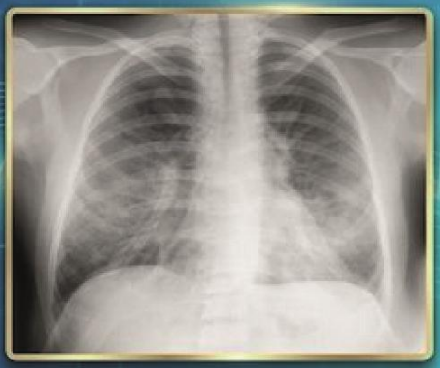
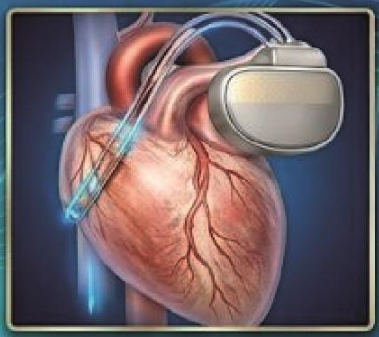
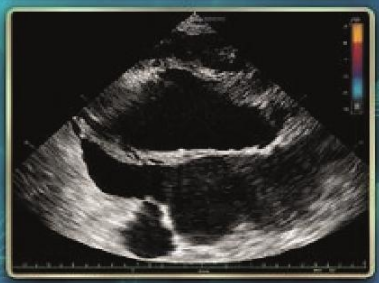
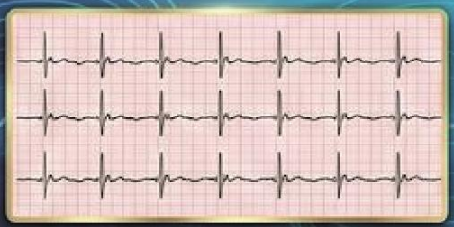
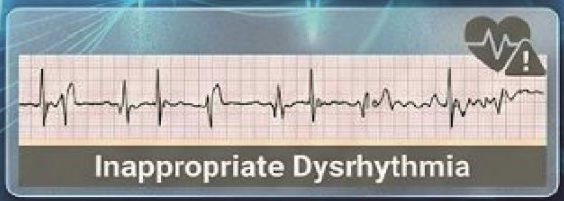
Critical Syndromes in Acute and Intensive Cardiovascular Care











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CONTENTS

Preface

Acute and intensive cardiovascular care remains one of the most demanding fields in modern medicine, requiring rapid decision-making, pathophysiological insight, and timely evidence-based interventions. *Critical Syndromes in Acute and Intensive Cardiovascular Care* has been developed to provide a structured and clinically oriented overview of the most critical cardiovascular emergencies encountered in practice.

Despite significant advances in diagnostics and therapeutics, acute heart failure, cardiogenic shock, and malignant arrhythmias continue to be major causes of morbidity and mortality worldwide. Contemporary clinical practice requires not only adherence to guidelines but also a nuanced understanding of disease mechanisms and clinical phenotypes. This volume aims to bridge this gap by integrating pathophysiological concepts with practical management strategies.

A key strength of this book lies in its emphasis on early, time-sensitive evaluation and multidimensional clinical assessment. The integration of etiological classification, hemodynamic profiling, and left ventricular ejection fraction-based stratification forms the cornerstone of modern management. In particular, the first critical hour of care demands a systematic approach focused on the rapid identification of life-threatening conditions and prompt initiation of appropriate therapy.

The contributors have combined scientific rigor with clinical practicality, presenting complex conditions in a clear and accessible manner while remaining aligned with current international guidelines.

This book is intended as both a reference and a practical guide for clinicians involved in the care of critically ill

cardiovascular patients, with the aim of improving clinical understanding and patient outcomes.

ETIOLOGY AND PRECIPITATING FACTORS OF ACUTE HEART FAILURE

ELİF ALÇIK[1]

Etiology and Classification of Acute Heart Failure

Acute heart failure (AHF) is not a single disease but rather a clinical syndrome arising from a heterogeneous spectrum of underlying cardiac and non-cardiac conditions (McDonagh, et al., 2021: 3599–3726).

A precise understanding of etiology is indispensable in the acute setting: it determines the specific therapeutic approach, guides the urgency of invasive investigation, identifies reversible precipitating factors, and defines the long-term management pathway. The 2021 ESC Guidelines and subsequent updates classify AHF etiologically according to the primary mechanism of decompensation, the nature of the precipitating event, and the status of baseline cardiac structure and function (McDonagh, et al., 2021: 3599–3726).

Epidemiologically, AHF may present as de novo heart failure-in a patient without prior known cardiac disease — or as

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acute decompensation of pre-existing chronic heart failure (ADHF). In most registries, including the EuroHeart Failure Survey II and the ESC-EORP HF Long-Term Registry, ADHF accounts for approximately 60–75% of all AHF hospitalizations; de novo presentations, often associated with acute coronary syndromes, hypertensive emergencies, or new-onset arrhythmias, comprise the remainder (Ponikowski, et al., 2016: 2129–2200).

Primary Etiological Categories

Coronary Artery Disease and Acute Myocardial Infarction

Coronary artery disease (CAD) remains the single most common underlying substrate for AHF in Western populations, accounting for approximately 50–70% of cases across major registries (McDonagh, et al., 2021: 3599–3726).

Acute Myocardial Infarction (AMI) with LV Dysfunction: ST-elevation MI (STEMI) and non-ST-elevation MI (NSTEMI) can precipitate AHF through acute loss of contractile myocardium. The extent of jeopardized territory, time to reperfusion, and presence of pre-existing LV dysfunction determine the severity of hemodynamic compromise. AHF complicating AMI carries a substantially higher in-hospital mortality than AMI without hemodynamic compromise (van Diepen, et al., 2017: e232–e268).

Mechanical Complications of AMI: Represent life-threatening causes of de novo AHF and cardiogenic shock occurring within hours to days after the index infarction. These include (Mebazaa, et al., 2016: 147–163).

Acute mitral regurgitation due to papillary muscle rupture (typically involving the posteromedial papillary muscle supplied by a single coronary artery)

Ventricular septal defect (VSD): occurs in 1–3% of AMI cases pre-reperfusion era; associated with biventricular failure

Free wall rupture and pseudoaneurysm formation: frequently fatal unless surgically repaired

Right ventricular infarction: seen in 30–50% of inferior STEMI; causes disproportionate RV failure with preserved LV systolic function

Echocardiographic assessment is mandatory in all AMI patients with sudden hemodynamic deterioration to differentiate primary pump failure from mechanical complications, as each demands a distinct and urgent treatment strategy (Lancellotti, et al., 2015: 3–5).

Ischemic Cardiomyopathy: Chronic CAD leading to progressive LV remodeling, scar formation, and systolic dysfunction constitutes the most prevalent substrate for recurrent ADHF. Episodes may be precipitated by recurrent ischemia, arrhythmia, or excessive fluid intake (McDonagh, et al., 2021: 3599–3726).

Non-Ischemic Cardiomyopathies

Non-ischemic cardiomyopathies are a morphologically and genetically diverse group that collectively represent the dominant cause of AHF in younger patients and a significant proportion of all AHF hospitalizations (Heidenreich, et al., 2022: e895–e1032).

Dilated Cardiomyopathy: Characterized by LV or biventricular dilation with impaired systolic function in the absence of sufficient CAD or abnormal loading conditions. Familial DCM accounts for 25–30% of cases; causative genes include TTN (titin), LMNA (lamin A/C), SCN5A, RBM20 and PLN (Metra & Teerlink, 2017: 1981–1995).

Hypertrophic Cardiomyopathy: Although predominantly associated with preserved or hyperdynamic systolic function, HCM may cause AHF via diastolic dysfunction, dynamic LV outflow tract obstruction, mitral regurgitation, or supraventricular arrhythmias. AHF in HCM is typically triggered by atrial fibrillation or dehydration.

Arrhythmogenic Cardiomyopathy: Predominantly right ventricular disease caused by desmosomal gene mutations (PKP2, DSP, DSG2). Acute RV failure may develop with exercise or during disease progression. Biventricular and left-dominant forms are increasingly recognized.

Peripartum Cardiomyopathy (PPCM): Defined as LV systolic dysfunction developing in the last month of pregnancy or within five months of delivery in the absence of another identifiable cause. Mortality and recovery rates vary by geography; up to 50% of patients recover LV function within 6 months, particularly with prompt treatment including bromocriptine in select cases (McDonagh, et al., 2021: 3599–3726).

Takotsubo Cardiomyopathy (Stress Cardiomyopathy): A transient, reversible LV dysfunction syndrome predominantly affecting postmenopausal women, triggered by physical or emotional stress. Characterized by apical ballooning with basal hyperkinesis and mimics AMI clinically and on ECG. May cause severe AHF and cardiogenic shock. Crucially, inotropes are relatively contraindicated due to the risk of worsening LV outflow tract obstruction; vasopressors and volume management are preferred (Mebazaa, et al., 2016: 147–163).

Myocarditis: Inflammatory cardiomyopathy, most commonly viral (enterovirus, parvovirus B19, adenovirus) or autoimmune in origin. Fulminant myocarditis presents with acute severe LV dysfunction, cardiogenic shock, and high-degree

atrioventricular block. Cardiac MRI is the diagnostic standard; endomyocardial biopsy guides immunosuppressive therapy in autoimmune and giant cell variants (McDonagh, et al., 2023: 3627–3639).

Cardiac Sarcoidosis: Granulomatous infiltration of the myocardium causing conduction abnormalities, ventricular arrhythmias, and progressive cardiomyopathy. AHF may be the initial presentation (McDonagh, et al., 2021: 3599–3726).

Toxic/Drug-Induced Cardiomyopathy: Anthracycline chemotherapy (cumulative dose-dependent), trastuzumab, checkpoint inhibitors, alcohol, cocaine, and amphetamines may all precipitate AHF through direct myocardial toxicity, inflammatory mechanisms, or coronary vasospasm (McDonagh, et al., 2023: 3627–3639).

Valvular Heart Disease

Acute valvular pathology is a critical and time-sensitive cause of AHF that frequently requires urgent surgical or catheter-based intervention (Heidenreich, et al., 2022: e895–e1032).

Acute Severe Aortic Regurgitation: May result from infective endocarditis, aortic dissection, or trauma. The unprepared LV faces sudden massive volume overload, resulting in acute pulmonary edema. Aortic valve surgery is the definitive treatment; medical stabilization with vasodilators (nitroprusside) serves as a bridge (Heidenreich, et al., 2022: e895–e1032).

Acute Severe Mitral Regurgitation: Most commonly due to papillary muscle rupture in AMI, chordal rupture in mitral valve prolapse, or infective endocarditis. Rapid onset of pulmonary edema and low-output state. Echocardiographic identification is urgent; emergent surgical repair or replacement is often required (Lancellotti, et al., 2015: 3–5).

Critical Aortic Stenosis (CAS): Severe low-flow, low-gradient aortic stenosis can present with acute pulmonary edema, particularly when triggered by atrial fibrillation or volume overload. Medical management is limited; transcatheter aortic valve implantation (TAVI) should be considered even in the acute phase in stable patients (Heidenreich, et al., 2022: e895–e1032).

Mitral Stenosis: Elevated LA pressure transmitted to the pulmonary circulation causes flash pulmonary edema, commonly precipitated by atrial fibrillation with rapid ventricular response, pregnancy, or infection (McDonagh, et al., 2021: 3599–3726).

Prosthetic Valve Dysfunction: Valve thrombosis, pannus formation, or structural failure of bioprostheses can cause sudden hemodynamic deterioration and acute heart failure (McDonagh, et al., 2023: 3627–3639).

Arrhythmias as Primary Precipitants

Cardiac arrhythmias may either precipitate AHF in a structurally abnormal heart or — in extreme tachycardia — cause AHF even in a structurally normal heart (tachycardia-induced cardiomyopathy) (McDonagh, et al., 2023: 3627–3639).

Atrial Fibrillation (AF): The most common arrhythmic precipitant of AHF. Rapid ventricular response reduces diastolic filling time, increases myocardial oxygen demand, and eliminates the atrial contribution to cardiac output. AF is identifiable as the primary trigger in approximately 30–40% of ADHF episodes, particularly in HFpEF (Ponikowski, et al., 2016: 2129–2200).

Ventricular Tachyarrhythmias: Sustained VT or VF in the setting of structural heart disease causes acute hemodynamic collapse. Prompt cardioversion/defibrillation is essential; underlying

substrate must subsequently be addressed (van Diepen, et al., 2017: e232–e268).

Bradyarrhythmias / High-Degree AV Block: Complete heart block, sick sinus syndrome, or high-degree AV block — particularly in the context of inferior AMI or LMNA cardiomyopathy — may reduce cardiac output sufficiently to precipitate AHF. Temporary pacing is the immediate treatment (McDonagh, et al., 2023: 3627–3639).

Tachycardia-Induced Cardiomyopathy: Persistent uncontrolled tachycardia (typically AF, atrial flutter, or inappropriate sinus tachycardia) for weeks to months can result in reversible LV systolic dysfunction. Rate or rhythm control leads to recovery of LVEF (McDonagh, et al., 2021: 3599–3726).

Hypertensive Heart Disease and Hypertensive Emergency

Severe, uncontrolled hypertension precipitates acute pulmonary edema primarily through two mechanisms: (1) acute afterload excess impairing LV systolic function, and (2) diastolic dysfunction and impaired LV relaxation causing rapid elevation of filling pressures (Heidenreich, et al., 2022: e895–e1032).

Hypertensive emergency with pulmonary edema is typically characterized by flash-onset dyspnea, dramatically elevated blood pressure (systolic > 180 mmHg), and a relatively preserved or even hyperdynamic LVEF on echocardiography — distinguishing it from low-output HFrEF. Intravenous vasodilators (nitroglycerin, nitroprusside) are the cornerstone of acute therapy. Rapid blood pressure reduction leads to prompt improvement in pulmonary congestion (Stevenson & Perloff, 1989: 884–888).

Pulmonary Causes and Right Heart Failure

Acute right heart failure is increasingly recognized as a distinct AHF phenotype with specific therapeutic implications (Monteagudo-Vela, et al., 2023: 998382).

Acute Pulmonary Embolism (APE): Massive or submassive PE causes acute RV pressure overload and dilation, interventricular septal shift, and reduced LV filling — resulting in obstructive shock rather than true cardiogenic shock. Systemic thrombolysis or catheter-directed therapy is indicated in massive PE with hemodynamic compromise (McDonagh, et al., 2023: 3627–3639).

Acute-on-Chronic Pulmonary Hypertension: Patients with pre-existing pulmonary arterial hypertension may present with acute RV decompensation triggered by infection, arrhythmia, or discontinuation of pulmonary vasodilator therapy. Inhaled nitric oxide, intravenous prostacyclin, and RV-specific inotropes (dobutamine, milrinone) form the therapeutic framework (Monteagudo-Vela, et al., 2023: 998382).

Chronic Obstructive Pulmonary Disease (COPD) Exacerbation: Severe hypoxia, hypercapnia, and elevated pulmonary vascular resistance during COPD exacerbation may cause or exacerbate RV failure; the clinical distinction from primary AHF requires echocardiographic evaluation and BNP measurement (McDonagh, et al., 2021: 3599–3726).

High-Output Heart Failure

High-output heart failure occurs when an elevated metabolic demand or pathological arteriovenous shunting overwhelms normal or increased cardiac output, resulting in pulmonary congestion and peripheral hypoperfusion. This entity is characterized by an elevated

or normal cardiac output with simultaneously elevated filling pressures (McDonagh, et al., 2023: 3627–3639).

Causative conditions include: severe anemia (hemoglobin < 7 g/dL), sepsis and systemic inflammatory states, thyrotoxicosis (thyroid storm), Paget's disease of bone, large arteriovenous fistulae (including hemodialysis fistulae), and beriberi (thiamine deficiency) (McDonagh, et al., 2021: 3599–3726).

Recognition of high-output failure is clinically important because vasodilators and inotropes are of limited value; treatment of the underlying cause (iron supplementation, thyroid suppression, antibiotic therapy) is the primary therapeutic target (McDonagh, et al., 2023: 3627–3639).

Pericardial Disease

Cardiac Tamponade: Pericardial effusion accumulating under pressure causes hemodynamic compromise through diastolic collapse of cardiac chambers and equalization of filling pressures. The classic Beck's triad (hypotension, elevated JVP, muffled heart sounds) has limited sensitivity; echocardiography is diagnostic. Emergency pericardiocentesis is life-saving (Lancellotti, et al., 2015: 3–5).

Constrictive Pericarditis: Chronic pericardial fibrosis restricts cardiac filling and causes a syndrome of elevated venous pressure with preserved systolic function, mimicking HFpEF. Distinguished by specific echocardiographic features (septal bounce, respiratory variation in E-wave velocities, pericardial thickening on CT/MRI) (McDonagh, et al., 2021: 3599–3726).

Systemic Diseases and Infiltrative Cardiomyopathies

Systemic diseases may involve the myocardium and cause AHF through infiltration, inflammation, or metabolic derangement (McDonagh, et al., 2023: 3627–3639).

Cardiac Amyloidosis: Deposition of misfolded protein fibrils (AL or ATTR amyloid) causes progressive diastolic dysfunction and restrictive cardiomyopathy. AHF typically presents with disproportionate dyspnea relative to apparent systolic function. Tafamidis, diflunisal, and patisiran/inotersen (for ATTR) represent disease-modifying therapies. Early recognition using multimodality imaging and tissue characterization is crucial, as timely initiation of disease-modifying therapy significantly alters prognosis (McDonagh, et al., 2023: 3627–3639).

Hemochromatosis, Fabry Disease, Glycogen Storage Diseases: Each may cause myocardial infiltration, hypertrophy, and progressive AHF; genetic testing and specific enzyme replacement or chelation therapy are indicated. These conditions should be suspected particularly in unexplained left ventricular hypertrophy, where early diagnosis may prevent irreversible myocardial damage (McDonagh, et al., 2021: 3599–3726).

Systemic Lupus Erythematosus and Autoimmune Myocarditis: Myocardial inflammation mediated by autoantibodies or T-cell infiltration may cause AHF; immunosuppressive therapy forms the treatment basis. Endomyocardial biopsy and advanced imaging modalities may be required in selected cases to confirm diagnosis and guide immunosuppressive strategies (McDonagh, et al., 2021: 3599–3726).

Acute Precipitants of Decompensation in Chronic HF

In ADHF, an identifiable acute precipitant is present in the majority of cases. Recognition and targeted treatment of the precipitant is as important as symptomatic decongestion (McDonagh, et al., 2023: 3627–3639). The most common precipitants and their corresponding clinical implications are summarized in Table 1.

Table 1: *Common Acute Precipitants of Decompensation in Chronic Heart Failure*

Category	Specific Precipitant	Clinical Implication
Cardiac	New-onset or uncontrolled atrial fibrillation	Rate/rhythm control; anticoagulation
Cardiac	Acute coronary syndrome (ACS)	Urgent coronary angiography ± revascularization
Cardiac	Myocarditis / pericarditis	Immunosuppression; anti-inflammatories
Hemodynamic	Hypertensive emergency	IV vasodilators; blood pressure control
Hemodynamic	Acute valve dysfunction (endocarditis, rupture)	Urgent cardiac surgery or transcatheter therapy
Extracardiac	Pulmonary embolism	Anticoagulation; thrombolysis if massive
Extracardiac	Pneumonia / respiratory infection	Antibiotics; respiratory support; BIPAP
Metabolic	Renal failure / fluid overload	Diuretics; dialysis/ultrafiltration
Metabolic	Thyrotoxicosis / severe anemia	Treat underlying cause; transfusion

Category	Specific Precipitant	Clinical Implication
Pharmacological	Non-adherence to medications	Patient education; adherence monitoring
Pharmacological	NSAIDs / corticosteroids / negative inotropes	Cessation of offending agents
Dietary	Excessive sodium/fluid intake	Dietary restriction; patient education

ESC Classification by Clinical Presentation

The 2021 ESC Guidelines define three major clinical presentations of AHF that guide initial assessment, triage, and therapeutic urgency (McDonagh, et al., 2023: 3627–3639).

Acute Decompensated Heart Failure (ADHF): The most common presentation (~50–70% of AHF hospitalizations). Characterized by gradually worsening dyspnea, peripheral edema, and weight gain over days. Usually managed with intravenous diuretics and optimization of background therapy without hemodynamic emergency (Chioncel, et al., 2017: 1242–1254).

Acute Pulmonary Edema: Characterized by acute onset severe dyspnea, respiratory distress, hypoxemia, and bilateral pulmonary crackles. Precipitants include hypertensive emergency, acute MR/AR, arrhythmia, and massive fluid overload. Non-invasive ventilation and intravenous vasodilators are cornerstone therapies; intubation may be required (Guiha, et al., 1974: 587–592).

Cardiogenic Shock (CS): Defined by tissue hypoperfusion due to reduced cardiac output. Represents the most severe AHF phenotype with the highest mortality. Requires emergent evaluation for revascularization, mechanical circulatory support, and

multidisciplinary management (van Diepen, et al., 2017: e232–e268).

Classification by Left Ventricular Ejection Fraction

The LVEF-based classification is fundamental to guiding both acute management and long-term therapy (Heidenreich, et al., 2022: e895–e1032). The key distinctions between these categories and their therapeutic implications are summarized in Table 2.

In the acute setting, HFpEF frequently presents with a dramatically elevated blood pressure and flash pulmonary edema. These patients — predominantly elderly, female, obese, and with multiple comorbidities — typically respond well to rapid decongestion with intravenous diuretics and vasodilators; however, they are sensitive to excessive preload reduction, which can result in acute hypotension and renal impairment (McDonagh, et al., 2023: 3627–3639).

Table 2: *AHF Classification by LVEF and Key Clinical Distinctions*

Category	LVEF	Dominant Mechanism	Acute Therapy Focus
HFrEF	< 40%	Systolic dysfunction; low output; neurohormonal activation	Inotropes, diuretics, GDMT optimization, ICD evaluation
HFmrEF	40–49%	Mixed systolic/diastolic dysfunction; heterogeneous	Diuretics; consider SGLT2i, MRA, ACEi/ARB
HFpEF	≥ 50%	Diastolic dysfunction; elevated filling pressures	Diuretics, vasodilators, treat precipitant; SGLT2i (Class I-A)

Classification by Hemodynamic Profile and Onset

A complementary classification stratifies AHF by the rate of clinical deterioration and predominant hemodynamic disturbance, providing a practical framework for distinguishing between rapid-onset and more gradual presentations while simultaneously guiding initial diagnostic and therapeutic strategies based on congestion and perfusion status (van Diepen, et al., 2017: e232–e268). The major hemodynamic profiles and their clinical correlates are outlined in Table 3.

Table 3: *AHF Classification by Onset Pattern and Hemodynamic Profile*

Profile	Onset	BP at Presentation	Typical Precipitant	Treatment Priority
Hypertensive AHF	Acute (hours)	High (>160 mmHg)	Hypertensive emergency, AF	Vasodilators, diuretics
Normotensive ADHF	Subacute (days)	Normal	Non-adherence, infection	IV diuretics, precipitant treatment
Low-Output / Hypotensive AHF	Acute or subacute	Low (<90 mmHg)	AMI, end-stage HF, arrhythmia	Inotropes, vasopressors, MCS
Right Heart Failure	Variable	Variable (often low)	PE, RV infarction, PHT exacerbation	RV-specific inotropes; preload management

Table 3: *AHF Classification by Onset Pattern and Hemodynamic Profile*

Profile	Onset	BP at Presentation	Typical Precipitant	Treatment Priority
Cardiogenic Shock	Acute	Low + hypoperfusion	AMI, mechanical complication	MCS, urgent revascularization

Integrated Etiological Framework: Clinical Decision Algorithm

In clinical practice, etiological classification and hemodynamic profiling should proceed in parallel and be integrated within the first 30–60 minutes of presentation. The following systematic approach is recommended (McDonagh, et al., 2023: 3627–3639). A comprehensive summary of etiological categories and recommended diagnostic approaches is provided in Table 4.

Table 4: *Summary: Etiological Classification of Acute Heart Failure*

Category	Key Conditions	Specific Assessment
Coronary Artery Disease	AMI, mechanical complications, ischemic CMP	ECG, troponin, urgent coronary angiography
Non-Ischemic Cardiomyopathy	DCM, HCM, PPCM, myocarditis, Takotsubo, toxic	Echo, MRI, genetic testing, biopsy (selected)
Valvular Disease	Acute MR/AR, critical AS, prosthetic dysfunction	Echo (TEE if needed), urgent surgical assessment
Arrhythmias	AF, VT/VF, complete heart block, tachycardia CMP	ECG, Holter, electrophysiology study

Category	Key Conditions	Specific Assessment
Hypertensive Heart Disease	Hypertensive emergency, LVH decompensation	BP monitoring, Echo, renal function
Right Heart Failure	Pulmonary embolism, PHT crisis, RV infarction	Echo, CT-PA, RHC if needed
High-Output States	Anemia, sepsis, thyrotoxicosis, AV fistula	CBC, TFTs, blood cultures, AV fistula assessment
Pericardial Disease	Cardiac tamponade, constrictive pericarditis	Echo, CT/MRI pericardium
Systemic/Infiltrative	Amyloidosis, sarcoidosis, autoimmune myocarditis	Cardiac MRI, PET, biopsy, serology

Step 1 — Life-Threatening Conditions First: Is there CS? Acute MI? Mechanical complication? Cardiac tamponade? Massive PE? Malignant arrhythmia? These require immediate specific intervention and must not be missed (Lancellotti, et al., 2015: 3–5).

Step 2 — LVEF Assessment: Emergency POCUS to classify as HFrEF, HFmrEF, or HFpEF and to identify RV function, valvular abnormalities, and pericardial pathology (Lancellotti, et al., 2015: 3–5).

Step 3 — Hemodynamic Profile (Wet/Dry/Cold/Warm): Position the patient within the 2×2 matrix to guide the choice between diuretics, vasodilators, inotropes, or vasopressors (Stevenson & Perloff, 1989: 884–888).

Step 4 — Identify the Acute Precipitant: Is the decompensation driven by infection, ACS, arrhythmia, medication

non-adherence, or dietary indiscretion? Specific treatment of the precipitant is essential for durable recovery (Chioncel, et al., 2017: 1242–1254).

Step 5 — SCAI Staging (if CS present): Classify CS severity using SCAI stages A–E to determine the urgency and type of escalation required (Naidu, et al., 2022: 933–946).

