosis.

- Immunological analyses

The quantification of cytokines such as interferon-gamma also belongs to the immunological evaluation, since this marker reflects the cellular immune response to *M. tuberculosis*. Elevated levels (> 200 pg/ml) can reinforce the diagnostic suspicion, especially in conjunction with other parameters.⁴⁴

Pericardial diseases in patients with cancer

Pericardial diseases are frequently observed in patients with cancer. Recent studies have shown that pericardial involvement is present in 2% to 30% of autopsies of patients with cancer, with approximately 12% presenting pericardial metastasis. Etiologies are diverse and maybe related both to the underlying disease and to radiological, clinical, and chemotherapy treatment.⁴⁸

Direct invasion of the pericardium can cause malignant pericardial effusion, especially in lung, breast, gastrointestinal tract, and hematologic malignancies, as well as cardiac sarcomas, which can produce hemorrhagic or exudative effusion due to necrosis, vascular invasion, or metastasis.^{48–50} Lymphatic or hematogenous dissemination also contributes to malignant effusions.⁵¹

In addition to tumor infiltration, oncological treatments can trigger pericarditis. Radiation therapy leads to the formation of reactive oxygen species and pericardial injury, predisposing to effusion and possible progression to constrictive pericarditis. Immunosuppression increases the risk of infectious pericarditis, and chemotherapeutic agents, such as anthracyclines, cyclophosphamide, cytarabine, and immunotherapies (including checkpoint inhibitors), can cause cardiotoxicity and trigger pericardial effusion or constrictive pericarditis.⁴⁸

Laboratory analyses

- Cytological analysis

Initially, optical microscopic examination of cells present in the fluid may reveal the presence of neoplastic cells. The collected material is centrifuged, and the sediment is placed on a slide, which is then stained, allowing observation of cell morphology. Tumor cells are distinguished by characteristics such as enlarged nucleus, nuclear irregularity, and hyperchromasia. However, these cells can be confused with reactive mesothelial cells, requiring further investigation with other complementary methods.⁴⁵

- Immunological analysis

Measurement of tumor markers, such as carcinoembryonic antigen (CEA), alpha-fetoprotein (AFP), carbohydrate antigen 72-4 (CA.72-4), GATA-binding protein 3, CYFRA 21.1 (a tumor marker that measures a soluble fragment of cytokeratin 19), carbohydrate antigen 19-9 (CA-19.9), neuron-specific enolase (NSE), carbohydrate antigen 125 (CA-125), and vascular endothelial growth factor (VEGF) can provide clues to malignancy. High concentrations of these tumor markers in pericardial fluid confirm the possibility of neoplasia and help identify its origin.^{8,45}

- Immunohistochemical analysis

For more precise diagnosis, immunohistochemical staining is used to differentiate tumor cells from reactive cells, using antibodies directed against antigens such as CEA, epithelial membrane antigen, and vimentin.^{31,45} The cell block technique with immunostaining for vimentin and for the monoclonal antibody to detect epithelial cell adhesion molecules (BerEP4) exemplifies this process: BerEP4 recognizes epitopes of epithelial cell adhesion molecules (EpCAM), characteristic of epithelial cells and epithelial tumors, while vimentin marks cells of mesenchymal origin. Thus, positive vimentin with negative BerEP4 suggests reactive mesenchymal cells, whereas negative vimentin with positive BerEP4 indicates a higher probability of malignancy.³¹ This approach allows for a more precise characterization of the cells present in the pericardial fluid and is essential in the differential diagnosis between neoplasms, inflammatory processes, and reactive processes.⁴⁵

Pericardial diseases in patients with autoimmune diseases

In suspected autoimmune pericarditis, whose estimated prevalence ranges from 2% to 7% of acute pericarditis and about 10% of recurrent pericarditis, complementary laboratory tests are necessary for diagnostic clarification.^{52,53} Systemic lupus erythematosus, rheumatoid arthritis, Sjögren's syndrome, systemic sclerosis, and systemic vasculitis are the autoimmune diseases most associated with pericarditis.^{54–56}

