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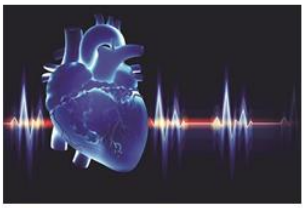
ΠΡΟΓΡΑΜΜΑ ΜΕΤΑΠΤΥΧΙΑΚΩΝ ΣΠΟΥΔΩΝ

«ΚΑΡΔΙΑΚΗ ΑΝΕΠΑΡΚΕΙΑ - ΚΑΡΔΙΟ-ΟΓΚΟΛΟΓΙΑ - ΚΑΡΔΙΑΓΓΕΙΑΚΗ ΑΠΟΚΑΤΑΣΤΑΣΗ»

(MSc in Heart Failure - Cardio-oncology - Cardiac Rehabilitation)



Μεταπτυχιακή Διπλωματική Εργασία

«Οξεία καρδιακή ανεπάρκεια: Επιδημιολογία - Διάγνωση – Αντιμετώπιση»

υπό

Λεωνίδου Έλενας

Ειδικευόμενης Ιατρού Καρδιολογίας

Υπεβλήθη για την εκπλήρωση μέρους των απαιτήσεων για την απόκτηση του

Διπλώματος Μεταπτυχιακών Σπουδών

«Καρδιακή ανεπάρκεια – Καρδιο-ογκολογία – Καρδιαγγειακή αποκατάσταση»

Λάρισα, Φεβρουάριος 2024

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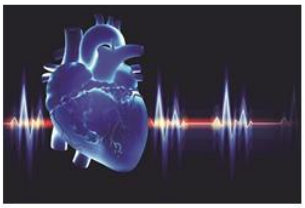

Acute Heart Failure: Epidemiology - Diagnosis – Management

Larissa, February 2024

«Βεβαιώνω ότι η παρούσα διπλωματική εργασία είναι αποτέλεσμα δικής μου δουλειάς και δεν αποτελεί προϊόν αντιγραφής. Στις δημοσιευμένες ή μη δημοσιευμένες πηγές έχω χρησιμοποιήσει εισαγωγικά και όπου απαιτείται έχω παραθέσει τις πηγές τους στο τμήμα της βιβλιογραφίας».

Υπογραφή:

ΛΕΩΝΙΔΟΥ ΕΛΕΝΑ

Πανεπιστήμιο Θεσσαλίας, Σχολή Επιστημών Υγείας, Τμήμα Ιατρικής, 2024

ΔΙΕΥΘΥΝΤΗΣ ΤΟΥ ΠΡΟΓΡΑΜΜΑΤΟΣ ΜΕΤΑΠΤΥΧΙΑΚΩΝ ΣΠΟΥΔΩΝ

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Acute Cardiac Failure: Epidemiology - Diagnosis – Management

Ευχαριστίες

Με την ολοκλήρωση της μεταπτυχιακής διπλωματικής μου εργασίας θα ήθελα να ευχαριστήσω θερμά τον επιβλέποντα Καθηγητή μου, κύριο Γρηγόριο Γιαμούζη για την επιστημονική του καθοδήγηση, το ενδιαφέρον και τις υποδείξεις του.

Επίσης ιδιαίτερες ευχαριστίες θα ήθελα να απευθύνω στον σύμβουλο της διπλωματικής μου εργασίας, Επιμελητή Α΄ του Πανεπιστημιακού Νοσοκομείου Λάρισας, κύριο Κωνσταντίνο Τσαρούχα για τις εποικοδομητικές του υποδείξεις, τις συμβουλές και την ευγενική διαθεσιμότητα του σε όλη τη διάρκεια εκπόνησης της.

Επίσης, θα ήθελα να εκφράσω τις ευχαριστίες μου προς τον κύριο Κυριακό Γιάγκου για την ενθάρρυνση που μου παρείχε να συμμετάσχω στο συγκεκριμένο Πρόγραμμα Μεταπτυχιακών Σπουδών (ΠΜΣ), καθώς επίσης και για τη γενναιοδωρία του προς τους Κύπριους συμμετέχοντες μέσω της χορηγίας υποτροφιών.

Τέλος θα ήθελα να εκφράσω την ευγνωμοσύνη μου στην οικογένεια μου και το σύζυγο μου για τη στήριξη, τη συμπαράσταση και την κατανόηση τους, καθ' όλη τη διάρκεια των σπουδών μου.

ΛΕΩΝΙΔΟΥ ΕΛΕΝΑ

Οξεία καρδιακή ανεπάρκεια: Επιδημιολογία - Διάγνωση – Αντιμετώπιση

Περίληψη

Υπόβαθρο: Η Καρδιακή Ανεπάρκεια είναι κλινικό σύνδρομο που χαρακτηρίζεται από ανατομική ή λειτουργική καρδιακή ανωμαλία, και έχει ως αποτέλεσμα τη μειωμένη καρδιακή παροχή και/ή την αύξηση των ενδοκαρδιακών πιέσεων. Σε αντίθεση με την χρόνια καρδιακή ανεπάρκεια που εξελίσσεται βαθμιαία, η οξεία καρδιακή ανεπάρκεια (ΟΚΑ) απαιτεί άμεση ιατρική παρέμβαση, με συχνές περιπτώσεις νοσηλείας. Η πολυπλοκότητα στην διάγνωση και η μεταβλητότητα των θεραπευτικών αποτελεσμάτων υπογραμμίζουν την ανάγκη για πλήρη κατανόηση του συνδρόμου.

Στόχος: Η παρούσα διπλωματική εργασία εστιάζει στην ανάδειξη των βασικών χαρακτηριστικών της ΟΚΑ, από τις επιδημιολογικές της τάσεις μέχρι τη διάγνωση και τις σύγχρονες θεραπευτικές προσεγγίσεις. Μέσω της σύνθεσης της τρέχουσας έρευνας και των κλινικών γνώσεων, η μελέτη επιδιώκει να εντοπίσει τομείς που απαιτούν περαιτέρω εξερεύνηση.

Μέθοδοι: Μέσω εκτενούς βιβλιογραφικής ανασκόπησης, συγκεντρώθηκαν και αναλύθηκαν πληροφορίες από διάφορες επιστημονικές πηγές, συμπεριλαμβανομένων του PubMed και του Google Scholar.

Αποτελέσματα: Η παθοφυσιολογία της ΟΚΑ είναι πολυπαραγοντική, επηρεάζεται από παράγοντες όπως η παρόξυνση χρόνιας καρδιακής ανεπάρκειας, το οξύ έμφραγμα του μυοκαρδίου και η βαλβιδική καρδιοπάθεια. Οι διαγνωστικές προκλήσεις προκύπτουν από τη μη ειδική φύση των συμπτωμάτων ΟΚΑ. Οι παραδοσιακές θεραπείες όπως τα διουρητικά και τα αγγειοδιασταλτικά παρουσιάζουν ποικίλη αποτελεσματικότητα, προτρέποντας την εξερεύνηση νέων μορφών θεραπείας. Οι παράγοντες κινδύνου, συμπεριλαμβανομένης της ηλικίας, των συννοσηροτήτων και των επιλογών τρόπου ζωής, περιπλέκουν περαιτέρω τη διαχείριση του ΟΚΑ.

Συμπέρασμα: Η ΟΚΑ θέτει σημαντικές κλινικές προκλήσεις, που χαρακτηρίζονται από την ξαφνική εμφάνισή της, τη σοβαρή συμπτωματολογία και τις σχετικές επιβαρύνσεις της υγειονομικής περίθαλψης. Ενώ έχουν σημειωθεί θεραπευτικές εξελίξεις, εξακολουθούν να υπάρχουν κενά στην ακρίβεια της διάγνωσης και στη βελτιστοποίηση της θεραπείας. Αυτή η διπλωματική εργασία υπογραμμίζει την επιτακτική ανάγκη για συνεχή έρευνα, με στόχο την καινοτομία και τη βελτίωση των αλγορίθμων διαχείρισης της ΟΚΑ για βελτίωση της έκβασης των ασθενών.

Λέξεις-κλειδία: Οξεία Καρδιακή Ανεπάρκεια, Καρδιακή Ανεπάρκεια, Επιδημιολογία, Διάγνωση, Διαχείριση, Διαγνωστικές Προκλήσεις

Acute Heart Failure: Epidemiology - Diagnosis – Management

Abstract

Background: Acute Heart Failure (AHF) emerges as a distinct syndrome in the continuum of heart failure, characterized by its abrupt and intense symptomatology. Unlike chronic heart failure, which manifests gradually, AHF's rapid symptom escalation necessitates immediate clinical attention, frequently culminating in hospital admissions. The complexities of its diagnosis and the variability in therapeutic outcomes emphasize the need for a thorough understanding of this syndrome.

Purpose: This thesis offers a comprehensive exploration of AHF, spanning its epidemiological trends, diagnostic complexities, and therapeutic modalities. The study seeks to pinpoint gaps in knowledge and areas necessitating further exploration by synthesizing current research and clinical insights.

Methods: A meticulous examination of literature was undertaken using platforms such as PubMed, Google Scholar, and other renowned databases. The research encompassed studies related to AHF epidemiology, diagnostic tools, therapeutic strategies, and patient outcomes.

Results: The pathophysiology of AHF is multifactorial, influenced by factors like chronic heart failure exacerbation, acute myocardial infarction, and valvular heart disease. Diagnostic challenges arise from the nonspecific nature of AHF symptoms. Traditional therapies like diuretics and vasodilators present varied efficacy, prompting the exploration of novel treatment avenues. Risk factors including age, comorbidities, and lifestyle choices further complicate AHF management.

Conclusion: AHF poses significant clinical challenges, marked by its sudden onset, severe symptomatology, and associated healthcare burdens. While therapeutic advancements have been made, gaps persist in diagnosis precision and treatment optimization. This thesis underscores the imperative for continued research, aiming to innovate and refine AHF management paradigms for improved patient outcomes.