Summary

The etiological and clinical classification of acute heart failure is a multidimensional process that integrates the underlying cardiac substrate, the precipitating mechanism, the hemodynamic consequence, and the LVEF-based phenotype. No single classification fully captures the complexity of AHF; rather, they function as complementary frameworks that guide real-time clinical decision-making. The first 30–60 minutes of management must prioritize the exclusion of life-threatening, immediately reversible causes — particularly AMI, mechanical complications, tamponade, and malignant arrhythmias — before transitioning to comprehensive etiological workup and individualized pharmacological or device-based therapy. This integrative diagnostic framework underpins all subsequent management decisions discussed in the sections that follow (Heidenreich, et al., 2022: e895–e1032).

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MANAGEMENT AND THERAPEUTIC STRATEGIES FOR ACUTE HEART FAILURE

ELİF MİRAY ALPAY[2]

Modern Classification of Acute Heart Failure

Acute heart failure (AHF) is defined as the rapid onset or worsening of symptoms and signs secondary to abnormal cardiac function, resulting in reduced cardiac output and/or elevated filling pressures. This syndrome may manifest either as new-onset (de novo) heart failure or as acute decompensation of pre-existing chronic heart failure. On a global scale, AHF remains one of the leading causes of cardiovascular hospitalization and mortality each year (McDonagh et al., 2021a) (Heidenreich et al., 2022). The 2021 ESC Guidelines and their 2023 Focused Update have structured the classification of AHF according to clinical profile, ejection fraction, and underlying pathophysiology (McDonagh et al., 2024).

Clinical Profile: The Wet/Dry – Cold/Warm Matrix

The most widely used practical classification in AHF management is built on two clinical axes: 'wet versus dry'

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(congestion) and 'cold versus warm' (perfusion) (McDonagh et al., 2021a) (Stevenson & Perloff, 1989). This 2×2 matrix provides a rapid hemodynamic summary that directly guides therapy:

- **Wet (Congestion+):** Elevated filling pressures manifesting as orthopnea, paroxysmal nocturnal dyspnea, peripheral edema, elevated jugular venous pressure, and pulmonary crackles.
- **Dry (Congestion−):** Filling pressures near normal; typically corresponds to a stable chronic heart failure profile.
- **Cold (Hypoperfusio+):** Reduced cardiac output manifesting as cool extremities, oliguria, altered mental status, and narrow pulse pressure.
- **Warm (Hypoperfusion−):** Perfusion preserved; no signs of peripheral vasoconstriction.

In clinical practice, patients are commonly categorized into four groups: (1) Cold and wet — cardiogenic shock or severe low-output syndrome; (2) Warm and wet — the most frequently encountered profile, with volume overload predominating; (3) Cold and dry — low cardiac output state with hypovolemia; (4) Warm and dry— compensated profile (McDonagh et al., 2021a) (Stevenson & Perloff, 1989). The patient's position within this matrix directly determines treatment selection — primarily guiding the choice among diuretic, vasodilator, or inotropic therapy.

EF vs. HFrEF: Distinct Approaches in the Acute Setting

The 2021 ESC Guidelines and the 2022 AHA/ACC/HFSA Guidelines have adopted a three-tier classification based on left ventricular ejection fraction (LVEF): HFrEF (LVEF <40%), HFmrEF (LVEF 40–49%), and HFpEF (LVEF ≥50%) (McDonagh et al., 2024)(Heidenreich et al., 2022). Although this distinction is

most impactful in chronic management, important differences also apply in the acute setting.

- **HFrEF in the Acute Setting:** The dominant mechanism is systolic dysfunction with reduced cardiac output and impaired perfusion. Inotropic support is more frequently required; patients with LVEF ≤35% who survive the acute episode should be evaluated for ICD implantation (McDonagh et al., 2024)(Heidenreich et al., 2022).
- **HFpEF in the Acute Setting:** These patients frequently present with elevated systolic blood pressure; elevated filling pressures are the principal finding while LVEF remains preserved. Vasodilator and diuretic therapy are effective; however, inotropes must be used with caution. The 2023 ESC Focused Update assigned a Class I-A recommendation to SGLT2 inhibitors in HFpEF and HFmrEF (Heidenreich et al., 2022)(McDonagh et al., 2024). Acute decompensation in HFpEF is most commonly triggered by hypertensive crisis, atrial fibrillation, or myocardial ischemia; identification and treatment of these precipitating factors is of paramount importance.

First 60 Minutes: What Must Be Done

Assessment and treatment performed within the first hour have a decisive impact on short-term outcomes in AHF. The ESC guidelines recommend that the following steps be carried out without delay during this critical window:

- **Rapid Clinical Assessment:** Exclusion of life-threatening conditions (acute coronary syndrome, acute valve regurgitation, cardiogenic shock, hypertensive emergency). Continuous monitoring of oxygen saturation, blood pressure, heart rate, and respiratory rate.

- **Urgent Investigations:** 12-lead ECG, chest X-ray, arterial blood gas, BNP/NT-proBNP, troponin, biochemistry, complete blood count, and coagulation studies. In the presence of ST-elevation or new left bundle branch block, urgent coronary angiography must be arranged (McDonagh et al., 2021b).
- **Point-of-Care Echocardiography:** It should be performed as soon as possible assessment of LVEF, right ventricular size and function valvular pathology guides immediate treatment decisions (Lancellotti et al., 2015)(Harrison et al., 2022). Repeated measures of inferior vena cava (IVC) diameter and collapsibility via echocardiography are used to assess fluid status, particularly during concomitant sepsis Echocardiography is useful to evaluate for mechanical complications such as papillary muscle rupture, ventricular septal defects, or cardiac tamponade (Damluji et al., 2021).
- **Oxygen and Ventilatory Support:** Oxygen support is not used routinely in non-hypoxaemic patients, as it can cause vasoconstriction and reduce cardiac output. It is specifically recommended for when SpO_2 <90% or PaO_2 <60mmHg. Non-invasive positive pressure ventilation (CPAP or BiPAP) reduces mortality and the need for intubation. While CPAP and BPAP can often be used interchangeably. BPAP is more useful for patients with hypercapnia, chronic lung disease, or severe respiratory failure (Hernández et al., 2017)(Laghlam et al., 2024).
- **Intravenous Diuretic Therapy:** In the presence of congestion, intravenous furosemide is the first-line agent. The initial dose should be at least 2.5 times the patient's daily oral equivalent (ter Maaten et al., 2022).

- **Vasopressor/Inotrope in Hemodynamic Instability:** If systolic BP <90mmHg with signs of hypoperfusion, initiation of norepinephrine or dobutamine should be considered (Van Diepen et al., 2017).

Current Pharmacological Management

The pharmacological treatment of AHF rests on three fundamental pillars: diuretics, vasodilators, and inotropes. The choice of agent, timing, and dosing must be individualized according to the patient's hemodynamic profile, underlying etiology, and the degree of organ perfusion (McDonagh et al., 2021a)(Heidenreich et al., 2022).

Diuretic Resistance: Definition, Mechanisms, and Strategies to Overcome It

Diuretic resistance is defined as the failure to achieve adequate natriuresis and volume removal despite maximum doses of furosemide (400–600 mg/day)(ter Maaten et al., 2022). The natriuretic response to intravenous loop diuretics is measured by urine output, urinary sodium concentration, and weight loss. Diuretic resistance is a common feature in the clinical course of patients with advanced heart failure and is frequently associated with kidney dysfunction. If urinary sodium is <50–70mEq/L or urine output is <100mL/hour at 6 hours and failing to achieve a weight loss of 0.5–1.5kg within 24 hours diuretic resistance is present (Wilcox et al., 2020).

Pathophysiological Mechanisms: The principal mechanisms underlying diuretic resistance include: (1) Reduced renal perfusion due to low cardiac output; (2) 'Diuretic braking' — distal nephron hypertrophy secondary to chronic high-dose diuretic use; (3) Aldosterone activation and neurohormonal upregulation; (4) Decreased oral bioavailability secondary to gut wall edema; (5)

Concurrent use of NSAIDs, intravenous contrast agents, or nephrotoxic medications (Wilcox et al., 2020).

The DOSE Trial and Urine Sodium-Guided Therapy: The NHLBI-sponsored DOSE trial demonstrated that high-dose furosemide (2.5 times the oral dose administered intravenously) was superior to low-dose (IV dose equivalent to oral dose) in terms of symptom relief and decongestion. Continuous infusion showed no significant advantage over bolus dosing; however, continuous infusion may provide better decongestion in higher-risk patients (Moon, 2012). The 2023 PUSH-AHF trial demonstrated that urinary sodium-guided diuretic titration was superior to standard care in achieving complete decongestion (ter Maaten et al., 2022).

Strategies to Overcome Diuretic Resistance: If the response to loop diuretics is inadequate, the following steps can be applied sequentially:

- **Addition of thiazide diuretics:** Metolazone or hydrochlorothiazide achieves sequential nephron blockade and produces synergistic diuresis.
- **Acetazolamide:** The ADVOR trial demonstrated that the addition of acetazolamide to IV furosemide significantly increased the rate of successful decongestion (McDonagh et al., 2024).
- **SGLT2 inhibitors:** The EMPULSE and DICTATE-AHF trials showed that early in-hospital initiation of empagliflozin or dapagliflozin in AHF enhances natriuresis, promotes volume removal, and improves clinical outcomes (McDonagh et al., 2021b).
- **Hypertonic saline + furosemide:** In selected patients, hypertonic saline combination may augment diuretic efficacy

by increasing the osmotic gradient; however, it is not recommended for routine use (Gandhi et al., 2014).

- **Ultrafiltration:** When all pharmacological strategies have failed and the patient's hemodynamic status permits, ultrafiltration is considered.

Vasodilators: Who, When, and Which Agent?

Intravenous vasodilators are indicated in AHF when systolic blood pressure is ≥90–100mmHg (McDonagh et al., 2024). Vasodilators provide to a reduction in venous return to the heart (preload) and lower systemic vascular resistance (afterload). This effect of them results in less congestion, increased stroke volume, and the relief of heart failure symptoms. These agents are particularly effective in hypertensive AHF and acute pulmonary edema.

Nitroglycerin (GTN): Acts primarily via venodilation to reduce preload; at higher doses, arterial dilation and afterload reduction are also achieved. Sublingual or inhaled formulations provide rapid relief prior to IV infusion initiation in acute pulmonary edema. Nitrate tolerance develops within 24–48 hours; therefore, intermittent administration is preferred over continuous infusion.

Sodium Nitroprusside (SNP): A potent arterial and venous vasodilator that rapidly reduces afterload. Particularly useful in hypertensive emergencies and AHF secondary to acute valve regurgitation; however, cyanide toxicity risk and the requirement for invasive blood pressure monitoring are limiting factors (Heidenreich et al., 2022).

Nesiritide (BNP Analog): Has vasodilatory and modest diuretic properties; however, the ASCEND-HF trial failed to demonstrate a mortality benefit (Fudim et al., 2018).

Contraindications: Vasodilators are contraindicated when systolic BP <90mmHg, in severe aortic stenosis, and in preload-dependent states (right ventricular infarction, cardiac tamponade).Aortic stenosis can cause increasing LV afterload and causing LV hypertrophy, leading to a further worsening of heart failure (McDonagh et al., 2024).

Inotrope Selection: Dobutamine vs. Milrinone

Inotropes are indicated when cardiac index is <2.2L/min/m², severe signs of hypoperfusion are present, or organ dysfunction accompanies shock (Van Diepen et al., 2017). Although these agents have not demonstrated a mortality benefit, they have an established role as short-term bridge therapy (to heart transplantation or mechanical circulatory support) or for palliation.

Dobutamine: A β1-adrenergic agonist that increases cardiac output; moderate β2 and α1 activity reduces peripheral vascular resistance. Standard dosing ranges from 2–20μg/kg/min (McDonagh et al., 2021a). Tachyphylaxis with prolonged use, arrhythmia risk, and increased myocardial oxygen consumption are key disadvantages. Efficacy is reduced in patients receiving beta-blockers.

Milrinone: A phosphodiesterase-3 inhibitor with inotropic, lusitropic (improves diastolic relaxation), and significant vasodilatory properties (Van Diepen et al., 2017). Preferred particularly when pulmonary hypertension or right ventricular failure coexists. Dose reduction is required in renal failure; the risk of hypotension is greater than with dobutamine. The OPTIME-CHF trial demonstrated better tolerability in non-ischemic patients (Felker et al., 2003).

Levosimendan: A calcium sensitizer and K-ATP channel opener with combined inotropic and vasodilatory effects that does

not increase myocardial oxygen consumption. Efficacy is preserved in patients receiving beta-blockers. Because levosimendan acts through a mechanism independent of beta-adrenoceptors, it may be preferred over dobutamine for patients who are already on chronic beta-blocker therapy. The SURVIVE and REVIVE trials failed to demonstrate superiority over standard care; however, levosimendan may be used as an alternative to dobutamine in selected patients with acute decompensation (Mebazaa et al., 2007). It is widely used in Turkey and many other European countries.

Epinephrine: An agent of last resort; used in severe cardiogenic shock and refractory ventricular arrhythmias. Carries a high arrhythmogenic risk and notable myocardial toxicity.

Vasopressor Selection: Norepinephrine vs. Dopamine

Vasopressor therapy is unavoidable in vasodilatory shock or catecholamine-requiring AHF/cardiogenic shock. The choice between norepinephrine and dopamine has been largely resolved by the SOAP-II trial.

Norepinephrine (First-Line): Potent α1-adrenergic vasoconstriction combined with moderate β1 inotropic effect. Effectively raises mean arterial pressure with less chronotropic effect than dopamine (Van Diepen et al., 2017). The SOAP-II trial demonstrated that norepinephrine was associated with fewer arrhythmic events and similar mortality compared to dopamine in cardiogenic shock.

Dopamine (Second-Line): At low doses (1–5μg/kg/min), dopaminergic effects produce renal and mesenteric vasodilation; however, the clinical benefit of this 'renal dose' concept remains controversial. At intermediate doses (5–10μg/kg/min), β1-adrenergic effects predominate; at high doses, α1 effects take over.

Its tachycardia-inducing and arrhythmogenic properties place it behind norepinephrine for cardiogenic shock.

Vasopressin: May be considered as an adjunct in catecholamine-resistant cases or to reduce catecholamine dose requirements; however, evidence supporting its routine use in AHF remains insufficient.

Cardiogenic Shock

Cardiogenic shock (CS) is a high-mortality clinical syndrome characterized by systemic signs of tissue hypoperfusion resulting from inadequate cardiac output. Despite more than three decades of progress, mortality associated with AMI-related CS remains approximately 30–50%, a rate that has not declined dramatically despite advances in mechanical circulatory support (MCS) devices and percutaneous revascularization (Baran et al., 2019).

Diagnostic Criteria: CS is defined by: (1) Persistent hypotension: systolic BP <90mmHg for >30 minutes or requiring vasopressors; (2) Reduced cardiac output: cardiac index <2.2L/min/m² (or <1.8 L/min/m² unsupported); (3) Signs of tissue hypoperfusion: cool extremities, oliguria (<0.5mL/kg/hour), altered mental status, elevated lactate (>2mmol/L) (Baran et al., 2019)(Naidu et al., 2022).

SCAI Classification: Severity Staging from A to E

The SCAI (Society for Cardiovascular Angiography and Interventions) shock classification, developed in 2019 and updated in 2022, defines CS across five stages from A to E (Naidu et al., 2022)(Hill et al., 2023). This classification has been endorsed by the ACC, AHA, ESC ACVC, SCCM, and STS:

Stage A (At-Risk): No active signs of shock; however, the underlying cardiac condition (acute MI, decompensated HF) confers

CS risk. Normal hemodynamic parameters, normal lactate, no end-organ damage.

Stage B (Beginning): Relative hypotension or tachycardia is present without hypoperfusion. Systolic BP <90mmHg or heart rate >100bpm. Normal lactate, preserved mental status.

Stage C (Classic Cardiogenic Shock): Classic CS features are present; vasopressors or inotropes are required. Cold-wet profile, lactate ≥2mmol/L, elevated serum creatinine, elevated BNP.

Stage D (Deteriorating): CS not responding to initial therapy. Multiple vasopressors/inotropes or temporary MCS required. Lactate continues to rise.

Stage E (Extremis): Cardiac arrest and/or ongoing resuscitative efforts. pH ≤7.2, lactate >8–10mmol/L, PEA or VF. Survival probability is extremely low.

The SCAI stage at admission and 24-hour reclassification are strong independent predictors of in-hospital mortality. Failure to downstage (i.e., non-improvement) at 24 hours is a critical alarm signal for treatment escalation (Naidu et al., 2022)(Hill et al., 2023).

The Fluid Trap in Cardiogenic Shock

Fluid resuscitation in cardiogenic shock must be approached with great caution. In the context of CS, where elevated coronary bed and capillary pressures coexist with circulatory failure, excessive fluid administration can lead to right ventricular volume overload, interstitial pulmonary edema, and worsening of cardiac tamponade physiology. This phenomenon is referred to as the 'fluid trap.'

By its nature, cardiogenic shock is a state of reduced cardiac output; the primary problem is pump failure, not hypovolemia. Therefore, ESC and SCAI guidelines caution against routine

aggressive fluid loading in CS, recommending that fluid administration be performed only after assessing preload adequacy via echocardiography, CVP measurement, or invasive monitoring (Van Diepen et al., 2017). Intracavitary pressure measurements (pulmonary capillary wedge pressure, CVP) and IVC assessment guide this distinction.

Invasive Monitoring: Lactate, $ScvO_2$, and Pulmonary Artery Catheter

Hemodynamic monitoring in CS forms the foundation of treatment optimization.

Serum Lactate: The most practical and reliable indicator of tissue hypoperfusion. A value >2mmol/L at presentation is considered significant; >4mmol/L is associated with markedly increased in-hospital mortality (Baran et al., 2019). Lactic acidosis ($pH \leq 7.2$ combined with lactate elevation) corresponds to SCAI Stage E and signals an extremely poor prognosis. Serial lactate measurements (at 6, 12, and 24 hours) should be performed to assess treatment response.

$ScvO_2$ (Central Venous Oxygen Saturation): The target value is above 70%. $ScvO_2$ <60% indicates an imbalance between oxygen delivery and consumption at the tissue level; it signals the need to escalate inotropic support and/or mechanical circulatory support.

Pulmonary Artery Catheter (Swan-Ganz): Enables measurement of pulmonary capillary wedge pressure (PCWP), cardiac output, systemic vascular resistance, and mixed venous oxygen saturation (SvO_2). Evidence supports that PAC-guided management in CS studies is associated with reduced mortality (Van Diepen et al., 2017). The ESC guidelines recommend pulmonary

artery catheterization particularly in CS of unclear etiology or refractory to therapy.

Mechanical Circulatory Support

When pharmacological therapy proves insufficient in cardiogenic shock, temporary mechanical circulatory support (MCS) devices serve as life-saving bridging strategies (Ahmad et al., 2023)(Farhat et al., 2025). Over the fundamentally transformed this field — with the IABP falling to the background and Impella, VA-ECMO, and combination strategies emerging to the forefront.

Intra-Aortic Balloon Pump: Why It Has Receded

The intra-aortic balloon pump (IABP), long used as the first-line MCS device in cardiogenic shock, now has only limited indications (Ahmad et al., 2023). The IABP-SHOCK II trial (n=600) demonstrated that IABP did not reduce 30-day mortality in AMI-related CS; this finding was maintained at 6 and 12 months of follow-up (Baran et al., 2019). Following these findings, ESC and ACC/AHA guidelines downgraded IABP recommendations; routine use in AMI-CS has been downgraded to Class III (no benefit, not recommended).

IABP augments diastolic blood pressure to support coronary perfusion and modestly reduces systolic aortic pressure to lower afterload; however, the resulting increase in cardiac output is only 0.3–0.5L/min. This limited hemodynamic effect is insufficient in severe CS. Nevertheless, IABP may still retain value in early-stage (SCAI B–C) CS or as a bridging strategy in carefully selected patients.

Impella: Mechanism, Indications, and the DanGer Shock Trial

Impella is a percutaneous microaxial pump that provides continuous flow from the left ventricular cavity into the aorta

(Ahmad et al., 2023)(Modi et al., 2024). By unloading the left ventricle, it reduces end-diastolic volume and pressure, decreases myocardial oxygen consumption, and augments cardiac output and mean arterial pressure. A characteristic leftward and downward shift is observed in the pressure-volume loop.

Currently available models include: Impella 2.5 (2.5L/min), Impella CP (3.7L/min), and Impella 5.0/5.5 (5–5.5L/min). Larger models (5.0/5.5) require an axillary approach and implantation in an operating theatre, while the CP model can be deployed in the catheterization laboratory (Modi et al., 2024).

DanGer Shock Trial (2024): Following previous non-randomized studies, the DanGer Shock trial — published in 2024 — was the first randomized controlled trial to demonstrate that Impella CP significantly reduced 180-day mortality compared to standard care in AMI+CS. This trial represents the strongest evidence to date supporting the use of Impella CP in STEMI-related CS; however, increased rates of bleeding, hemolysis, and limb ischemia were also reported.

Patient Selection: The population most likely to benefit are patients with SCAI C–D stage CS without prior cardiac arrest in whom the device is placed before reperfusion, matching the DanGer Shock enrollment profile (Ahmad et al., 2023)(Farhat et al., 2025). The benefit in advanced-stage (SCAI E) and post-cardiac arrest patients remains uncertain.

VA-ECMO: Patient Selection and Complications

Venoarterial extracorporeal membrane oxygenation (VA-ECMO) is the most powerful temporary MCS device, providing simultaneous circulatory and respiratory support (Thiele et al., 2023)(Ahmad et al., 2023). It oxygenates venous blood and returns

it to the aorta, replacing cardiac output; however, this retrograde flow may increase left ventricular afterload.

Pathophysiological Paradox: VA-ECMO does not assume the mechanical function of the left ventricle; on the contrary, retrograde aortic flow may increase LV filling pressure. This can cause to increased LV end-diastolic pressure and pulmonary congestion. In that cases, requiring the use of "unloading" devices like an Impella or intra-aortic balloon pump use to protect the heart (Thiele et al., 2023)(Grandin et al., 2022). As a result, when ECMO is initiated alone, the addition of a left ventricular unloading strategy is frequently required.

VA-ECMO Indications: Refractory CS (SCAI D–E), cardiac arrest, mechanical complications of myocardial infarction, massive pulmonary embolism, and as a bridging strategy (Farhat et al., 2025).

VA-ECMO Complications: Major bleeding (25–40%), lower limb ischemia (10–20%), stroke (5–15%), infection, thrombosis, and hemolysis. These high complication rates necessitate careful patient selection, an experienced multidisciplinary team, and protocolized management.

ECpella: VA-ECMO + Impella Combination

The simultaneous use of VA-ECMO and Impella (ECpella) is gaining traction to prevent LV distension caused by retrograde ECMO flow and to achieve more aggressive LV unloading (Morici et al., 2023). Impella counteracts the afterload increase imposed by ECMO and reduces LV filling pressure.

Evidence Base: Multiple observational studies and a meta-analysis have shown that the ECpella combination is associated with lower mortality compared to VA-ECMO alone. However, ECpella is associated with significantly higher rates of bleeding, embolism,

sepsis, and limb ischemia compared to ECMO alone (Morici et al., 2023). Randomized controlled trials have not yet been completed, and prospective evidence is needed before routine recommendation.

Patient Selection Guidance: ECpella should be considered primarily in patients who develop LV distension despite VA-ECMO, those in SCAI D–E stage, and patients with evidence of salvageable myocardium (Modi et al., 2024).

The 'Too-Late ECMO' Syndrome

The 'too-late ECMO' syndrome refers to the initiation of ECMO after multi-organ failure has inflicted irreversible damage. This concept carries a critical warning for clinicians: when ECMO is started in patients in whom the therapeutic window has largely been missed, mortality may be comparable to or higher than in patients not receiving ECMO.

Risk Factors: Multi-organ failure (hepatic, renal, neurological), prolonged prior cardiac arrest, severe lactic acidosis (lactate >10–15mmol/L), prolonged and uncontrolled shock duration, and advanced age in combination are warning signs identifying patients unlikely to benefit from ECMO.

Time-Sensitive Approach: Transition from SCAI Stage C to D/E must be detected early; MCS decisions should be made promptly within escalation protocols without delay. Protocolized shock management (as exemplified by the National Cardiogenic Shock Initiative model), early MCS use, and the establishment of dedicated shock teams are the strategies that need to be implemented in this context.

The Decision-Altering Role of Emergency Echocardiography

Point-of-care echocardiography (POCUS) has become a revolutionary tool in the management of acute heart failure and cardiogenic shock (Harrison et al., 2022)(Monteagudo-Vela et al.,

2023). By providing bedside, real-time information equivalent to that of standard echocardiography, it confirms the diagnosis, monitors treatment response, and directly guides critical clinical decisions. The 2021 ESC Guidelines endorse echocardiographic evaluation as early as possible in AHF with a Class I recommendation.

Recognition of Mechanical Complications

Mechanical complications arising after acute myocardial infarction include acute mitral regurgitation (papillary muscle rupture), ventricular septal rupture (VSD), and free wall rupture (Lancellotti et al., 2015)(Monteagudo-Vela et al., 2023). These complications cause sudden, dramatic hemodynamic deterioration; echocardiography is indispensable for differentiating this presentation from primary cardiogenic shock.

Mitral Valve Rupture: Acute severe MR secondary to papillary muscle rupture rapidly progresses to acute pulmonary edema. An eccentric jet is conspicuous on color Doppler; it may occasionally be difficult to distinguish from papillary muscle vegetation.

VSD: Shunt flow across the apical or basal septum is detected with Doppler; right and left ventricular loading conditions can be compared in real time.

Free Wall Rupture /Pseudoaneurysm: A loculated pericardial fluid collection, tamponade physiology, and disrupted myocardial contour can be rapidly identified with POCUS.

Assessment of Right Ventricular Failure

Right ventricular (RV) failure is an underrecognized but treatment-altering condition in AHF and CS (Monteagudo-Vela et al., 2023)(Astengo et al., 2024). The rapid bedside assessment of RV function with POCUS determines the treatment trajectory, since

fluid management strategy and inotrope selection differ substantially in RV failure.

