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REVIEW

Cardiovascular Involvement in Hantavirus Infection-Pathophysiology, Clinical Manifestations, and Management

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ABSTRACT

Hantavirus infection can lead to hemorrhagic fever with renal syndrome and hantavirus cardiopulmonary syndrome, and cardiovascular (CV) involvement is increasingly recognized as an important feature of severe disease. The present review summarizes the epidemiology, clinical manifestations, pathophysiological mechanisms, diagnostic evaluation, and management of CV involvement in hantavirus infection. The available evidence includes experimental studies, observational cohorts, case series, and clinical reports. Reported CV manifestations include myocardial injury, myocarditis, ventricular dysfunction, cardiogenic shock, pericardial involvement, conduction abnormalities, and atrial or ventricular arrhythmias. Proposed mechanisms include endothelial dysfunction, increased vascular permeability, inflammatory and cytokine activation, autonomic nervous system dysregulation, and microvascular abnormalities. Clinical assessment may reveal hypotension, elevated cardiac biomarkers, ventricular dysfunction, and circulatory collapse. Echocardiography, cardiac biomarker assessment, electrocardiography, speckle-tracking echocardiography, and cardiac magnetic resonance imaging may aid diagnosis and risk stratification. Management is largely supportive and may include individualized fluid management, vasopressors and inotropes as needed, hemodynamic monitoring, and mechanical circulatory support or extracorporeal membrane oxygenation for refractory shock. The current evidence base is limited by the predominance of observational data and heterogeneity in diagnostic and follow-up strategies. Prospective studies are needed to clarify the mechanisms of myocardial injury, identify prognostic biomarkers, and establish evidence-based approaches to CV assessment and management.

Keywords: Arrhythmia, capillary leak syndrome, cardiogenic shock, endothelial dysfunction, myocarditis

INTRODUCTION

Hantaviruses are zoonotic, enveloped viruses with negative-sense, single-stranded RNA genomes belonging to the family Hantaviridae. Rodents serve as their natural reservoirs, and humans become infected by inhaling aerosols containing infected rodent excreta. Hantavirus infections are a global public health concern and can cause severe disease. Their geographic distribution is closely associated with the distribution of their reservoir species. In Europe and Asia, hantavirus infections typically manifest as hemorrhagic fever with renal syndrome (HFRS), whereas in the Americas, the most common presentation is hantavirus cardiopulmonary syndrome (HCPS). HFRS is characterized by fever, thrombocytopenia, vascular leakage, and renal failure, whereas HCPS is primarily associated with pulmonary edema, respiratory failure, and circulatory collapse. Despite differences in their clinical presentations, both syndromes are associated with increased vascular permeability and endothelial dysfunction.[1-3]

Research on hantavirus infection has traditionally focused on its pulmonary and renal manifestations. However, accumulating evidence suggests that cardiovascular (CV) involvement may also contribute to disease severity and clinical outcomes. Reported CV manifestations range from mild myocardial injury and hemodynamic abnormalities to myocarditis, ventricular dysfunction, arrhythmias, cardiogenic shock, and, rarely, sudden cardiac death. The CV effects of hantavirus infection may involve endothelial activation, capillary leakage, systemic inflammation, and hemodynamic disturbances. Nevertheless, the mechanisms underlying CV involvement and the extent to which individual mechanisms contribute to clinical outcomes remain poorly understood. Accordingly, this review examines the pathophysiological mechanisms, clinical manifestations, diagnostic approaches, and therapeutic implications of hantavirus-associated CV involvement.[4-6]

Citation Strategy

Citations were reassessed throughout the manuscript to improve the alignment between individual statements and their supporting

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sources. Hantavirus-specific and CV references were prioritized for claims concerning CV manifestations, myocardial injury, hemodynamic abnormalities, imaging, biomarkers, and clinical outcomes. Broader reviews and general critical care or CV sources were retained primarily to support general concepts and management principles when hantavirus-specific evidence was limited. Duplicate citations were reduced where appropriate, and citation placement was reviewed to ensure that each reference supports the corresponding statement.

Literature Review Methodology

This article is a narrative review. The relevant literature was identified through a focused search of the biomedical literature using combinations of the following terms: "hantavirus," "hantavirus infection," "hemorrhagic fever with renal syndrome," "hantavirus cardiopulmonary syndrome," "cardiovascular," "cardiac," "myocarditis," "heart failure," "shock," "arrhythmia," "echocardiography," "speckle-tracking echocardiography," "cardiac magnetic resonance," "biomarkers," and "extracorporeal membrane oxygenation." Original research articles, observational studies, case series, case reports, reviews, and guideline or consensus documents were considered based on their relevance to the CV manifestations, mechanisms of injury, diagnostic evaluation, management, and long-term outcomes of hantavirus infection. The reference lists of relevant publications were also screened to identify additional studies. Because this was a narrative review, no formal systematic review protocol, meta-analysis, or quantitative risk-of-bias assessment was undertaken. The available evidence was critically appraised, with particular attention to the predominantly observational nature of the published literature and the methodological heterogeneity among studies.