Keywords: Acute Heart Failure, Heart Failure, Epidemiology, Diagnosis, Management, Diagnostic Challenges, Knowledge gaps

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Introduction

Acute heart failure (AHF) is a syndrome defined as the new onset (de novo heart failure (HF)) or worsening (acutely decompensated heart failure (ADHF)) of symptoms and signs of HF, presenting unique challenges in terms of both diagnosis and management.(1)Unlike chronic heart failure, which manifests gradually and can often be stabilized with long-term treatments, AHF often erupts unexpectedly, with symptoms that escalate rapidly, impairing the patient's well-being. It is characterized by an abrupt decline in cardiac output stemming from myocardial dysfunction or structural heart abnormalities. This leads to systemic congestion, impaired tissue perfusion, and a spectrum of symptoms ranging from mild discomfort to severe dyspnea, accompanied by fluid accumulation manifesting as edema, weight gain, and reduced exercise tolerance. The sudden onset and severity of AHF necessitate prompt intervention, often requiring hospitalization.(2)

The significance of AHF becomes evident when considering its clinical impact. Patients with AHF experience reduced quality of life and increased mortality rates. AHF is associated with a higher risk of rehospitalization, often within a short timeframe, placing a substantial burden on healthcare systems and leading to increased healthcare costs.(3, 4) Furthermore, it is not only the acute episode itself that poses risks but also the potential for long-term consequences, such as the worsening of chronic heart failure, which may further compromise cardiac function. (5)

Understanding the pathophysiology of AHF is essential in appreciating its clinical significance. Several factors contribute to the development of AHF, including exacerbation of chronic heart failure, acute myocardial infarction, valvular heart disease, and other precipitating factors. The interplay of neurohormonal activation, fluid overload, and ventricular dysfunction drives the symptomatic cascade in AHF. Furthermore, the exact pathophysiological mechanisms may vary among patients, making the condition even more challenging to manage and treat effectively.(6)

The clinical diagnosis of AHF presents its own set of challenges. The symptoms of AHF, such as dyspnea and edema, are nonspecific and can mimic other medical conditions.(7) Accurate and timely diagnosis is crucial for initiating appropriate treatment and optimizing outcomes.(8) Diagnostic tools, including physical examination, imaging studies, and biomarker assessments, have advanced over the years, but there remains a need for improved accuracy and precision in AHF diagnosis.(9)

Considering the significance of AHF, research and clinical efforts consistently improve therapeutic strategies. Traditional approaches involve diuretics to alleviate fluid overload and vasodilators to improve cardiac output. However, the efficacy of these therapies varies among patients, and their long-term impact is not well defined. (10-12)

In this thesis, we aim to provide a thorough review of AHF, covering its epidemiology, diagnostics, and therapeutic methods, to gain a deeper understanding of this complex syndrome. We will provide a comprehensive survey of the latest research findings and clinical insights. Additionally, through our review, we intend to identify gaps in the existing evidence and highlight areas that require further research. This approach will promote the development of innovative diagnostic and treatment strategies.

Exploring the definition of AHF

HF is a clinical syndrome characterized by diverse causes and pathophysiological mechanisms, that usually develops gradually and worsens over time. Table 1 offers an overview of the latest definitions of HF according to the American College of Cardiology/American Heart Association (ACC/AHA) and the Heart Failure Association / European Society of Cardiology (HFA/ESC) guidelines. Existing definitions have typically focused on specific aspects of this highly complex physiological condition, including factors like ventricular filling pressures, cardiac preload and afterload, oxygen

consumption, left ventricular remodeling and dysfunction, neurohormonal responses, and exercise capacity.(13)

Table 1: Definitions of Heart Failure in Modern Clinical Practice Guidelines

ESC (2021)(10)	HF manifests as a clinical syndrome marked by symptoms like breathlessness, ankle swelling, and fatigue, often accompanied by signs such as increased jugular venous pressure, pulmonary crackles, and peripheral edema. It arises from structural and/or functional heart abnormalities that lead to elevated intracardiac pressures and/or insufficient cardiac output, both at rest and during physical exertion.
ACC-AHA (2022)(14)	HF is a complex clinical syndrome that results from any structural or functional impairment of ventricular filling or ejection of blood. The cardinal manifestations of HF are dyspnea and fatigue, which may limit exercise tolerance, and fluid retention, which may lead to pulmonary and/or splanchnic congestion and/or peripheral edema. Some patients have exercise intolerance but little evidence of fluid retention, whereas others complain primarily of edema, dyspnea, or fatigue.

Although there may be variations in specific details between the definitions of HF in current practice guidelines from the HFA/ESC and ACC/AHA, they do share common elements. Essentially, the existing HF definitions comprise three primary components: evidence of structural heart disease, a history of symptoms commonly associated with HF, and objective signs frequently observed in HF.

Conversely, our understanding of the occurrence and management of individuals presenting with AHF is not as comprehensive. This broad category covers individuals who are either experiencing typical heart failure symptoms and signs for the first time

(de novo AHF) or those with a deterioration of their pre-existing cardiomyopathy (ADHF).

De novo AHF

De novo AHF refers to the abrupt onset of new or exacerbated heart failure symptoms, often necessitating immediate medical attention and unplanned hospitalization. This condition requires prompt evaluation and treatment.(12)

This sudden manifestation typically occurs due to elevated intracardiac filling pressures or acute myocardial dysfunction, resulting in reduced peripheral blood flow and pulmonary edema. Cardiac ischemia, commonly caused by blocked coronary arteries, is the leading factor, demanding stabilization of the patient's hemodynamics and efforts to restore myocardial contractile function through reperfusion.

Less frequently, non-ischemic factors like viral infections, drug-induced cardiomyopathy, peripartum cardiomyopathy, or unknown causes can trigger de novo AHF. Hospitalization for this condition may lead to a chronic HF diagnosis due to the long-term effects of these acute insults. Additionally, AHF can arise from conditions such as arrhythmogenic cardiomyopathy, Takotsubo cardiomyopathy, or endocrine-related issues, necessitating immediate hemodynamic support and the identification and correction of the underlying problem.

Valvular issues, often related to ischemic damage, can also induce AHF by causing acute mitral regurgitation. External factors such as pulmonary embolism or pericardial effusion, leading to tamponade, can reduce left ventricular output and peripheral blood flow.

The management of de novo AHF involves addressing hemodynamic instability, either through pharmaceutical interventions or mechanical support, and addressing the underlying cause.(15)

Acute Decompensated HF

Most patients with AHF typically present with underlying cardiomyopathy, referred to as ADHF. Notable distinctions exist between these individuals and those with new-onset AHF, impacting the assessment of hemodynamic compromise and treatment approaches.(16)

In contrast to new-onset AHF, ADHF patients typically display signs of congestion and fluid retention (e.g., weight gain, exertional dyspnea, orthopnea, dependent edema), rather than the pulmonary edema or cardiogenic shock seen in acute left ventricular systolic dysfunction. This discrepancy results from the chronic and often dysregulated compensatory mechanisms aimed at maintaining hemodynamic stability despite deteriorating left ventricular function. Decompensation occurs when these mechanisms prove inadequate or fail entirely.(17)

Like new-onset AHF, decompensation of CHF can manifest in various clinical settings. Demographic studies of decompensated CHF patients reveal a high prevalence of comorbid conditions, including atrial fibrillation/flutter (30-46%), valvular heart disease (44%), and dilated cardiomyopathy (25%).(18) The balance of these conditions is delicate in individuals with pre-existing myocardial dysfunction, and any disruption, such as an episode of atrial fibrillation with a rapid heart rate, can trigger decompensation, leading to AHF admission.

ADHF patients present with a more gradual onset of symptoms, complicated by multiple medical comorbidities, with congestion often as the predominant clinical

feature. Management primarily focuses on addressing concurrent triggers and encouraging adherence to disease-modifying therapy.

Epidemiology of AHF

HF represents a significant and growing clinical concern in the field of cardiology and healthcare, affecting more than 63 million patients worldwide.(19, 20) The economic burden associated with HF is ranging from under 1,000 USD per patient in low-income nations to approximately 5,000-15,000 EUR in Europe, and 17,000-30,000 USD in the United States.(21) The burden of HF is on the rise, driven by several factors. The aging population, increasing rates of cardiovascular risk factors like hypertension and diabetes, and improved survival from other conditions that may lead to heart failure all contribute to this growing healthcare challenge. While the estimates may differ based on the specific population being studied, the prevalence of heart failure typically ranges from 1% to 2%. However, this prevalence significantly increases to over 10% among individuals aged 70 years or older, underscoring the substantial impact of AHF on the aging population. (22) Adding to the complexity of HF's epidemiology, a registry led by Mercier, G. et al. in France estimated the incidence of AHF in Western countries to be approximately 5 to 10 new cases per 1000 person-years.(23)

AHF is a condition affecting individuals of all ages, with its global prevalence steadily increasing. Additionally is recognized as one of the most frequent reasons for hospital admissions, primarily to emergency departments, making it a paramount public health concern.(24) However, when compared to CHF, there is a significant lack of comprehensive data on the frequency of AHF occurrences worldwide. Inconsistent data collection, variations in healthcare reporting practices, and limited research in certain regions all contribute to this inadequate documentation and understanding of AHF's epidemiology. This knowledge gap underscores the need for standardized data collection methods.

Gender differences in AHF have been a subject of significant research and analysis. Various studies and registries have provided valuable insights into these disparities. The European Society of Cardiology Heart Failure Long-Term (ESC-HF-LT) registry, which included patients with AHF, provides critical information about the demographics of AHF patients. The average age of the participants in this registry was approximately 70 years, reflecting the predominance of elderly individuals among AHF cases. In this registry, 61% of the patients were male, while 33% were classified as New York Heart Association (NYHA) class IV. (4) In the same manner, the EuroHeart Failure Survey II (EHFS II) encompassed a broad European scope, spanning 30 countries and engaging 133 participating hospitals. Among the 3580 patients enrolled in EHFS II, 1384 (39%) were women, with an average age of 73 years, while 2196 (61%) were men, with a mean age of 68 years.(17)

Furthermore, as reported in the registry led by Spinar, J. and their research team, the patients had a mean age of 70.3 years, with a notable proportion (32.5%) falling within the age range of 70 to 79 years. Notably, female patients were comparatively older, with an average age of 76.3, in contrast to their male counterparts with an average age of 69.2. Additionally, the incidence of new-onset AHF was notably higher among female patients, accounting for 41% of cases, compared to male subjects, where it represented 35% of the cases.(25) Building on these findings, the Acute Heart Failure Database (AHEAD) registry, conducted within a single university center with 24-hour catheterization laboratory services, provided additional insights. This registry encompassed 1253 patients, with 534 females and 719 males, and was conducted between 2006 and 2007. Among these patients, 56% had de novo AHF, and 43.9% experienced ADHF, with the majority (61.7%) being male. Notably, women exhibited a higher likelihood of experiencing de novo, representing 60.3% of cases, compared to men, where de novo HF accounted for 53.4% of cases.(26)

Cardiac and non-cardiac comorbidities are highly prevalent among both chronic and acute patients worldwide. In the case of AHF, data from the ESC-HF-LT registry revealed that more than half of all AHF patients (56%) had a known history of ischemic heart disease, which was complicated by myocardial infarction in 20-30% of cases.