TAPSE (Tricuspid Annular Plane Systolic Excursion): ≥17mm is considered normal; <17mm indicates longitudinal RV systolic dysfunction. TAPSE <14mm is associated with significant RV failure (Monteagudo-Vela et al., 2023)(Astengo et al., 2024).

RV/LV Diameter Ratio: An RV-to-LV diameter ratio >0.6 at the apex is abnormal; >1.0 indicates advanced RV dilation.

D-Sign: In the parasternal short-axis view, the "D sign" in clinical practice refers to the flattening of the interventricular septum, causing the left ventricle to appear D-shaped on echocardiography, typically due to RV pressure or volume overload.

Inferior Vena Cava (IVC) Assessment: IVC >21mm with <50% respiratory collapse indicates elevated right atrial pressure — an important guide for fluid management in CS. For instance, a dilated, non-collapsible IVC is often associated with the "wet" clinical profiles which are characterized by high filling pressures and systemic congestion

In the presence of RV infarction (AMI from right coronary artery involvement), inotropic support should be prioritized for the RV; fluid loading must be cautious, and any maneuver that reduces LV preload should be avoided (Lancellotti et al., 2015)(Astengo et al., 2024).

Volume Status Assessment

Accurate assessment of volume status in cardiogenic shock is critical to avoid the fluid trap while optimizing perfusion. POCUS offers multiple parameters for this assessment:

IVC Diameter and Collapsibility Index: IVC diameter <15mm with >50% respiratory collapse supports low right atrial pressure. IVC >21mm, rigid with reduced respiratory variation, indicates elevated filling pressure.

Lung Ultrasound (LUS): B-lines indicate alveolar-interstitial pulmonary edema and serve as an excellent tool for monitoring diuretic efficacy (Lancellotti et al., 2015). A decreasing number of B-lines with diuretic therapy signifies successful decongestion. Three or more B-lines in the left and right hemithorax combined is significantly associated with pulmonary congestion.

Cardiac-Lung POCUS Integration: Simultaneous bedside assessment of the heart and lungs provides a comprehensive perspective on LV filling pressures, RV function, and volume responsiveness. This multiparametric approach has been elevated to guideline-level recommendation for directing treatment decisions.

E/e' Ratio: E/e' >15 obtained by tissue Doppler predicts elevated LV filling pressures; however, reliability may diminish in the acute phase of CS.

POCUS-Guided Clinical Decision Points

Rapid POCUS evaluation supports the following critical clinical decisions: (Lancellotti et al., 2015)(Harrison et al., 2022) (Astengo et al., 2024)

•Pericardial tamponade → urgent pericardiocentesis

•Severe aortic stenosis → pharmacological treatment limitations, TAVI assessment

•Acute severe MR /VSD → emergent surgery or temporary MCS decision

•HFrEF vs HFpEF → inotropic support vs vasodilator therapy selection

•RV failure → fluid restriction, norepinephrine, RV-specific inotropes

•Hyperdynamic LV (Takotsubo) → avoidance of inotropes, consideration of beta-blockers

•IVC collapsibility <50% + empty-appearing LV → fluid loading decision

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TROPONIN ELEVATION WITHOUT ACUTE CORONARY SYNDROME: PATHOPHYSIOLOGY, DIFFERENTIAL DIAGNOSIS, AND CLINICAL MANAGEMENT IN THE EMERGENCY DEPARTMENT

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Introduction

Cardiac troponins (cTn) are the most sensitive and specific biomarkers of myocardial injury and have become the cornerstone of acute myocardial infarction (AMI) diagnosis. Their clinical utility was further amplified by the introduction of high-sensitivity troponin (hs-cTn) assays, which are capable of detecting previously undetectable degrees of myocardial damage. This advancement, however, has created a diagnostic challenge: troponin elevation is no longer synonymous with acute coronary syndrome (ACS) (Chauin, 2021: 601–617; Savic, et al., 2025).

Studies consistently demonstrate that among emergency department (ED) patients with detectable troponin elevations,

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approximately **49–60%** do not have ACS as the underlying cause (Maayah, et al., 2024). The Fourth Universal Definition of Myocardial Infarction reinforces this concept by defining troponin elevation as evidence of myocardial injury — whether ischemic or non-ischemic — and requiring additional clinical criteria (symptoms, ECG changes, or imaging evidence) to diagnose AMI (Thygesen, et al., 2018: e618–e651). The term "false positive troponin" is therefore conceptually misleading: in virtually all cases, real myocardial damage exists; it simply does not arise from plaque rupture or acute ischemic occlusion.

This distinction carries enormous clinical weight. Misattributing a non-ACS troponin elevation to acute MI can result in inappropriate antithrombotic therapy, unwarranted coronary angiography with its associated procedural risks, and — most importantly — a missed or delayed diagnosis of the true underlying condition. Conversely, dismissing troponin elevation in a patient with genuine MINOCA, Takotsubo cardiomyopathy, or myocarditis may deprive them of appropriate, potentially life-saving management (Chauin, 2021: 601–617; Thygesen, et al., 2018: e618–e651).

This chapter provides a comprehensive review of the major non-ACS causes of troponin elevation encountered in the ED. The following conditions are addressed in depth: cerebrovascular events (ischemic stroke, subarachnoid hemorrhage, intracerebral hemorrhage), pulmonary embolism, hypoxia and acute respiratory failure, carbon monoxide poisoning, acute pancreatitis, Takotsubo syndrome (stress cardiomyopathy), myocardial infarction with non-obstructive coronary arteries (MINOCA), and ischemia with non-obstructive coronary arteries (INOCA). Each section covers pathophysiology, biomarker kinetics, diagnostic approach, and clinical management implications, with reference to current PubMed literature.

Biochemical and Pathophysiological Basis of Troponin Elevation

Structure and Function of the Troponin Complex

The troponin complex resides on the thin actin filament of striated muscle and is composed of three subunits: troponin C (cTnC), which binds calcium; inhibitory troponin I (cTnI); and tropomyosin-binding troponin T (cTnT). The cardiac-specific isoforms cTnI and cTnT are not expressed in skeletal muscle, conferring their high organ specificity for myocardial injury (Parmacek & Solaro, 2004: 159–176).

Within the cardiomyocyte, troponins exist in two distinct pools: the structurally bound myofibrillar fraction (approximately 94–97% of total content) and the free cytosolic fraction (~3–6%). Following myocardial injury, the cytosolic pool is released first — rapidly entering the circulation — followed by the structurally bound fraction released during proteolytic degradation of myofibrils. This biphasic release kinetic is more apparent with hs-cTn assays, enabling earlier detection than was possible with conventional assays (Parmacek & Solaro, 2004: 159–176).

Non-Ischemic Mechanisms of Troponin Release

Troponin elevation can occur through multiple distinct pathophysiological pathways that do not require plaque rupture or coronary occlusion (Collet, et al., 2021: 1289–1367). Understanding these mechanisms is essential for appropriate clinical interpretation:

Reversible myocyte injury involves transient sarcolemmal permeability without irreversible cell death, as occurs in myocardial "stunning," early Takotsubo syndrome, or transient ischemia (Collet, et al., 2021: 1289–1367; Prandin, et al., 2024: 107844). Cytokine/neurohormonal-mediated damage, seen in sepsis and critical illness, involves TNF-alpha, IL-1beta, and IL-6 activating calpain-mediated proteolysis, generating low-molecular-weight

troponin fragments that traverse the membrane without frank necrosis. Neurogenic myocardial injury arises from sympathetic storms generating catecholamine-mediated contraction band necrosis, as in subarachnoid hemorrhage. Direct cellular toxicity through reactive oxygen species, mitochondrial inhibition, and membrane peroxidation underlies carbon monoxide-induced myocardial damage. Mechanical wall stress in the setting of elevated ventricular afterload (pulmonary embolism, hypertensive emergency) activates stretch-mediated signaling and apoptosis. Reduced renal clearance of troponin fragments accounts for the chronic low-level elevation consistently seen in advanced chronic kidney disease (Favory & Neviere, 2006: 224).

High-Sensitivity Assays and the Delta Troponin Concept

The ESC 0h/1h and 0h/2h rapid rule-out/rule-in algorithms, endorsed by the 2020 ESC NSTEMI Guidelines, exploit the kinetic properties of hs-cTn to differentiate acute from chronic myocardial injury (Collet, et al., 2021: 1289–1367). A delta troponin rise of ≥5 ng/L (hs-cTnT) or ≥6 ng/L (hs-cTnI) within the first hour is highly specific for acute AMI. In non-ACS conditions, troponin changes are typically slow or plateau rather than showing rapid rise and fall. However, these algorithms were calibrated primarily for ischemic causes; several non-ACS conditions (Takotsubo, myocarditis, MINOCA) can produce dynamic kinetics that mimic AMI, making them particularly treacherous (Mueller, et al., 2016: 76–87 e74).

Table 1. Mechanisms of Troponin Release and Associated Clinical Conditions

Mechanism	Pathophysiology	Clinical Example
Ischemic Necrosis	Sarcolemmal disruption, ATP depletion	AMI, Type 1 MI
Reversible Injury	Transient membrane permeability	Takotsubo, MINOCA
Cytokine /Neurohormonal	TNF-α, IL-6, calpain activation	Sepsis, critical illness
Neurogenic	Catecholamine surge, contraction band necrosis	SAH, ischemic stroke
Direct Toxicity	CO-Hb, ROS, mitochondrial Complex IV inhibition	Carbon monoxide poisoning
Mechanical Stress	Wall tension, stretch-activated channels, apoptosis	PE, pulmonary hypertension, HF
Reduced Clearance	Decreased renal clearance of troponin fragments	CKD, dialysis

SAH: subarachnoid hemorrhage; CO-Hb: carboxyhemoglobin; ROS: reactive oxygen species; PE: pulmonary embolism; HF: heart failure; CKD: chronic kidney disease

Cerebrovascular Events

Acute Ischemic Stroke

Acute ischemic stroke (AIS) is one of the most clinically important non-cardiac causes of troponin elevation presenting to the ED. Using standard troponin assays, elevations are reported in 10–34% of AIS patients; with hs-cTn, this proportion may approach 50%. Gulia and colleagues' 2024 meta-analysis — encompassing 53 studies — demonstrated that troponin elevation in AIS patients was associated with a 3.80-fold increase in in-hospital mortality (RR: 3.80; 95% CI: 2.82–5.12), establishing troponin as an independent prognostic marker in this population (Becker, et al., 2024: 830–839).

The principal pathophysiological mechanism is neurogenic myocardial injury through the brain-heart axis. Cerebral ischemia — particularly involving the insular cortex, which exerts strong autonomic regulatory influence — triggers activation of the hypothalamic-adrenal axis, resulting in a massive catecholamine surge. Excessive norepinephrine release causes coronary microvascular vasoconstriction, cardiomyocyte apoptosis, and contraction band necrosis, leading to troponin release in the absence of epicardial coronary occlusion (Prandin, et al., 2024: 107844). This mechanism bears a close pathophysiological resemblance to Takotsubo syndrome, and transient left ventricular dysfunction indistinguishable from Takotsubo can occur in stroke.

A critical clinical decision-making challenge is distinguishing two scenarios: (1) the stroke is itself caused by cardiac embolism (cardioembolic stroke), in which case troponin elevation may reflect the underlying cardiac pathology (e.g., atrial fibrillation, cardiomyopathy, or LV thrombus); or (2) the stroke itself has generated neurogenic myocardial injury. This distinction directly impacts the diagnostic workup and secondary prevention strategy. Current AHA/ASA guidelines recommend troponin measurement in

all patients presenting with acute stroke (Prandin, et al., 2024: 107844).

Subarachnoid Hemorrhage

Subarachnoid hemorrhage (SAH) carries the highest risk of cardiac complications and troponin elevation among all cerebrovascular events. Zhao and colleagues' 2025 meta-analysis — encompassing 33 studies and 6,349 SAH patients — found an overall troponin elevation prevalence of 24.55%, with a pooled odds ratio for in-hospital mortality of 3.13 (95% CI: 1.87–5.26) (Zahid, et al., 2020: e9792). The landmark study by Naidech and colleagues in 253 SAH patients demonstrated that troponin elevation was independently associated with poor clinical grade, intraventricular hemorrhage, and global cerebral edema — independent of aneurysm location or intervention timing (Naidech, et al., 2005: 2851–2856).

The pathophysiological mechanism of cardiac injury in SAH is mediated by acute hypothalamic-cardiac reflex pathways. Sudden intracranial pressure elevation and hypothalamic ischemia trigger massive sympathoadrenal activation. The resulting catecholamine storm produces widespread contraction band necrosis — a pattern of perivascularity distributed injury distinct from coronary artery territory infarction and histologically identical to the myocardial injury seen in Takotsubo syndrome (Mayer, et al., 1999: 780–786). This pathological substrate explains both the EKG changes and the regional wall motion abnormalities frequently observed in SAH.

ECG manifestations in SAH may include QTc prolongation, diffuse T-wave inversions, prominent U waves, ST-segment elevation, and new left bundle branch block. These changes can be clinically indistinguishable from AMI. Crucially, thrombolytic therapy or emergent coronary angiography driven by misdiagnosis of AMI in a patient with SAH carries catastrophic risk. Echocardiography — demonstrating a regional wall motion

abnormality pattern inconsistent with a single coronary territory — is an essential diagnostic step (Zahid, et al., 2020: e9792).

Intracerebral Hemorrhage and Transient Ischemic Attack

Intracerebral hemorrhage (ICH) can also cause troponin elevation, particularly when the bleed involves the thalamus, basal ganglia, or insular cortex. However, in Gulia et al.'s meta-analysis, the association between troponin elevation and in-hospital mortality in ICH did not reach statistical significance (RR: 1.13; 95% CI: 0.46–2.79), suggesting that the prognostic weight of troponin elevation may differ across cerebrovascular subtypes (Becker, et al., 2024: 830–839). In transient ischemic attack (TIA), clinically significant troponin elevation is rare, though NT-proBNP elevation correlates more consistently, reflecting underlying cardiac pathology (Wira, et al., 2011: 414–420).

Diagnostic Approach in Cerebrovascular Troponin Elevation

Key clinical principles for interpreting troponin elevation in the context of cerebrovascular disease include the following: First, the onset and character of neurological symptoms relative to the onset of chest pain or ECG changes must be carefully sequenced. Second, troponin kinetics in neurogenic injury typically show a slower rise and more prolonged plateau than classic AMI. Third, in the ED, ECG, bedside echocardiography, and urgent non-contrast head CT provide the most rapid diagnostic clarity. Fourth, cardioembolic workup (prolonged ECG monitoring, transesophageal echocardiography, hypercoagulability screen) should follow rather than precede neurological stabilization, unless AMI cannot be excluded (Prandin, et al., 2024: 107844).

Pulmonary Embolism, Hypoxia, and Acute Respiratory Failure

Pulmonary Embolism

Pulmonary embolism (PE) is one of the most important non-ACS causes of troponin elevation in the ED — and one of the most clinically dangerous to misclassify. Using hs-cTn assays, troponin elevation is detectable in up to 64% of PE patients. The primary mechanism is right ventricular (RV) pressure overload: acute elevation of pulmonary vascular resistance leads to RV dilation, interventricular septal shift ("D-shaped septum"), impaired RV coronary perfusion, and RV ischemia with subsequent troponin release (Freund, et al., 2011: R147; Konstantinides & Meyer, 2019: 3453–3455).

Troponin elevation in PE is a robust independent prognostic marker. The ESC 2019 PE guidelines incorporate troponin positivity into risk stratification (intermediate-high risk) to guide decisions on reperfusion therapy (Konstantinides & Meyer, 2019: 3453–3455). Importantly, PE-associated troponin kinetics are typically slower in both rise and decline compared to AMI. Pleuritic chest pain, dyspnea, hypoxia, sinus tachycardia, signs of DVT, and elevated D-dimer in the context of troponin elevation should always prompt PE as a primary differential diagnosis before proceeding to coronary angiography.

Hypoxia and Acute Respiratory Failure

The myocardium — with its high oxidative metabolic demands and near-maximal baseline oxygen extraction ratio — is exceptionally vulnerable to systemic hypoxia. Any condition acutely reducing oxygen delivery below myocardial demand generates Type 2 MI physiology: supply-demand mismatch without plaque rupture, mediated by ATP depletion, impaired sarcoplasmic reticulum

calcium handling, and reactive oxygen species accumulation (Amgalan, Pekson, & Kitsis, 2017: 118–121).

Conditions producing acute hypoxemia and clinically significant troponin elevation include: acute respiratory distress syndrome (ARDS), severe pneumonia, status asthmaticus, acute-on-chronic exacerbations of COPD, pneumothorax, and massive pleural effusion. Troponin elevation in these settings serves as a biochemical indicator of respiratory compromise severity and independently predicts ICU requirement and mortality. Additional mechanisms include RV pressure loading from hypoxic pulmonary vasoconstriction and neurohormonal activation driven by physiological stress (Amgalan, Pekson, & Kitsis, 2017: 118–121).

Sepsis and Septic Cardiomyopathy

Sepsis-induced myocardial injury is among the most well-characterized non-ischemic causes of troponin elevation, with clinically significant elevations reported in 30–85% of ICU patients with septic shock (Savic, et al., 2025). The pathophysiological cascade is multifactorial: pro-inflammatory cytokines (TNF-alpha, IL-1beta, IL-6) directly activate calpain-mediated intracellular proteolysis of the cytosolic troponin pool, generating low-molecular-weight fragments that traverse the sarcolemma through increased permeability without obligatory necrosis. Simultaneously, reactive oxygen species cause mitochondrial dysfunction, nitric oxide-mediated myocardial depression, and impaired beta-adrenergic receptor responsiveness.

Sepsis-associated troponin elevation is an independent predictor of 30-day mortality. Critically, this elevation does not by itself indicate ACS and does not require invasive coronary evaluation. Management should be directed at the underlying septic process, with hemodynamic stabilization, source control, and evidence-based sepsis bundle implementation as priorities. Routine

coronary angiography for troponin elevation in the absence of other ACS features in septic patients is not supported by current evidence (Savic, et al., 2025).

Severe Anemia

Severe anemia (typically hemoglobin <7 g/dL) impairs oxygen-carrying capacity sufficiently to produce supply-demand mismatch-mediated myocardial injury, classified as Type 2 MI under the Fourth Universal Definition (Thygesen, et al., 2018: e618–e651). This mechanism is particularly relevant in patients with pre-existing coronary artery disease in whom the ischemic threshold is already reduced. Management centers on identifying and treating the underlying cause of anemia, with red blood cell transfusion when appropriate. Troponin elevation in this context should not trigger anti-thrombotic therapy without additional evidence of obstructive coronary pathology.

Carbon Monoxide Poisoning

Epidemiology and Cardiac Manifestations

Carbon monoxide (CO) poisoning causes over 50,000 emergency department visits and approximately 1,200 deaths annually in the United States, making it the leading cause of poisoning-related mortality in many high-income countries (Patel, et al., 2023). Cardiac involvement is a frequent and clinically underappreciated complication that can mimic ACS. The clinical triad of headache, nausea, and altered consciousness may co-exist with chest pain, dyspnea, and troponin elevation, creating a diagnostic challenge that, if unrecognized, leads to inappropriate management.

Patel and colleagues' 2023 retrospective cohort study — the largest dedicated analysis of troponin I in CO poisoning to date — found that among 119 patients with available troponin measurement

within a 900-patient CO cohort, 22 (18.5%) met criteria for myocardial injury based on elevated troponin I. The presence of myocardial injury was strongly associated with in-hospital mortality (OR: 6.82), ICU admission, and mechanical ventilation, confirming the prognostic weight of troponin elevation in this toxidrome. The authors propose that routine troponin measurement be incorporated into the standard ED assessment of all CO-poisoned patients with moderate-to-severe exposure (Patel, et al., 2023).

Taghdiri's 2024 systematic review further demonstrated that combining high-sensitivity troponin I with BNP substantially improves the sensitivity of cardiac injury detection in CO poisoning over either marker alone (Taghdiri, 2024: 9). In pediatric populations, Ipek and colleagues showed that NT-proBNP elevation predicted troponin I positivity with 70% sensitivity and 86% specificity, suggesting a complementary screening role for natriuretic peptides in younger patients (Ipek, et al., 2023: 2457–2466).

Pathophysiology

Carbon monoxide exerts cardiac toxicity through four convergent mechanisms (Park, et al., 2020: 183–189; Patel, et al., 2023). First and most well-known: CO binds hemoglobin with 200–250-fold greater affinity than oxygen, forming carboxyhemoglobin (COHb) and dramatically reducing oxygen-carrying capacity. Because the myocardium operates near its maximal oxygen extraction at rest, even modest reductions in oxygen delivery produce profound cellular energy deficit.

Second, CO binds myoglobin — the primary intracellular oxygen reservoir in cardiomyocytes — impairing intracellular oxygen storage and utilization independent of COHb levels. This explains the well-documented dissociation between COHb levels and the severity of cardiac injury: patients with relatively modest

COHb elevations may sustain significant myocardial damage because myoglobin binding has already depleted cellular oxygen reserves (Park, et al., 2020: 183–189).

Third — and arguably the most important mechanism at the cellular level — CO is a potent inhibitor of mitochondrial cytochrome c oxidase (Complex IV), the terminal electron acceptor of the respiratory chain. This direct mitochondrial blockade halts ATP synthesis and initiates cardiomyocyte necrosis through energy depletion, calcium overload, and intrinsic apoptotic pathway activation. Fourth, CO markedly amplifies reactive oxygen species production, leading to lipid peroxidation, membrane structural damage, and inflammatory cascade initiation (Park, et al., 2020: 183–189).

Kim and colleagues' study of 905 CO patients found a 11.9% incidence of CO-induced cardiomyopathy; hs-cTnI and CK-MB demonstrated high diagnostic accuracy for echocardiographic dysfunction (AUC: 0.894 and 0.874, respectively). Cho and colleagues' 2024 cardiac MRI study revealed that among CO-poisoned patients with troponin elevation, 69.2% had late gadolinium enhancement (LGE) on CMR — suggesting that myocardial fibrosis is far more prevalent in CO poisoning than previously appreciated, with implications for long-term cardiac prognosis (Park, et al., 2020: 183–189).

ECG Findings and Clinical Management

ECG manifestations of CO-induced myocardial injury include: sinus tachycardia (most common), ST-segment changes, T-wave inversions, QTc prolongation, and ventricular arrhythmias. These findings can be indistinguishable from AMI. The key to correct diagnosis is exposure history — including occupational exposure, household gas appliances, or fire-related inhalation —

combined with COHb measurement on co-oximetry (Patel, et al., 2023).

Treatment centers on high-flow normobaric oxygen (100% FiO2 via non-rebreather mask) or hyperbaric oxygen therapy (HBO) in eligible patients. Cardiac management includes serial troponin and ECG monitoring, bedside echocardiography, and cardiology consultation for significant troponin elevation. A critical safety point: in patients with confirmed CO poisoning, troponin elevation alone does not indicate antithrombotic therapy. Such therapy should only be initiated if ACS cannot be excluded after comprehensive evaluation, including correlation with clinical kinetics and echocardiography (Patel, et al., 2023; Taghdiri, 2024: 9).

Acute Pancreatitis

Clinical Importance and Incidence

Acute pancreatitis (AP) is a systemic inflammatory disease in which local pancreatic injury can progress to systemic inflammatory response syndrome (SIRS) and multi-organ dysfunction. Cardiac involvement — manifesting as troponin elevation, ECG changes, and occasionally severe hemodynamic compromise — is increasingly recognized as a clinically important complication (Khan, et al., 2023: 1–11; Yegneswaran, Kostis, & Pitchumoni, 2011: 225 e211–228).

Khan and colleagues' comprehensive 2023 review of 34 individual case reports of AP mimicking ACS — published in Cardiology — systematically characterized the clinical, ECG, and biomarker features of this phenomenon. The inferior wall STEMI pattern was the most frequently reported ECG finding, underscoring the risk of misdiagnosis. The authors specifically warned that erroneous antithrombotic therapy — including thrombolysis — initiated in AP patients misidentified as having STEMI carries

serious hemorrhagic risk, including intra-abdominal bleeding from an inflamed, edematous pancreas (Khan, et al., 2023: 1–11).

Broader epidemiological data on troponin elevation prevalence in AP remain limited, but published series suggest elevations occur in up to 30–54% of patients with severe AP and multi-organ dysfunction. Troponin elevation in this context correlates with AP severity scores and independently predicts ICU requirement and 30-day mortality (Khan, et al., 2023: 1–11; Zaki, et al., 2021: e18637).

Pathophysiological Mechanisms

Multiple overlapping mechanisms underlie myocardial injury in AP. The systemic cytokine storm (TNF-alpha, IL-1beta, IL-6, IL-8) is the dominant driver: activated by the acute-phase inflammatory response, these mediators directly induce cardiomyocyte apoptosis, activate intracellular proteases, and increase sarcolemmal permeability to facilitate troponin release. Oxidative stress generated by activated pancreatic enzymes and inflammatory cells produces reactive oxygen species that cause mitochondrial dysfunction and myocardial lipid peroxidation. Autonomic dysregulation driven by pain and systemic stress triggers catecholamine release, which may exacerbate myocardial injury via adrenergic mechanisms similar to those seen in Takotsubo syndrome (Khan, et al., 2023: 1–11; Zaki, et al., 2021: e18637).

Hemodynamic factors are equally important: fluid sequestration, third-spacing, and capillary leak syndrome can produce significant hypovolemia, reducing coronary perfusion pressure and generating Type 2 MI physiology. Electrolyte disturbances are common in AP — hypokalemia, hypocalcemia, and hypomagnesemia may prolong the QT interval and contribute to ST-segment changes that further complicate ECG interpretation (Zaki, et al., 2021: e18637).

Diagnostic Approach and Clinical Pitfalls

The combination of epigastric pain, nausea/vomiting, and troponin elevation requires active differentiation between AP and ACS. Diagnostic clues favoring AP include: pain predominantly localized to the epigastrium with dorsal radiation, postprandial symptom worsening, abdominal tenderness on examination, and markedly elevated serum lipase (>3 times the upper limit of normal). Abdominal CT with contrast provides the definitive diagnosis of AP and allows severity grading (Khan, et al., 2023: 1–11).