Host and Viral Responses

Hantaviruses are enveloped viruses with negative-sense, single-stranded RNA genomes belonging to the family Hantaviridae. Hantavirus genomes are tripartite and consist of three segments (S, M, and L) that encode the nucleocapsid protein, the envelope glycoproteins (Gn and Gc), and the RNA-dependent RNA polymerase. The envelope glycoproteins are involved in viral attachment to and entry into host cells, whereas the nucleocapsid protein plays a role in viral replication and interactions with host immune responses. Hantaviruses are transmitted by rodents, with each viral species typically associated with a specific rodent reservoir. Infected animals may shed the virus in their urine, feces, and saliva, resulting in environmental contamination and subsequent aerosol transmission to humans. South American hantavirus strains are associated with HCPS, and person-to-person transmission has been reported for some strains.[7,8]

Hantavirus glycoproteins interact with β3 integrins expressed on endothelial and other vascular cells, platelets, and additional cell types. Following receptor-mediated entry, viral replication takes place in the cytoplasm. Endothelial involvement is associated with increased vascular permeability and capillary leakage, both of which are prominent features of severe disease. Available evidence suggests that host immune responses are major determinants of disease severity. Although hantaviruses are generally considered non-cytopathic, infection can activate T-cells, macrophages, and natural killer cells. Endothelial dysfunction and increased vascular permeability have been associated with inflammatory mediators, including tumor necrosis factor-α (TNF-α), interleukin (IL)-6, and interferon-γ. Severe hantavirus infection may therefore be accompanied by cardiac and hemodynamic abnormalities, although the relative contributions of immune-mediated mechanisms remain incompletely understood.[9,10]

Pathophysiology of CV Injury

CV involvement in hantavirus infection likely results from interactions among viral infection, endothelial dysfunction, immune dysregulation, and hemodynamic disturbances. Experimental and pathological observations suggest that hantaviruses predominantly affect vascular endothelial cells rather than cardiomyocytes. Systemic inflammatory responses have also been reported. Together, these processes have been proposed to contribute to ventricular dysfunction, arrhythmias, circulatory collapse, and multiorgan dysfunction.[11]

Endothelial Dysfunction

Endothelial dysfunction is a well-recognized feature of severe hantavirus infection. The effects of viral particles on endothelial cells may be mediated through mechanisms that are not directly related to cytolysis. Endothelial dysregulation may lead to the disruption of intercellular junctions, increased vascular permeability, and impaired regulation of vascular tone. Experimental studies show that hantavirus glycoproteins bind to β3 integrins and disrupt endothelial signaling and barrier function. Endothelial barrier dysfunction has also been linked to permeability mediators such as vascular endothelial growth factor and angiopoietins. These pathological changes may cause hypotension, tissue edema, and reduced organ perfusion.[12]

Capillary Leak Syndrome

Severe hantavirus infection is characterized by CV instability and capillary leak syndrome. Increased endothelial permeability allows proteins and fluid to extravasate into the interstitial space, causing tissue edema and intravascular volume depletion. In HCPS, pulmonary capillary leakage may lead to pulmonary edema and profound hypoxia. Reduced effective intravascular volume may also cause hypotension and shock secondary to reduced cardiac preload. Severe capillary leakage may further impair ventricular filling and oxygen delivery to myocardial cells, thereby contributing to reduced ventricular function. The extent of vascular leakage has been associated with adverse clinical outcomes.[13]

Cytokine Activation and Inflammation

Inflammatory pathways are considered important contributors to CV involvement in hantavirus infection. Proinflammatory cytokines, such as TNF-α, IL-1β, IL-6, IL-8, and interferon-γ, have been reported in clinical and experimental studies. The upregulation of these cytokines has been associated with increased endothelial permeability, leukocyte recruitment, and vascular inflammation. Inflammatory mediators may also exert negative inotropic effects. For example, TNF-α and IL-6 have been associated with abnormalities in calcium handling, reduced myocardial contractility, and mitochondrial dysfunction. Transient myocardial dysfunction has been reported in severe hantavirus

infection, and cytokine-mediated myocardial depression has been proposed as one of the mechanisms contributing to this finding.[14]

Pathogenesis of Myocardial Injury

Myocardial injury in hantavirus infection likely has a multifactorial etiology. Current evidence suggests that immune-mediated and endothelial mechanisms may contribute to myocardial injury, whereas the extent of direct cardiomyocyte infection remains uncertain. Myocarditis has not been characterized in detail in patients with hantavirus infection. However, clinicopathological findings suggestive of myocarditis have been reported in some cases, along with ventricular dysfunction and elevated cardiac troponin levels. Cytokines are thought to contribute to myocardial depression, although microvascular dysfunction, systemic hypoperfusion, oxidative stress, and inflammatory cell infiltration may also play a role. These processes may lead to myocardial dysfunction, myocarditis, and cardiogenic shock in susceptible patients. The recovery of ventricular function reported in many cases suggests that reversible functional impairment may predominate over irreversible myocyte injury in at least some patients.[15] The proposed pathophysiological mechanisms linking hantavirus infection to CV injury and their potential clinical consequences are illustrated in Figure 1.