Furthermore, approximately 70% and 40% of AHF patients, respectively, had a prior history of hypertension and atrial fibrillation. Non-cardiac co morbidities, including diabetes mellitus (39%), chronic kidney disease (26%), and chronic obstructive pulmonary disease (21%), were also highly prevalent.(4) When examining gender disparities, female patients exhibited specific characteristics, including higher systolic blood pressure, a greater prevalence of hypertension (67.4% vs. 59.4%), diabetes mellitus (35.0% vs. 31.4%), anemia (18.5% vs. 12.4%), or thyroid disease (11.1% vs. 4.4%), and less coronary artery disease (44.1% vs. 59.4%). Conversely, male patients were more commonly current smokers (19.8% vs. 6.9%) and had a higher incidence of chronic obstructive pulmonary disease (22.1% vs. 15.0%).(17)

One notable comorbidity prevalent in AHF patients is iron deficiency, affecting approximately 35-55% of individuals with chronic HF and reaching higher proportions of up to 70-80% in those with AHF. Addressing this, the AFFIRM-AHF trial evaluated the effectiveness of intravenous ferric carboxymaltose (FCM) therapy, a recommended disease-modifying treatment for AHF. Compared to a placebo, FCM therapy substantially reduced the risk of recurrent hospitalizations for heart failure and simultaneously enhanced the quality of life in iron-deficient patients with left ventricular ejection fraction (LVEF) less than 50%, which had stabilized following an episode of AHF.(27)

Hospitalizations and rehospitalizations represent significant components of the AHF landscape. While hospitalization for heart failure is estimated to account for 1–5% of hospital admissions in Western countries, it takes a more substantial toll on individuals aged 65 and older, remaining the leading cause of hospitalization within this demographic. Over the course of one year, approximately 12–45% of patients with heart failure will experience hospitalizations for heart failure. Furthermore, all-cause hospitalizations affect the majority of HF patients, with a staggering 63% facing hospitalizations for various causes.(28) The prognosis for AHF patients is alarming, with in-hospital mortality rates ranging from 4% to 7%, while 60- to 90-day mortality rates vary between 7% and 11%. Additionally, a substantial proportion of patients (25% to 30%) experience rehospitalization within 60 to 90 days of their initial

hospitalization.(24) Patients with cardiogenic shock had the highest in-hospital mortality rate, with 50% of deaths occurring on the first day of admission.(29) Clinical outcomes also exhibit gender-related differences. For instance, women tend to have a lower all-cause readmission rate during the one-year follow-up. However, the proportion of heart failure-related hospitalization and one-year mortality after discharge remains similar in both genders. This suggests that while the immediate post-discharge outcomes may differ, long-term prognosis and healthcare utilization exhibit some level of parity between men and women.(17)

The complex nature of AHF results from a multitude of factors, both cardiovascular and non-cardiovascular, along with patient-related and iatrogenic influences, which can swiftly precipitate the development or deterioration of heart failure symptoms. This, in turn, necessitates hospitalization to manage the acute episode effectively. Post-discharge, the risk of rehospitalization is prominent, with roughly one-fourth of patients readmitted within the first three months and two-thirds experiencing rehospitalization within a year. Furthermore, the readmission pattern exhibits a biphasic course, characterized by two peaks – an early surge during the first 2 to 3 months post-discharge and a subsequent rise during the later stages of the syndrome, separated by an extended plateau phase marked by lower admission rates.(30) Despite these daunting statistics, gender disparities do not significantly influence the duration of hospitalization for AHF patients. The mean length of in-hospital stay remains relatively consistent at nine days, with no noticeable gender-based difference in this regard. Whether considering female or male patients, the average duration of hospitalization remains quite similar, highlighting that the complex clinical course and prognosis of AHF are not markedly affected by gender.(24)

While the exact prevalence of AHF can vary based on geographic location and population demographics, it remains a considerable public health issue worldwide. Recent multinational cohort studies, like INTERnational Congestive Heart Failure Study (INTER-CHF), have shed light on these disparities. In China, the 1-year mortality rate for AHF is notably lower at 7%, whereas South America and the Middle East report a 9% rate, and African countries exhibit a much higher 34% mortality rate. These

differences suggest that diverse factors, including disparities in healthcare infrastructure, quality, and accessibility, along with environmental and genetic influences, may contribute to regional variations in AHF mortality.

Similar regional disparities are observed in Asian countries, where the economic differences between nations play a role. In the context of patients with HF with reduced ejection fraction (HFrEF), Southeast Asia experiences the highest 1-year mortality rate, reaching 13.6%. In contrast, Northeast Asia reports an 8.9% rate, and South Asia records an 8.3% rate. Remarkably, despite having relatively younger populations, individual countries like Indonesia (21.4%) and the Philippines (14.3%) exhibit higher mortality rates, whereas Japan, characterized by an older population, reports the lowest 1-year mortality rate at 4.4%. This data highlights how the economic, environmental, and demographic factors within regions can significantly impact the epidemiology and outcomes of AHF.(21)

In summary, AHF is a global public health concern characterized by a substantial and escalating burden on healthcare systems. The epidemiology of AHF is diverse, influenced by various factors including demographic, gender-related, comorbidities, and regional variations. Understanding these nuances is essential for tailoring effective prevention and management strategies. Despite the challenges posed by this multifaceted condition, consistent data collection methods and international collaboration are critical steps toward improving our understanding and addressing the growing burden of acute heart failure worldwide.

Diagnosis of AHF

The diagnosis of AHF, whether it manifests as de novo or ADHF, is a multifaceted process that demands a combination of clinical expertise, medical history assessment, and various diagnostic tools. AHF is a critical condition characterized by a sudden

decrease of cardiac output, leading to a cascade of distressing symptoms. Distinguishing between the two forms—de novo, occurring without a prior heart disease history, and acute decompensated, marked by an abrupt worsening of CHF—is essential for tailoring appropriate treatment strategies. The clinical presentation of both forms shares common features, although they may differ in terms of the patient's medical history.

HF patients display significant heterogeneity concerning cardiac structure, function, etiology, exacerbating factors for AHF, comorbidities, and medication regimens. Timely and accurate diagnosis is important, as any delays or diagnostic errors have been linked to a heightened risk of adverse outcomes and mortality. It's noteworthy that up to one-third of patients experience misdiagnosis during their initial presentation, with chronic obstructive pulmonary disease (COPD) being the most common reason for misdiagnosis.(31-33) This highlights the crucial necessity for increased clinical vigilance and the adoption of improved diagnostic approaches in the management of this complex and potentially life-threatening medical condition.

Patients with AHF typically exhibit a range of distressing symptoms. In most cases, patients with AHF experience a gradual emergence of HF symptoms, which usually develop over days to weeks. This gradual progression is thought to be driven, at least in part, by a complex interplay of factors, including renal and dietary influences, leading to systemic congestion. Remarkably, changes in filling pressure of the heart and, on occasion, body weight are observed to increase at least one week prior to the onset of acute decompensation.(34) In the study conducted by Goldberg et al., patients predominantly cited dyspnea (93%) as their primary concern, with peripheral edema (70%), cough (51%), orthopnea (37%), and chest pain or discomfort (30%) following as other commonly reported symptoms. Dyspnea (shortness of breath) is a hallmark sign, often severe and triggered by minimal exertion or when lying down, which is known as orthopnea. Patients may also experience paroxysmal nocturnal dyspnea, a sudden awakening from sleep with extreme breathlessness. Fluid retention is another key feature, leading to rapid weight gain, swelling in the legs (peripheral edema), and sometimes abdominal bloating. Fatigue and weakness are prevalent, and patients may report a persistent cough, often accompanied by frothy or pink-tinged sputum.

Tachycardia is a compensatory response to maintain cardiac output, and chest discomfort can occur, mimicking symptoms of a heart attack. In severe cases, inadequate blood flow to the brain can result in confusion or altered mental status.(7, 32, 35, 36)

The clinical examination of patients with AHF is a pivotal component of the diagnostic process and plays a crucial role in guiding appropriate therapeutic interventions. This examination encompasses several key aspects that collectively provide a comprehensive assessment of the patient's condition. Symptoms of AHF are often accompanied by a range of clinical signs that provide invaluable insights into the patient's condition and serve as essential guides for healthcare professionals involved in diagnosis and management. Among these clinical signs, tachypnea, characterized by rapid and labored breathing, and tachycardia, involving an elevated heart rate, are frequently observed. The presence of low or normal blood pressure reflects the heart's compromised ability to effectively pump blood, contributing to the overall clinical picture of AHF. Another cardinal sign is raised jugular venous pressure (JVP). Measurement of the JVP is performed by examining the pulsations of the internal jugular vein in the neck. An elevated JVP can indicate increased central venous pressure, which reflects elevated right atrial pressure—a common finding in AHF. The measurement of JVP demonstrates a specificity of 87% and a sensitivity of 37.2% in identifying HF. (36-38) Monitoring JVP is essential not only for diagnosis but also for guiding therapeutic decisions, such as the appropriate use of diuretics to address fluid overload. The identification of the 3rd or 4th heart sound, referred to as gallops, during auscultation is indicative of abnormalities in the heart's rhythm and filling, further assisting in diagnosis. The S3 heart sound demonstrates an impressive level of specificity, falling within the range of 97.7% to 99%. Nevertheless, it is important to note that its sensitivity is notably lower, measuring at only 12.7%. (39) Additionally, the detection of rales, characterized by crackling sounds during lung auscultation, is a strong indicator of pulmonary congestion and fluid accumulation in the lungs. Peripheral edema, often localized in the legs and ankles, is a common clinical finding, reflecting the retention of excess fluid, while patients may experience intolerance of the supine position due to aggravated dyspnea when lying down.(12, 39-42)

In a meta-analysis assessing diverse signs and symptoms in patients experiencing dyspnea, it was determined that no individual sign or symptom possessed sufficient discriminatory power to conclusively rule out AHF, COPD, asthma, or pulmonary embolism. However, findings such as elevated JVP, the presence of a third heart sound, and lung crepitations were strongly indicative of a potential diagnosis of AHF.(43)

These clinical signs collectively contribute to the comprehensive assessment of AHF, aiding in the prompt diagnosis and appropriate interventions to alleviate symptoms and enhance cardiac function. The recognition of these signs is vital in distinguishing HF from other medical conditions that may present with similar symptoms, ultimately improving patient care and outcomes in the management of this challenging cardiac condition.