Coronary angiography should be deferred until the clinical and biochemical assessment renders ACS likely rather than possible. If urgent coronary evaluation is genuinely necessary, the procedural approach must account for the hemodynamic instability and coagulopathy that may accompany severe AP. The use of echocardiography in AP patients with troponin elevation is valuable: regional wall motion abnormalities in a coronary distribution favor ischemic etiology, while global or non-coronary-territory dysfunction may suggest non-ischemic cardiomyopathy secondary to SIRS or Takotsubo physiology (Khan, et al., 2023: 1–11; Yegneswaran, Kostis, & Pitchumoni, 2011: 225 e211–228).

Takotsubo Syndrome (Stress Cardiomyopathy)

Definition and Epidemiology

Takotsubo syndrome (TTS) — also known as stress cardiomyopathy, apical ballooning syndrome, or "broken heart syndrome" — is an acute, transient left ventricular (LV) dysfunction syndrome characterized by ECG changes and troponin elevation that clinically mimics ACS, in the absence of obstructive epicardial coronary artery disease. First described in Japan in the 1990s, TTS accounts for approximately 1–3% of all suspected ACS presentations. Women are disproportionately affected, constituting

up to 89.8% of cases in the International Takotsubo Registry (InterTAK); the female-to-male ratio is approximately 5–9:1, with postmenopausal women at highest risk (Ghadri, et al., 2018: 2032–2046; Schweiger, et al., 2024: 1178–1189).

A paradigm shift in understanding TTS has emerged from large registry data: Schweiger and colleagues' 2024 analysis of the InterTAK Registry — the largest TTS cohort in the literature — demonstrated that annual all-cause mortality in TTS is 5.6%, a figure comparable to that of NSTEMI patients. Long-term outcomes across a decade of follow-up are equally sobering, dispelling earlier impressions of TTS as a uniformly benign, self-limiting condition (Schweiger, et al., 2024: 1178–1189).

Pathophysiology

The precise mechanisms of TTS remain incompletely understood. The central hypothesis involves catecholamine excess and sympathetic over-activation. Acute physiological or emotional stress triggers a surge of circulating catecholamines (particularly epinephrine), which interact with beta-2 adrenergic receptors (beta2-AR) predominantly expressed on cardiomyocytes. In the apical myocardium, beta2-AR density is significantly higher than in the basal segments. Excessive catecholamine stimulation at the apex induces G-protein switching (Gs to Gi), cyclic AMP reduction, and negative inotropy, resulting in the characteristic apical hypokinesis or akinesis (Ghadri, et al., 2018: 2032–2046).

Several concurrent mechanisms contribute: epicardial coronary artery vasospasm causing transient ischemia, coronary microvascular dysfunction impairing subendocardial perfusion, direct catecholamine-mediated myocardial stunning, and activation of the brain-heart axis (explaining the high co-occurrence of TTS with neurological events, particularly stroke and SAH). Histologically, myocardial biopsy specimens show contraction band

necrosis and mononuclear inflammatory infiltrates — a pattern more consistent with catecholamine toxicity than atherothrombotic infarction (Ghadri, et al., 2018: 2032–2046).

Biomarker Profile: Differentiation from ACS

The biomarker profile of TTS is diagnostically distinctive and represents one of the most valuable practical tools for distinguishing TTS from ACS at the bedside, prior to coronary angiography (Frohlich, et al., 2012: 328–332; Rallidis, et al., 2024: 22–30).

Troponin in TTS is elevated at presentation but the peak value is disproportionately low relative to the degree of LV dysfunction — a hallmark feature. Pik troponin levels in TTS average approximately 1.6 times the upper reference limit (URL), compared to approximately 6-fold in STEMI patients. This discordance — severe regional wall motion abnormality with modest troponin rise — is the biochemical fingerprint of myocardial "stunning" rather than extensive necrosis (Rallidis, et al., 2024: 22–30).

Conversely, BNP and NT-proBNP are markedly elevated in TTS, reflecting acute LV failure and myocardial wall stress disproportionate to the degree of necrosis. Doyen and colleagues demonstrated a BNP/troponin I ratio of 642 (IQR: 332–1,227) in TTS, compared to 184.5 (IQR: 50.5–372.3) in NSTEMI — with an AUC of 0.98 versus STEMI and 0.81 versus NSTEMI. Froehlich and colleagues demonstrated that the NT-proBNP/myoglobin and NT-proBNP/troponin T ratios provided excellent discrimination between TTS and ACS (Frohlich, et al., 2012: 328–332).

Rallidis and colleagues' 2024 prospective study validated an NT-proBNP/cTnT ratio threshold of ≥7.5 on day 2 — achieving 91% sensitivity and 95% specificity for TTS over ACS — making this

ratio a practical bedside tool applicable even before angiography (Rallidis, et al., 2024: 22–30).

Table 2. Comparison of Biomarker Profiles in Takotsubo Syndrome versus ACS

Biomarker	Takotsubo Syndrome	ACS / AMI
Troponin (presentation)	Elevated, similar to ACS	Elevated
Troponin (peak)	Low (~1.6x URL)	High (~6–8x URL in STEMI)
CK-MB	Minimal elevation	Significant elevation
BNP / NT-proBNP	Markedly elevated	Moderately elevated
BNP/TnI ratio	High: ~642 pg/mcg	Low: ~184.5 (NSTEMI)
NT-proBNP/TnT (day 2)	≥7.5: 91% Sn, 95% Sp for TTS	Low ratio
TnT vs LV dysfunction	Disproportionately low TnT	Proportionate correlation

URL: upper reference limit; TTS: Takotsubo syndrome; Sn: sensitivity; Sp: specificity; LV: left ventricular

InterTAK Diagnostic Score and Diagnostic Criteria

The InterTAK Diagnostic Score assigns points to seven clinical variables: female sex (25 pts), emotional trigger (24 pts), physical trigger (13 pts), absence of ST-segment depression (except

in aVR) (12 pts), psychiatric disorder history (11 pts), neurological disorder history (9 pts), and QTc prolongation (6 pts). A score ≥70 points predicts TTS with approximately 90% probability, providing valuable pre-angiographic decision support (Ghadri, et al., 2018: 2032–2046; Schweiger, et al., 2024: 1178–1189).

Definitive diagnosis requires coronary angiography demonstrating the absence of flow-limiting obstructive disease, combined with left ventriculography or echocardiography confirming a characteristic regional wall motion abnormality extending beyond a single coronary territory. The classic apical ballooning pattern accounts for approximately 80% of cases; mid-ventricular, basal (inverted Takotsubo), and focal patterns represent recognized variants. Cardiac MRI is the gold standard for tissue characterization: TTS typically demonstrates myocardial edema on T2-weighted imaging with absent or minimal late gadolinium enhancement (LGE), distinguishing it from AMI (subendocardial LGE) and myocarditis (midmyocardial or subepicardial LGE) (Ghadri, et al., 2018: 2032–2046; Schweiger, et al., 2024: 1178–1189).

Complications and Prognosis

Life-threatening complications occur in approximately 10–20% of TTS patients, including ventricular arrhythmias (Torsades de Pointes, VF/VT, 3–8.6% of cases — particularly in the subacute phase during QTc prolongation), LV outflow tract obstruction (LVOTO), apical thrombus formation, cardiogenic shock, and acute mitral regurgitation. Recurrence rate is approximately 5% over 10 years; long-term mortality matches that of NSTEMI cohorts, driven primarily by the often serious underlying triggering condition (neurological disease, malignancy, or psychiatric illness) rather than the cardiac syndrome itself (Schweiger, et al., 2024: 1178–1189).

MINOCA: Myocardial Infarction with Non-Obstructive Coronary Arteries

Definition and Prevalence

Myocardial infarction with non-obstructive coronary arteries (MINOCA) is defined as meeting the Fourth Universal Definition criteria for AMI — including troponin elevation with at least one of: ischemic symptoms, new ischemic ECG changes, imaging evidence of new regional wall motion abnormality, or identification of intracoronary thrombus — while coronary angiography demonstrates no epicardial stenosis ≥50% in any major vessel. A third mandatory criterion is the exclusion of a specific diagnosis that clinically accounts for the presentation (PE, myocarditis, Takotsubo syndrome) at the time of initial evaluation (Parwani, et al., 2023: 561–570; Tamis-Holland, et al., 2019: e891–e908).

MINOCA accounts for approximately 5–10% of all AMI presentations, with recent large registry analyses suggesting the figure may be higher in women and younger patients. Demographically, MINOCA disproportionately affects women (>50% of cases in most registries), younger individuals, and patients of Black, Maori, Pacific Islander, and Hispanic ethnicity. MINOCA is a working diagnosis, not a final diagnosis — the underlying ischemic mechanism must be identified through systematic further evaluation (Tamis-Holland, et al., 2019: e891–e908).

Pathophysiological Mechanisms

The pathophysiology of MINOCA is heterogeneous, encompassing both atherosclerotic and non-atherosclerotic ischemic mechanisms (Takahashi, et al., 2024: 17–24).

Atherosclerotic mechanisms in MINOCA include: plaque rupture or plaque erosion with overlying thrombus in a non-obstructive plaque (confirmed by optical coherence tomography

[OCT] or intravascular ultrasound [IVUS] even when angiographically non-obstructive), spontaneous coronary artery dissection (SCAD), and coronary embolism from a proximal cardiac or aortic source. Non-atherosclerotic mechanisms include: epicardial coronary vasospasm (Prinzmetal angina), which may be precipitated by emotional stress, cold exposure, or cocaine use; coronary microvascular dysfunction (CMD) with impaired flow reserve (CFR <2.0) or elevated index of microcirculatory resistance (IMR >25); and oxygen supply-demand mismatch (Type 2 MI physiology).

Takahashi and colleagues' 2024 review emphasized the value of multimodality imaging in elucidating MINOCA mechanisms: OCT detects plaque disruption or SCAD not visible on angiography, while CMR identifies the pattern and extent of myocardial injury to discriminate ischemic (subendocardial LGE) from non-ischemic (midmyocardial LGE in myocarditis) causes. A 2023 meta-analysis found that among patients initially labeled MINOCA, definitive CMR identified myocarditis in 33%, Takotsubo in 18%, other cardiomyopathy in 12%, and confirmed true MI in only 24% — highlighting the diagnostic imperative of CMR in this population (Parwani, et al., 2023: 561–570; Takahashi, et al., 2024: 17–24).

Prognosis

MINOCA was historically regarded as a benign condition; contemporary data refute this assumption. Quesada and colleagues' 2023 study demonstrated that in patients with STEMI-presentation MINOCA, 5-year mortality was actually higher than in obstructive STEMI patients (HR: 1.93), likely reflecting the severity of the underlying precipitating conditions and the absence of targeted secondary prevention. Annual recurrent MI rates of approximately 5–7% have been reported, with major adverse cardiovascular events (MACE) occurring in 10–15% of patients within 3 years (Parwani, et al., 2023: 561–570).

Management

Because MINOCA is a working diagnosis, management must be directed at the underlying ischemic mechanism once identified (Tamis-Holland, et al., 2019: e891–e908). For vasospasm: calcium channel blockers (CCBs) and long-acting nitrates. For CMD: ACE inhibitors, statins, and ranolazine have shown benefit in observational studies. For SCAD: conservative management is preferred over PCI in most cases due to risk of dissection propagation. For plaque-related MINOCA: dual antiplatelet therapy, high-intensity statin, and evidence-based secondary prevention. Observational data support that statin and ACE inhibitor use reduce MACE in unselected MINOCA cohorts. Cardiac MRI should be performed in all MINOCA patients prior to discharge or within 2 weeks when feasible (Kunadian, et al., 2021: 1049–1069).

INOCA: Ischemia with Non-Obstructive Coronary Arteries

Definition and Clinical Relevance

Ischemia with non-obstructive coronary arteries (INOCA) describes a clinical syndrome of recurrent angina or myocardial ischemia with objective evidence of ischemia but no angiographic flow-limiting coronary stenosis (≥50%). While MINOCA is an acute presentation with AMI-level troponin elevation, INOCA encompasses the chronic symptomatic manifestation of the same underlying pathophysiology — and may also produce troponin elevation in acute exacerbations, making it relevant to ED presentations (Kunadian, et al., 2021: 1049–1069).

The two principal pathophysiological subtypes of INOCA are: (1) Microvascular angina (MVA) — impaired coronary flow reserve (CFR <2.0) and/or elevated index of microcirculatory resistance (IMR >25) secondary to structural or functional coronary microvascular dysfunction; and (2) Vasospastic angina (VSA) —

focal or diffuse epicardial or microvascular coronary vasospasm precipitating transient ischemia, classically provoked by emotional stress, cold exposure, or exertion (Kunadian, et al., 2021: 1049–1069).

Diagnostic Evaluation

The 2023 Japanese Society of Cardiology/CVIT/JCC Focused Update — and supporting 2021 ESC guidelines — recommend a structured diagnostic approach to INOCA following exclusion of obstructive coronary disease. After angiography confirms non-obstructive disease, acetylcholine or ergonovine provocation testing identifies vasospasm (sensitivity 80–90%), while adenosine- or papaverine-based coronary physiology assessment (CFR, IMR) quantifies microvascular dysfunction. Cardiac MRI with stress perfusion can detect subendocardial hypoperfusion in CMD even with normal angiography (Hokimoto, et al., 2023: 879–936).

The boundary between INOCA and MINOCA is not always sharp. A patient presenting acutely with troponin elevation and normal angiography (MINOCA) may, on further evaluation, be found to have CMD or VSA — reclassifying the mechanism as INOCA-mediated Type 2 MI. This continuum underscores the importance of functional coronary assessment in all MINOCA patients when anatomical causes (OCT, SCAD, embolism) have been excluded (Hokimoto, et al., 2023: 879–936; Kunadian, et al., 2021: 1049–1069).

Management Principles

INOCA management is mechanism-directed. For MVA: beta-blockers, CCBs, ACE inhibitors, and statins form the pharmacological backbone; ranolazine, nicorandil, and — in refractory cases — coronary sinus reducer may provide additional

relief. For VSA: CCBs are first-line, with long-acting nitrates as second-line; provocative triggers (smoking, cocaine, alcohol, ergot alkaloids, 5-fluorouracil) must be identified and avoided; ICDs may be considered for patients with documented life-threatening arrhythmias associated with vasospasm. The WARRIOR trial provided further support for intensive medical therapy in symptomatic INOCA patients (Hokimoto, et al., 2023: 879–936).

Other Important Causes of Non-ACS Troponin Elevation

Myocarditis

Viral myocarditis — particularly Coxsackievirus B, adenovirus, and SARS-CoV-2 — is one of the most clinically important non-ischemic causes of troponin elevation, particularly in younger patients. The presentation may be indistinguishable from STEMI: acute chest pain, ST-segment elevation, and rising troponin in the absence of obstructive coronary disease. Cardiac MRI using Lake-Louise criteria (T1/T2 elevation indicating edema, early gadolinium enhancement for hyperemia, and late gadolinium enhancement in a non-ischemic midmyocardial or subepicardial distribution) remains the gold standard for diagnosis (Chauin, 2021: 601–617).

Heart Failure Exacerbation

Acute decompensated heart failure (ADHF) frequently causes troponin elevation through increased wall stress, neurohormonal activation, endocardial ischemia from subendocardial malperfusion, and concurrent hypoxemic injury. Troponin elevation in ADHF is an independent predictor of 30-day and 1-year mortality. The presence of troponin elevation in ADHF does not automatically indicate ACS and should not reflexively trigger coronary angiography without additional supporting

evidence. BNP and clinical context guide the distinction (Bhatt, Lopes, & Harrington, 2022: 662–675; Chauin, 2021: 601–617).

Chronic Kidney Disease and Dialysis

Troponin elevation is near-universal in advanced CKD and end-stage renal disease (ESRD). Mechanisms include: reduced renal clearance of troponin fragments (particularly cTnT fragments, which are smaller and more readily accumulate), chronic subclinical myocardial injury from LV hypertrophy and uremic cardiomyopathy, and the proarrhythmic milieu of chronic electrolyte dysregulation. Serial troponin measurement is essential in CKD; an additional delta-cTn rise above the patient's chronic baseline is required to diagnose acute MI in this population (Bhatt, Lopes, & Harrington, 2022: 662–675; Chauin, 2021: 601–617).

Tachyarrhythmias and Hypertensive Emergency

Sustained supraventricular or ventricular tachyarrhythmias increase myocardial oxygen consumption while shortening diastolic filling time, producing supply-demand mismatch-mediated troponin elevation (Type 2 MI). Troponin typically normalizes with rate or rhythm control. Hypertensive emergency produces troponin elevation through increased afterload, subendocardial ischemia from LVH-related microvascular rarefaction, and activation of the renin-angiotensin-aldosterone axis. Both conditions require addressing the primary hemodynamic disturbance rather than initiating anti-thrombotic therapy for the troponin elevation per se (Bhatt, Lopes, & Harrington, 2022: 662–675; Chauin, 2021: 601–617).

Cardiac Contusion

Blunt chest trauma — from motor vehicle collisions, falls, or sports injuries — can cause myocardial contusion with direct cardiomyocyte disruption and troponin elevation. The combination of trauma history, anterior ST changes, echocardiographic RV or LV

wall motion abnormality, and troponin kinetics (proportional to the degree of mechanical injury) guides diagnosis. Coronary angiography is reserved for cases where a traumatically induced coronary dissection or LAD contusion cannot be excluded clinically (Bhatt, Lopes, & Harrington, 2022: 662–675).

Emergency Department Diagnostic Algorithm

Initial Systematic Assessment

When troponin elevation is detected in the ED, a structured approach that does not default to ACS as the only hypothesis is essential. Initial assessment should comprehensively gather: troponin kinetics (serial measurements at 0/1h or 0/2h per ESC protocol), symptom characterization (chest pain quality, location, radiation, onset timing relative to neurological or systemic symptoms), associated system symptoms (dyspnea, abdominal pain, neurological deficits, fever, altered consciousness), relevant history (comorbidities, prior cardiac history, medications, drug/toxin exposures, recent physiological or emotional stressors), 12-lead ECG with attention to dynamic changes and non-coronary-territory patterns, and initial laboratory panel (CBC, metabolic panel, D-dimer, lipase, arterial blood gas, COHb if indicated, BNP/NT-proBNP) (Collet, et al., 2021: 1289–1367; Thygesen, et al., 2018: e618–e651).

Clinical Pattern Recognition

Several clinical phenotypes should trigger immediate reconsideration of the ACS hypothesis. Troponin elevation with focal neurological deficit or altered consciousness: prioritize cerebrovascular event, rule out stroke/SAH before proceeding with cardiac workup. Troponin elevation with pleuritic chest pain, dyspnea, hypoxia, and elevated D-dimer: CTPA for PE before coronary angiography. Troponin elevation with epigastric pain and

elevated lipase: AP must be excluded before any ACS-directed intervention. Troponin elevation with COHb > 10% or CO exposure history: CO poisoning — treat with oxygen therapy, defer anti-thrombotic decisions. Troponin elevation with acute onset severe headache (thunderclap): SAH until proven otherwise — urgent CT head and neurosurgery before any coronary intervention.

Advanced Cardiac Imaging

In patients where non-ACS etiology is suspected or coronary angiography demonstrates non-obstructive disease (MINOCA working diagnosis), cardiac MRI should be performed as the definitive imaging modality. CMR provides tissue characterization that is critical for distinguishing: ischemic injury (subendocardial LGE in coronary distribution — confirms MINOCA of ischemic mechanism), myocarditis (midmyocardial or subepicardial LGE — excludes MINOCA, establishes inflammatory diagnosis), Takotsubo syndrome (apical myocardial edema on T2 with absent or minimal LGE), and stress-related cardiomyopathy with neurogenic substrate. Functional coronary physiology testing (CFR, IMR, acetylcholine provocation) should be considered in MINOCA patients without ischemic CMR findings to evaluate for CMD and vasospasm (Parwani, et al., 2023: 561–570; Takahashi, et al., 2024: 17–24).

Discussion: Clinical Implications and Diagnostic Pitfalls

The integration of high-sensitivity troponin assays into emergency medicine has unquestionably improved the speed and accuracy of AMI diagnosis. However, their exquisite sensitivity has simultaneously rendered troponin a non-specific signal that requires rigorous clinical contextualization. The "troponin positive = ACS" heuristic, which dominated ED management for decades, is now demonstrably inadequate and potentially harmful (Chauin, 2021: 601–617; Savic, et al., 2025).

Several pitfalls deserve specific emphasis. In cerebrovascular emergencies, the simultaneous occurrence of neurological and cardiac crises can create competing diagnostic urgencies. EMS and triage protocols that automatically redirect stroke patients to catheterization laboratories based on troponin and ST elevation — without cranial CT — risk catastrophic intervention in SAH or hemorrhagic stroke. The clinical principle that headache preceding chest pain or ECG change should prompt CT head before ECG-guided catheterization deserves broad dissemination (Zahid, et al., 2020: e9792).

In Takotsubo syndrome, the BNP-to-troponin disproportion and the non-coronary-territory wall motion pattern are powerful bedside discriminators that are widely underutilized. Similarly, the InterTAK score, though not validated for emergency settings specifically, provides a structured clinical framework applicable even without angiography. The emotional or physical trigger — elicited only if specifically asked — is present in the majority of TTS patients (Ghadri, et al., 2018: 2032–2046; Schweiger, et al., 2024: 1178–1189).

In MINOCA, the historic tendency to reassure patients that their "angiogram was clean" and discharge them without further workup has been replaced — too slowly — by recognition that these patients carry meaningful risk and deserve CMR, functional coronary testing, and tailored secondary prevention. The WARRIOR trial and observational data supporting statin/ACE inhibitor use provide a framework, but evidence remains sparse compared to obstructive CAD (Parwani, et al., 2023: 561–570; Tamis-Holland, et al., 2019: e891–e908).

Carbon monoxide poisoning illustrates the catastrophic consequences of missed non-cardiac troponin elevation from a different angle: a patient presenting with altered consciousness,

troponin elevation, and ST changes following a house fire may be inappropriately anticoagulated or referred for urgent PCI without the clinician recognizing CO as the etiology. CO oximetry should be reflexively obtained in all troponin-positive patients with exposure to confined spaces, heating systems, or fire-related products (Patel, et al., 2023).

Conclusion

Troponin elevation is a sensitive and clinically indispensable marker of myocardial injury but is not a specific marker for acute coronary syndrome. As the complexity of hs-cTn interpretation in the ED has grown, so has the imperative for clinicians to move beyond a binary ACS/non-ACS framework and engage with the full spectrum of conditions that generate myocardial damage.

The conditions reviewed in this chapter — cerebrovascular events, pulmonary embolism, sepsis, hypoxia, carbon monoxide poisoning, acute pancreatitis, Takotsubo syndrome, MINOCA, and INOCA — each have distinct pathophysiological mechanisms, characteristic biomarker profiles, and specific management implications. Recognition of these patterns prevents diagnostic errors with potentially life-threatening consequences: antithrombotic therapy in acute pancreatitis or CO poisoning, invasive angiography in SAH, or reassurance without further workup in MINOCA (Savic, et al., 2025; Thygesen, et al., 2018: e618–e651).

The ideal approach to non-ACS troponin elevation integrates serial biomarker kinetics, clinical context, 12-lead ECG interpretation, bedside echocardiography, and — when indicated — cardiac MRI with functional coronary physiology testing. As diagnostic technologies continue to evolve and MINOCA/INOCA registries accumulate long-term data, individualized, mechanism-directed management will become increasingly achievable for this heterogeneous and clinically important population.

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ARRHYTHMIAS AND ACUTE CLINICAL DETERIORATION TACHYARRHYTHMIAS REQUIRING CARDIOVERSION AND BRADYCARDIA SYNDROMES REQUIRING INTERVENTION IN THE EMERGENCY SETTING

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Arrhythmia Management in Hemodynamic Compromise

Cardiac arrhythmias causing hemodynamic compromise represent some of the most time-critical presentations in emergency medicine. The fundamental question — whether the arrhythmia is *causing* the hemodynamic deterioration, or whether the deterioration is coexisting with it — shapes the entire management pathway. A structured approach grounded in physiological principles and supported by current guideline evidence is essential for providers managing these patients in the prehospital and emergency department settings (Al-Khatib, et al., 2018: e210–e271; Panchal, et al., 2020: S366–S468).

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Is It the Rhythm or the Rate That Kills?

The clinical question of whether the rhythm or the rate is primarily responsible for hemodynamic instability is not academic — it has direct and immediate therapeutic implications. Most hemodynamic instability attributed to arrhythmias is mediated by one or more of three core pathophysiological mechanisms (Al-Khatib, et al., 2018: e210–e271; Stevenson & Perloff, 1989: 884–888).

Loss of Atrioventricular Synchrony: In conditions such as complete heart block, ventricular pacing, or junctional rhythms, the atrial contribution to ventricular filling — accounting for 15–30% of cardiac output under normal conditions and up to 50% in a stiff, hypertrophied, or diastolic-dysfunctional ventricle — is lost. The consequence is a reduction in stroke volume and cardiac output that may be tolerated in a structurally normal heart but can be catastrophic in hypertrophic cardiomyopathy or severe LV diastolic dysfunction (Al-Khatib, et al., 2018: e210–e271; Stevenson & Perloff, 1989: 884–888).

Inadequate Diastolic Filling Time: Tachycardia — regardless of its mechanism — reduces diastolic duration disproportionately relative to systole. At heart rates exceeding 150 bpm, diastolic filling time is critically abbreviated, reducing left ventricular end-diastolic volume and stroke volume by the Frank-Starling mechanism. The threshold at which rate alone becomes hemodynamically significant varies with diastolic compliance: in the setting of LV hypertrophy, acute ischemia, or HFpEF, rates exceeding 110–120 bpm can precipitate acute pulmonary edema. In atrial fibrillation, the additional loss of atrial kick compounds the hemodynamic impairment (Panchal, et al., 2020: S366–S468; Stevenson & Perloff, 1989: 884–888).

Loss of Hemodynamically Effective Contractions: In ventricular fibrillation, polymorphic VT, or atrial flutter with very rapid ventricular response, coordinated ventricular contraction is absent or severely disorganized; cardiac output drops precipitously and cannot be sustained regardless of any measured rate. These arrhythmias constitute hemodynamic emergencies independent of any rate measurement (Al-Khatib, et al., 2018: e210–e271; Panchal, et al., 2020: S366–S468).