Microvascular Dysfunction

Microvascular dysfunction has been proposed as an additional mechanism contributing to CV involvement in hantavirus infection. Microcirculatory blood flow may be compromised by endothelial and complement activation, inflammatory cytokines, and coagulopathy. Increased vascular permeability and interstitial edema may increase the diffusion distance for oxygen, while platelet activation and local thrombus formation may further impair microvascular perfusion. These abnormalities may impair myocardial perfusion even in the presence of minimal epicardial coronary artery disease. Microvascular dysfunction has therefore been proposed as a potential contributor to myocardial ischemia, ventricular dysfunction, arrhythmias, and hemodynamic deterioration. Systemic microcirculatory impairment may also contribute to multiorgan dysfunction. However, the relative importance of these mechanisms and their prognostic significance in hantavirus infection remain incompletely established.[16]

The pathophysiological processes outlined above-including endothelial dysfunction, capillary leakage, systemic inflammation, myocardial injury, and microvascular abnormalities-provide a plausible basis for the range of CV manifestations reported in hantavirus infection. These processes may manifest clinically as transient hemodynamic disturbances, subclinical myocardial injury, overt ventricular dysfunction, myocarditis, arrhythmias, or cardiogenic shock. Understanding the links between these underlying mechanisms and their clinical consequences is important for recognizing and managing CV involvement. The next section therefore examines the principal CV manifestations reported in patients with hantavirus infection.[16]

CV Manifestations

CV manifestations are increasingly recognized as contributors to morbidity and mortality in hantavirus infection. Although pulmonary and renal complications have been studied more extensively, CV involvement is an important feature of severe HCPS. The clinical spectrum ranges from mild hemodynamic abnormalities to severe ventricular dysfunction and circulatory collapse. Endothelial dysfunction, increased vascular permeability, systemic inflammation, and myocardial injury have been implicated in the CV manifestations of severe disease.[17]

Shock and Hypotension

Hypotension is a common CV manifestation of severe hantavirus infection. Inflammatory mediators induce vasodilation, leading to decreased systemic vascular resistance, while increased vascular permeability causes plasma leakage into the tissues and reduces effective intravascular volume. Consequently, shock may be hypovolemic, distributive, cardiogenic, or mixed. In patients with significant myocardial dysfunction, fluid therapy may exacerbate pulmonary edema and hemodynamic instability. Persistent hypotension should prompt a comprehensive hemodynamic evaluation and the initiation of vasopressor support, as indicated.[18]

Myocarditis

Myocarditis has been reported in patients with HFRS and HCPS, although its frequency and clinical significance remain uncertain. Clinical features have included chest pain, electrocardiographic changes, elevated cardiac biomarkers, and reversible ventricular dysfunction. Histopathological analyses have revealed interstitial inflammatory infiltrates, myocardial edema, and focal myocyte injury. In patients with suspected myocarditis, cardiac magnetic resonance (CMR) imaging may demonstrate myocardial edema and late gadolinium enhancement. Immune-mediated mechanisms and cytokine-associated myocardial depression have been proposed, although direct viral injury to the myocardium cannot be excluded. Ventricular function appears to recover in many patients after the acute illness.[15]

Pericardial Involvement

Pericardial involvement appears to be less common than myocardial dysfunction but has been reported in patients with hantavirus infection. Acute pericarditis may present with chest pain and electrocardiographic changes, whereas echocardiography may reveal a small pericardial effusion. Pericardial abnormalities may develop in the setting of systemic inflammation and increased vascular permeability. Although clinically significant cardiac tamponade appears to be rare, hemodynamic deterioration should prompt echocardiographic assessment. Echocardiography is useful for diagnosing and monitoring pericardial involvement.[19,20]

Acute Heart Failure

Severe hantavirus infection may be complicated by acute heart failure. Rapid-onset ventricular dysfunction has been associated with myocardial inflammation, cytokine-mediated myocardial depression, microvascular abnormalities, and acute changes in ventricular loading conditions. Clinical features may include dyspnea, pulmonary congestion, elevated natriuretic peptide concentrations, and reduced left ventricular ejection fraction (LVEF). In HCPS, acute ventricular

dysfunction may contribute to pulmonary edema and complicate the differentiation of cardiogenic from non-cardiogenic respiratory failure. In some patients, transient inflammatory and hemodynamic disturbances may play a greater role than irreversible structural myocardial damage.[15]

Right Ventricular Dysfunction

Right ventricular dysfunction may be underrecognized in severe hantavirus infection. Pulmonary edema, hypoxic pulmonary vasoconstriction, and pulmonary vascular abnormalities may increase right ventricular afterload. Echocardiography in critically ill patients may reveal right ventricular enlargement associated with impaired function or elevated pulmonary artery pressure. Because right ventricular function is essential for maintaining cardiac output, significant right ventricular dysfunction may contribute to hemodynamic deterioration. A comprehensive echocardiographic examination should therefore include an assessment of right ventricular size and systolic function.[21]

Cardiogenic Shock

Cardiogenic shock is a severe manifestation of CV involvement in HCPS and has been associated with high mortality in reported cohorts. Myocardial depression and ventricular failure may occur even in the absence of obstructive coronary artery disease. Patients