Another crucial component of the diagnostic cascade for AHF is the comprehensive medical history of the patient. It holds considerable diagnostic and therapeutic significance. It is a cornerstone of the clinical assessment, providing vital information about the patient's underlying risk factors, previous cardiac conditions, and ongoing medical management. The comprehensive medical history should encompass details regarding the patient's cardiovascular risk factors, as these can contribute to the development of heart failure.

Risk factors for AHF include hypertension, renal disease, pre-existing heart disease, diabetes, male gender, older age, and obesity. Advanced age, renal disease, and lower blood pressure are associated with increased mortality in cases of AHF.(24, 37, 44, 45) Precipitating factors for AHF exacerbations can be attributed to both cardiac and non-cardiac causes. Cardiac triggers include uncontrolled hypertension, dietary or medication noncompliance, aortic dissection, dysrhythmias, and cardiac ischemia. Non-cardiac triggers encompass pulmonary disease, endocrine disorders, infections, worsening renal function, anemia, and medication side effects.(37, 46) It has been observed that patients who exhibit non-compliance with their prescribed diet and medications tend to have lower ejection fractions, higher brain-type natriuretic peptide

(BNP) levels, and more severe congestion when compared to their counterparts.(47) Dysrhythmias, with atrial fibrillation being the most common among them, frequently serve as precipitating causes. Acute coronary syndrome (ACS) is more commonly associated with de novo HF.(7) A patient's medical history, including factors like weight gain, dyspnea, chest pain, peripheral edema, substance use, new medications, past complications, previous hospitalizations, diet modifications (e.g., salt or fluid intake), and medication adherence, plays a vital role in determining the underlying cause of HF, with an identifiable trigger being found in approximately 60% of patients.(37, 38)

In the context of AHF, a thorough diagnostic assessment is paramount for accurate diagnosis, risk stratification, and appropriate management. This multifaceted evaluation involves a range of diagnostic tests that serve distinct roles, collectively contributing to a comprehensive understanding of the patient's condition.

Laboratory Testing

Routine biochemical examinations during hospital admission include hemogram, blood glucose, urea, creatinine, BUN, estimated glomerular filtration rate (eGFR), electrolytes, transaminases, C-reactive protein, and thyroid-stimulating hormone (TSH) level should be conducted. Biochemical analysis can provide information on the precipitating factors of AHF (e.g., anemia, infection, hyper- or hypothyroidism, renal failure, etc.) and assist in deciding for suitable drug treatment.(48-50) Abnormalities in liver function are prevalent in approximately 75% of patients with AHF and are associated with the severity of the disease. When the right ventricle is involved, bilirubin and alkaline phosphatase levels may rise, while left-sided disease is more commonly associated with elevated transaminase levels.(51, 52) Renal function assessment is vital, serving as a predictor of disease severity and mortality. A decreased GFR is linked to prolonged in-hospital stays, short-term mortality, and long-term mortality. Notably, in patients with AHF, every 10 mL/minute decrease in GFR is associated with a 7% increase in mortality. Creatinine and electrolytes should be

monitored at short intervals during AHF treatment, especially with ongoing signs of congestion, as deterioration in renal function is associated with a poor prognosis.(53-56)

In addition to a basic metabolic profile and complete blood count, it is advisable to include cardiac enzymes, particularly troponins, in the evaluation of patients with AHF, especially when there is suspicion of a myocardial infarction. Notably, elevated cTn (cardiac Troponin) levels are not exclusive to ACS and can also be observed in various other conditions, including AHF, where they carry significant prognostic implications. The elevation of cTn is intricately linked to diverse pathophysiological processes, such as subendocardial ischemia, activation of inflammatory markers, and heightened myocardial demand associated with fixed coronary disease. Elevated troponin levels are linked to higher rates of re-hospitalization and increased 90-day mortality, and both BNP and troponin are recommended in guidelines for the comprehensive evaluation and risk stratification of patients with AHF.(40, 57, 58)

Additionally, the inclusion of arterial blood gas measurement is advisable for patients exhibiting signs of dyspnea or hypoxia, facilitating the recognition of respiratory failure and acidosis in individuals with AHF. When contemplating non-invasive or invasive ventilation strategies, a critical aspect is the assessment of oxygen saturation and partial oxygen pressure. In situations where obtaining arterial samples presents challenges, venous samples can serve as a viable alternative for evaluating blood gases. The interpretation of arterial acidosis and hypercapnia from venous samples involves specific cut-off limits, with a blood pH below 7.32 and pCO2 exceeding 51.3 mm Hg being indicative of these conditions.(59)

Furthermore, natriuretic peptides, particularly BNP and N-terminal pro-B-type natriuretic peptide (NT-proBNP), serve as crucial adjuncts in achieving diagnostic precision. Synthesized primarily by cardiac myocytes in the ventricles, these peptides respond to elevated tension in ventricular walls.(60) Their assessment is pivotal in the emergency room for differentially diagnosing dyspnea. In the specific context of dyspnea, both BNP (with a cutoff of <100 pg/mL) and NT-proBNP (with a cutoff of

<300 pg/mL) are valuable tools, aiding in excluding AHF.(61) However, it's essential to recognize that natriuretic peptide levels can rise in various conditions, such as pulmonary embolism, pulmonary hypertension, valvular heart disease, acute respiratory distress syndrome, impaired kidney function, elevated body mass index (BMI), and obesity. Noteworthy is the potential impact of obesity, which may distort natriuretic peptide levels downward, while renal disease can falsely elevate them, particularly with a GFR below 60 mL/min.(62-66) Based on the review by Long et al., increased levels moderately raise the probability of AHF, demonstrating a specificity of 72.9% at 1550 pg/mL for NT-proBNP. Levels surpassing 400 pg/mL for BNP or 900 pg/mL for NT-proBNP suggest the presence of AHF, with an adjustment to 1800 pg/mL for NT-proBNP applicable to individuals over 75 years old.(7)

Despite their role in distinguishing conditions, the application of these biomarkers has not consistently demonstrated improved patient-centered outcomes in various studies. Observational trial data highlight notable sensitivity but poor specificity for natriuretic peptides. Findings from randomized controlled trials suggest that awareness of BNP levels may not significantly impact emergency department treatment, mortality, or readmission rates.(7, 67, 68) However, it could contribute to a reduction in hospital length of stay and overall cost.(69) The integration of these biomarkers and routine laboratory tests adds an important dimension to the diagnostic process, providing quantitative data for risk assessment and therapeutic monitoring.

Imaging

Imaging is a vital component in assessing patients with suspected HF, offering crucial information about both the structural and functional aspects of the heart. Alongside imaging, electrocardiograms (ECGs) play a key role in providing insights into the electrical activity of the heart. In AHF, ECGs can reveal changes associated with acute myocardial ischemia, such as ST-segment deviations or T-wave abnormalities. These findings are indicative of cardiac abnormalities contributing to AHF, whether it be

ischemic in nature or related to other cardiac pathologies. ECG findings are pivotal for identifying the underlying cause and guiding immediate treatment decisions. Furthermore, the details furnished by the ECG complement the findings from biomarker assessments, aiding in confirming the diagnosis of AHF in situations where the cause of dyspnea is uncertain. Moreover, the ECG in patients hospitalized for AHF holds substantial prognostic implications in both the short and long term and requires thorough analysis. According to Vaclavik, J. et al. and Chertan, A. et al., QT prolongation emerged as an independent predictor of overall mortality in individuals with HF, while left ventricular hypertrophy (LVH) was frequently observed in the ECGs of patients experiencing AHF, respectively.(70, 71)

Chest X-ray is a pivotal diagnostic tool in the assessment of patients admitted with suspected AHF. This imaging modality plays a crucial role in identifying cardiac enlargement and manifestations of pulmonary congestion, such as vascular redistribution, interstitial or alveolar edema, and pleural effusion. The classic "bat-wing" appearance, indicative of alveolar edema, is a hallmark finding on chest X-rays in cases of AHF. Additionally, it serves as a valuable tool in ruling out alternative causes of dyspnea, including pulmonary diseases. Despite its significance, it's important to note that a normal chest X-ray, observed in around 20% of cases, does not definitively exclude the diagnosis of AHF. The chest X-ray findings, encompassing pleural effusions, cardiomegaly, Kerley B-lines, dilated upper lobe vessels, increased cardiothoracic ratio and upper lobe pulmonary venous congestion, provide a comprehensive overview of the signs of acute pulmonary congestion. Notably, radiographic interpretation regarding the presence or absence of CHF may have limitations, as demonstrated by the breathing not properly study, underlining the importance of a comprehensive clinical evaluation.(72-74)

Moreover, echocardiography is a recommended diagnostic procedure for differentiating and planning the treatment of AHF. Both the updated 2022 recommendation from the AHA and the 2021 ESC guidelines agree that echocardiography is the most useful imaging tool in the evaluation and initial diagnosis of systolic and diastolic cardiac dysfunction and, at times, can reveal the etiology of new onset HF.(14, 65) According to