The emergency clinician's cardinal discriminator is not arrhythmia mechanism identification, but hemodynamic stability assessment. Hemodynamic instability — defined as systolic BP < 90 mmHg, altered mental status, signs of acute pulmonary edema, or ischemic chest pain attributable to the arrhythmia — mandates immediate electrical therapy irrespective of arrhythmia diagnosis. Any attempt to pharmacologically identify the arrhythmia mechanism in an unstable patient wastes critical minutes and may precipitate further hemodynamic collapse. This principle cannot be overstated and is foundational to all modern advanced cardiac life support training (Kotalczyk, Lip, & Calkins, 2021: 65–67; Panchal, et al., 2020: S366–S468).

Synchronized Cardioversion: Indications, Energy, and Technique

Synchronized direct-current cardioversion (DCCV) delivers a precisely timed electrical shock synchronized to the R wave of the QRS complex, avoiding discharge during the vulnerable T-wave period that could induce ventricular fibrillation. This precise synchronization is the critical technical distinction between cardioversion — used for organized tachyarrhythmias — and defibrillation — used for VF or pulseless VT (Al-Khatib, et al., 2018: e210–e271; Page, et al., 2016: e471–505).

Absolute Indications for Immediate Synchronized Cardioversion:

— Sustained VT with hemodynamic instability (systolic BP < 90 mmHg, altered consciousness, ischemic chest pain, acute pulmonary edema)

— Atrial fibrillation with rapid ventricular response causing acute hemodynamic compromise

— Atrial flutter with hemodynamic compromise

— Supraventricular tachycardia refractory to vagal maneuvers and adenosine with associated hemodynamic instability

Energy Protocols: For atrial fibrillation, biphasic energies of 120–200 J are recommended as the initial shock; monophasic protocols begin at 200 J and escalate to 360 J. For atrial flutter and SVT, initial energies of 50–100 J biphasic are typically sufficient for termination. Monomorphic VT responds to 100 J initial biphasic shock with escalation if unsuccessful. For synchronization to function reliably, the defibrillator must clearly identify QRS complexes; if QRS amplitude is insufficient, repositioning leads, increasing gain, or switching to a different lead configuration improves signal recognition (Page, et al., 2016: e471–505; Panchal, et al., 2020: S366–S468).

Pre-Cardioversion Checklist (Elective/Semi-Elective Settings)

— AF duration: < 48 hours vs. ≥ 48 hours. AF of ≥ 48 hours duration requires either 3 weeks of therapeutic anticoagulation prior to cardioversion, or transesophageal echocardiography to exclude left atrial appendage thrombus, followed by cardioversion and at least 4 weeks of post-cardioversion anticoagulation regardless of CHA_2DS_2-VASc score.

— Electrolyte correction: Hypokalemia and hypomagnesemia increase post-cardioversion arrhythmia recurrence and proarrhythmic risk. Correct to $K^+ > 4.0$ mEq/L and $Mg^{2+} \geq 2.0$ mEq/L prior to elective cardioversion.

— Digoxin toxicity: Cardioversion in digoxin-toxic patients carries high risk of refractory ventricular fibrillation. Toxicity should be excluded or treated before elective cardioversion.

— Procedural sedation: IV propofol (0.5–1.5 mg/kg), etomidate (0.15–0.3 mg/kg), or midazolam (1–3 mg) with fentanyl (1–2 μg/kg) is required for all non-emergency cardioversions.

When Cardioversion Fails: Strategies to improve DCCV success include: increasing energy to maximum device output; repositioning pads to anterior-posterior position (left parasternal 4th ICS anteriorly, inferior left scapular region posteriorly — this position reduces transthoracic impedance by 20–30%); pharmacological pretreatment to lower the defibrillation threshold (ibutilide 1 mg IV, amiodarone, or flecainide in structurally normal heart); and repeating cardioversion after 10–15 minutes. Patients with recurrent immediate reinitiation of AF after successful cardioversion may benefit from antiarrhythmic drug preloading (Joglar, et al., 2024: e1–e156; Page, et al., 2016: e471–505).

***Table 1**: Emergency Synchronized Cardioversion: Energy Recommendations and Clinical Priorities*

Arrhythmia	Initial Energy (Biphasic)	If Failure	Priority Caveat
Atrial fibrillation	120–200 J	Escalate to 200 J; A-P pads	Anticoagulation before elective CV
Atrial flutter	50–100 J	Escalate to 200 J	Often very low energy responsive
AVNRT / AVRT (SVT)	50–100 J	Escalate; consider IV adenosine first if stable	Vagal maneuvers first if stable
Monomorphic VT	100 J	Escalate to 200 J; amiodarone pre-treatment	Do NOT give verapamil/diltiazem
Polymorphic VT / VF	200 J (unsynchronized)	Escalate to max; CPR; amiodarone	Immediate defibrillation; check QT

Wide QRS Tachycardias: VT vs. SVT — A Practical Approach

Wide complex tachycardia (WCT), defined as a regular or irregular tachycardia with QRS duration ≥ 120 ms, represents one of

the highest-stakes diagnostic challenges in acute medicine. The differential diagnosis encompasses: ventricular tachycardia (VT), supraventricular tachycardia (SVT) with bundle branch block (BBB), SVT with rate-dependent aberrant conduction, pre-excited tachycardia (antidromic AVRT or AF over an accessory pathway), and drug- or electrolyte-induced QRS widening. The therapeutic consequences of misclassification can be fatal (Kashou, et al., 2022: 32–39; Moccetti, et al., 2022: 831–839; Wellens, 2001: 579–585).

The cardinal rule of WCT management: In any patient with WCT of unknown etiology, the presumptive diagnosis is ventricular tachycardia until proven otherwise (Moccetti, et al., 2022: 831–839). VT accounts for approximately 80% of all regular WCTs encountered in the emergency setting, rising to > 90% in patients with known structural heart disease or prior myocardial infarction. The catastrophic consequence of administering AV nodal blocking agents — calcium channel blockers, digoxin, adenosine in the wrong context — to a patient with VT mandates that every WCT be assumed to be VT unless definitive evidence excludes it (Kashou, et al., 2022: 32–39; Wellens, 2001: 579–585).

Clinical Context: Prior Probability of VT vs. SVT with Aberrancy

The clinical presentation substantially modifies the prior probability of VT versus SVT with aberrancy:

Clinical features strongly favoring VT: History of ischemic cardiomyopathy or dilated cardiomyopathy; prior myocardial infarction; history of sustained VT; prior ICD with documented VT therapies; age > 70 years; known left ventricular dysfunction; prior cardiac surgery including CABG or valve repair; hemodynamic instability (Moccetti, et al., 2022: 831–839).

Clinical features favoring SVT with aberrancy: Young age without structural heart disease; known pre-existing BBB identical to the WCT morphology; prior documented SVT with aberrancy; prior documented LBBB or RBBB with identical morphology on baseline ECG; tachycardia terminating with vagal maneuver (Kashou, et al., 2022: 32–39).

ECG Diagnostic Algorithms: From Brugada to Basel

The Brugada Algorithm (1991) — Sequential Four-Step Analysis

The most historically validated and widely known WCT algorithm (Brugada, et al., 1991: 1649–1659; Sun, et al., 2023: e069273). Applied sequentially — if any step diagnoses VT, no further criteria are assessed:

Step 1: Absence of RS complex in *all* precordial leads V1–V6 → VT. An RS pattern requires at least one dominant positive then negative deflection. If all precordial leads show only R, QS, or QR morphologies without an RS transition, VT is confirmed at this step.

Step 2: In any precordial lead with an RS complex: the interval from onset of R wave to the nadir of the S wave > 100 ms → VT. This criterion reflects the slow, cell-to-cell myocardial conduction characteristic of ventricular ectopic activation, contrasting with the rapid Purkinje-mediated conduction of SVT.

Step 3: AV dissociation demonstrable on ECG → VT. This is pathognomonic when present. Manifestations include: visible P waves at a rate independent of QRS complexes; capture beats (a narrow QRS complex appearing during VT when a sinus impulse captures the ventricle before the next VT beat); and fusion beats (intermediate-morphology QRS complexes created when a sinus impulse fuses with a VT complex).

Step 4: QRS morphology criteria in V1 and V6 examining for features atypical of bundle branch block morphology → VT if morphology is inconsistent with classic BBB. This is the most complex step: for RBBB-pattern WCT, VT is suggested by a monophasic R in V1 or qR in V1, and by R < S in V6; for LBBB-pattern WCT, VT is suggested by R duration > 30 ms, notching on the S-wave downstroke in V1, or any Q wave in V6 (Brugada, et al., 1991: 1649–1659; Sun, et al., 2023: e069273).

Original published accuracy: sensitivity 98.7%, specificity 96.5% for VT. Real-world accuracy in subsequent validation studies: 77–85%, reflecting difficulty in applying Step 4 morphological criteria under time pressure in acute settings (Brugada, et al., 1991: 1649–1659; Sun, et al., 2023: e069273; Vereckei, et al., 2008: 89–98).

The Vereckei Algorithm (2008) — Lead aVR Only

A simplified, single-lead algorithm assessing only lead aVR, designed for more rapid application:

Step 1: Initial positive (R) deflection in aVR → VT.

Step 2: Initial q or r wave width > 40 ms in aVR → VT.

Step 3: Notching on the descending limb of an initially entirely negative QRS in aVR → VT.

Step 4: Ventricular activation-velocity ratio (Vi/Vt): measure the vertical excursion (in mV) during the initial 40 ms (Vi) and the terminal 40 ms (Vt) of the QRS in aVR. If Vi/Vt ≤ 1 → VT; if Vi/Vt > 1 → SVT with aberrancy. Reported overall test accuracy 91.5%; superior to the Brugada algorithm in some studies by virtue of its single-lead design, though Step 4 remains technically demanding at the bedside (Vereckei, et al., 2007: 589–600, 2008: 89–98).

The Basel Algorithm (2022) — Three Criteria, Two Needed for VT

Developed and validated by Moccetti, Reichlin, and colleagues at the University of Basel in 2022, specifically designed to maximize practical applicability in emergency settings for non-electrophysiologists (Moccetti, et al., 2022: 831–839). VT is diagnosed when ≥ 2 of the following 3 criteria are met:

Criterion 1 — Clinical High-Risk Features: Any of the following: age > 70 years; known coronary artery disease or prior MI; history of heart failure with reduced EF; prior sustained VT; ICD in situ.

Criterion 2 — Lead II Time to First Peak > 40 ms: Measured from QRS onset to the first peak or nadir in lead II.

Criterion 3 — Lead aVR Time to First Peak > 40 ms: Measured from QRS onset to the first peak or nadir in lead aVR.

Diagnostic performance in the derivation cohort (206 WCTs, EP-confirmed): sensitivity 92%, specificity 89%, accuracy 91%. In the external validation cohort (203 consecutive WCTs): sensitivity 93%, specificity 90%, accuracy 93%. Importantly, the Basel algorithm showed *comparable* diagnostic accuracy to the Brugada and Vereckei algorithms but significantly faster diagnosis time: median 36 seconds vs. 105 seconds for Brugada ($p = 0.002$). This time advantage is clinically meaningful in acute situations. The algorithm is also suitable for incorporation into automated ECG interpretation software given its reliance on only two limb leads (Moccetti, et al., 2022: 831–839).

Table 2: *Comparison of WCT Differentiation Algorithms in Clinical Practice*

Algorithm	Year	Key Feature	Real World Accuracy	Practical Limitation
Brugada	1991	4 sequential precordial + morphological criteria	77–85%	Complex; time-consuming; Step 4 difficult
Vereckei (aVR)	2008	4 sequential steps, lead aVR only	~82–91%	Vi/Vt measurement challenging bedside
Basel	2022	2 of 3 criteria: clinical + lead II + aVR peaks	91–93%	Clinical criterion subjective; needs validation in diverse populations
Limb Lead (Chen)	2020	Q waves in inferior leads	~88%	Limited data on diverse WCT types

ECG Features: High-Yield Bedside Indicators

Table 3: *High-Yield ECG Features for VT vs. SVT with Aberrancy*

ECG Feature	Suggests VT	Suggests SVT with Aberrancy
AV Dissociation	Pathognomonic when visible (P waves independent of QRS)	Not present
Capture Beats	Narrow QRS among wide QRS complexes — diagnostic	Not present
Fusion Beats	Intermediate morphology QRS — diagnostic	Not present
Precordial Concordance	All V1–V6 positive or all negative	Never concordant
QRS Duration	> 140 ms (RBBB-pattern) or > 160 ms (LBBB-pattern)	Typically < 140 ms
QRS Axis	Extreme NW axis (−90° to ±180°)	Typically −60° to +120°
Lead aVR (initial)	Dominant initial R wave	Dominant initial negativity
RS Interval	> 100 ms in any precordial lead (Brugada Step 2)	≤ 100 ms in all leads
V6 in LBBB-Pattern	QR or RS complex (any Q wave pathological)	Broad monophasic R, no Q
Josephson Sign	Notch near S-wave nadir in precordial leads	Absent

The Adenosine Trap: When Adenosine Caused Harm

Adenosine (6–12 mg rapid IV push) is a rational initial pharmacological approach to a hemodynamically stable, regular narrow-complex tachycardia when SVT is suspected (Al-Khatib, et al., 2018: e210–e271; Moccetti, et al., 2022: 831–839; Panchal, et al., 2020: S366–S468). Its administration in WCT, however, carries significant and potentially lethal risks:

Scenario 1 — VT Misdiagnosed as SVT with Aberrancy: Adenosine does not terminate VT. Its administration causes profound transient hypotension that may unmask or worsen hemodynamic compromise. More critically, by causing transient high-degree AV block, adenosine may unmask an underlying AF with accessory pathway, allowing all impulses to conduct via the fast accessory pathway — potentially precipitating VF (Moccetti, et al., 2022: 831–839).

Scenario 2 — Pre-excited AF (AF with WPW) — A Potentially Fatal Error: In patients with atrial fibrillation conducting rapidly over an accessory pathway, the irregular, wide-complex tachycardia may superficially resemble VT but is, in fact, AF with pre-excitation. Adenosine blocks the AV node and causes *all* atrial impulses to conduct exclusively via the accessory pathway, dramatically accelerating the ventricular rate — sometimes to 300–400 bpm — and precipitating hemodynamic collapse and VF. The distinguishing ECG feature is **irregularity** of the QRS complexes and varying QRS morphology, reflecting varying degrees of fusion between normal AV nodal conduction and accessory pathway conduction. Pre-excited AF is an absolute contraindication to adenosine, verapamil, diltiazem, and digoxin (Moccetti, et al., 2022: 831–839).

The PROCAMIO Trial (Ortiz et al., Eur Heart J 2017): The only randomized controlled trial comparing pharmacological

management strategies for stable WCT. In 74 patients with hemodynamically tolerated WCT (presumed VT), IV procainamide (10 mg/kg over 20 min) was compared with IV amiodarone (5 mg/kg over 20 min). The primary endpoint — major cardiac adverse events within 40 minutes — occurred in 9% of procainamide patients versus 41% of amiodarone patients (OR 0.1; 95% CI 0.03–0.6; p = 0.006). Tachycardia terminated within 40 minutes in 67% of procainamide vs. 38% of amiodarone patients (OR 3.3; p = 0.026). This landmark trial establishes procainamide as the preferred pharmacological agent for hemodynamically stable WCT of uncertain or ventricular origin when electrical cardioversion is deferred (Ortiz, et al., 2017: 1329–1335).

Practical Management Algorithm

Table 4: *Management Algorithm for Wide QRS Tachycardia by Hemodynamic Status*

Clinical Scenario	Immediate Action	Agent of Choice	Strict Avoidance
ANY WCT + hemodynamic instability	Immediate synchronized DCCV 100–200 J	Electrical cardioversion — no delay	No pharmacological diagnosis attempt
Stable WCT — VT confirmed or high probability (SHD, positive VT criteria)	IV procainamide or amiodarone; prepare defibrillation	Procainamide 10 mg/kg over 20 min (PROCAMIO); amiodarone 150 mg over 10 min	Verapamil, diltiazem, digoxin, adenosine

Clinical Scenario	Immediate Action	Agent of Choice	Strict Avoidance
Stable WCT — SVT with BBB suspected (no SHD, meets SVT criteria)	Vagal maneuvers first; then adenosine 6–12 mg IV	Adenosine; if SVT confirmed: verapamil or metoprolol	If VT not excluded: NO verapamil
Irregular WCT — Pre-excited AF suspected (varying morphology)	DCCV if unstable; procainamide/ibutilide if stable	IV procainamide 10 mg/kg or ibutilide 1 mg	ABSOLUTE: adenosine, verapamil, diltiazem, digoxin

Acute Atrial Fibrillation: Rate or Rhythm Control?

Atrial fibrillation (AF) is the most prevalent sustained cardiac arrhythmia globally, affecting more than 37 million individuals. In the emergency setting, AF accounts for a significant proportion of all arrhythmia-related presentations, and the decision between rate control and rhythm control remains among the most clinically nuanced in acute medicine. The 2020 ESC Guidelines on Atrial Fibrillation and the 2023 ACC/AHA/ACCP/HRS Guideline for Diagnosis and Management of Atrial Fibrillation represent the most contemporary evidence-based frameworks for this decision (Joglar, et al., 2024: e1–e156; Kotalczyk, Lip, & Calkins, 2021: 65–67).

The 2020 ESC Framework: ABC Pathway and the 4S-AF Scheme

The 2020 ESC AF Guidelines introduced a paradigm shift from arrhythmia-centric treatment to a holistic, patient-centered

framework using the 'ABC' integrated care pathway(Kotalczyk, Lip, & Calkins, 2021: 65–67; Potpara, et al., 2021: 270–278).

A — Anticoagulation / Avoid Stroke: Stroke risk assessment using the CHA_2DS_2-VASc score. Oral anticoagulation — preferably a NOAC (non-vitamin K oral anticoagulant) — is recommended for men with score ≥ 1 and women with score ≥ 2. The reduction in stroke risk from anticoagulation is the single most important intervention in AF management.

B — Better Symptom Management: Rate control versus rhythm control decision, individualized to patient symptoms (EHRA symptom classification), clinical profile, age, and comorbidities. The 2020 ESC Guidelines affirm that both strategies are acceptable for most patients but emphasize the emerging role of early rhythm control.

C — Cardiovascular Risk and Comorbidity Optimization: Treatment of hypertension, diabetes, obesity, obstructive sleep apnea, and alcohol consumption, all of which are independently associated with AF progression, recurrence after cardioversion, and response to antiarrhythmic therapy.

The complementary **4S-AF scheme** (Stroke risk, Symptoms, Severity of AF burden, Substrate) provides comprehensive characterization of each patient's individual AF phenotype, moving beyond the simple rate-versus-rhythm binary to guide individualized management (Potpara, et al., 2021: 270–278).

The EAST-AFNET 4 Trial: The Case for Early Rhythm Control

A landmark shift in AF management was catalyzed by the EAST-AFNET 4 trial (Kirchhof et al., N Engl J Med, 2020). In this international, investigator-initiated, randomized, blinded-outcome-assessment trial, 2,789 patients with recently diagnosed AF (≤ 12 months prior to enrollment) and at least two cardiovascular risk

factors were randomized to early systematic rhythm control versus usual care (predominantly rate control) (Kirchhof, et al., 2020: 1305–1316).

Over a median follow-up of 5.1 years, early rhythm control was associated with a significantly lower risk of the composite primary endpoint of cardiovascular death, stroke, hospitalization for heart failure, or hospitalization for acute coronary syndrome (HR 0.79; 95% CI 0.66–0.94; p = 0.005). Importantly, the benefit was present regardless of symptom status at baseline — challenging the long-held assumption that rhythm control is only beneficial for symptomatic patients. A subsequent mediation analysis demonstrated that the presence of sinus rhythm at 12 months accounted for 81% of the treatment effect of early rhythm control. This trial has fundamentally altered the threshold for pursuing rhythm control and is the evidence base for the 2022 ACC/AHA AF guideline upgrade of early rhythm control to a Class IIa recommendation (Eckardt, et al., 2022: 4127–4144; Kirchhof, et al., 2020: 1305–1316).

Emergency Decision Framework: Rate vs. Rhythm in Acute AF

Table 5: *Emergency Rate vs. Rhythm Control Decision Framework in Acute AF*

Clinical Scenario	Strategy	First-Line Agent	Key Principle
AF + hemodynamic instability (any duration)	Immediate DCCV	Biphasic DCCV 120–200 J	No delay; no pharmacology first

Clinical Scenario	Strategy	First-Line Agent	Key Principle
AF < 48h, stable, symptomatic, no SHD	Rhythm control (pharmacological or electrical)	Flecainide 2 mg/kg IV or 200–300 mg PO; vernakalant 3 mg/kg IV	Anticoagulate before/after; no flecainide if SHD
AF < 48h, stable, SHD present	Rhythm control with safe agents	IV amiodarone 5 mg/kg over 1h	Avoid flecainide/propafenone in SHD
AF ≥ 48h or unknown duration, stable	Rate control pending anticoagulation; delayed DCCV	IV metoprolol 2.5–5 mg or diltiazem 0.25 mg/kg	TEE or 3w anticoagulation before cardioversion
AF + HFrEF (LVEF < 40%)	Rate control; amiodarone if rhythm control needed	IV amiodarone or digoxin; avoid CCBs	Beta-blockers safe only if compensated HF
Pre-excited AF / AF + WPW	DCCV if unstable; procainamide/ibutilide if stable	IV procainamide 10 mg/kg	NEVER AV nodal blockers — risk of VF
Postoperative AF (cardiac surgery)	Rate control; spontaneous reversion common	IV metoprolol or amiodarone	70% spontaneous reversion within 24–48h

Who Should Undergo Acute Rhythm Restoration?

The 2020 ESC and 2023 ACC/AHA/ACCP/HRS guidelines identify the following as candidates for early cardioversion (Joglar, et al., 2024: e1–e156; Kotalczyk, Lip, & Calkins, 2021: 65–67).

Strong Candidates for Cardioversion: (1) First-detected or recent-onset AF (< 48 hours) with significant symptoms; (2) AF clearly precipitating acute heart failure or hemodynamic compromise; (3) younger patients with no significant atrial substrate; (4) AF of < 48 hours duration with adequate anticoagulation coverage; (5) patients in whom rhythm control is preferred as long-term strategy (EAST-AFNET 4 criteria: recent AF, ≤ 12 months, with cardiovascular risk factors) (Joglar, et al., 2024: e1–e156; Kirchhof, et al., 2020: 1305–1316; Kotalczyk, Lip, & Calkins, 2021: 65–67).

Rate Control Preferred: (1) AF of uncertain or prolonged duration without TEE exclusion of left atrial appendage thrombus or adequate anticoagulation; (2) elderly patients with minimal symptoms and high recurrence risk (large LA > 55 mm, significant mitral valve disease, extensive atrial fibrosis); (3) patient preference for rate control; (4) permanent AF classification (Kotalczyk, Lip, & Calkins, 2021: 65–67).

Wait-and-Watch Strategy: Endorsed by the 2020 ESC Guidelines for hemodynamically stable patients with recent-onset AF (< 48 hours). The RACE 7 ACWAS trial (Pluymaekers et al., NEJM 2019) demonstrated that 69% of patients with AF < 48 hours spontaneously reverted to sinus rhythm within 48 hours of observation with rate control alone. A period of monitored observation with rate control therapy before committing to active cardioversion is therefore a reasonable, guideline-supported strategy in stable patients, avoiding unnecessary procedural risk and sedation (Pluymaekers, et al., 2019: 1499–1508).

Rate Control Agents in the Emergency Setting

Target resting heart rate for rate control: < 110 bpm as a lenient strategy (validated by the RACE II trial); tighter control to < 80 bpm may be appropriate for symptomatic patients (Kotalczyk, Lip, & Calkins, 2021: 65–67).

Beta-blockers: IV metoprolol 2.5–10 mg over 2 minutes (repeat up to 3 doses); oral bisoprolol or metoprolol succinate for maintenance. First-line for most hemodynamically stable patients. Avoid in acute decompensated HF, bronchospasm, or high-degree AV block.

Non-DHP Calcium Channel Blockers: IV diltiazem 0.25 mg/kg over 2 min (repeat 0.35 mg/kg); IV verapamil 2.5–10 mg. Contraindicated in HFrEF (LVEF < 40%), pre-excited AF, and cardiogenic shock.

Digoxin: IV loading 0.25–0.5 mg; slower onset; predominantly effective at rest; less effective during adrenergic states. Useful adjunct or sole agent in HFrEF where beta-blockers and CCBs are not tolerated (Kotalczyk, Lip, & Calkins, 2021: 65–67).

Amiodarone: IV 300 mg over 1 hour (then 900 mg over 24h); provides combined rate and rhythm control properties. Preferred in AF with acute HF or when other agents are contraindicated. Also appropriate when rhythm control is the ultimate goal (Kotalczyk, Lip, & Calkins, 2021: 65–67).

Pharmacological Cardioversion: Agent Selection

Pharmacological cardioversion is most effective when AF duration is < 48 hours (Kotalczyk, Lip, & Calkins, 2021: 65–67; Page, et al., 2016: e471–505).

Flecainide (2 mg/kg IV over 10 min, or 200–300 mg oral 'pill-in-the-pocket'): Highly effective for recent-onset AF without structural heart disease; conversion rates 70–90% within 6 hours. Contraindicated in ischemic heart disease, reduced LVEF, and significant conduction abnormalities.

Propafenone (2 mg/kg IV over 10 min, or 450–600 mg oral): Similar efficacy and contraindications to flecainide. The Class Ic agents are particularly attractive for the pill-in-the-pocket approach for self-cardioversion in paroxysmal AF patients.

Amiodarone (5–7 mg/kg IV over 1–2 hours): Lower acute conversion rate (40–60% at 24 hours) but safe across all structural heart disease substrates. The agent of choice when flecainide and propafenone are contraindicated (Kotalczyk, Lip, & Calkins, 2021: 65–67).

Ibutilide (1 mg IV over 10 min; repeat once): Effective for AF and flutter (60–90%); QT-prolongation and torsades de pointes risk (2–4%); continuous monitoring for 4 hours post-administration required (Page, et al., 2016: e471–505).

Vernakalant (3 mg/kg IV over 10 min; repeat 2 mg/kg): Atrial-selective Kv1.5 channel blocker; approved in Europe for recent-onset AF < 7 days. Faster cardioversion than amiodarone: 51.7% vs. 5.2% termination at 90 min in the AVRO trial (Joglar, et al., 2024: e1–e156).