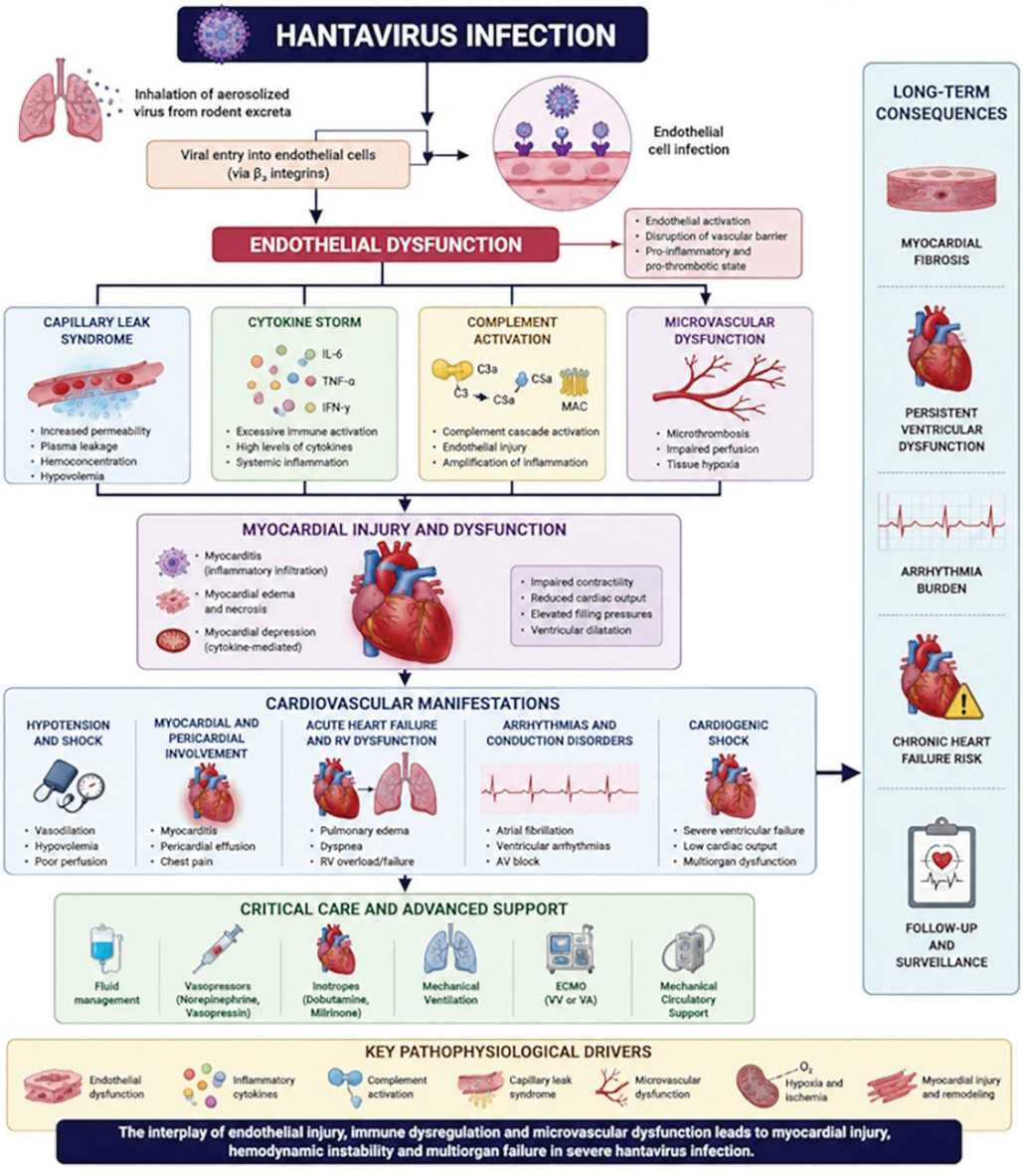


Figure 1. Central illustration. Hantavirus infection is associated with endothelial dysfunction, capillary leak syndrome, inflammatory and complement activation, and microvascular abnormalities. These processes have been proposed to contribute to myocardial dysfunction, arrhythmias, heart failure, and cardiogenic shock. Although ventricular function appears to recover in many survivors, the frequency and clinical significance of persistent myocardial abnormalities remain uncertain

IL-6: Interleukin-6, TNF-α: Tumor necrosis factor-alpha, AV: Atrioventricular, RV: Right ventricular

may present with persistent hypotension, elevated lactate levels, end-organ hypoperfusion, and reduced cardiac output. Hemodynamic assessment may reveal reduced myocardial contractility and elevated filling pressures. Supportive management may require vasopressors, inotropes, and mechanical ventilation. In selected patients with refractory shock, extracorporeal membrane oxygenation (ECMO) may be considered. Observational studies and case reports suggest that venoarterial ECMO can provide cardiopulmonary support in selected patients with severe hantavirus-associated cardiac failure; however, the available evidence remains limited.[22]

Conduction and Rhythm Disturbances

Conduction abnormalities and arrhythmias may occur during severe hantavirus infection. Reported abnormalities include atrial and ventricular arrhythmias, as well as atrioventricular and intraventricular conduction disturbances. These abnormalities may be secondary to myocarditis, autonomic nervous system dysfunction, electrolyte imbalances, microvascular dysfunction, hypoxemia, or the direct electrophysiological effects of cytokines. Serious arrhythmias may contribute to morbidity and mortality, although rhythm disturbances may resolve as the acute illness improves.