Laboratory analysis is broad and diverse. In autoimmune pericarditis, erythrocyte sedimentation rate and C-reactive protein are frequently elevated.⁵⁷ Antinuclear factor, rheumatoid factor, and specific testing for various autoantibodies, when positive, suggest diagnoses. Among the various autoantibodies, positive anti-DNA and anti-Sm antibodies, together with reduced complement levels, are characteristic of systemic lupus erythematosus. Positive rheumatoid factor, in turn, indicates rheumatoid arthritis, but it can also be positive in Sjögren's syndrome.^{58,59} Positive anti-CCP antibody suggests rheumatoid arthritis. Anti-Ro and anti-La antibodies may indicate systemic lupus erythematosus, Sjögren's syndrome, or both.^{58,59} Antineutrophil cytoplasmic antibodies (ANCA) are present in ANCA-associated systemic vasculitis. Anticentromere, antitopoisomerase I, anti-U1 RNP, and anti-RNA polymerase III antibodies may be present in systemic sclerosis.^{58,59}

In clinical practice, pericardial fluid examination in autoimmune pericarditis is not routine, as similar autoantibody titers are expected in blood and pericardial fluid, and it is reserved for specific situations. It should be indicated mainly when there are suspected complications, diagnostic uncertainty, or a need to rule out other etiologies.⁸ In any case, if autoimmune pericarditis and concomitant fever are suspected, a complete and detailed analysis of the pericardial fluid may be crucial for diagnostic clarification.⁸

characteristics of the pericardial fluid, whether or not they are associated with a suggestive clinical picture, can significantly assist in establishing diagnosis. For example, in systemic lupus erythematosus, the pericardial fluid usually presents as an inflammatory exudate, with lymphocytic predominance, and antinuclear factor and anti-DNA may be positive; in contrast, in rheumatoid arthritis, the pericardial fluid may present positive rheumatoid factor and/or anti-CCP.⁶⁰⁻⁶²

Pericardiogram

Finally, the authors propose the pericardiogram (Figure 2) as a tool that can contribute to the diagnosis and organization of pericardial syndromes. Analogous to a complete blood count, it is a structured form that should be filled out with personal data (such as name, age, address, and healthcare facility), as well as clinical information, including past medical history and medication use. Additionally, specific data regarding the pericardial syndrome should be collected, encompassing etiology and cytological, microbiological, immunohistochemical, and biochemical laboratory information. In this manner, the pericardiogram will allow for the standardization of the steps in diagnosing pericardial syndrome, guiding healthcare professionals on the procedures necessary to achieve greater diagnostic accuracy.

Conclusion

Advanced cardiovascular imaging methods have significantly expanded the ability to non-invasively characterize morphological alterations in pericardial syndromes. Currently, these exams complement echocardiographic assessment, enabling detection of pericardial fibrosis, inflammation, fibrin deposition, changes in pericardial fluid density, and thickening of the pericardial sac. This integrated approach constitutes a multimodal evaluation, which aims not only to clarify the etiology of the disease, but also to assess its functional impact and prognosis in acute or chronic presentations.

The constant evolution of imaging technologies and laboratory techniques highlights the need to update diagnostic and treatment protocols for pericarditis and associated conditions, with careful attention to standardizing diagnostic steps. This organization is fundamental to optimize the use of available tools and ensure that patients promptly receive appropriate care.

Despite these advances, barriers persist, including resource scarcity, the absence of standardized protocols,

and limited access to invasive methods. Another relevant limitation is the possibility of loss of the material collected for analysis or biopsy. If the collection, transport, and analysis do not follow predefined safety standards, there is a risk of compromising the sample, resulting in delayed diagnosis and reduced quality of care provided to patients.