Bradyarrhythmias and AV Conduction Disorders

Bradyarrhythmias — encompassing all conditions with pathologically slow heart rates (< 60 bpm) or with significant AV conduction delay — span a clinical spectrum from asymptomatic findings requiring no treatment to hemodynamic collapse requiring emergency pacing. The 2018 ACC/AHA Guideline on the Evaluation and Management of Patients With Bradycardia and

Cardiac Conduction Delay and the 2021 ESC Guidelines on Cardiac Pacing provide the current framework for emergency management (Glikson, et al., 2022: 71–164; Kusumoto, et al., 2019: e51–e156).

Classification: From Sinus Node to Infra-Hisian

Sinus Node Dysfunction (SND): Encompasses sinus bradycardia, sinus arrest, sinoatrial exit block, and tachycardia-bradycardia syndrome. In the emergency setting, symptomatic SND presenting with hemodynamic compromise requires treatment regardless of the absolute heart rate. The underlying mechanism may be intrinsic (fibrosis, ischemia, infiltrative disease) or extrinsic (vagal tone, drug effect, hypothyroidism, hypothermia).

Atrioventricular Block — Three Degrees of Severity:

— **First-Degree AV Block:** PR interval > 200 ms with all P waves conducted; no emergency treatment required. May indicate significant conduction system disease if PR > 300 ms.

— **Second-Degree Mobitz Type I (Wenckebach):** Progressive PR prolongation until a P wave is non-conducted; block is at the AV node level. Generally benign and well-tolerated; reversible causes (inferior MI, drug toxicity) must be sought. Hemodynamically significant cases require atropine and pacing preparation.

— **Second-Degree Mobitz Type II:** Sudden non-conduction of P waves without prior PR prolongation; block is infra-Hisian (His bundle or bundle branches). This pattern carries significantly higher risk of progression to complete heart block and sudden asystole. Emergency pacing preparation is mandatory.

— **Third-Degree (Complete) AV Block:** Complete dissociation between atrial and ventricular activation; ventricular rate determined by the escape pacemaker. **Junctional escape** (40–60 bpm, narrow QRS) is more hemodynamically tolerated;

ventricular escape (20–40 bpm, wide QRS) is unstable, pharmacologically resistant to atropine, and carries risk of asystole. Complete AVB with ventricular escape rhythm in the context of anterior STEMI (infra-Hisian mechanism) demands immediate temporary pacing (Glikson, et al., 2022: 71–164; Kusumoto, et al., 2019: e51–e156).

Table 6: *AV Block Classification: Mechanism, Risk, and Emergency Action*

Degree	PR Behavior	Level of Block	Risk of Progression	Emergency Action
First degree	Prolonged PR; all P conducted	AV node	Minimal	None required; investigate cause
Second degree Mobitz I (Wenckebach)	Progressive PR → dropped beat	AV node	Low	Atropine if symptomatic; monitor
Second degree Mobitz II	Fixed PR → sudden dropped beat	Infra-Hisian	High — may progress to 3°	Prepare pacing; atropine may be ineffective
High-degree AVB (2:1, 3:1)	Fixed PR with multiple non-conducted P	Variable	High	Pacing preparation mandatory

Degree	PR Behavior	Level of Block	Risk of Progression	Emergency Action
Third degree (complete)	Complete P-QRS dissociation	AV node or infra-Hisian	Asystole risk if escape fails	Emergency pacing; atropine for narrow QRS escape only

Emergency Transcutaneous Pacing: Indications and Technique

Transcutaneous pacing (TCP) is the fastest available pacing modality and should be initiated without delay in patients with hemodynamically significant bradycardia unresponsive to pharmacological measures (Glikson, et al., 2022: 71–164; Kusumoto, et al., 2019: e51–e156).

Indications for Emergency TCP:

—Symptomatic bradycardia with hemodynamic compromise (systolic BP < 90 mmHg, altered mental status, acute pulmonary edema, signs of shock) not responding to atropine

— Second-degree Mobitz II or complete AV block with hemodynamic instability

— Bradycardia-induced syncope or near-syncope

— As bridge to transvenous pacing while preparations are made

— Post-cardiac arrest due to symptomatic bradycardia or asystole

Technique: Pacing pads in anterior-posterior position (anterior: left parasternal 4th ICS; posterior: inferior left scapular region) or anterior-lateral position. Initial output set at 60–80 mA;

increase in 10 mA increments until electrical capture (wide QRS after each pacing spike). Mechanical capture (palpable pulse coinciding with each QRS) must be confirmed by femoral palpation away from artifact. Target rate 60–80 bpm. Due to chest wall stimulation discomfort, sedation/analgesia (morphine 2–4 mg IV + midazolam 1–2 mg IV) is mandatory in conscious patients (Glikson, et al., 2022: 71–164; Kusumoto, et al., 2019: e51–e156).

Pharmacological Bridge While Preparing for Pacing:

Atropine 0.5–1 mg IV (repeat every 3–5 min to maximum 3 mg): First-line for sinus bradycardia and AV nodal block (Wenckebach). *Important:* Atropine is **ineffective** for infra-nodal block (Mobitz II, complete heart block with wide-QRS escape) and may paradoxically worsen block by increasing sinus rate without improving infra-Hisian conduction.

Isoprenaline (Isoproterenol) 2–10 μg/min IV infusion: Accelerates escape rhythm and AV conduction via beta-1 stimulation. Useful for complete AV block awaiting pacing. Use cautiously in acute ischemia.

Dopamine 5–20 μg/kg/min or **Epinephrine** 2–10 μg/min: Useful when bradycardia is accompanied by hypotension requiring vasopressor support; both have chronotropic properties (Kusumoto, et al., 2019: e51–e156).

Transvenous Temporary Pacing

Transvenous temporary pacing provides more reliable, comfortable, and durable pacing than TCP and is indicated when: (1) TCP fails to maintain stable mechanical capture; (2) pacing is required for > 30–60 minutes; (3) the patient requires monitored transfer; or (4) permanent pacemaker implantation is anticipated but cannot be performed immediately (Glikson, et al., 2022: 71–164; Kusumoto, et al., 2019: e51–e156).

Access is obtained via the right internal jugular vein (preferred) or subclavian vein. A 5–7 Fr pacing catheter is advanced to the right ventricular apex under fluoroscopic guidance. Pacing threshold should be < 1 mA at pulse width 0.5 ms; pacing output is programmed to 2–3 times threshold for an adequate safety margin. Complications include: lead displacement (most common), cardiac perforation, pneumothorax, air embolism, and infection. Daily threshold checks are essential (Glikson, et al., 2022: 71–164; Kusumoto, et al., 2019: e51–e156).

Drug-Induced Bradyarrhythmias: Recognition and Reversal

Table 7: Drug-Induced Bradyarrhythmias: Mechanisms and Antidotes

Drug / Class	Arrhythmia Produced	Mechanism	Emergency Antidote Management
Beta-blockers	Sinus bradycardia, AVB	β1 blockade: reduces SA/AV automaticity and conduction	Atropine; glucagon 3–10 mg IV bolus; high-dose insulin (HIET); pacing
Non-DHP CCBs (verapamil, diltiazem)	Sinus bradycardia, AVB	L-type Ca^{2+} channel block in SA/AV node	IV calcium chloride 1 g; atropine; isoproterenol; HIET; pacing

Drug / Class	Arrhythmia Produced	Mechanism	Emergency Antidote Management
Digoxin toxicity	Sinus bradycardia, 2°/3° AVB, junctional rhythm	Enhanced vagal tone + Na/K ATPase inhibition	Digoxin-specific Fab (DigiFab) 10–20 vials; pacing if hemodynamically unstable; NO cardioversion
Amiodarone (chronic)	Sinus bradycardia, 1°-2° AVB	Non-competitive β-blockade + $K^+/Na^+/Ca^{2+}$ channel effects	Dose reduction; temporary pacing if symptomatic; rarely drug discontinuation
Class Ic (flecainide, propafenone)	Infra-Hisian block, wide-QRS bradycardia	Sodium channel blockade; slows His-Purkinje conduction	IV sodium bicarbonate 1–2 mEq/kg; hypertonic saline 3%; pacing
Ivabradine	Sinus bradycardia	Selective If-current (HCN) channel block in SA node	Dose reduction or cessation; rarely pacing needed

Beta-blocker or calcium channel blocker overdose may produce profound, refractory bradycardia and hypotension unresponsive to standard resuscitative measures. Current toxicological guidance recommends (St-Onge, et al., 2017: e306–e315).

High-Dose Insulin Euglycemic Therapy (HIET): Regular insulin 1 unit/kg IV bolus followed by 0.5–1 unit/kg/hr infusion.

Dextrose 50% titrated to maintain glucose 100–250 mg/dL. HIET improves myocardial calcium handling and energy metabolism and is now considered the most effective pharmacological intervention for severe CCB and beta-blocker toxicity. Onset of hemodynamic improvement: 15–30 minutes (St-Onge, et al., 2017: e306–e315).

Intravenous Lipid Emulsion (ILE): 20% Intralipid 1.5 mL/kg IV bolus, repeated up to 3 doses with 5-minute intervals; effective for lipophilic drug toxicity (verapamil, propranolol).

VA-ECMO as Bridge Therapy: For refractory hemodynamic collapse due to severe drug toxicity unresponsive to maximal pharmacological intervention; provides time for drug metabolism and clearance (St-Onge, et al., 2017: e306–e315).

Bradyarrhythmias in Acute Myocardial Infarction

The location of the infarct-related artery determines the mechanism, reversibility, and severity of AV conduction abnormality in AMI:

Inferior STEMI (RCA occlusion): AV nodal ischemia (the AV nodal artery arises from the RCA in 90% of patients). Produces Wenckebach second-degree AVB or complete AV block with junctional escape (narrow QRS, 40–60 bpm). Generally transient (resolving within 3–7 days), pharmacologically responsive to atropine, and associated with favorable prognosis. Temporary pacing reserved for hemodynamically unstable patients not responding to atropine. Right ventricular infarction complicates 30–50% of inferior STEMI and may produce profound hemodynamic compromise requiring careful fluid management and pacing (Al-Khatib, et al., 2018: e210–e271; Kusumoto, et al., 2019: e51–e156).

Anterior STEMI (LAD occlusion): Infra-Hisian block due to necrosis of the interventricular septum and both bundle branches. Complete AVB produces a wide-QRS ventricular escape rhythm

(20–40 bpm). **Atropine is ineffective** (infra-nodal mechanism). Pacing-resistant, hemodynamically unstable, and associated with large MI and poor prognosis reflecting extensive myocardial damage. Immediate transvenous or transcutaneous pacing is mandatory (Al-Khatib, et al., 2018: e210–e271; Kusumoto, et al., 2019: e51–e156).

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PERICARDIAL TAMPONADE

ARİF ARISOY[5]

Introduction and Definition

Pericardial tamponade is a life-threatening cardiovascular emergency resulting from the accumulation of fluid, blood, gas, or pus within the pericardial sac under sufficient pressure to impair diastolic filling of all cardiac chambers. The pericardium is a fibrous sac composed of two layers — the visceral (epicardium) and the parietal pericardium — normally containing 15–50 mL of serous fluid. The parietal pericardium is relatively non-compliant, and this property dictates that the physiological consequences of an effusion depend critically on the ***rate of fluid accumulation*** rather than the absolute volume alone (Adler, et al., 2015: 2921–2964; Spodick, 2003: 684–690).

When fluid accumulates slowly, the pericardium can accommodate up to 1–2 liters before hemodynamic compromise occurs due to pericardial stretch. Conversely, as little as 150–200 mL of rapidly accumulating hemorrhage — as in cardiac rupture or

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iatrogenic injury — can precipitate fatal tamponade (Spodick, 2003: 684–690). The pathophysiological hallmark is equalization of diastolic pressures across all cardiac chambers (right atrial, right ventricular, pulmonary capillary wedge, and left atrial pressures), leading to impaired ventricular filling, reduced stroke volume, and ultimately circulatory collapse (Hoit, 2007: S355–364).

Tamponade exists on a spectrum from subclinical effusion with preserved hemodynamics to pulseless electrical activity requiring emergency drainage. Prompt clinical recognition, echocardiographic confirmation, and timely intervention are the cornerstones of management and determine patient survival (Bodson, Bouferrache, & Vieillard-Baron, 2011: 416–424; Imazio & Adler, 2013: 1186–1197).

Epidemiology and Incidence

The true incidence of pericardial tamponade is difficult to ascertain due to variability in case definition and clinical presentation. Large pericardial effusions are detected in approximately 3–5% of patients undergoing echocardiography in tertiary referral centers, but only a minority require drainage (Imazio, et al., 2005: 1393–1394). In the intensive care unit (ICU), tamponade may complicate 0.1–2% of post-cardiac surgery cases, and up to 1–6% of patients undergoing percutaneous cardiac interventions such as catheter ablation, pacemaker implantation, or structural interventions (Cappato, et al., 2009: 1798–1803; Malouf, et al., 1993: 1451–1457).

Malignancy is the most common cause of large pericardial effusion requiring drainage in developed countries, followed by idiopathic/viral pericarditis and iatrogenic causes (Tsang, et al., 2002: 429–436). In endemic regions, Mycobacterium tuberculosis remains the predominant etiology and carries a substantially higher mortality if untreated (Mayosi, et al., 2014: 1121–1130). In-hospital

mortality from tamponade varies widely from <5% in hemodynamically stable patients undergoing elective drainage to >50% in traumatic hemopericardium or aortic dissection.

Etiology and Classification

The causes of pericardial tamponade are diverse and encompass virtually all categories of disease affecting the pericardium. Understanding the etiology is essential not only for pathophysiological appreciation but also for guiding the choice of fluid analysis, additional diagnostics, and long-term therapy. A comprehensive etiological classification is presented in Table 1.

Table 1: *Etiological Classification of Pericardial Tamponade*

Category	Common Causes	Rare/Special Causes
Infectious	Viral (Coxsackievirus, Echovirus, EBV, CMV, HIV)	Bacterial (S. aureus, M. tuberculosis), Fungal, Parasitic
Neoplastic	Breast, lung, lymphoma (metastatic)	Primary cardiac tumors (mesothelioma, angiosarcoma)
Iatrogenic	Post-cardiac surgery, post-catheterization, post-pacemaker/ICD implantation	Post-radiation therapy, esophageal perforation
Traumatic	Blunt chest trauma, penetrating thoracic injury	Aortic dissection with pericardial extension
Autoimmune/ Inflammatory	SLE, rheumatoid arthritis, systemic sclerosis	Dressler syndrome, post-MI pericarditis
Metabolic	Uremia, hypothyroidism	Chylous effusion, amyloidosis
Idiopathic	Up to 50% of cases in developed countries	Presumed viral/ autoimmune in most

Abbreviations: *EBV = Epstein-Barr virus; CMV = cytomegalovirus; ICD = implantable cardioverter-defibrillator; SLE = systemic lupus erythematosus; MI = myocardial infarction.*

Among the most clinically relevant high-risk etiologies in the cardiac intensive care unit are: (1) post-cardiac surgery effusion, which may be delayed (Dressler-like syndrome) presenting days to weeks after surgery; (2) hemopericardium complicating type A aortic dissection, which is a surgical emergency and an absolute

contraindication to pericardiocentesis as a standalone intervention; (3) procedure-related perforation during electrophysiology procedures; and (4) malignant effusion, typically exudative and frequently recurrent. The distinction between these etiologies profoundly impacts management strategy (Maisch, et al., 2004: 587–610).

Pathophysiology

The pericardial pressure-volume curve has a characteristic biphasic shape: initially relatively flat (allowing significant fluid accumulation with minimal pressure rise), followed by a steep upward inflection representing the limits of pericardial compliance. Once this inflection point is exceeded, even small additional fluid volumes produce disproportionately large pressure increases (Shabetai, 1976: 67–89).

The central pathophysiological mechanism is ***ventricular interdependence***: as pericardial pressure rises and approximates diastolic filling pressures, the interventricular septum shifts leftward during inspiration (when right-sided filling transiently exceeds left-sided), reducing left ventricular preload. This phenomenon — which is the anatomical basis of pulsus paradoxus — results in a measurable reduction of systolic blood pressure during normal inspiration (Appleton, Hatle, & Popp, 1988: 1020–1030).

The Frank-Starling mechanism becomes increasingly impaired as cardiac filling is restricted. The compensatory adrenergic response (tachycardia, peripheral vasoconstriction, and increased contractility) initially preserves blood pressure and organ perfusion. However, as pericardial pressure rises further, these mechanisms become insufficient, resulting in hypotension, reduced coronary perfusion pressure, myocardial ischemia, and ultimately cardiac arrest in pulseless electrical activity (Fowler & Gabel, 1985: 154–157).

Right-sided chambers are more vulnerable to collapse because of their lower intracavitary pressures. Right atrial collapse in systole is the earliest echocardiographic sign, followed by right ventricular diastolic collapse when intrapericardial pressure exceeds right ventricular diastolic pressure. Left-sided chamber collapse is a late and ominous finding indicating extreme elevation of pericardial pressure (Singh, et al., 1984: 966–971).

Symptoms and Clinical Presentation

The clinical presentation of pericardial tamponade spans a broad spectrum from insidious and subacute to abrupt and catastrophic, largely determined by the rate of fluid accumulation, underlying etiology, and baseline hemodynamic reserve (Ristic, et al., 2014: 2279–2284).

Symptoms

- In subacute and chronic presentations, patients typically report:
- Dyspnea on exertion, progressing to dyspnea at rest — the most frequent presenting symptom (>85%)
- Chest discomfort or pressure, often positional (relieved by leaning forward), reflecting pericardial inflammation
- Fatigue and progressive exercise intolerance due to reduced cardiac output
- Orthopnea — paradoxically less common than in left heart failure due to different mechanism
- Palpitations — often tachycardia felt by the patient
- Nausea, anorexia, and abdominal fullness from hepatic venous congestion and reduced gut perfusion
- Syncope or presyncope in patients with significant hemodynamic compromise

Acute traumatic or iatrogenic tamponade may present with sudden hemodynamic deterioration without antecedent symptoms,

directly proceeding to cardiogenic shock or pulseless electrical activity. In contrast, malignant effusions may be discovered incidentally on imaging in patients who present with dyspnea and only modest hemodynamic compromise (Ristic, et al., 2014: 2279–2284).

Physical Examination Findings

The physical examination remains central to the diagnosis of tamponade. The classic triad described by Claude Beck in 1935 — hypotension, elevated jugular venous pressure (JVP), and muffled heart sounds — remains clinically valuable but is present simultaneously in only 10–40% of cases (Ristic, et al., 2014: 2279–2284; Singh, et al., 1984: 966–971). A comprehensive summary of physical findings, their mechanisms, and diagnostic accuracy is provided in Table 2.

Table 2: *Physical Examination Findings in Pericardial Tamponade*

Clinical Feature	Mechanism	Sensitivity / Specificity
Hypotension	Reduced stroke volume due to cardiac compression	~26% / High — often late sign
Elevated JVP / Distended neck veins	Impaired right ventricular filling, elevated RA pressure	~76% — most consistent sign
Muffled heart sounds	Pericardial fluid attenuates transmitted sounds	~28% — often subtle
Pulsus paradoxus >10 mmHg	Exaggerated ventricular interdependence during respiration	~82% sensitivity, ~70% specificity
Tachycardia	Compensatory sympathetic activation	>100/min common; earliest sign
Kussmaul's sign	JVP rises on inspiration (uncommon in tamponade vs. constrictive pericarditis)	Rare in pure tamponade; if present suggests effusive-constrictive disease

Abbreviations: *JVP = jugular venous pressure; RA = right atrium.*

Pulsus Paradoxus — Measurement and Interpretation

Pulsus paradoxus — an exaggerated fall in systolic blood pressure of >10 mmHg during normal inspiration — is the most diagnostically useful bedside finding. It is measured using a sphygmomanometer: the cuff is inflated above systolic pressure, then slowly deflated. The pressure at which Korotkoff sounds are

first heard only during expiration is recorded, followed by the pressure at which sounds are audible throughout the respiratory cycle. The difference between these two values represents the pulsus paradoxus (Curtiss, et al., 1988: 391–398).

A value >10 mmHg is considered abnormal. Values >20–25 mmHg are strongly suggestive of hemodynamically significant tamponade. However, pulsus paradoxus may be absent or diminished in conditions that prevent ventricular interdependence: severe aortic regurgitation, atrial septal defect, positive pressure ventilation, low pressure tamponade, and regional (loculated) tamponade — an important consideration in post-cardiac surgery patients (Swami & Spodick, 2003: 215–217).

Peripheral Perfusion and Shock

In advanced tamponade, signs of low cardiac output predominate: cool and clammy extremities, prolonged capillary refill time (>3 seconds), altered consciousness, and oliguria or anuria. Hepatomegaly and peripheral edema may develop in chronic tamponade with persistent venous hypertension. The paradox of tamponade is markedly elevated neck veins co-existing with hypotension — the combination of which should always prompt consideration of obstructive shock (Leimgruber, et al., 1983: 612–620).

Electrocardiographic Findings

The 12-lead electrocardiogram is a readily available bedside tool that can provide important diagnostic clues. While no ECG finding is pathognomonic for tamponade, certain patterns raise clinical suspicion and should prompt urgent echocardiography. Key ECG findings are summarized in Table 3 (Ristic, et al., 2014: 2279–2284; Singh, et al., 1984: 966–971).

Table 3: *Electrocardiographic Findings in Pericardial Tamponade*

ECG Finding	Description	Clinical Significance
Sinus tachycardia	Most common and earliest finding; HR typically >100 bpm	Nonspecific; compensatory response
Low voltage QRS	<5 mm limb leads; <10 mm precordial leads	Fluid attenuating electrical signal
Electrical alternans	Beat-to-beat alternation of QRS axis, amplitude, or both; may involve P waves	Highly specific; due to pendular heart motion
Diffuse ST elevation	Concave upward pattern in multiple leads; PR depression	Suggests underlying pericarditis
PR depression	PR segment below baseline, most prominent in II, V4-V6	Indicates pericardial/atrial inflammation
Sinus arrest / Bradyarrhythmia	May occur in severe/terminal tamponade	Indicates severe hemodynamic compromise; pre-terminal

Electrical Alternans

Electrical alternans — the most specific ECG finding for tamponade — results from the pendular oscillatory motion of the heart within a large pericardial effusion, producing beat-to-beat variation in the electrical axis. It is most commonly observed as alternating QRS amplitude and morphology, but may also involve P waves and T waves in total electrical alternans. When electrical

alternans is combined with sinus tachycardia and low voltage, the positive predictive value for large hemodynamically significant effusion approaches 80% (Bruch, et al., 2001: 219–226).

The combination of low QRS voltage across limb leads (<5 mm) and electrical alternans should prompt immediate echocardiographic evaluation. Serial ECG monitoring is valuable as electrical alternans may be intermittent and not captured on a single recording. In the post-operative cardiac surgery patient, new sinus tachycardia with unexplained hemodynamic instability should always raise suspicion for tamponade even in the absence of classical ECG findings (Bruch, et al., 2001: 219–226).

Echocardiographic Assessment

Transthoracic echocardiography (TTE) is the diagnostic modality of choice for pericardial tamponade, providing real-time assessment of effusion size, distribution, chamber compression, hemodynamic compromise, and guidance for intervention. The 2015 ESC Guidelines on pericardial diseases and the 2019 ACC/AHA appropriateness criteria endorse echocardiography as the primary imaging tool in suspected tamponade (Adler, et al., 2015: 2921–2964; Imazio & Adler, 2013: 1186–1197).

Standard Echocardiographic Views and Protocol

A focused echocardiographic protocol for tamponade should include: subcostal four-chamber view (optimal for detecting effusion and RA/RV collapse), parasternal long axis and short axis views, apical four-chamber view, and assessment of inferior vena cava (IVC) diameter and collapsibility. M-mode echocardiography complements 2D imaging by providing high temporal resolution for detection of chamber collapse during specific phases of the cardiac cycle (Lancellotti, et al., 2015: 3–5).

Table 4: *Echocardiographic Findings and Their Diagnostic Significance in Tamponade*

Echo Finding	Description	Notes
Pericardial effusion	Echo-free space; large if circumferential >20 mm; fibrinous strands may be seen	Size alone does not define tamponade
RA collapse	Systolic invagination of RA free wall; earliest chamber sign	Sensitivity ~55%, specificity ~68%
RV diastolic collapse	Diastolic invagination of RV free wall; confirms elevated pericardial pressure	Sensitivity ~90%, specificity ~85%
IVC plethora	<50% inspiratory collapse of IVC (normal >50%)	Reflects elevated RA pressure; ~92% sensitivity
Respirophasic flow variation	Mitral E velocity decreases >25% with inspiration; tricuspid increases >40%	Echo correlate of pulsus paradoxus
Swinging heart	Pendular motion of heart within pericardial sac	Correlates with electrical alternans on ECG
Effusion localization	Post-surgical effusions may be loculated, posterior, or localized	May require TEE or CT for full characterization

Abbreviations: *RA = right atrium; RV = right ventricle; IVC = inferior vena cava; TEE = transesophageal echocardiography.*

Doppler Assessment and Respirophasic Variation

Spectral Doppler interrogation of mitral and tricuspid inflow velocities provides the echocardiographic correlate of pulsus paradoxus. A >25% decrease in mitral E-wave velocity with inspiration (compared to expiration) and a >40% increase in tricuspid E-wave velocity are characteristic of tamponade physiology. These Doppler findings may be blunted in patients on positive pressure mechanical ventilation, where the normal respiratory variation in intrathoracic pressure is reversed (Himelman, et al., 1988: 1470–1477).

Tissue Doppler imaging (TDI) of the mitral annulus can demonstrate reduced e' velocity in tamponade, while E/e' ratio may be misleading due to the unique pathophysiology of diastolic restriction. Three-dimensional echocardiography can accurately quantify effusion volume but is not routinely required for clinical decision-making (Himelman, et al., 1988: 1470–1477).

Transesophageal Echocardiography

Transesophageal echocardiography (TEE) is particularly valuable in post-cardiac surgery patients with suboptimal TTE windows, in mechanically ventilated ICU patients, or when loculated posterior effusions are suspected. TEE provides superior visualization of posterior pericardial space, left atrial compression, and aortic root in the context of suspected aortic dissection. Intraoperative TEE is essential when surgical drainage is performed (Russo, O'Connor, & Waxman, 1993: 71–78).