Sudden Cardiac Death

Sudden cardiac death has rarely been reported in association with hantavirus infection. It may occur in the setting of conduction abnormalities, fulminant myocarditis, severe cardiogenic shock, or malignant ventricular arrhythmias. The available evidence is limited, and the incidence and predictors of sudden cardiac death remain uncertain. Continuous electrocardiographic monitoring should be considered in patients with severe CV involvement or clinically significant rhythm abnormalities. Table 1 summarizes the principal CV manifestations of hantavirus infection and their proposed mechanisms.

Cardiac Biomarkers

Cardiac biomarkers may help identify and assess myocardial involvement in hantavirus infection; however, they should always be interpreted in conjunction with clinical findings and cardiac imaging. Cardiac troponin levels may be elevated in myocardial injury but are not specific to myocarditis. Levels may also increase in association with severe systemic illness, hypoxemia, hemodynamic instability, or renal dysfunction. In HFRS, biomarker concentrations may also be affected by acute kidney injury, making serial measurements and clinical context important for interpretation. N-terminal pro-B-type natriuretic peptide is a marker of ventricular function and myocardial wall stress, but its levels are also influenced by age, renal function, volume status, and hemodynamic stress. The prognostic value of these biomarkers in hantavirus disease remains poorly characterized and warrants further investigation in prospective cohorts. The clinical assessment of cardiac involvement in hantavirus infection should incorporate clinical findings, cardiac biomarkers, and imaging. Echocardiography is usually the first-line imaging modality because of its rapid availability, repeatability, and ability to provide bedside hemodynamic assessment. Myocardial strain can be assessed using speckle-tracking echocardiography (STE), while CMR imaging can provide additional tissue characterization when indicated.[23] The principal cardiac biomarkers and imaging modalities used for the assessment of CV involvement in hantavirus infection, together with their clinical applications and limitations, are summarized in Table 2.

Transthoracic Echocardiography

Transthoracic echocardiography is the principal bedside imaging modality for CV assessment in hantavirus infection. It allows rapid, non-invasive evaluation of ventricular size and systolic function, regional wall motion, diastolic function, and pericardial effusion. Echocardiography can also support hemodynamic assessment, including the estimation of stroke volume, filling pressures, and pulmonary artery pressure. Serial examinations may help monitor changes in ventricular function during acute illness and subsequent recovery.[20]

STE

STE provides a quantitative assessment of myocardial deformation and may offer information beyond that obtained from conventional measures of ventricular systolic function. In hantavirus infection, STE may help identify subtle myocardial dysfunction that is not apparent from LVEF alone. Findings should be interpreted in the context of image quality and the rapidly changing loading conditions that may occur during acute hantavirus infection.

CMR Imaging

CMR is useful in cases of suspected myocarditis or chronic myocardial injury and provides detailed information about ventricular function and myocardial tissue characteristics. Native T1 and T2 mapping, assessment of myocardial edema, and late gadolinium enhancement may indicate inflammatory or fibrotic myocardial injury, while cine imaging allows the assessment of left and right ventricular volumes and systolic function. However, experience with CMR in hantavirus infection remains limited. Gadolinium-based contrast agents require particular consideration in patients with severe renal dysfunction or acute kidney injury. Renal function and the clinical indication for contrast-enhanced CMR should therefore be assessed before imaging. Non-contrast techniques, including native T1/T2 mapping and cine imaging, may provide useful information when gadolinium administration is inappropriate.[24]

Computed Tomography

Computed tomography (CT) may demonstrate cardiopulmonary involvement in hantavirus infection but is not routinely used as the initial cardiac imaging modality. Chest CT may reveal bilateral ground-glass opacities, interlobular septal thickening, pleural effusions, and pulmonary edema consistent with capillary leakage. When clinically indicated, cardiac CT may demonstrate cardiomegaly, pericardial effusion, or right ventricular dilation. Coronary CT angiography may be considered selectively when obstructive coronary artery disease is included in the differential diagnosis. Data on CT assessment specifically in hantavirus infection remain scarce. Overall, multimodality imaging should be guided by the clinical question, with echocardiography serving as the principal bedside modality and STE or CMR used selectively when they are likely to provide additional information.[25]

CV and Critical Care Management

Management of severe hantavirus infection is primarily supportive and requires close collaboration among intensivists, cardiologists, infectious disease specialists, and other critical care professionals. CV status can deteriorate rapidly, leading to hemodynamic instability and cardiogenic shock. Therefore, early recognition and supportive treatment of CV involvement are essential. The primary goals are to maintain tissue perfusion and oxygenation, support ventricular function, and prevent or mitigate multiorgan failure.[26]

Vasopressor Use

If hypotension does not resolve with judicious fluid therapy, vasopressor support may be required. Norepinephrine is commonly used to maintain arterial pressure and systemic vascular tone. Vasopressin may be considered an adjunct in patients with persistent vasodilatory shock. Hemodynamic monitoring can help guide fluid administration and vasoactive therapy while minimizing excessive fluid administration and its potential adverse effects on pulmonary and microvascular perfusion.[27]

Inotropic Support

Inotropic support may be required in patients with severe ventricular dysfunction and low cardiac output. Dobutamine may improve myocardial contractility and increase cardiac output, whereas milrinone may be considered in selected patients because of its combined inotropic and pulmonary vasodilatory effects. The choice of agent should be individualized according to ventricular function, systemic blood pressure, pulmonary vascular resistance, and the overall hemodynamic profile. Serial echocardiography may help assess the need for treatment and monitor the patient's response.[20]