Papadimitriou, L. et al, a feasible and reasonable window for baseline assessment is within 24h from hospital admission.(75) This non-invasive imaging modality offers dynamic assessment of cardiac function, providing information on LVEF, valve function, and chamber size. Echocardiography aids in distinguishing between systolic and diastolic HF, offering critical insights into the specific nature of cardiac dysfunction. This diagnostic tool proves valuable in establishing a diagnosis and identifying potential causes such as ischemia, pericardial tamponade, or valvular disease in HF. It is invaluable for assessing structural and functional aspects of the heart, helping clinicians make informed decisions about treatment strategies and prognosis.(7, 76)

Lung ultrasound is emerging as a highly sensitive tool in AHF diagnosis, enabling real-time visualization of pulmonary congestion. This test is particularly useful for differentiating AHF from other causes of acute respiratory distress. Lung ultrasound reveals characteristic artifacts, such as B-lines, which indicate fluid accumulation in the interstitial and alveolar spaces - comet tails - while A-lines signify COPD. These findings can assist in rapid diagnosis and assessing the response to treatment. The portability and immediacy of lung ultrasound make it a valuable tool in various clinical settings, facilitating quick decision-making in emergency situations.(77, 78) According to Russell, F. et al, by using a combination of lung, cardiac, and inferior vena cava ultrasound, the authors were able to improve diagnostic accuracy by 20%.(79)

In conclusion, the integration of these diagnostic tests is pivotal in diagnosing AHF, determining its etiology, assessing its severity, and guiding appropriate treatment. They collectively contribute to a comprehensive understanding of the patient's condition, facilitating timely and tailored interventions, which are essential in the management of this critical cardiac condition. The differential diagnosis of AHF is a crucial clinical challenge, as it requires distinguishing between acute heart failure from alternative causes of acute dyspnea and non-cardiac causes of acute respiratory distress and other associated symptoms. While AHF is a common cause, other medical conditions can mimic its presentation.

Factors that Initiate AHF

Precipitating factors refer to the specific events, conditions, or triggers that lead to or contribute to the occurrence of a medical situation. In the context of AHF, precipitating factors are the factors that initiate or contribute to the conversion of stable CHF into a decompensated state, causing acute exacerbation of symptoms. These precipitating factors are categorized into two main groups: cardiac and non-cardiac.

Cardiac factors contributing to the onset of de novo HF or ADHF encompass a spectrum of issues, including uncontrolled hypertension, non-compliance with HF medication, arrhythmias, valvular disease, and ischemia—particularly ACS. Insights gathered from patient admissions to the EHFS II and other registry studies shed light on the predominant causes of decompensation. Ischemia and ACS were identified as the primary factors initiating de novo HF, constituting 14.7% of cases. Arrigo, M. et al. highlight in the intercontinental GREAT registry that patients experiencing AHF triggered by ACSs or infections face elevated short-term mortality in contrast to those initiated by atrial fibrillation (AF) or uncontrolled hypertension.(80) Furthermore, arrhythmias, notably AF and atrial flutter, along with valvular diseases like moderate to severe mitral regurgitation (MR) or tricuspid regurgitation (TR), and less common severe aortic stenosis (AS), emerged as the second major factor. AF and atrial flutter not only worsen AF but also increase the risk of thromboembolic complications, such as stroke, thereby contributing to higher mortality rates.

Additionally, valvular diseases further complicate matters by disrupting normal blood flow within the heart, leading to heightened pressure and volume overload. This additional strain compromises the myocardium's ability to effectively pump blood, contributing to the progressive nature of HF. Uncontrolled hypertension ranked as the third most prevalent factor, contributing to 10.7% of cases, underscoring the critical role of blood pressure management in preventing HF exacerbations. Non-compliance with HF medication represented the fourth most common cause, emphasizing the need for

patients to adhere to prescribed treatment regimens for optimal HF management. valvular diseases and treatment non-compliance more frequently lead to decompensated AHF.

Non-cardiac factors significantly contribute to the initiation or exacerbation of CHF across various domains. These include pulmonary conditions such as COPD, pneumonia, or pulmonary embolism, which can impose an additional burden on the heart by compromising oxygenation and increasing pulmonary vascular resistance. Opasich, C. et al found that pulmonary infections are the second most common reason for the decompensation of CHF.(81) Renal causes, encompassing worsening renal function or chronic kidney disease, contribute to fluid retention and elevate systemic pressure, exacerbating CHF symptoms. Liver diseases, such as cirrhosis, can lead to an increase in systemic venous pressure, impacting cardiac function. Additionally, endocrine disorders, including thyroid dysfunction or diabetes, introduce hormonal imbalances that can impact cardiovascular function, contributing to HF progression.

Anemia, characterized by a reduced oxygen-carrying capacity of the blood, places increased strain on the heart to meet the body's oxygen demands. Drug-induced causes, particularly certain medications like nonsteroidal anti-inflammatory drugs (NSAIDs), specific antihypertensive medications such as calcium antagonists and beta-blockers, and chemotherapeutic agents like anthracyclines, may trigger or worsen HF. Furthermore, alcoholism, with its impact on the cardiovascular system and potential toxicity to the heart muscle, represents another non-cardiac factor capable of initiating or exacerbating CHF.(17, 50, 82)

Understanding and addressing these precipitating factors are crucial for managing and preventing the exacerbation of HF symptoms. This is evidenced by numerous studies that establish a correlation between these factors and both mortality and readmission rates.

Management of AHF

The effective management of AHF demands a multifaceted and comprehensive approach, encompassing various phases of care to address the complex nature of this medical condition. From the initial pre-hospital phase to in-hospital interventions and subsequent pre-discharge and early post-discharge phases, a careful strategy is essential to navigate the complexities of AHF. In recent years, clinical practice guidelines have emphasized the significance of a 'time-to-treatment' concept in AHF, advocating for early intervention ideally before hospital admission.(12, 41, 83) Consistent evidence from randomized controlled trials and observational studies (Takahashi et al., Plaisance et al., Peacock et al., Packer et al., Metra et al., Maisel et al., and Park et al.) underscores the impact of timely medical attention, related to approaches seen in other acute cardiovascular conditions, on shaping favorable patient outcomes.(34)

On the other hand, a comprehension of the disease's pathophysiology is essential. Despite the gradual increase in intracardiac pressure/pulmonary artery pressure in AHF, irrespective of the LVEF, patients present with varied clinical courses and manifestations. Therefore, a critical element of effective management involves accurately categorizing patients according to their underlying pathophysiology and clinical phenotypes, facilitating precise and tailored interventions.(84) Finally, it is crucial that pre-hospital interventions do not delay the transportation of the patient to the hospital, as longer transportation times by EMS have been linked to increased mortality rates.(85)

Pre-hospital Phase of Management: Embracing the Time-to-Treatment Concept

The pre-hospital phase of AHF management is crucial, emphasizing the 'Time-to-Treatment' concept as we discuss. Early intervention plays a significant role in patient

outcomes.(12, 86) The first medical contact for a patient experiencing AHF symptoms is Emergency Medical Services (EMS), which plays an important role in the initial assessment and treatment of AHF. Studies have shown that EMS can achieve high specificity (98%) and diagnostic accuracy (77%) for AHF.(87) In this pre-hospital setting, individuals displaying AHF symptoms should undergo an immediate clinical examination, focusing on the patient's airway, breathing, circulation, and disability, with special attention to the presenting problem. Vital signs are swiftly assessed through non-invasive diagnostic tools, to measure pulse oximetry, blood pressure, respiratory rate, and to perfume an ECG to gauge the severity of the condition.

Additionally, during this initial encounter, EMS should gather essential information regarding the patient's chief complaint, medical history, allergies, medications, and events leading to the present situation. Identifying the root cause of symptoms in AHF constitutes a crucial component of the initial management strategy. This proactive approach not only addresses the immediate concern but also sets the stage for subsequent interventions aligned with the specific etiology contributing to AHF symptoms. These interventions may encompass myocardial revascularization in the case of ACS, antimicrobial treatment if the cause is an infection, and, in certain situations, the consideration of ventricular assist devices, particularly if arrhythmias are identified as contributing factors to AHF.(65)

Clinical guidelines emphasize the prompt relief of symptoms in AHF.(14, 65) In cases of detected hypoxia (SpO2 <90% to 94%), oxygen supplementation is recommended. While supplemental oxygen has been a longstanding therapy for hypoxemic patients with AHF, recent clinical observations highlight potential negative consequences, particularly in normoxemic patients with HF. Studies reveal that supplemental oxygen is often prescribed in the Emergency Department for AHF patients, irrespective of oxygen saturation levels. The benefits or harms of oxygen therapy in AHF remain uncertain, and guidelines provide varying recommendations, reflecting the lack of robust evidence.(88, 89) Also, when respiratory distress, characterized by increased efforts to breathe or rapid breathing, is identified, the consideration of non-invasive ventilation becomes crucial. Compared with conventional oxygen therapy, NIV improves

oxygenation and rapidly reduces breathing effort, thereby leading to a prompt restoration of respiratory function, consequently reducing the risk of tracheal intubation and mortality.(90)

Moreover, once the diagnosis of AHF is established, the administration of intravenous (IV) diuretics, such as furosemide, along with non-invasive ventilation, is crucial to achieving early decongestion of the patient and relieving the symptoms. Studies have indicated that early IV administration of furosemide is associated with favorable outcomes, including a lower mortality rate. This underscores the importance of timely and targeted interventions in AHF management, with a focus on IV therapies to address fluid overload and alleviate symptoms.(86, 91-93) Together with diuretics, another medication that can improve the symptoms of the patient are vasodilators (e.g. nitrates or natriuretic peptides). The systematic combination of IV vasodilators with diuretics is recommended for patients with elevated systolic blood pressure (>110 mmHg). It is crucial to note that the use of vasodilators is not indicated in AHF cases where the systolic blood pressure is below 90 mmHg. Some studies have collectively demonstrated that vasodilatory agents, when used in AHF, do not confer prognostic benefits.(1, 89, 94)

Also, the administration of bronchodilators (e.g., albuterol) in the prehospital setting is suggested as another intervention in the pre-hospital management of AHF. Notably, the administration of bronchodilators in the prehospital and emergency department settings for patients with AHF has been linked to an increased risk of in-hospital mechanical ventilation, intensive care unit admission, and longer hospital stays, prompting careful consideration of treatment strategies in the pre-hospital phase.(87)

Upon reaching the hospital, patients should undergo triage to assess cardiopulmonary stability, ruling out conditions such as cardiogenic shock and respiratory failure. Following triage, a thorough clinical evaluation, including simultaneous diagnostic tests, physical assessments, as well as pharmacologic and nonpharmacologic treatments, is imperative.