Low-Pressure Tamponade

A clinically important variant is low-pressure tamponade, in which chamber collapse and hemodynamic compromise occur with small or moderate effusions in the context of intravascular volume depletion. In hypovolemic patients, right atrial collapse may occur

with ICP as low as 5–10 mmHg. Recognition of this entity is critical, as the clinical signs may be subtle and the condition responds dramatically to volume loading and pericardiocentesis (Antman, Cargill, & Grossman, 1979: 403–406).

Other Imaging Modalities

Chest Radiography

Chest radiography may demonstrate an enlarged cardiac silhouette ("water bottle" or "flask-shaped" configuration) when effusion exceeds 200–250 mL; however, this sign is neither sensitive nor specific. The lung fields are typically clear, helping differentiate tamponade from acute left heart failure. Cardiomegaly with clear lungs in a dyspneic patient should raise suspicion for pericardial effusion. Chest radiography is useful for identifying concurrent pathology (pneumothorax, pulmonary infiltrate, mediastinal mass) but should never delay echocardiography in hemodynamically unstable patients.

Cardiac Computed Tomography

Cardiac computed tomography (CT) provides excellent delineation of pericardial anatomy, effusion distribution, density, and loculation, and is superior to echocardiography for assessing adjacent mediastinal and pulmonary structures. CT attenuation values can provide information on effusion composition: simple transudates measure 0–20 HU, hemorrhagic effusions 40–70 HU, and purulent exudates variably. CT is the modality of choice in trauma assessment (hemopericardium in the context of aortic injury), in characterizing complex pericardial disease, and in planning surgical drainage in loculated effusions (Maisch, et al., 2004: 587–610).

ECG-gated cardiac CT can visualize pericardial thickness (normal <2 mm), pericardial calcification, and provide a global

assessment of cardiac anatomy. A limitation is the inability to provide real-time hemodynamic assessment or guide drainage procedures, and the risk of radiation and contrast nephropathy in critically ill patients.

Cardiac Magnetic Resonance Imaging

Cardiac magnetic resonance imaging (CMR) offers the most comprehensive tissue characterization and is superior for diagnosing inflammatory, fibrotic, or malignant pericardial disease. Late gadolinium enhancement (LGE) of the pericardium indicates active inflammation or malignant infiltration. CMR can differentiate constrictive pericarditis from restrictive cardiomyopathy with high accuracy. However, its role in acute tamponade is limited by prolonged acquisition time, limited availability in the acute setting, and contraindication in patients with non-MR-compatible devices (Maisch, et al., 2004: 587–610).

Point-of-Care Ultrasound

Focused cardiac ultrasound (FOCUS) protocols — including FATE (Focused Assessment with Transthoracic Echocardiography) and RUSH (Rapid Ultrasound for Shock and Hypotension) — enable rapid bedside diagnosis of pericardial effusion and tamponade in undifferentiated shock. Emergency physicians and intensivists trained in FOCUS can reliably identify large effusions and chamber collapse, enabling timely therapeutic decisions without awaiting formal echocardiography (Bodson, Bouferrache, & Vieillard-Baron, 2011: 416–424).

Diagnostic Algorithm and Differential Diagnosis

The diagnosis of pericardial tamponade is ultimately a clinical-echocardiographic diagnosis. Hemodynamic compromise alone is insufficient — a demonstration of pericardial effusion with echocardiographic signs of elevated intrapericardial pressure is

required. The diagnostic algorithm should proceed as follows: (1) clinical suspicion based on history, symptoms, and examination; (2) ECG for supportive findings; (3) urgent point-of-care echocardiography; (4) hemodynamic confirmation if invasive monitoring is available; and (5) decision for intervention based on integrated assessment (Adler, et al., 2015: 2921–2964; Imazio & Adler, 2013: 1186–1197).

The differential diagnosis includes other causes of obstructive shock — acute massive pulmonary embolism, tension pneumothorax, and constrictive pericarditis — as well as right ventricular infarction, which can mimic tamponade with elevated JVP and hypotension. Differentiation is guided by clinical context, ECG, and echocardiography. In constrictive pericarditis, echocardiography demonstrates ventricular interdependence, pericardial thickening/calcification, and characteristic septal bounce, distinguishing it from tamponade (Maisch, et al., 2004: 587–610).

Hemodynamic Monitoring and Invasive Assessment

Right heart catheterization (Swan-Ganz catheterization) can confirm tamponade physiology by demonstrating equalization of diastolic pressures (right atrial, right ventricular diastolic, pulmonary artery diastolic, and pulmonary capillary wedge pressures all within 5 mmHg of each other). This is particularly useful when echocardiographic windows are limited or clinical presentation is atypical. The characteristic y-descent blunting of the right atrial tracing (reflecting impaired RV filling) and the respiratory variation in pulmonary artery pressures are additional confirmatory findings (Shabetai, 1976: 67–89).

In mechanically ventilated ICU patients, invasive arterial line monitoring provides continuous blood pressure tracing and allows quantification of pulse pressure variation (a surrogate for pulsus paradoxus) under positive pressure ventilation. Central venous

pressure monitoring typically demonstrates elevated CVP (>10–15 mmHg) with blunted y-descent. Pulmonary artery catheterization, while rarely required for diagnosis, may be necessary to guide management in complex cases (e.g., post-operative tamponade with concurrent right ventricular dysfunction) (Hoit, 2007: S355–364).

Medical and Supportive Management

Medical management of tamponade is temporizing and must not delay definitive drainage. No pharmacological agent reverses the mechanical obstruction of cardiac filling. However, supportive measures are essential in stabilizing the patient while preparations for drainage are underway.

Volume Resuscitation

Cautious intravenous fluid administration (250–500 mL normal saline bolus) may transiently increase right-sided filling pressures and improve cardiac output in patients with relative hypovolemia. This is particularly important in low-pressure tamponade. However, excessive volume loading risks worsening venous congestion and organ edema, and does not reverse the underlying hemodynamic impairment (Kerber, et al., 1982: 929–931).

Vasopressors and Inotropes

Catecholamine support (dopamine or norepinephrine) may be required to maintain adequate mean arterial pressure during preparation for drainage. Dobutamine (a positive inotrope) is less preferable as it reduces systemic vascular resistance and may worsen hypotension. Beta-blockers and vasodilators are absolutely contraindicated in tamponade, as they eliminate the compensatory tachycardia and peripheral vasoconstriction that sustain blood pressure (Kerber, et al., 1982: 929–931).

Mechanical Ventilation Considerations

The institution of positive pressure mechanical ventilation in a patient with tamponade carries substantial risk and must be approached with extreme caution. Positive intrathoracic pressure reduces venous return, further impairing already compromised cardiac filling. If intubation is unavoidable, high-dose vasopressors should be immediately available, and pericardiocentesis should ideally be performed before or immediately after induction of anesthesia (Hoit, 2007: S355–364).

Treatment of Underlying Cause

Specific medical treatment directed at the underlying etiology is indicated after hemodynamic stabilization: NSAIDs and/or colchicine for idiopathic/viral pericarditis; corticosteroids for autoimmune or systemic inflammatory conditions; anti-tuberculosis therapy for tuberculous tamponade; antibiotics for bacterial pericarditis. In malignant effusion, systemic oncological treatment may reduce recurrence, though the efficacy of intrapericardial therapy (sclerosants, chemotherapeutic agents) remains incompletely established (Imazio & Adler, 2013: 1186–1197).

Pericardiocentesis: Technique and Procedural Aspects

Pericardiocentesis — percutaneous aspiration of the pericardial effusion — is the primary interventional treatment for pericardial tamponade. Echocardiography-guided pericardiocentesis is the standard of care, associated with a success rate >95% and a complication rate of approximately 1–4% in experienced centers (Tsang, et al., 2002: 429–436).

Indications and Contraindications

Pericardiocentesis is indicated in all patients with hemodynamically significant tamponade (Class I, Level B) and in

large symptomatic effusions without hemodynamic compromise when diagnostic drainage is required. Relative contraindications include: uncorrected coagulopathy (INR>1.5, platelets <50,000/μL), aortic dissection (where surgical drainage is mandatory), small or loculated effusions not amenable to needle access, and active chest wall or skin infection at the planned access site (Adler, et al., 2015: 2921–2964).

Table 5: *Step-by-Step Echocardiography-Guided Pericardiocentesis Protocol*

Step	Action	Key Consideration
1	Position patient semi-recumbent at 30–45°	Fluid gravitates anteriorly and inferiorly
2	Connect ECG monitoring; obtain IV access; prepare resuscitation drugs	Atropine, dopamine, epinephrine at bedside
3	Echocardiography to select optimal window (subcostal vs. apical vs. parasternal)	Largest fluid pocket, shortest needle path, no intervening structures
4	Subcostal approach: insert 18-gauge needle between xiphoid and left costal margin, angle 45° toward left shoulder	Needle tip visible on echo at all times
5	Advance with continuous aspiration; entry confirmed by return of fluid and echo visualization	Bloody fluid: check for clotting (hemopericardium clots; effusion does not)

6	Insert guidewire via Seldinger technique; exchange for pigtail catheter (6–8 French)	Confirm wire position in pericardial space not ventricle
7	Drain fluid slowly; assess hemodynamic response after each 100–200 mL	Rapid drainage may cause acute RV dilatation (tamponade release syndrome)
8	Leave catheter in situ; remove when <25 mL/24h drainage	Reduces recurrence; send fluid for analysis

Abbreviations: *All steps should be performed with continuous ECG monitoring and hemodynamic assessment. Resuscitation equipment must be immediately available.*

Access Routes

The subcostal (subxiphoid) approach is the most commonly used and safest route: the needle is inserted at a 45° angle between the xiphoid process and the left costal margin, directed toward the left shoulder. This route avoids the coronary arteries and minimizes risk of lung injury. The apical approach (lateral to the cardiac apex) is used when effusion is predominantly posterior or lateral. The parasternal approach (second or third intercostal space, left sternal border) is an alternative when posterior effusions or post-surgical loculated collections are targeted. Real-time echocardiographic guidance reduces complications in all approaches (Tsang, et al., 2002: 429–436).

Complications

Potential complications include: cardiac perforation with hemopericardium worsening (most feared; 0.5–1%), pneumopericardium or pneumothorax, coronary artery laceration, intercostal vessel injury, vasovagal reaction, infection/pericarditis, and rarely, acute pulmonary edema following rapid decompression (acute RV dilation syndrome). Ventricular premature beats on ECG

monitoring during advancement suggest proximity to myocardium and necessitate immediate repositioning of the needle (Mayosi, et al., 2014: 1121–1130).

Pericardial Fluid Analysis

Analysis of pericardial fluid is essential for establishing etiology and guiding further management. A comprehensive panel should be sent routinely. Key findings and their diagnostic implications are summarized in Table 6.

Table 6: Pericardial Fluid Analysis: Characteristics and Diagnostic Implications

Effusion Type	Key Laboratory Features	Likely Etiology
Exudate	LDH >200 U/L; protein >3 g/dL; glucose < serum	Infectious, malignant, autoimmune, post-MI
Transudate	LDH <200 U/L; protein <3 g/dL; clear/straw colored	Heart failure, hypoalbuminemia, hypothyroid
Hemorrhagic	RBCs >10,000/μL; hematocrit >50% of serum suggests hemopericardium	Trauma, iatrogenic, aortic dissection, malignancy
Purulent	WBC >10,000/μL (neutrophilic); organisms on Gram stain/culture	Bacterial pericarditis, contiguous spread
Chylous	Milky appearance; triglycerides >500 mg/dL	Post-thoracic surgery, lymphoma, trauma
Cytology/ Histology	Malignant cells (sensitivity 50–60%); TB ADA >40 U/L	Strongly guides treatment decisions

Abbreviations: *ADA = adenosine deaminase; LDH = lactate dehydrogenase; WBC = white blood cell count. ADA >40 U/L has sensitivity ~87% and specificity ~89% for tuberculous pericarditis.*

Surgical Drainage and Pericardiectomy

Surgical drainage is indicated when pericardiocentesis is contraindicated, technically unfeasible, or has failed to provide adequate drainage. It is the treatment of choice in: aortic dissection with hemopericardium, purulent pericarditis requiring debridement, traumatic hemopericardium (cardiac laceration), post-cardiac surgery tamponade with organized clot or adhesions, and recurrent effusions following two or more failed drainage attempts (Maisch, et al., 2004: 587–610).

Subxiphoid Pericardiostomy

The subxiphoid (subxiphoid window) approach is the most commonly performed surgical drainage technique. It can be performed under local anesthesia with sedation and is associated with lower morbidity than full sternotomy. A 3–5 cm incision inferior to the xiphoid allows pericardial access; a pericardial window of approximately 2 × 2 cm is created, and a drain is placed. This technique is preferred in patients at high surgical risk, malignant effusion, and recurrent effusion for diagnostic or palliative purposes (Tsang, et al., 2002: 429–436).

Video-Assisted Thoracoscopic Surgery

Video-assisted thoracoscopic surgery (VATS) allows creation of a larger pericardial window with excellent visualization, enabling biopsy of pericardial tissue and drainage of loculated effusions. The pericardiopleuropericardial window drains fluid into the pleural space, reducing recurrence. VATS is preferred when tissue diagnosis is needed and in patients with adequate cardiorespiratory reserve.

Emergency Thoracotomy

In cases of traumatic cardiac tamponade with imminent cardiac arrest (pulseless electrical activity or extreme hemodynamic

instability), emergency department thoracotomy may be lifesaving. Resuscitative thoracotomy allows direct pericardiotomy and control of cardiac injury. Survival rates are highly dependent on mechanism of injury (penetrating trauma has better outcomes than blunt trauma) and time from injury to intervention.

Pericardiectomy for Recurrent Effusion

Total or subtotal pericardiectomy may be required in patients with recurrent or chronic effusions refractory to drainage (particularly malignant, tuberculous, and radiation-induced effusions), or in effusive-constrictive pericarditis. Surgical mortality ranges from 5–15% depending on patient selection and institutional experience, and is significantly higher in radiation-induced pericardial disease (Maisch, et al., 2004: 587–610).

Special Clinical Scenarios

Tamponade in the ICU and Post-Cardiac Surgery

Post-cardiac surgery tamponade represents a distinct entity: effusions are frequently hemorrhagic and loculated, often posterior or lateral, and may not follow classical echocardiographic criteria. Beck's triad is often incomplete. Diagnostic delay is common because symptoms may be attributed to the expected postoperative course. Any unexplained hemodynamic deterioration in the first 2–4 weeks following cardiac surgery should prompt urgent echocardiography, with particular attention to posterior and apical pericardial spaces (Russo, O'Connor, & Waxman, 1993: 71–78).

Tamponade Complicating Catheter Ablation

Pericardial perforation during catheter ablation (particularly pulmonary vein isolation for atrial fibrillation) is a serious but manageable complication with an incidence of 0.5–1.5%. Early recognition requires continuous hemodynamic monitoring and

fluoroscopic surveillance during the procedure. Prompt pericardiocentesis via the subcostal approach, with placement of a pigtail catheter, resolves tamponade in the majority of cases without surgical intervention (Cappato, et al., 2009: 1798–1803).

Malignant Pericardial Effusion

Malignant effusions — most commonly from lung, breast, lymphoma, and leukemia — account for a significant proportion of large pericardial effusions requiring drainage. Cytological analysis has modest sensitivity (50–60%), and pericardial biopsy increases diagnostic yield. Recurrence after pericardiocentesis alone occurs in 40–60% of cases. Prolonged catheter drainage reduces recurrence. Intrapericardial instillation of cisplatin or thiotepa has been used in selected cases of malignant effusion, with variable results (Tsang, et al., 2002: 429–436).

Tuberculous Pericarditis

Tuberculous tamponade is a medical emergency in endemic regions (sub-Saharan Africa, Asia, Eastern Europe). Standard anti-tuberculosis quadruple therapy is the cornerstone of treatment. The addition of adjunct corticosteroids (prednisolone 1 mg/kg/day) is recommended by WHO to reduce pericardial inflammation and lower the risk of developing constrictive pericarditis, though evidence from randomized trials (including the IMPI trial) has yielded mixed results regarding mortality benefit (Tsang, et al., 2002: 429–436).

Outcomes and Prognosis

The prognosis of pericardial tamponade depends primarily on the underlying etiology and speed of diagnosis and treatment. Idiopathic and viral tamponade have an excellent prognosis with appropriate drainage and anti-inflammatory therapy, with recurrence rates of 15–30%. Malignant effusion carries a median survival of 3–

12 months depending on the primary tumor type and extent of disease (Imazio & Adler, 2013: 1186–1197; Imazio, et al., 2005: 1393–1394).

Iatrogenic tamponade, when recognized promptly and treated with pericardiocentesis, has a favorable outcome with complication-related mortality below 1% in experienced centers. Traumatic hemopericardium mortality depends on injury mechanism: penetrating cardiac injuries managed with emergency thoracotomy have survival rates of 15–40%, while blunt injury outcomes are generally worse.

In-hospital complications following pericardiocentesis include: recurrence of effusion (15–20% within 30 days), infection, pneumopericardium, and the rare post-drainage acute pulmonary edema. Long-term follow-up with serial echocardiography is recommended to monitor for recurrence and development of constrictive pericarditis, which complicates approximately 1–10% of cases depending on etiology (Imazio & Adler, 2013: 1186–1197).

Summary: Key Management Principles

- Pericardial tamponade is a clinical-echocardiographic diagnosis; hemodynamic instability plus echocardiographic signs of pericardial pressure elevation confirm the diagnosis.
- Rate of fluid accumulation determines clinical severity more than absolute effusion volume.
- Pulsus paradoxus >10 mmHg is the most sensitive bedside sign (>82%); Beck's triad is present in <40% of cases.
- Electrical alternans on ECG combined with sinus tachycardia and low voltage has ~80% PPV for hemodynamically significant tamponade.
- RV diastolic collapse and IVC plethora are the most specific echocardiographic signs of tamponade.

- Echocardiography-guided pericardiocentesis is the treatment of choice (Class I, Level B); surgical drainage is reserved for specific indications.
- Avoid positive pressure ventilation, beta-blockers, and vasodilators in tamponade.
- All drained pericardial fluid should be sent for comprehensive analysis (cell count, protein, LDH, glucose, culture, cytology, ADA) to guide etiological diagnosis.
- In suspected aortic dissection, never perform pericardiocentesis as a definitive treatment — surgical drainage and aortic repair are mandatory.
- Long-term follow-up with serial echocardiography is essential given 15–30% recurrence rates and the risk of constrictive pericarditis.

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IMPLANTABLE CARDIOVERTER DEFIBRILLATOR RELATED INAPPROPRIATE SHOCKS: MECHANISMS, CLINICAL IMPACT, DIAGNOSIS, AND CONTEMPORARY MANAGEMENT STRATEGIES

GÖKHAN CABRİ[6]

Introduction

Implantable cardioverter-defibrillator (ICD) and cardiac resynchronization therapy-defibrillator (CRT-D) systems are regarded as the gold standard therapeutic modalities in modern cardiology for the prevention of sudden cardiac death (SCD) due to ventricular tachyarrhythmias (Li, et al., 2016: 110–116). These devices are capable of detecting life-threatening arrhythmias such as ventricular tachycardia (VT) and ventricular fibrillation (VF) within milliseconds and delivering timely and effective therapy. Despite these well-established benefits and ongoing advancements in ICD technology, inappropriate shocks (IS) remain one of the principal limitations affecting the overall clinical efficacy of this treatment

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approach (Chiu, et al., 2025: 2861–2869; Stiles, et al., 2019: 485–493).

In its most fundamental definition, an inappropriate shock refers to an unwarranted high-energy discharge delivered by the device in the absence of malignant ventricular arrhythmias (VT/VF). Current literature indicates that approximately 12–29% of ICD recipients experience at least one inappropriate shock during the lifetime of the device (Stiles, et al., 2019: 485–493). The clinical consequences of such events extend beyond acute physical discomfort; they are associated with significant reductions in quality of life and increased incidence of psychiatric comorbidities, including anxiety, depression, and post-traumatic stress disorder (PTSD). More importantly, large-scale randomized trials such as MADIT-II and SCD-HeFT have demonstrated that inappropriate shocks are independently associated with increased mortality risk. Even a single inappropriate shock has been shown to adversely affect survival, whereas repeated shocks confer a cumulative increase in mortality risk, with the hazard ratio rising up to 3.7 after the fifth shock (Stiles, et al., 2019: 485–493; van Rees, et al., 2011: 556–562).

The pathophysiology of inappropriate shocks can be broadly categorized into two principal mechanisms: misclassification of physiological rhythms and device-related sensing errors. Approximately 80% of cases are attributable to supraventricular tachyarrhythmias (SVTs). Among these, atrial fibrillation (AF) represents the most common trigger, primarily due to its rapid ventricular response and irregular R–R intervals, which challenge the device's discrimination algorithms (Bifulco, et al., 2014: 579526). In addition, "oversensing" defined as the inappropriate detection of T waves, myopotentials, or electromagnetic interference (EMI) as ventricular activity—may lead to erroneous interpretation of cardiac electrical signals by the device. Structural abnormalities related to the lead system, including lead fracture, insulation defects,

or connection failures, are also important contributors and may result in recurrent and clinically dramatic inappropriate discharges, occasionally manifesting as electrical storm (Stiles, et al., 2019: 485–493).

Epidemiological data suggest that certain patient populations are at a higher risk for inappropriate shocks. In particular, pediatric patients and individuals with congenital heart disease (CHD) exhibit substantially higher incidence rates, reaching up to 40–50%. This increased risk is largely attributed to sinus tachycardia associated with higher levels of physical activity in childhood, as well as mechanical stress on the lead system during somatic growth. In the adult population, younger age (<70 years) and the presence of concomitant AF have been identified as independent risk factors for inappropriate shocks (Dichtl, et al., 2011: 433–436; Fleeman & Aleong, 2019: 3623–3632).

Over the past decade, a significant paradigm shift has occurred in ICD programming strategies. Landmark trials such as MADIT-RIT and ADVANCE III have demonstrated the superiority of a “delayed and selective therapy” approach, based on higher rate thresholds and prolonged detection durations, over earlier aggressive treatment strategies. Increasing tachycardia detection thresholds to ≥200 bpm, prolonging detection intervals (e.g., NID [Number of Intervals to Detect] 30/40 or 60/80), and implementing antitachycardia pacing (ATP) during capacitor charging have been shown to significantly reduce not only inappropriate shocks but also unnecessary appropriate shocks delivered for self-terminating arrhythmias. These findings have been incorporated into clinical practice through international consensus documents published in 2015 and 2019 (Dichtl, et al., 2011: 433–436; Fleeman & Aleong, 2019: 3623–3632).

The aim of this chapter is to systematically review the pathophysiological mechanisms underlying inappropriate shocks, evaluate their clinical and psychosocial impact, and provide a comprehensive management framework for their prevention, incorporating contemporary programming strategies, remote monitoring technologies, and pharmacological approaches.

Definitions and Terminology

The classification of therapies delivered within the scope of ICD treatment is based on the clinical nature of the underlying arrhythmic event that triggers device intervention. Clear and standardized definition of these terminological distinctions is of critical importance both for scientific reporting and for optimizing clinical decision-making processes (Frodi, et al., 2025: 125–139; Garnreiter, 2017: 2898–2906).

Antitachycardia Pacing

Antitachycardia pacing (ATP) is a low-energy electrical intervention developed in ICD systems as an alternative to high-energy, painful shock therapy. The primary objective of this approach is to terminate of potentially life-threatening ventricular tachyarrhythmias. ATP exerts its effect through short sequences of ventricular stimuli delivered at a rate exceeding the tachycardia' rate ; typically, the pacing cycle length is programmed to approximately 81–88% of the tachycardia R–R interval. This strategy aims to suppress re-entrant circuits via entrainment or to interrupt ectopic focus activity (Biffi, 2014: S88–100; Chiu, et al., 2025: 2861–2869).

Clinical studies have demonstrated that ATP is highly effective in slow VT and, with appropriate patient selection, can also successfully terminate fast VT (up to 250 beats per minute), with success rates reaching approximately 70%. One of its major advantages is that it is painless, thereby protecting patients from the

physical discomfort and psychological distress associated with high-voltage shocks. Furthermore, considering that each high-energy shock significantly depletes device battery life—equivalent to approximately 15 days of battery consumption—the use of ATP contributes positively to long-term device longevity (Chiu, et al., 2025: 2861–2869).

Despite these benefits, ATP is not entirely without risks. Rare cases of arrhythmia acceleration, including transition to VF, have been reported following ATP delivery. Therefore, careful consideration of arrhythmia characteristics and patient-specific factors is essential when programming ATP therapies.

Appropriate and Inappropriate Shock Concepts

An appropriate shock is defined as the timely delivery of high-energy therapy by the device following accurate detection of life-threatening ventricular arrhythmias such as VT or VF (Marcus, Chan, & Redberg, 2011: 348–353). In contrast, an inappropriate shock refers to an unwarranted discharge delivered in the absence of malignant ventricular arrhythmias, typically resulting from supraventricular tachycardias (SVTs), AF, sensing errors, or device/lead-related technical issues (Dichtl, et al., 2011: 433–436).

Between these two core concepts lies a clinically distinct category termed unnecessary appropriate shock. This refers to shocks delivered for correctly detected arrhythmias that are hemodynamically tolerable or have the potential for spontaneous termination and therefore may not actually require therapy. This distinction is particularly relevant in the evaluation of contemporary ICD programming strategies (Chiu, et al., 2025: 2861–2869).

Sensing and Detection Terminology

In ICD systems, rhythm analysis is performed through two fundamental processes: sensing and detection. Sensing refers to the

identification and timing of cardiac depolarization signals by the device using amplitude thresholds and filtering mechanisms. Detection, on the other hand, involves the analysis of these signals through specific algorithms to determine whether the rhythm is of ventricular or supraventricular origin (Kossaify, 2020: 308–317; Mukherjee, et al., 2021: 235–240).

Oversensing, the most common technical cause of inappropriate shocks, is defined as the erroneous interpretation of signals that do not represent true ventricular depolarization as ventricular activity (Powell, et al., 2012: 863–869). This phenomenon may arise through several mechanisms:

T-wave oversensing: Occurs when reduced R-wave amplitude or prominent T-wave morphology leads the device to interpret each cardiac cycle as two separate events, resulting in an overestimation of ventricular rate (Biffi, 2014: S88–100; Fleeman & Aleong, 2019: 3623–3632).

Double counting: A single QRS complex is detected as two distinct events via both the R wave and T wave, artificially increasing the calculated heart rate into tachycardia detection zones (Stiles, et al., 2019: 485–493).