Mechanical Ventilation

Severe HCPS is characterized by acute respiratory failure resulting from pulmonary capillary leakage and non-cardiogenic pulmonary edema. Mechanical ventilation can reduce the work of breathing and improve oxygenation. When invasive ventilation is required, a lung-protective strategy using low tidal volumes and appropriate positive end-expiratory pressure should be employed. Careful monitoring of oxygenation and hemodynamics is essential because increased intrathoracic pressure may compromise venous return and worsen CV dysfunction. Respiratory failure may develop rapidly, necessitating timely intervention and transfer to the intensive care unit.[28]

Extracorporeal Membrane Oxygenation

ECMO may be considered in selected patients with severe hantavirus infection and refractory respiratory or circulatory failure. Veno-venous ECMO may provide support in patients with life-threatening respiratory failure that is refractory to conventional treatment, whereas venoarterial ECMO may be considered when severe myocardial dysfunction and cardiogenic shock predominate. Observational studies and case series have reported successful use of ECMO in selected patients. However, comparative evidence remains limited, and patient selection, timing of initiation, and institutional expertise are important determinants of outcomes.[29]

Mechanical Circulatory Support

Mechanical circulatory support may be considered in patients with refractory cardiogenic shock and severe ventricular failure. Percutaneous or surgical ventricular assist devices and intra-aortic balloon counterpulsation may be used in selected cases. Experience with these approaches in hantavirus infection remains limited, but

Table 1. Cardiovascular manifestations of hantavirus infection

Manifestation	Proposed mechanism	Clinical findings	Prognostic impact
Hypotension	Capillary leak, vasodilation, intravascular volume depletion	Low blood pressure, dizziness, shock	Associated with severe disease
Myocarditis	Immune-mediated myocardial inflammation	Troponin elevation, ventricular dysfunction	May progress to heart failure or shock
Pericardial involvement	Inflammation and vascular leakage	Pericardial effusion, chest pain	Usually mild, rarely tamponade
Acute heart failure	Myocardial depression, inflammation, microvascular dysfunction	Dyspnea, pulmonary edema, reduced LVEF	Major determinant of mortality
Right ventricular dysfunction	Pulmonary hypertension, hypoxia, RV overload	RV dilation, reduced RV function	Associated with hemodynamic deterioration
Cardiogenic shock	Severe myocardial dysfunction	Hypoperfusion, elevated lactate, low cardiac output	High mortality risk
Atrial arrhythmias	Inflammation, atrial stretch, autonomic activation	Atrial fibrillation, atrial tachycardia	May worsen hemodynamics
Ventricular arrhythmias	Myocarditis, ischemia, myocardial edema	VT, VF, PVCs	Potentially life-threatening
Conduction disorders	Conduction system inflammation	AV block, bundle branch block	May require pacing support
Sudden cardiac death	Malignant arrhythmias or severe myocardial injury	Unexpected cardiovascular collapse	Rare but catastrophic

AV: Atrioventricular, HCPS: Hantavirus cardiopulmonary syndrome, HF: Heart failure, LVEF: Left ventricular ejection fraction, PVCs: Premature ventricular complexes, RV: Right ventricular, VF: Ventricular fibrillation, VT: Ventricular tachycardia

they may provide temporary hemodynamic support while myocardial function recovers. Decisions should therefore be individualized and made by a multidisciplinary team with the appropriate institutional expertise. Hemodynamic monitoring, individualized volume management, and early initiation of vasoactive agents are important components of managing severe hantavirus-associated cardiac complications. Mechanical circulatory support may be considered when conventional treatment fails.[29]

Long-Term CV Outcomes

Long-term CV outcomes after hantavirus infection remain poorly characterized. To date, most studies have focused on the acute phase, and longitudinal data are limited. Some studies have suggested that CV abnormalities may persist after the resolution of clinical symptoms; however, their prevalence, duration, and clinical significance remain unknown. Prospective longitudinal studies are needed to clarify the long-term CV consequences of hantavirus infection.

Long-Term Ventricular Dysfunction

In HCPS, ventricular dysfunction appears to be reversible in many survivors, with recovery reported over a period of weeks to months. Nevertheless, residual left or right ventricular dysfunction has also been described. Potential contributing factors include severe myocarditis, acute myocardial injury, persistent inflammation, and myocardial remodeling, although their relative contributions remain uncertain. Follow-up assessment of ventricular function may therefore be appropriate for patients who experienced documented CV involvement during the acute illness.[30]

CV Follow-Up

Evidence regarding CV follow-up after hospital discharge following hantavirus infection is limited, and no standardized follow-up strategy has been established. In patients with documented CV involvement or persistent symptoms, clinical assessment and electrocardiography may be considered after recovery. Transthoracic echocardiography can be used to assess ventricular function recovery and identify residual structural abnormalities. CMR imaging may be useful in selected patients with suspected myocarditis, persistent biomarker elevation, reduced ejection fraction, or otherwise unexplained symptoms. Ambulatory rhythm monitoring may be considered when clinically indicated. Prospective longitudinal studies are needed to determine the frequency and clinical relevance of persistent ventricular dysfunction, myocardial fibrosis, and arrhythmias and to establish evidence-based follow-up strategies.[29]

Future Perspectives and Research Gaps

Hantavirus infection has well-characterized renal and pulmonary manifestations, but its CV effects remain less well understood. Most available data come from small observational cohorts, case series, case reports, and retrospective studies. Consequently, the frequency, underlying mechanisms, and long-term clinical significance of CV involvement remain uncertain. Future studies should use standardized definitions and risk-stratification approaches and prospectively assess CV outcomes.