In-hospital management: Navigating Congestion and Perfusion Dynamics

The in-hospital management of AHF can pose a significant challenge for clinicians. The high hospitalization rate of AHF, particularly among the elderly, correlates significantly with subsequent mortality, especially in cases involving recurrent hospitalizations.(95) Patients struggling with AHF not only face the risk of cardiovascular failure-related mortality, but also deal with the consequences of organ dysfunction resulting from congestion and hypoperfusion.(96) The initial phase of managing AHF in the hospital focuses on promptly improving acute congestion symptoms, stabilizing hemodynamics, preserving tissue perfusion and oxygenation, and preventing additional damage to vital organs like the heart and kidneys. These objectives are primarily achieved by administering IV therapies, which may include loop diuretics, vasodilators, inotropes, and/or vasopressors.(89, 97)

Table 2: In-hospital Management of patients with AHF (10, 14, 98)

In-hospital Phase	
Treatment goal	Achieve Decongestion and Optimize Perfusion
Continuous Patient Assessment Parameters	1. Clinical presentation of the patient (symptoms/signs) 2. Vital signs (systolic BP/mean arterial pressure, heart and respiratory rate, saturation (SpO2)) 3. Urine output
Supplementary evaluation tests	1. Blood tests (Hb, Na+/K+, Creatinine, BNP/NT-proBNP, Troponin, ABGs, Lactate) 2. Echocardiography

In managing AHF, the initial focus is on achieving hemodynamic stability and relieving symptoms. This starts in the Emergency Department, where a thorough clinical assessment, including history, vital signs, and additional tools like pulse oximetry and lab tests, guides further decisions.(99) These assessments aim to identify precipitating factors and comorbidities and classifies patients based on their congestion and perfusion

status. Understanding the patient's perfusion status and fluid congestion level is critical, categorized as warm-dry, warm-wet, cold-dry, or cold-wet. (Table 3)

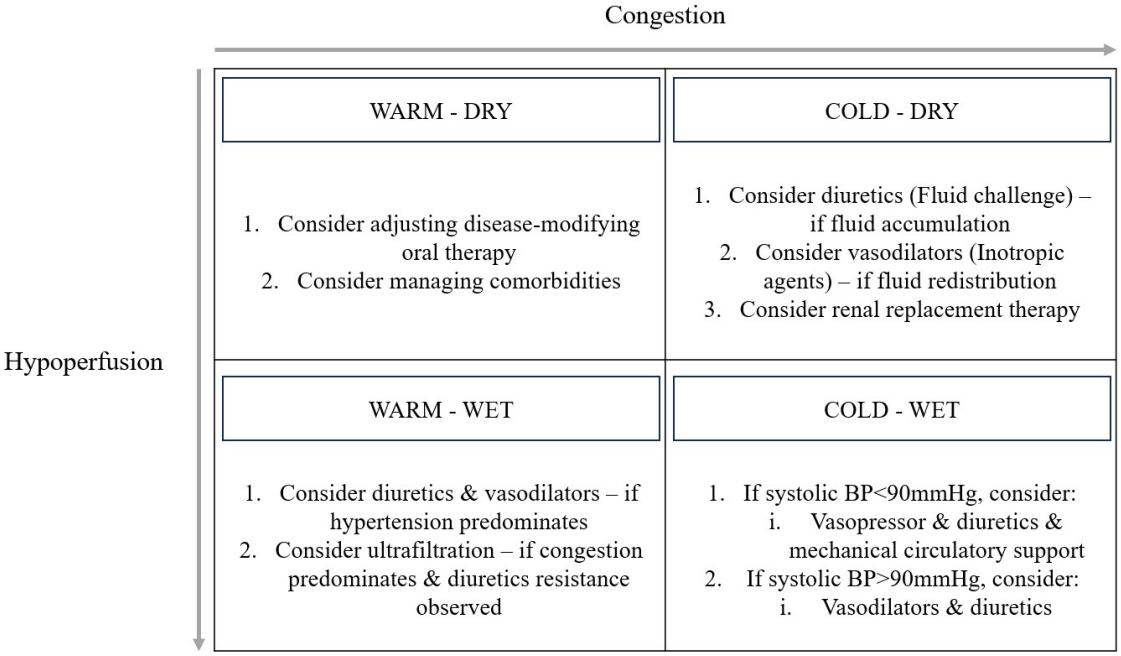
In the warm-dry category of AHF, where patients exhibit adequate perfusion and minimal fluid congestion, the primary goal is to maintain a delicate balance without resorting to aggressive diuretics. Concurrently, considering adjustments to disease-modifying oral therapy and managing comorbidities becomes crucial for comprehensive patient care.

Conversely, for patients categorized as warm-wet, characterized by sufficient perfusion but noticeable fluid congestion, a personalized approach is adopted. This involves a careful diuretic strategy to subside congestion while safeguarding perfusion. Options such as diuretics and vasodilators are considered based on the predominant clinical features, with a tailored focus on optimizing both aspects without compromising either. Ultrafiltration may be explored in cases where congestion is prominent, and resistance to diuretics is observed, especially if hypertension predominates.

Patients identified as cold-dry, indicating inadequate perfusion despite minimal congestion, may require interventions like diuretics through fluid challenges to address fluid accumulation or vasodilators, acting as inotropic agents, if fluid redistribution is evident. For those in the cold-wet category, facing impaired perfusion and significant congestion, a cautious and balanced approach is essential to prevent exacerbating either condition. Depending on systolic blood pressure levels, interventions range from vasopressors, diuretics, and mechanical circulatory support if systolic blood pressure is below 90mmHg, to vasodilators and diuretics if the systolic BP exceeds 90mmHg. (1, 2)

In short, customizing decongestion therapy in AHF requires a careful understanding of the patient's condition, allowing personalized interventions to effectively tackle both congestion and low blood flow.

Table 3: Therapeutic Approach for patients with AHF (10, 14, 98)



Diuretics play a vital role in relieving congestion-symptoms, a critical component of the therapeutic strategy for managing AHF.(1, 89, 93, 98-100) Among these, IV administered loop diuretics, like furosemide, are frequently used for their rapid and effective decongestant properties. Furosemide acts by inhibiting the Na-K-2Cl symporter at the ascending loop of Henle, leading to sodium and chloride excretion and subsequent diuresis. The initial recommended dose for new-onset AHF patients is typically 20–40 mg, or an equivalent IV dose for those on chronic diuretic therapy. Evaluating diuretic response involves monitoring urinary volume output and post-diuretic spot urinary sodium content, with adjustments made if deemed insufficient, such as doubling the bolus dose. Loop diuretics also function as immediate vasodilators, contributing to swift relief of respiratory symptoms. The timely administration of diuretics, especially early in AHF, is associated with positive outcomes, including reduced mortality rates.(89)

However, the use of diuretics in AHF is not one-size-fits-all, emphasizing the need for a personalized approach. Some patients may display resistance to diuretic therapy, necessitating alternative strategies or combinations with other agents. Combinatorial

approaches, incorporating thiazide diuretics, mineralocorticoid receptor antagonists, and vasopressin antagonism, aim to enhance diuretic efficacy.(101, 102) Emerging treatments like Tolvaptan, a selective vasopressin V2 receptor antagonist, and Sodium-Glucose Linked Transporter Type 2 (SGLT2) inhibitors show promise in augmenting decongestion.(103, 104) Yet, striking a balance between the decongestive benefits of diuretics and potential risks, such as electrolyte imbalances and renal dysfunction, underscores the importance of vigilant monitoring and dose adjustments based on individual patient responses.

Continued decongestive therapies, such as the administration of loop diuretics, should be maintained until the patient reaches a state of euvolemia, indicating a balanced fluid volume. The determination of euvolemia is a complex procedure involving various indicators. Clinical signs, such as the resolution of peripheral edema and improvement in respiratory distress, serve as observable markers. Imaging modalities, like chest X-rays or ultrasounds, can provide visual evidence of reduced pulmonary congestion or normalized cardiac dimensions. Biomarkers such as BNP or NT-proBNP can be tracked to assess the neurohormonal response and guide the decongestive progress. For instance, a decrease in BNP levels over successive measurements may indicate a positive response to therapy. Once these parameters collectively indicate euvolemia, the transition to oral forms of diuretics may be initiated for ongoing management. This careful and multifaceted approach optimizes the decongestive process and contributes to the overall success of acute heart failure treatment.(93, 99, 105)

In the complex domain of AHF management, the critical role of maintaining optimal oxygenation for patients cannot be overstated. Vigilant monitoring, particularly of oxygen saturation (SpO2) and arterial blood gases (ABGs), is paramount, especially when SpO2 levels dip below the crucial threshold of 90%. Clinicians are tasked with the continuous observation of patients, ready to swiftly address any signs of respiratory distress that may emerge. Non-invasive positive pressure ventilation (NIPPV) stands out as a recommended intervention when respiratory distress becomes evident.(34, 88, 89) Notably, non-invasive ventilation (NIV) emerges as a superior alternative to conventional oxygen therapy, exhibiting enhanced outcomes by swiftly improving

respiratory distress and oxygenation. This not only reduces the likelihood of tracheal intubation but also contributes to a rapid restoration of respiratory function, subsequently lowering mortality risks.(106) Recent meta-analyses, including the 3CPO trial, substantiate the effectiveness of NIV in diminishing both intubation and mortality rates, particularly in patients struggling with pulmonary congestion.(107) Furthermore, insights from Girardis et al. underscore the potential benefits of conservative oxygen therapy, maintaining a SpO2 range of 94–98%, as opposed to conventional oxygen therapy targeting SpO2 levels of 97–100%, revealing a lower ICU mortality rate. This is likely because maintaining SpO2 at 100% can result in vasoconstriction and a reduction in cardiac output.(108) It is crucial to consider intubation if NIPPV proves ineffective or is contraindicated, taking into account factors like patient cooperation, apnea, vomiting, or suspicion of pneumothorax.(109)