Myopotential sensing: Electrical signals generated by skeletal muscle activity, particularly from pectoral muscles, are interpreted as high-frequency noise, potentially mimicking VF (Stiles, et al., 2019: 485–493).

Hardware and Environmental Interaction Terminology

Structural or mechanical abnormalities related to the lead system constitute an important category of causes for inappropriate shocks and are described using specific terminology. Lead fracture refers to disruption of conductor integrity and is typically characterized by irregular, high-frequency “make-and-break”

signals. In contrast, a loose set screw—commonly observed in the early postoperative period—is associated with inadequate contact between the lead and the generator, resulting in position-dependent signal noise and impedance fluctuations (Bera, et al., 2021: 54–58; Pai, Abedin, & Rawling, 2008: 69–71).

EMI occurs when external electrical signals are misinterpreted by the device as cardiac activity, potentially triggering inappropriate therapies (Pai, Abedin, & Rawling, 2008: 69–71).

Clinical and Psychological Phenomena

Several specific clinical and psychological phenomena experienced by patients following ICD therapy have been described in the literature. Phantom shock refers to the perception of a shock in the absence of an actual device discharge and is commonly associated with anxiety or post-traumatic stress disorder. Electrical storm is defined as a high-risk clinical condition characterized by three or more appropriate or inappropriate shocks occurring within a 24-hour period, with at least 5-minute intervals between episodes (F, et al., 2023: 1029–1039).

Discrimination Algorithms

ICD systems employ multiparametric discrimination algorithms to differentiate between ventricular and supraventricular arrhythmias (Mukherjee, et al., 2021: 235–240). The principal components of these algorithms include:

Stability: Analysis of R–R interval variability to distinguish irregular rhythms (e.g., AF) from regular VT.

Onset: Evaluation of whether tachycardia begins abruptly (suggestive of VT) or gradually (suggestive of sinus tachycardia).

Morphology analysis (template matching): Comparison of the QRS complex recorded during tachycardia with a stored sinus rhythm template, allowing similarity-based classification.

Epidemiology

The prevalence of inappropriate shocks (IS) in ICD and CRT-D systems demonstrates substantial heterogeneity depending on follow-up duration, device type, programming strategies, and the clinical characteristics of the patient population. Large-scale randomized trials and meta-analyses indicate that approximately 12–29% of ICD recipients experience at least one inappropriate shock during the lifetime of the device. Although historical cohorts have reported a five-year cumulative incidence of up to 18%, a significant reduction in these rates has been observed with the adoption of contemporary programming strategies. Recent real-world data suggest that the annual incidence of inappropriate shocks has declined to approximately 0.49 events per 100 patient-years (Corzani, et al., 2015: 56–59; Goncalves & Pereira, 2013: 141–148).

High-Risk Populations and Demographic Determinants

From an epidemiological perspective, pediatric patients and individuals with congenital heart disease (CHD) constitute the highest-risk groups. In these populations, the incidence of inappropriate shocks typically ranges between 20% and 30%, with some studies reporting rates as high as 40–50%. This increased risk is attributed to sinus tachycardia associated with higher levels of physical activity, a greater burden of supraventricular arrhythmias, and lead dysfunction related to mechanical stress imposed by somatic growth (Garnreiter, 2017: 2898–2906).

Age is one of the most robust independent predictors of inappropriate shocks. Patients younger than 70 years exhibit approximately a 1.8-fold higher risk compared with older

individuals. Additionally, a clinical history of AF independently increases the risk of inappropriate shocks by approximately twofold, primarily due to misclassification of tachyarrhythmias (Fleeman & Aleong, 2019: 3623–3632).

Device-Type–Related Epidemiological Differences

The relationship between device type (ICD vs. CRT-D) and the incidence of inappropriate shocks is complex and multifactorial. No clear superiority has been demonstrated between single-chamber (VR) and dual-chamber (DR) ICD systems in terms of inappropriate shock reduction. In fact, some meta-analytic data suggest a modest increase in inappropriate shock risk in dual-chamber systems, potentially due to atrial sensing errors (odds ratio [OR]: 1.53) (Dorian, et al., 2004: 540–547; Kutyifa, et al., 2016: e001965).

In contrast, patients with CRT-D devices exhibit a significantly lower risk of inappropriate shocks, likely related to reverse ventricular remodeling and a reduced arrhythmic burden. This reduction has been estimated at approximately 62% compared with conventional ICD populations. Subcutaneous ICD (S-ICD) systems demonstrate overall inappropriate shock rates comparable to transvenous systems (approximately 7%); however, the predominant mechanism differs, with T-wave oversensing—rather than supraventricular arrhythmias—being the leading cause in this group (Corzani, et al., 2015: 56–59).

Recurrent Events and Temporal Trends

Inappropriate shocks are rarely isolated events and tend to recur within specific patient subgroups. Approximately 37.9% of patients who experience an initial inappropriate shock will develop recurrent episodes during follow-up. Furthermore, epidemiological evidence supports a dose–response relationship between inappropriate shock burden and mortality. Recurrent shocks have

been shown to adversely affect survival, with a marked increase in mortality risk after the fifth shock (hazard ratio ~3.7) (Frodi, et al., 2025: 125–139; van Rees, et al., 2011: 556–562).

Over the past decade, the most notable trend in the epidemiology of inappropriate shocks has been a substantial decline in incidence. The integration of programming strategies based on higher rate thresholds and prolonged detection durations—established by landmark trials such as MADIT-RIT and ADVANCE III—has reduced inappropriate shock rates from historical levels of approximately 13–17% to as low as 1.6–1.9% in contemporary cohorts. This trend clearly highlights the direct and measurable impact of advances in device technology and evidence-based programming on patient outcomes (Fleeman & Aleong, 2019: 3623–3632).

Mechanisms of Inappropriate Shocks

The pathophysiology of inappropriate shocks in patients receiving ICD therapy can be broadly categorized into two principal mechanisms: (i) misclassification of physiological rhythms (discrimination errors) and (ii) oversensing of non-cardiac signals or artifacts. A detailed understanding of these mechanisms is essential for accurate interpretation of post-shock intracardiac electrograms (EGMs) and for optimizing patient-specific therapeutic strategies (Dichtl, et al., 2023).

Supraventricular Tachyarrhythmias

Approximately 80% of inappropriate shocks are attributable to SVTs. In such cases, the device correctly detects an increased ventricular rate; however, limitations in discrimination algorithms lead to erroneous classification of the arrhythmia (Daubert, et al., 2008: 1357–1365).

Atrial fibrillation: AF is the most common cause, accounting for approximately 40–45% of inappropriate shocks. AF with rapid ventricular response can easily exceed programmed rate thresholds. Furthermore, marked irregularity in R–R intervals may disrupt stability algorithms, resulting in misclassification as VF (Pestrea, et al., 2024: 248).

Sinus tachycardia: Particularly in young and physically active individuals, exercise-induced high sinus rates may occasionally enter tachycardia detection zones despite their gradual onset, leading to inappropriate therapy delivery (Cardoso, et al., 2015: 236–244).

Atrioventricular nodal reentrant tachycardia (AVNRT): In AVNRT, atrial signals may fall within the post-ventricular atrial blanking (PVAB) period, resulting in underdetection of atrial activity. Consequently, the device may incorrectly interpret a ventricular-dominant rhythm (V>A) and classify it as VT (Swerdlow, et al., 2000: 878–885).

Oversensing Mechanisms

Oversensing refers to the inappropriate detection of signals that do not represent true ventricular depolarization as ventricular events. This leads to artificial inflation of the calculated heart rate and erroneous entry into tachycardia or defibrillation zones (Corzani, et al., 2015: 56–59).

T-wave oversensing: In the presence of low-amplitude R waves or prominent T-wave morphology, the device may interpret each cardiac cycle as two separate events (double counting). This phenomenon is particularly common in S-ICD systems (Bifulco, et al., 2014: 579526).

Myopotential sensing: Electrical signals generated by pectoral or diaphragmatic muscle activity may be interpreted as

high-frequency noise, mimicking VF. In clinical practice, myopotential-induced inappropriate shocks triggered by upper extremity activity are well recognized (Pearman, et al., 2023: 101–104).

Far-field signals: In cases of suboptimal lead positioning, atrial signals may be sensed on the ventricular channel (atrial far-field sensing), leading to erroneous ventricular rate calculations and inappropriate therapies (Ferretto, et al., 2019: 562–564).

Hardware Failure and Lead Dysfunction

Structural abnormalities of the device or lead system frequently result in recurrent and clinically dramatic inappropriate shocks, often manifesting as electrical storm.

Lead fracture: Characterized by disruption of conductor integrity, producing short, high-frequency, non-physiological "make-and-break" signals. These signals may be interpreted as extremely rapid ventricular activity, triggering immediate shock delivery (Kella & Stambler, 2021: 3–7).

Loose set screw: Inadequate connection between the lead and the generator, typically occurring in the early postoperative period, leads to position-dependent signal artifacts and impedance fluctuations. Discrepancies between near-field (NF) and far-field (FF) signals provide important diagnostic clues (Bera, et al., 2021: 54–58).

Insulation defects: Disruption of lead insulation is associated with abrupt impedance drops and noise artifacts, potentially triggering inappropriate therapies (Oosterwerff, et al., 2024: 614–622).

Electromagnetic Interference (EMI)

EMI arises when external, non-cardiac electrical signals are misinterpreted by the device as cardiac activity (Ross, Milch, & Kongsgard, 2024: 102289).

Environmental and industrial sources: Ungrounded electrical devices, industrial equipment, faulty electrical systems, and certain physiotherapy devices (e.g., transcutaneous electrical nerve stimulation [TENS]) may generate EMI.

Effects of water and moisture: Reduced skin resistance in wet conditions facilitates the transmission of electromagnetic currents, thereby increasing the risk of EMI. Clinical reports have documented cases in which leakage currents during water exposure led to inappropriate detection of VF and subsequent inappropriate shocks.

Risk Factors

The development of inappropriate shocks in patients receiving ICD therapy represents a multidimensional process resulting from the interaction between patient characteristics, underlying cardiac pathology, device- and lead-related technical factors, and programming strategies. Systematic identification of these risk factors is essential for the development of patient-specific programming approaches, enabling preservation of the survival benefit of ICD therapy while optimizing quality of life (van Rees, et al., 2011: 556–562).

Demographic and Lifestyle Factors

Age is one of the most powerful independent predictors of inappropriate shocks. Patients younger than 70 years exhibit approximately a 1.8-fold higher risk compared with older individuals. This increased risk is attributed to higher levels of physical activity, enhanced sympathetic tone, and a greater burden

of SVTs. Pediatric patients and individuals with congenital heart disease (CHD) represent the highest-risk population, with reported rates reaching up to 40–50%. This elevated risk is explained by higher baseline heart rates, frequent episodes of sinus tachycardia, and increased mechanical stress on the lead system during somatic growth (Oosterwerff, et al., 2024: 614–622).

Smoking has also been identified as an independent risk factor for inappropriate shocks, particularly in relation to recurrent events. The impact of sex appears more heterogeneous; although some contemporary registry studies report lower rates of both appropriate and inappropriate shocks in women, these findings are likely influenced by differences in the underlying etiology of cardiomyopathy rather than sex alone (Sandgren, et al., 2015: e000249).

Clinical and Pathophysiological Risk Factors

AF is the most important and frequently encountered clinical risk factor for inappropriate shocks. Patients with a history of AF have approximately a twofold increased risk. This association is primarily explained by rapid ventricular response rates and irregular R–R intervals, which impair device discrimination algorithms, particularly stability analysis.

Elevated resting heart rate and the presence of sinus tachycardia significantly increase the likelihood of inappropriate shocks, especially in patients with ischemic cardiomyopathy (reported OR ~7.38). In addition, advanced heart failure, ventricular remodeling, and increased arrhythmic burden contribute to risk both by increasing arrhythmia frequency and by impairing signal quality. Chronic kidney disease has also been associated with a higher incidence of inappropriate shocks in some studies (Moradi, et al., 2022: 2372).

Technical and Device-Related Risk Factors

Technical characteristics of the device and lead system play a critical role, particularly in oversensing-related inappropriate shocks. Lead implantation technique is an important determinant; the subclavian puncture approach is associated with approximately a 1.4–1.5-fold higher risk of lead dysfunction and fracture compared with cephalic or axillary access. The "subclavian crush" phenomenon may lead to progressive conductor damage or insulation defects, resulting in noise sensing and recurrent inappropriate therapies (Oosterwerff, et al., 2024: 614–622).

Certain lead models have historically been associated with higher failure rates, underscoring the importance of device selection. Inadequate lead–generator connection (loose set screw), complex signal behavior in dual-coil systems, and insulation defects may all increase the risk of oversensing through position-dependent artifacts and impedance fluctuations. In patients with left ventricular assist devices (LVADs), inappropriate shock rates are notably higher, likely due to both an increased burden of supraventricular arrhythmias and electromagnetic interactions (Andreae, et al., 2025: 394–402).

Programming and Algorithm-Related Risk Factors

Device programming parameters represent the most critical and modifiable determinants of inappropriate shock risk. Low tachycardia rate thresholds and short detection durations increase the likelihood of inappropriate treatment of SVTs and self-terminating non-sustained VT. In contrast, contemporary programming strategies incorporating higher rate thresholds and delayed detection approaches have significantly reduced this risk (Fleeman & Aleong, 2019: 3623–3632).

Disabling discrimination algorithms or setting inappropriate thresholds—particularly those based on morphology analysis or atrioventricular relationship—can impair differentiation between SVT and VT, thereby increasing the risk of inappropriate shocks. In S-ICD systems, the extracardiac position of the sensing electrode predisposes to higher rates of T-wave oversensing and myopotential-related noise. Additionally, environmental EMI may further contribute to sensing errors and trigger inappropriate therapies in these systems (Ross, Milch, & Kongsgard, 2024: 102289).

Clinical Outcomes

Although ICD therapy is highly effective in preventing sudden cardiac death, the occurrence of inappropriate shocks can substantially limit its clinical benefits. The consequences of inappropriate shocks extend beyond an acute event and represent a complex clinical entity affecting multiple domains, including mortality, psychosocial status, quality of life, device performance, and healthcare system burden (Fleeman & Aleong, 2019: 3623–3632).

Impact on Mortality and Survival

Large-scale randomized trials and their sub-analyses (e.g., MADIT-II and SCD-HeFT) have demonstrated a significant and independent association between exposure to inappropriate shocks and increased mortality risk. Even a single inappropriate shock has been reported to adversely affect survival (hazard ratio ~1.6), while recurrent shocks are associated with a progressively increasing risk, reaching a hazard ratio of approximately 3.7 after the fifth shock (Dichtl, et al., 2011: 433–436).

The underlying mechanisms of this association remain incompletely understood. High-energy discharges may induce myocardial cellular injury, transient ischemia, and electroporation,

thereby creating a proarrhythmic substrate. Alternatively, some evidence suggests that inappropriate shocks may serve as a marker of underlying disease burden, particularly AF and advanced heart failure rather than exerting a direct causal effect (Dichtl, et al., 2011: 433–436).

Psychological Morbidity and Quality of Life

Inappropriate shocks exert some of the most profound and detrimental effects of ICD therapy at the psychosocial level. Among ICD recipients, the prevalence of anxiety (20–25%), depression (10–20%), and post-traumatic stress disorder (PTSD) (10–15%) is significantly elevated, and the experience of inappropriate shocks further exacerbates these conditions.

Patients often perceive inappropriate shocks not as life-saving interventions but as unpredictable and traumatic device malfunctions. This perception may lead to loss of trust in the device, persistent hypervigilance, and a chronic stress response characterized by fear of recurrent shocks. Additionally, the phenomenon of "phantom shock"—the perception of a shock in the absence of actual device discharge—represents a manifestation of this psychological burden. These factors may ultimately result in avoidance of physical activity, exercise intolerance, social withdrawal, and a marked deterioration in overall quality of life (Sears & Conti, 2002: 488–493; Torbey, et al., 2025: 101797).

Pain Perception and Device Acceptance

Inappropriate shocks are frequently perceived as more painful than appropriate shocks, largely because they often occur unexpectedly while the patient is fully conscious. Clinical studies have demonstrated significantly higher pain scores associated with inappropriate shocks compared to appropriate therapies.

Severe pain and the associated traumatic experience may lead to the development of a negative attitude toward device therapy. In a subset of patients, this may even prompt consideration of permanent device deactivation. This represents a significant challenge in terms of long-term acceptance and adherence to ICD therapy (Marcus, Chan, & Redberg, 2011: 348–353).

Physiological and Mechanical Consequences

Post-shock intracardiac electrogram (EGM) analyses have demonstrated transient electrical instability within the myocardium, manifested as changes described as “local injury current” (LIC). These findings suggest that repeated high-energy discharges may exert deleterious effects on myocardial function (Stempniewicz, et al., 2011: 554–560).

Furthermore, each defibrillation shock results in substantial battery depletion, thereby shortening device longevity. This increases the need for generator replacement procedures, exposing patients to additional surgical interventions and associated complications (Li, et al., 2016: 110–116).

Socioeconomic and Healthcare System Impact

Inappropriate shocks impose a considerable burden on the healthcare system. Increased emergency department visits, hospital admissions, and device evaluations contribute to higher direct healthcare costs. Additionally, indirect costs are amplified by reduced work productivity and diminished quality of life.

Although the incidence of syncope associated with inappropriate shocks is relatively low, this has led to ongoing debate regarding the necessity of restrictions such as driving limitations. Nevertheless, it is evident that inappropriate shocks represent a significant factor adversely affecting the cost-effectiveness profile of ICD therapy (Li, et al., 2016: 110–116).

Diagnostic Approach

The primary objective in the evaluation of a patient presenting with an ICD shock is to determine whether the event was appropriate (i.e., due to malignant ventricular arrhythmia) or inappropriate (resulting from supraventricular arrhythmias, oversensing, or device/lead dysfunction), and to accurately identify the underlying mechanism in order to prevent recurrence. This process requires a multilayered, multidisciplinary approach that includes detailed analysis of stored EGMs, systematic review of telemetric data, assessment of hardware integrity, and, when necessary, the application of targeted provocative testing (Mukherjee, et al., 2021: 235–240).

Intracardiac Electrogram (EGM) Analysis

Stored EGM recordings represent the gold standard for determining the etiology of ICD shocks (Mukherjee, et al., 2021: 235–240). Analysis should encompass the entire sequence from arrhythmia onset to therapy delivery and be conducted according to the following key parameters:

Near-field (NF) vs. far-field (FF) signal comparison: Simultaneous evaluation of NF (bipolar, tip-to-ring) and FF (unipolar, can-to-coil) channels is critical for identifying the source of artifacts. Noise due to lead fracture is typically confined to the NF channel, while organized QRS complexes remain visible in the FF channel. In contrast, EMI produces synchronous noise with similar morphology in both channels (Bera, et al., 2021: 54–58; Pai, Abedin, & Rawling, 2008: 69–71).

Rhythm discrimination criteria (SVT vs. VT)

Stability: Regularity of R–R intervals is assessed; irregular variability favors AF, whereas a fixed cycle length supports monomorphic VT.

Morphology analysis: Based on comparison of the QRS complex during tachycardia with a stored sinus rhythm template; high morphological concordance (>70%) suggests a supraventricular origin.

Atrioventricular (A–V) relationship: Particularly in dual-chamber systems, comparison of atrial and ventricular rates is essential; a ventricular rate exceeding the atrial rate (V > A) strongly favors VT (Mukherjee, et al., 2021: 235–240).

Assessment of Hardware Integrity

A substantial proportion of inappropriate shocks is attributable to mechanical or electrical abnormalities of the lead and connection system. Therefore, evaluation of the following technical parameters is essential:

Impedance trend analysis: Sudden decreases in impedance (<25 ohms) suggest insulation defects, whereas abrupt increases (>2000 ohms) or wide fluctuations are indicative of conductor fracture or loose connections (loose set screw) (Oosterwerff, et al., 2024: 614–622).

Lead Integrity Alert (LIA): This feature in modern devices analyzes impedance trends and short V–V intervals to detect potential lead dysfunction at an early stage and alert the clinician (Theuns & Jordaens, 2012: 82–85).

Radiological evaluation: Chest radiography and fluoroscopy are useful for assessing lead integrity, positioning, and generator connection. However, normal imaging findings do not exclude electrical dysfunction, as some lead abnormalities may only be detectable on EGM recordings (Oto, et al., 2000: 425–430).

Special Conditions and Provocative Testing

Certain mechanisms of inappropriate shocks manifest only under specific conditions; therefore, targeted provocative testing may support the diagnostic process:

Myopotential-related oversensing: In suspected cases, isometric upper extremity exercises or shoulder maneuvers performed under telemetry monitoring may reproduce noise artifacts (Corzani, et al., 2015: 56–59).

T-wave oversensing (TWOS): Particularly in S-ICD systems, this may be elicited during exercise. Treadmill testing or programmed pacing maneuvers can provoke the "double counting" phenomenon and aid diagnosis (Pearman, et al., 2023: 101–104).

LVAD and electromagnetic interference: In patients with left ventricular assist devices, device-related noise and environmental EMI sources (e.g., wet surfaces, electrical equipment) should be carefully investigated (Pai, Abedin, & Rawling, 2008: 69–71).

Remote Monitoring

Remote monitoring systems play a proactive role in the early detection of inappropriate shocks. Automated alerts transmitted by the device enable early identification of arrhythmia onset, oversensing patterns, and lead dysfunction. The TRUST trial demonstrated that remote monitoring detects clinical events significantly earlier than conventional follow-up methods (median 1 day vs. 5 days). This early detection is particularly critical for preventing recurrent inappropriate shocks and the development of electrical storm (Theuns & Jordaens, 2012: 82–85).

The diagnostic approach following an ICD shock is fundamentally based on systematic analysis of stored EGM data in conjunction with comprehensive assessment of hardware integrity.

Integrated interpretation of rhythm characteristics (rate, stability, morphology, and A–V relationship) alongside technical parameters (impedance trends, noise patterns) is essential for accurate etiological classification. Programming modifications implemented without a definitive diagnosis may expose the patient to untreated malignant arrhythmias; therefore, all interventions should be carefully planned within an evidence-based framework.

Management

The management of inappropriate shocks requires a comprehensive and multidisciplinary approach, ranging from acute control of recurrent discharges to definitive correction of underlying arrhythmic or device-related causes, as well as restoration of the patient's psychosocial well-being. The primary goal is to preserve the established survival benefit of ICD therapy while minimizing unnecessary and potentially harmful interventions, thereby optimizing quality of life (Fleeman & Aleong, 2019: 3623–3632).

Contemporary Programming Paradigms

At the core of current management strategies lies the implementation of evidence-based device programming approaches. Landmark trials such as MADIT-RIT and ADVANCE III have demonstrated the superiority of selective and delayed intervention over early and aggressive treatment strategies (Fleeman & Aleong, 2019: 3623–3632).

High-rate detection strategy: Increasing the VF detection threshold to ≥188–200 bpm reduces inappropriate shocks by excluding many SVTs from treatment zones. (Fleeman & Aleong, 2019: 3623–3632).

Delayed detection: Prolongation of detection intervals (e.g., NID 30/40 or time-based intervals of 6–12 seconds) prevents

unnecessary therapy for non-sustained VT (NSVT) and transient SVT episodes (Chiu, et al., 2025: 2861–2869).

Antitachycardia pacing (ATP): Even when programmed within the VF zone, ATP can terminate fast VT episodes painlessly, thereby significantly reducing shock burden.

Optimization of discrimination algorithms: Ensuring activation of morphology- and atrioventricular relationship–based algorithms (e.g., Wavelet, PR Logic, SMART) within appropriate rate zones, along with regular updating of patient-specific templates, improves SVT–VT discrimination (Fleeman & Aleong, 2019: 3623–3632).

Pharmacological and Interventional Approaches

In arrhythmia-driven inappropriate shocks, management focuses on eliminating the triggering mechanism.

Rate and rhythm control: In patients with AF or sinus tachycardia, beta-blockers and non-dihydropyridine calcium channel blockers represent first-line therapies (Garnreiter, 2017: 2898–2906).

Catheter ablation: In cases of drug-refractory SVTs and selected patients with AF, catheter ablation provides an effective and durable strategy for preventing inappropriate shocks (Fleeman & Aleong, 2019: 3623–3632).

“Pace-and-ablate” strategy: In patients with recurrent inappropriate shocks due to AF with rapid ventricular response, atrioventricular (AV) node ablation combined with physiological pacing (e.g., left bundle branch area pacing [LBBAP]) can achieve rate control while preserving ventricular function (Pestrea, et al., 2024: 248).

Technical and Device-Based Management

In device-related inappropriate shocks, the objective is correction of the underlying mechanical or electrical abnormality.

Acute management: In the setting of recurrent inappropriate discharges (electrical storm), application of a magnet over the device temporarily disables tachyarrhythmia detection and prevents further shocks (Sharma & Kapur, 2023: 222–226).

Lead revision and replacement: In cases of lead fracture or insulation failure, deactivation of the malfunctioning lead and implantation of a new lead is the standard approach. In early postoperative loose set screw scenarios, surgical revision is required (Bera, et al., 2021: 54–58).

Optimization of sensing parameters: Particularly in S-ICD systems, adjustment of sensing vectors and sensitivity settings is essential in cases of T-wave oversensing or myopotential-related noise (Corzani, et al., 2015: 56–59).

Remote Monitoring

Remote monitoring systems play a proactive role in preventing inappropriate shocks. Lead dysfunction, impedance changes, and asymptomatic arrhythmia episodes can be detected early without waiting for clinical presentation. Algorithms such as the LIA enable early identification of potential failures before shock delivery, allowing timely intervention (Theuns & Jordaens, 2012: 82–85).

Psychosocial Support and Patient Education

Given that inappropriate shocks may lead to anxiety, depression, and post-traumatic stress disorder (PTSD), psychosocial support represents an integral component of management. Structured communication strategies, such as the “4A” model (Ask, Advise,

Assist, Arrange), are recommended in clinical practice (Dichtl, et al., 2011: 433–436).

Through cognitive behavioral therapy (CBT), support groups, and patient education programs, it should be clearly communicated that inappropriate shocks represent a manageable clinical condition. Additionally, post-shock recommendations regarding driving and daily activity should be individualized, avoiding unnecessary physical and social restrictions in order to preserve quality of life (Dichtl, et al., 2011: 433–436).

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