Registries of Patients

International multicenter registries could help overcome the limitations of the current evidence base by collecting standardized clinical, laboratory, imaging, and outcome data. Such registries could help determine the incidence of myocardial injury, arrhythmias, ventricular dysfunction, heart failure, and cardiogenic shock according to hantavirus species and geographic region. Longitudinal follow-up may also help identify predictors of chronic CV changes and adverse clinical outcomes.

Advanced CV Imaging

Further advances in CV imaging may allow more detailed characterization of myocardial involvement in hantavirus infection. Echocardiography remains the principal modality for acute bedside assessment, whereas STE, tissue Doppler imaging, three-dimensional echocardiography, and CMR imaging may provide additional information in selected patients. However, the incremental diagnostic and prognostic value of these techniques in hantavirus infection remains uncertain and requires prospective evaluation. Longitudinal

Table 2. Biomarkers and imaging modalities in hantavirus-associated cardiac involvement

Parameter	Main clinical significance	Potential prognostic value
Troponin	Detection of myocardial injury and myocarditis	Higher levels associated with severe disease
NT-proBNP	Ventricular wall stress and heart failure	Predicts ventricular dysfunction
CK-MB	Myocardial injury marker	Limited specificity
CRP	Systemic inflammation	Correlates with disease severity
IL-6	Cytokine activation and endothelial dysfunction	Associated with shock and severe HCPS
TNF-α	Inflammation and myocardial depression	Linked to hemodynamic instability
Echocardiography	Assessment of ventricular function and hemodynamics	First-line imaging modality
Speckle-tracking echocardiography	Detection of subclinical myocardial dysfunction	May identify early cardiac involvement
Cardiac magnetic resonance	Myocardial edema, fibrosis, myocarditis	Gold standard for tissue characterization
Computed tomography	Cardiopulmonary involvement and pulmonary edema	Supports severity assessment
ECG/Holter monitoring	Detection of arrhythmias and conduction disorders	Useful for follow-up and risk assessment

CK-MB: Creatine kinase-myocardial band, CRP: C-reactive protein, ECG: Electrocardiography, HCPS: Hantavirus cardiopulmonary syndrome, IL-6: Interleukin-6, NT-proBNP: N-terminal pro-B-type natriuretic peptide, TNF-α: Tumor necrosis factor-alpha

imaging studies are particularly important for determining whether myocardial abnormalities persist after clinical recovery.

Future Therapeutic Directions

Treatment of severe hantavirus infection remains primarily supportive. Potential therapeutic targets include endothelial dysfunction and activation, complement signaling, and increased vascular permeability. Future translational studies should investigate these pathways and determine whether biomarkers or functional imaging can help identify patients who may benefit from targeted treatments. Machine learning and other computational approaches may also support risk stratification, but these approaches require validation in clinical practice. Further translational and clinical studies are needed to translate mechanistic findings into potential therapeutic strategies.

CONCLUSION

Future priorities include prospective longitudinal cohorts, standardized CV phenotyping, and multimodal assessment integrating biomarkers, echocardiography, STE, and selected CMR imaging. These studies should clarify the mechanisms of myocardial injury, identify reliable biomarkers and predictors, and determine whether residual ventricular dysfunction, fibrosis, or arrhythmias have clinical significance for long-term risk stratification. CV involvement is an important component of hantavirus infection, but the current evidence base remains limited by the predominance of observational studies and case series, as well as heterogeneous assessment strategies. Available data support the occurrence of myocardial injury, ventricular dysfunction, arrhythmias, and hemodynamic instability during acute disease, whereas the frequency and clinical significance of persistent abnormalities after recovery remain unknown.

Ethics Committee Approval: Not required, as this study is a narrative review based exclusively on previously published literature and does not involve human participants, animals, or the collection of patient data.

Informed Consent: Not required, as this study is a narrative review of previously published literature and does not involve direct patient participation, patient-specific data collection, or access to identifiable patient information.