In addition to the effective management of AHF, particularly in patients with elevated systolic blood pressure (BP), nitrovasodilators such as nitroglycerin, isosorbide mononitrate, isosorbide dinitrate, and sodium nitroprusside are recommended in combination with diuretics.(89, 110-112) Early administration of vasodilators, even in the pre-hospital setting, has been linked to a lower risk of mortality in patients with pulmonary congestion, prompting recent clinical guidelines to recommend vasodilators as first-line therapy for those presenting with pulmonary congestion.(34) Vasodilators have two key effects, lowering both preload and afterload by relaxing the tone of both veins and arteries. A widely acknowledged vasodilator in AHF, nitroglycerin, exhibits dose-dependent hemodynamic effects. At lower doses, it induces venous dilation, while higher doses (≥ 150–250 mcg/min) promote arterial vasodilation. High doses of nitroglycerin have been associated with reduced rates of endotracheal intubation and ICU admission, as revealed by a retrospective study. Bolus doses of IV nitroglycerin, specifically 2000 mg every 3-5 minutes, have been proven safe and correlated with improved outcomes, including decreased mortality and reduced intubation rates. (113)

However, caution is warranted as vasodilators are contraindicated in AHF cases where systolic BP is below 90 mmHg and should be used carefully, especially in patients with specific conditions such as low cardiac output, aortic stenosis, hypertrophic left

ventricle with a small cavity, predominant right ventricular failure, or recent use of phosphodiesterase-5 inhibitors (e.g., sildenafil, vardenafil).(114, 115) Beyond nitroglycerin, other vasodilators contribute to the therapeutic arsenal. Isosorbide dinitrate, a nitrate derivative, mirrors nitroglycerin's effects. Natriuretic peptides, like nesiritide foster vasodilation and alleviate fluid congestion, while hydralazine, often combined with nitrates, proves beneficial in HF with reduced LVEF. Phosphodiesterase inhibitors, such as milrinone, enhance vasodilation and cardiac output. ACE inhibitors and ARBs, integral to heart failure management, also exert vasodilatory effects. The selection of a specific vasodilator hinges on individual patient characteristics, ensuring tailored treatment for the multifaceted nature of AHF. (112) A newer treatment options with potentially more attractive therapeutic profiles, is serelaxin, a synthetic relaxin variant, shows promise in relieving dyspnea, even in patients with preserved ejection fraction and elevated systolic blood pressure, concurrently mitigating myocardial, renal, and hepatic injuries.(116) Preliminary evidence suggests a favorable impact on long-term outcomes, pending confirmation from ongoing clinical trials.

In cases of cardiogenic shock associated with AHF, vasopressors (or inotropic agents), including dopamine, norepinephrine, and epinephrine, are essential for managing the condition. These medications enhance myocardial contractility and increase vascular resistance, aiming to improve blood pressure and restore perfusion to vital organs. The use of vasopressors requires careful monitoring to achieve hemodynamic goals while minimizing side effects. Inotropic agents, such as beta-adrenergic receptor agonists, phosphodiesterase III inhibitors, and levosimendan (a calcium sensitizer), prove effective in increasing cardiac output and reducing filling pressures in critically ill patients. However, their benefits come with significant adverse events (mainly arrhythmias and myocardial ischemia), necessitating limited use in specific cases with clear indications, such as low cardiac output and elevated filling pressures.(117) Thus, inotropes should be administered only when there are explicit reasons to do so, particularly in individuals experiencing low cardiac output (cardiac index <2.0 Lt/min/m2), and when elevated filling pressures are evident (pulmonary capillary wedge pressure >18–20 mmHg and right atrial pressure >10–12 mmHg).(89, 98)

For patients unresponsive to initial treatments or experiencing rapid deterioration, short-term mechanical circulatory support (MCS), like extracorporeal membrane oxygenation (ECMO), is considered. ECMO provides circulatory and respiratory support, serving as a "bridge to recovery," "bridge to decision," or "bridge to bridge" in critically ill patients. Indications for ECMO include potentially reversible cardiogenic shock and failure to wean from cardiopulmonary bypass.(98)

Throughout the patient's hospitalization, it is imperative to identify the underlying precipitating factors and address them appropriately. Following the exclusion of urgent conditions, such as ACS, hypertensive emergency, rapid arrhythmias, severe bradycardia, conduction disturbances, acute mechanical causes like acute valve regurgitation, acute pulmonary embolism, infections, and tamponade, timely administration is crucial. The identification of comorbidities guides the customization of drug prescriptions, specifically for HF with amyloidosis, and the recommendation of surgeries, such as valve replacement for valvular heart disease, or mechanical circulatory support, like a left ventricular assist device (LVAD), or consideration of cardiac transplantation.(10)

Pre-discharge phase: A Transition in Treatment

Table 4: Switching from intravenous to oral medication (10, 14, 98)

Pre-discharge Phase	
Treatment goal	Switching from Intravenous to Oral Medication
Criteria for Achieving Stabilization	1. Enhanced or resolved symptoms/signs of congestion/hypoperfusion 2. Improved SpO2 and Vital signs (SBP, HR, RR) 3. Achieved adequate diuresis 4. Reduced body weight 5. Reduced NP levels

Surviving the initial episode of acute AHF places individuals at an elevated risk of recurrent episodes, underscoring the importance of effective pre-discharge management strategies.(118) The goals of AHF management are centered on improving survival rates and minimizing the risk of hospital readmission due to subsequent episodes. A pivotal element in achieving these objectives is ensuring the adequate stabilization of the individual's condition for a safe discharge during the pre-discharge phase. Patients with AHF are considered ready for discharge upon achieving crucial milestones, including sufficient decongestion and stable renal function through guideline-directed oral therapy.(10, 14, 99, 100)

Congestion emerges as a predominant factor contributing to AHF readmissions, with persistent congestion and renal dysfunction serving as ominous markers for a compromised post-discharge prognosis.(96) Various clinical and biochemical markers, such as weight and fluid loss, natriuretic peptides, cardiac troponins and soluble ST2 receptor, offer insights into the complex dynamics of fluid accumulation and redistribution in AHF patients. Notably, elevated pre-discharge natriuretic peptide levels are associated with adverse clinical outcomes, including heightened all-cause and cardiovascular mortality and morbidity.(58, 119)

Determining the appropriateness of discharging patients with AHF depends on precise stabilization criteria during the pre-discharge phase. These criteria serve as pivotal indicators of a patient's achievement of stability and readiness for transition to outpatient care. Essential elements encompass the resolution or substantial improvement of symptoms and signs associated with congestion and hypoperfusion, a comprehensive monitoring of vital signs, including systolic blood pressure, heart rate, and respiratory rate, a confirmation of improved or stable oxygen saturation, a verification of sufficient diuresis and a gradual reduction in body weight toward "dry" values are crucial for addressing fluid retention and congestion. These indicators represent key criteria for assessing a positive response to initial therapy, and their consideration is crucial in the decision-making process for discharge. (Table 4)

In addition to achieving optimal decongestion, the effective management of precipitating factors is crucial for improving post-discharge outcomes. For patients with HF with reduced LVEF (HFrEF), the continuation or initiation of disease-modifying oral HF therapy is recommended during hospitalization, adhering to established HF guidelines. In contrast, individuals with HF with preserved LVEF (HFpEF) should focus on optimal control of comorbidities and precipitating factors. The comprehensive treatment approach extends to evaluating additional therapies and potential surgical interventions during hospitalization, tailored to specific forms of HF.(10, 14, 119)

In the intricate transition from intravenous therapies to chronic HF medications, clinical judgment guides the process due to the lack of evidence-based guidance. As patients transition from intravenous therapies to the initiation or titration of chronic HF medications in this phase, careful consideration is given to the regulation of disease-modifying therapies (DMT). The step-by-step approach, encompassing neurohormonal inhibitors such as ACE inhibitors or ARBs (or combined with neprilysin-inhibitor), beta-blockers, mineralocorticoid receptor antagonists (MRA), and ivabradine, aligns with established guidelines for HF management.(1, 10, 14, 98, 100, 119, 120) Concurrently, careful handling of DMT during hospitalization includes evaluating criteria like blood pressure, heart rate, serum potassium, and renal function parameters. For a seamless discharge, a comprehensive approach ensures that DMT is appropriately initiated or titrated before patients leave the hospital, emphasizing caution when introducing ACEi or ARB in AHF patients on IV loop diuretics. The initiation of ACE inhibitors or ARBs in AHF patients receiving IV loop diuretics necessitates caution to prevent potential complications.(10, 14)

During the pre-discharge phase, the assessment of comorbid conditions, particularly non-cardiovascular comorbidities, assumes significance, given their prevalence and impact on the clinical status and prognosis of HF patients. Recognition and management of these comorbidities should be prioritized during hospitalization or scheduled for immediate post-discharge evaluation. Furthermore, a forward-looking approach involves evaluating patients for post-discharge HF treatment modalities, including the consideration of implantable devices like resynchronization and/or defibrillator systems.

In cases of advanced HF, the evaluation extends to potential interventions such as transplantation or ventricular assist device therapy.(121, 122) This multifaceted approach in the intermediate phase aims to optimize patient outcomes and provide comprehensive care, ensuring a seamless transition from hospitalization to outpatient management.

Early post-discharge phase: Entering Outpatient Care Following Hospital Discharge

AHF is associated with a concerning pattern of post-discharge readmissions, with approximately 30% occurring within the first week and 60% within the initial two weeks after leaving the hospital. This early recurrence of HF is particularly noteworthy, given its strong correlation with worse long-term outcomes. Significantly, at least 30% of these readmissions are attributed to HF itself, often linked to inadequate decongestion during the initial hospitalization.(123) Factors contributing to this trend include suboptimal identification of underlying causes, insufficient titration of chronic heart failure therapy, inadequate patient education, and a lack of specific post-discharge plans. Efforts to establish clear criteria for discharge readiness are essential to address these challenges.