Given these limitations, some specialized pericardial disease centers have been created to optimize diagnosis and management, representing a structured and multidisciplinary approach. These centers generally implement an organized workflow that includes initial screening with review of clinical records, laboratory and imaging tests, followed by appropriate referral by a healthcare professional. Patient follow-up is based on individualized treatment plans, as well as patient education on risk factors, warning symptoms, and therapeutic options. The approach is interdisciplinary, involving rheumatology, cardiothoracic surgery, clinical cardiology, specialized radiology, and pharmacy services. Continuous follow-up includes periodic in-person or telemedicine consultations, with repeated examinations as needed, ensuring accurate diagnosis and individualized management, aligned with the principles of precision medicine.¹⁰

An interdisciplinary approach combined with advanced imaging methods and standardized laboratory testing is essential to accelerate diagnosis and optimize prognosis in pericardial syndromes. In parallel, it is crucial to strengthen scientific production and specialized literature in order to develop clinical protocols that regulate and systematize the use of these tools, promoting more efficient, evidence-based care.

Author Contributions

Conception and design of the research: Vieira IL, Nunes LC; Acquisition of data, Writing of the manuscript and Critical revision of the manuscript for intellectual content: Vieira IL, Nunes LC, Nunes BD, Pimentel AML, Mesquita ET; Analysis and interpretation of the data: Vieira IL, Nunes LC, Nunes BD.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Study Association

This study is not associated with any thesis or dissertation work.

Ethics Approval and Consent to Participate

This article does not contain any studies with human participants or animals performed by any of the authors.

Review Article

PERICARDIOGRAM

NAME: _____ AGE: _____ ADDRESS: _____

PLACE OF BIRTH: _____

PAST MEDICAL HISTORY: _____

CURRENT MEDICATIONS: _____

RECENT VACCINATIONS: _____ DATE OF LAST DOSE: _____ RECENT TRAVEL HISTORY: _____

NEOPLASIA: _____ CHEMOTHERAPY: _____ RADIOTHERAPY: _____ IMMUNOTHERAPY: _____

RECENT SURGICAL PROCEDURES: _____

PERICARDIAL SYNDROME: _____

ACUTE PERICARDITIS ☐ RECURRENT PERICARDITIS ☐ INCESSANT PERICARDITIS ☐

CONSTRUCTIVE PERICARDITIS ☐ PERICARDIAL MASS ☐

PERICARDIAL EFFUSION? _____. MILD ☐ MODERATE ☐ LARGE ☐ CARDIAC TAMPONADE ☐

PERICARDIAL FLUID BIOCHEMICAL ANALYSIS: PROTEINS _____. GLUCOSE _____, TRIGLYCERIDES _____, CHOLESTEROL _____, AMYLASE _____, PH _____, LACTATE DEHYDROGENASE _____

IMMUNOLOGICAL ANALYSIS: ANTINUCLEAR FACTOR _____, COMPLEMENT C3 _____, COMPLEMENT C4 _____, RHEUMATOID FACTOR _____, ADENOSINE DEAMINASE _____, LUPUS ERYTHEMATOSUS CELLS _____, ANTINUCLEAR ANTIBODIES _____, OTHER: Tumor Markers: _____

ESTUDO IMUNOLOGICO DO LÍQUIDO PERICÁRDICO: FAN _____, C3 _____, C4 _____, FATOR REUMATÓIDE _____, ADA _____, CELS. LE _____, ANTIC ANTINUCLEAR _____, OUTROS: Marcadores tumorais _____

MICROBIOLOGY: GRAM STAIN _____, CULTURE _____, MYCOBACTERIAL TESTING _____

FUNGAL CULTURE _____, VIRAL PCR _____

CYTOPATHOLOGY: _____

CELL BLOCK: _____

ANATOMOPATHOLOGICAL FINDINGS: _____

IMMUNOHISTOCHEMISTRY: _____

ELECTRON MICROSCOPY: _____

LYMPH NODE BIOPSY: _____

FINAL RESULT:

VIRAL INFECTION (etiology) _____

BACTERIAL INFECTION (etiology) _____

AUTOIMMUNE DISEASE _____

NEOPLASM (specify primary site) _____

POST-PROCEDURAL (specify which procedure) _____

OTHER ETIOLOGIES (trauma, post-acute myocardial infarction, idiopathic, metabolic) _____

Figure 2 – Pericardiogram.

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