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REFERENCES

1. Chediack V, Calvo M, Cunto E, Santos A, Rodríguez A, Suberviola B. Hantavirus infection: a narrative review focusing on epidemiology, diagnosis, infection control and treatment in the era of globalisation. *Med Intensiva (Engl Ed).* 2026;50:502523.
2. Durante-Mangoni E, Cafarella I, Mercadante S, Scarpulla N; European Federation of Internal Medicine (EFIM) Infectious Diseases in Internal Medicine Working Group. Human infection with Andes hantavirus: an update for the general physician. *Eur J Intern Med.* 2026;149:106946.
3. Kraft L, Oberacker T, Schwab A, et al. Clinical course up to 20 years after hantavirus infection. *Nephrol Dial Transplant.* 2026;41:859-865.
4. Velavan TP, Schmidt-Chanasit J. When rare zoonoses travel: Andes virus, hantavirus cardiopulmonary syndrome, and the preparedness gap. *Int J Infect Dis.* 2026;169:108778.
5. Akram SM, Mangat R, Huang B. Hantavirus cardiopulmonary syndrome (Archived). 2023. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023.
6. Ghriss N, Mussini C, Kammoun S, et al. Diagnostic and clinical challenges of hantavirus-associated acute kidney injury. *Eur J Case Rep Intern Med.* 2026;13:006159.
7. Khaiboullina SF, St Jeor SC. Hantavirus immunology. *Viral Immunol.* 2002;15:609-625.
8. Singh S, Numan A, Sharma D, et al. Epidemiology, virology and clinical aspects of hantavirus infections: an overview. *Int J Environ Health Res.* 2022;32:1815-1826.
9. Koehler FC, Di Cristanziano V, Späth MR, et al. The kidney in hantavirus infection-epidemiology, virology, pathophysiology, clinical presentation, diagnosis and management. *Clin Kidney J.* 2022;15:1231-1252.
10. Saavedra F, Díaz FE, Retamal-Díaz A, Covián C, González PA, Kalergis AM. Immune response during hantavirus diseases: implications for immunotherapies and vaccine design. *Immunology*. 2021;163:262-277.
11. Munir N, Jahangeer M, Hussain S, et al. Hantavirus diseases pathophysiology, their diagnostic strategies and therapeutic approaches: a review. *Clin Exp Pharmacol Physiol*. 2021;48:20-34.
12. Connolly-Andersen AM, Thunberg T, Ahlm C. Endothelial activation and repair during hantavirus infection: association with disease outcome. *Open Forum Infect Dis.* 2014;1:ofu027.
13. Kallel H, Matheus S, Mayence C, et al. Capillary leak-syndrome triggered by Maripa virus in French Guiana: case report and implication for pathogenesis. *BMC Infect Dis.* 2019;19:260.
14. Sadeghi M, Eckerle I, Daniel V, Burkhardt U, Opelz G, Schnitzler P. Cytokine expression during early and late phase of acute Puumala hantavirus infection. *BMC Immunol.* 2011;12:65.
15. Saggioro FP, Rossi MA, Duarte MI, et al. Hantavirus infection induces a typical myocarditis that may be responsible for myocardial depression and shock in hantavirus pulmonary syndrome. *J Infect Dis*. 2007;195:1541-1549.
16. Mackow ER, Gavrilovskaya IN. Hantavirus regulation of endothelial cell functions. *Thromb Haemost*. 2009;102:1030-1041.
17. Rasmuson J, Lindqvist P, Sörensen K, Hedström M, Blomberg A, Ahlm C. Cardiopulmonary involvement in Puumala hantavirus infection. *BMC Infect Dis.* 2013;13:501.
18. Campen MJ, Milazzo ML, Fulhorst CF, Obot Akata CJ, Koster F. Characterization of shock in a hamster model of hantavirus infection. *Virology.* 2006;356:45-49.
19. Harris GH, Adalja AA. Recognition and management of infectious biothreats and emerging pathogens. *Crit Care Clin.* 2026;42:465-479.
20. Oliveira FMG, Esteves PA, Mendes RE. Epidemiological study of hantavirus in Southern Brazil, 2009-2019. *Rev Inst Med Trop Sao Paulo.* 2026;68:e28.

21. Ramos-Nino ME, Chiem NT, Ramdass PVAK. Hantavirus emergence in a changing world: virology, pathogenesis, surveillance, and one health preparedness. *Microorganisms*. 2026;14:1326.
22. Llah ST, Mir S, Sharif S, Khan S, Mir MA. Hantavirus induced cardiopulmonary syndrome: a public health concern. *J Med Virol*. 2018;90:1003-1009.
23. Rao A, Tariq H. Hantavirus cardiopulmonary syndrome: an emerging fatal zoonotic infection. *Infection*. 2026. doi: 10.1007/s15010-026-02994-6.
24. Krumm P, Zitzelsberger T, Gawaz M, Greulich S. Young patient with hantavirus-induced myocarditis detected by comprehensive cardiac magnetic resonance assessment. *BMC Infect Dis*. 2019;19:15.
25. Barbosa DL, Hochhegger B, Souza AS Jr, et al. High-resolution computed tomography findings in eight patients with hantavirus pulmonary syndrome. *Radiol Bras*. 2017;50:148-153.
26. Rose E, Fuher AN, Gergen DJ. C57-05 from rats to respiratory failure: a case of hantavirus pulmonary syndrome in Colorado. *Am J Respir Crit Care Med*. 2026;212(Suppl 1). doi: 10.1093/ajrccm/aamag162.205
27. Ulloa-Morrison R, Pavez N, Parra E, et al. Critical care management of hantavirus cardiopulmonary syndrome. A narrative review. *J Crit Care*. 2024;84:154867.
28. Montes JL, Juárez X, Lloveras S, Cordero AP, Saenz C. Seasonal influenza vaccination policies for poultry workers in 33 Pan American Health Organization Member States in 2026: a review. *Vaccines (Basel)*. 2026;14:871.
29. Lee DS, Hasan A. Cardiopulmonary failure in hantavirus disease: mechanisms, recognition, and ECMO-based management. *Viruses*. 2026;18:915.
30. Kumar AA, John J. Hantavirus: a comprehensive contemporary review of virology, global epidemiology, clinical variants, diagnosis, treatment, and intensive care management. Indian *J Crit Care Med*. 2026;30:430-442.