Table 5: Release and shift to outpatient care (10, 14, 98)

Early post-discharge Phase	
Treatment goal	Release and shift to outpatient care
Release criteria	1. Resolution of all symptoms and signs of congestion 2. Vital signs within target ranges: SBP ≥ 90 mmHg, HR < 80/min (< 100/min for AFib) 3. Adequate oxygen saturation (SpO2 ≥ 95%, or ≥ 90% in COPD) 4. Successful diuresis with a stable oral diuretic regimen for at least 24 hours 5. Discontinuation of vasodilators for a minimum of 24 hours 6. NP reduction of at least 30% 7. Initiation or titration of life-saving therapies 8. Comprehensive evaluation for additional therapies such as CRT or ICD 9. Thorough assessment of comorbidities 10. Patient education on the management and prevention of future events 11. Development of a specific post-discharge plan

To discuss the discharge of a patient hospitalized for an episode of HF, it is necessary to fulfill the discharge criteria for AHF, which are integral to ensuring the patient's stability and readiness for the transition to outpatient care. Successful management requires the complete resolution of symptoms and signs associated with congestion. Vital signs, including a systolic blood pressure equal to or greater than 90 mmHg and a heart rate less than 80/min (or less than 100/min for AF), should be within target ranges. Oxygen saturation levels should be maintained at 95% or higher (or 90% or higher in COPD). Effective diuresis, evidenced by a stable oral diuretic regimen for at least 24 hours, is crucial. Discontinuation of vasodilators for a minimum of 24 hours, a notable reduction (≥30%) in Natriuretic Peptide levels, and the initiation or titration of life-saving therapies further contribute to the criteria for discharge. (Table 5)

Reducing the length of hospital stay, while a potential means to control healthcare costs, has been associated with an increase in HF readmission rates.(124, 125) Incomplete decongestion during hospitalization, failure to identify precipitating factors, improper titration of chronic therapy, patient education gaps, and the absence of a comprehensive post-discharge plan collectively contribute to the heightened risk of readmission.(98) It underscores the importance of a well-defined post-discharge schedule, encompassing subsequent visits and investigations related to patient behavior, health information, and motivation for active engagement. Beyond supervised medical therapy, effective post-discharge management should prioritize symptom improvement, enhanced quality of life, and measures to delay disease progression. (10, 14)

Recognizing the persistent high risk of rehospitalization and death for AHF patients, guidelines recommend prompt post-discharge follow-up. The post-discharge follow-up plan for AHF is meticulously structured to ensure comprehensive monitoring and management of patients. The ACC/AHA advocates for the first contact within three days and a subsequent visit within 7–14 days, aligning with ESC guidelines recommending the first outpatient follow-up within seven days of discharge. Subsequent follow-ups occur at 3 to 6-month intervals. In addition to in-person visits, a phone follow-up protocol is established, commencing within the first week post-discharge and continuing at 2 or 4-week intervals. Patient education is a central

component, emphasizing self-assessment of congestion symptoms, body weight monitoring, dietary considerations, and adjustments in diuretic dosing. Laboratory investigations, including assessments of renal function and electrolytes, are conducted within a week from drug onset or titration and at 3-monthly intervals. Further assessments encompass evaluations for specific HF therapies, consideration of comorbid conditions, and examinations of quality of life, psychosocial status, and treatment compliance. For patients with advanced disease, the follow-up plan includes assessments for transplantation or LVAD implantation.(10, 14, 98)

Determinants of improved outcomes post-discharge involve optimal decongestion, the refinement of guideline-DMT, and the implementation of vigilant post-discharge monitoring. This holistic approach has demonstrated efficacy in significantly reducing mortality rates and incidents of new HF events following patient discharge. The success lies in the careful management of stabilization criteria, emphasizing the importance of decongestion, guideline-DMT optimization, and ongoing monitoring to ensure a smoother transition to outpatient care.

Conclusion: Limitations in current understanding and future directions

In conclusion, the study of AHF is important due to its life-threatening nature, significant impact on quality of life, heightened risks of morbidity and mortality, frequent hospitalizations, and the steadily growing burden, leading to increased healthcare costs for healthcare systems. The demographic challenge posed by an aging population further complicates the intricacies of managing AHF, with identified risk factors such as age, coronary artery disease, hypertension, diabetes, previous heart attack, obesity, kidney disease, smoking, and valvular heart disease.

Despite substantial progress in various fields of cardiology, the exploration for new and effective interventions for AHF has proven hard to attain over the past three decades.

Explorations of therapeutic avenues, including inotropic agents, vasodilators, and diuretics, have yielded largely neutral study results, raising questions about the efficacy of tested drugs or the adequacy of study designs.

The integration of diagnostic tests emerges as a pivotal aspect in the management of AHF. These tests play a crucial role in diagnosing AHF, determining its etiology, assessing its severity, and guiding appropriate treatment. By collectively contributing to a comprehensive understanding of the patient's condition, these diagnostic tools facilitate timely and tailored interventions, essential for effectively managing this critical cardiac condition. Additionally, recognizing the challenges posed by the differential diagnosis of AHF, which requires distinguishing it from alternative causes of dyspnea and non-cardiac respiratory distress, underscores the need for accurate diagnostic methods to ensure optimal patient outcomes.

Addressing precipitating factors linked to AHF exacerbation is imperative, as evidenced by numerous studies establishing correlations between these factors and increased mortality and readmission rates. A proactive approach to understanding and managing these factors is crucial for effective symptom management and the prevention of AHF exacerbations.

Despite significant progress in AHF research and management, several areas warrant further investigation. More extensive studies are needed in biomarker-guided risk stratification and treatment, highlighting the need for prospective investigations into the "time-to-treatment" concept. Determining the causes of readmissions and establishing appropriate strategies to prevent early readmissions after discharge are essential steps in improving the long-term prognosis of AHF patients. Circulating biomarkers, including natriuretic peptides, play a role in AHF treatment, but challenges remain. Biomarkers indicate myocardial stretch during acute episodes but do not reflect venous or whole-body congestion. A multimarker strategy, incorporating various biomarkers, may offer increased prognostic accuracy and risk prediction, but further investigation is required.

The main aim of this thesis has been to provide a thorough review of AHF, encompassing epidemiology, diagnostics, therapeutic approaches, and interventions. Through a comprehensive survey of the latest research findings and clinical insights, the thesis aims to identify gaps in existing evidence and highlight areas that require further research. This approach is designed to promote the development of innovative diagnostic and treatment strategies, ultimately contributing to the advancement of AHF management.

Looking forward, challenges in AHF management include early diagnosis, accurate risk stratification, individualized treatment, medication optimization, the development of novel therapies, remote monitoring, and enhanced patient engagement. Ongoing research explores ultrafiltration, vasopressin receptor antagonists, novel inotropic agents, and the integration of biomarkers for precision medicine. Telemedicine and remote monitoring show promise but require careful consideration of patient access and support, especially in underserved populations.

In summary, the multifaceted nature of AHF necessitates a holistic and evolving approach to its diagnosis, management, and ongoing research. The findings and insights presented in this thesis contribute to the broader understanding of AHF, aiming to guide future research and clinical practices toward more effective and patient-centric outcomes. The incorporation of personalized treatment, telemedicine, advanced therapies, and patient education represents promising avenues for further enhancing AHF management strategies.

Abbreviations

AHF: Acute Heart Failure

HF: Heart Failure

ADHF: Acutely Decompensated Heart Failure

ACC/AHA: American College of Cardiology/American Heart Association

HFA/ESC: Heart Failure Association / European Society of Cardiology

CHF: Chronic Heart Failure

ESC-HF-LT: European Society of Cardiology Heart Failure Long-Term

NYHA: New York Heart Association

EHFS II: EuroHeart Failure Survey II

AHEAD: Acute Heart Failure Database

AFFIRM-AHF: A Randomized, Double-Blind Placebo-Controlled Trial

FCM: Ferric Carboxymaltose

LVEF: Left Ventricular Ejection Fraction

INTER-CHF: INTERnational Congestive Heart Failure Study

HFrEF: Heart Failure with reduced Ejection Fraction

COPD: Chronic Obstructive Pulmonary Disease

JVP: Jugular Venous Pressure

BNP: Brain-type Natriuretic Peptide

ACS: Acute Coronary Syndrome

BUN: Blood Urea Nitrogen

eGFR: estimated Glomerular Filtration Rate

TSH: Thyroid-Stimulating Hormone

cTn: cardiac Troponin

NT-proBNP: N-Terminal pro-B-type Natriuretic Peptide

BMI: Body Mass Index

ECG: Electrocardiogram

LVH: Left Ventricular Hypertrophy

AF: Atrial Fibrillation

MR: Mitral Regurgitation

TR: Tricuspid Regurgitation

AS: Aortic Stenosis

NSAIDs: Non-Steroidal Anti-Inflammatory Drugs

EMS: Emergency Medical Services

IV: Intravenous

SGLT2: Sodium-Glucose Linked Transporter Type 2

SpO2: Oxygen saturation

ABG: Arterial Blood Gases

NIPPV: Non-Invasive Positive Pressure Ventilation

NIV: Non-Invasive Ventilation

ACE: Angiotensin Converting Enzyme

ARB: Angiotensin II Receptor Blocker

MCS: Mechanical Circulatory Support

ECMO: Extracorporeal Membrane Oxygenation

LVAD: Left Ventricular Assist Device

ST2: Soluble interleukin-1 receptor-like 1

DMT: Disease-Modifying Therapies

MRA: Mineralocorticoid Receptor Antagonist

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ΤΜΗΜΑ ΙΑΤΡΙΚΗΣ

ΣΧΟΛΗ ΕΠΙΣΤΗΜΩΝ ΥΓΕΙΑΣ

ΠΑΝΕΠΙΣΤΗΜΙΟ ΘΕΣΣΑΛΙΑΣ

ΠΡΟΓΡΑΜΜΑ ΜΕΤΑΠΤΥΧΙΑΚΩΝ ΣΠΟΥΔΩΝ

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