Anticoagulation In Heart Failure

Current Status and Future Direction

Essay

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Sherif Rabea Ahmed Mohammed

Aim of the work

This study aims at revealing the recent updates in anticoagulation management of heart failure.

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List of abbreviations

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

ACCP: American College of Chest Physicians

ACE: Angiotensin-Converting Enzyme

Ach: Acetylcholine

ACS: Acute Coronary Syndromes

AF: Atrial Fibrillation

ANP: Atrial Natriuretic Peptide

AT_1. Angiotensin Type 1

AT_2. Angiotensin Type 2

ATP: Adenosine Triphosphate

β- AR: β-Adrenergic Receptors

BNP: Brain Natriuretic Peptide

BUN: Blood Urea Nitrogen

CAD: Coronary Artery Disease

CD-NP: Chimeric Natriuretic Peptide

CE: Epinephrine

cGMP: Cyclic Guanosine Monophosphate

CMA: Cardiac Myosin Activators

CNP: C-type Natriuretic Peptide

CPAP: Continuous Positive Airway Pressure

DBP: Diastolic Blood Pressure

DNP: Dendroaspis NP

ECG: Electrocardiography

List of abbreviations

ESC: European Society of Cardiology

Fio_2: Fraction of Inspired Oxygen

HF: Heart Failure

HFLAS: Heart Failure Long-term Antithrombotic Study

HFpEF: Heart Failure with Preserved Ejection Fraction

HFrEF: Heart Failure with Reduced Ejection Fraction

HFSA: Heart Failure Society of America

IABC: Intra-Aortic Balloon Counterpulsation

ICDs: Implantable Cardiac Defibrillators

INR: International Normalized Ratio

JVP: Jugular Venous Pressure

LMWH: Low Molecular Weight Heparin

LV: Left Ventricle

LVEF: Left Ventricular Ejection Fraction

MI: Myocardial Infarction

MIBG: Metaiodobenzylguanidine

MRI: Magnetic Resonance Imaging

NE: Norepinephrine

NIPPV: Noninvasive Intermittent Positive-Pressure Ventilation

NS: Central Nervous System

NT-proBNP: N-Terminal Pro-BNP

PAC: Pulmonary Artery Catheter

$PaCO_2$: Arterial Partial Pressure of CO_2

List of abbreviations

PCWP: Pulmonary Capillary Wedge Pressure

PEEP: Positive End-Expiratory Pressure

RAAS: Renin-Angiotensin-Aldosterone System

RAS: Renin-Angiotensin System

SBP: Systolic Blood Pressure

sGC: Soluble Guanylate Cyclase

SVC: Superior Vena Cava

SvO2: Venous Oxygen Saturation

UF: Ultrafiltration

VKA: Vitamin K Antagonist

WARCEF: Warfarin and Antiplatelet Therapy in Reduced Ejection Fraction

WASH: Warfarin / Aspirin Study in Heart Failure

WATCH: Warfarin and Antiplatelet Therapy in Chronic Heart Failure

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Introduction

Heart failure is the pathophysiologic state in which the heart, via an abnormality of cardiac function (detectable or not), fails to pump blood at a rate commensurate with the requirements of the metabolizing tissues or is able to do so only with an elevated diastolic filling pressure **(Onwuanyl et al., 2007).**

Heart failure may be caused by myocardial failure but may also occur in the presence of near-normal cardiac function under conditions of high demand. Heart failure always causes circulatory failure, but the converse is not necessarily the case, because various noncardiac conditions (e.g. hypovolemic shock, septic shock) can produce circulatory failure in the presence of normal, modestly impaired, or even supranormal cardiac function. To maintain the pumping function of the heart, compensatory mechanisms increase blood volume, cardiac filling pressure, heart rate, and cardiac muscle mass. However, despite those mechanisms, there is progressive decline in the ability of the heart to contract and relax, resulting in worsening heart failure **(Fonarow et al., 2011)**.

The goals of pharmacotherapy are to reduce morbidity and to prevent complications. Along with oxygen, medications assisting with symptom relief include diuretics, digoxin, inotropes, oxygen, and morphine. Drugs that can exacerbate heart failure should be avoided (non steroidal anti-inflammatory drugs [NSAIDs], calcium channel blockers [CCBs], most anti-arrhythmic drugs) (**Moss et al., 2011).**

Despite therapeutic advances, patients with worsening heart failure (HF) requiring hospitalization have unacceptably high post-discharge mortality and re-admission rates soon after discharge. Evidence suggests hypercoagulable state is present in patients with HF. Although thromboembolism as a direct consequence of HF is not frequently clinically recognized, it may contribute to high mortality and morbidity **(Metra and Zannad, 2013).**

Additionally, many patients with HF have concomitant disorders conferring additional thrombotic risk, including atrial fibrillation (AF) and acute coronary syndrome (ACS), which is a common precipitating factor for worsening HF or sudden death. Because data are largely derived from observational studies or trials of modest size, guideline recommendations on anticoagulation for HF vary between organizations. These data suggest there is an urgent need to introduce newer agents in the management of patients hospitalized for HF who continue to have a high post-discharge event rate despite available therapies (**Gheorghiade and Vaduganathan, 2013*).***

PATHOPHYSIOLOGY OF HEART FAILURE

Heart failure is the pathophysiologic state in which the heart, via an abnormality of cardiac function (detectable or not), fails to pump blood at a rate commensurate with the requirements of the metabolizing tissues or is able to do so only with an elevated diastolic filling pressure **(Onwuanyl et al., 2007).**

Heart failure may be viewed as a progressive disorder that is initiated after an event either damages the heart muscle, with a resultant loss of functioning cardiac myocytes, or disrupts the ability of the myocardium to generate force, thereby preventing the heart from contracting normally. This index event may have an abrupt onset, as in the case of a myocardial infarction; it may have a gradual or insidious onset, as in the case of hemodynamic pressure or volume overloading; or it may be hereditary, as in the case of many of the genetic cardiomyopathies. Regardless of the nature of the event, the feature that is common to each of these index events is that they all, in some manner, produce a decline in pumping capacity of the heart ***(*Onwuanyl and Taylor, 2010*).***

In most instances, patients will remain asymptomatic or minimally symptomatic after the initial decline in pumping capacity of the heart or will develop symptoms only after the dysfunction has been present for some time. Although the precise reason that patients with LV dysfunction remain asymptomatic is not certain, one potential explanation is that a number of compensatory mechanisms become activated in the setting of cardiac injury or depressed cardiac output; these appear to modulate LV function within a physiologic-homeostatic range, such that the functional capacity of the patient is preserved or is depressed only minimally. However, as patients transition to symptomatic HF, the sustained activation of neurohormonal and cytokine systems leads to a series of end-organ changes within the myocardium referred to collectively as LV remodeling. LV remodeling is sufficient to lead to disease progression in HF independent of the neurohormonal status of the patient, (fig.1) ***(*Mann and Bristow, 2005).**

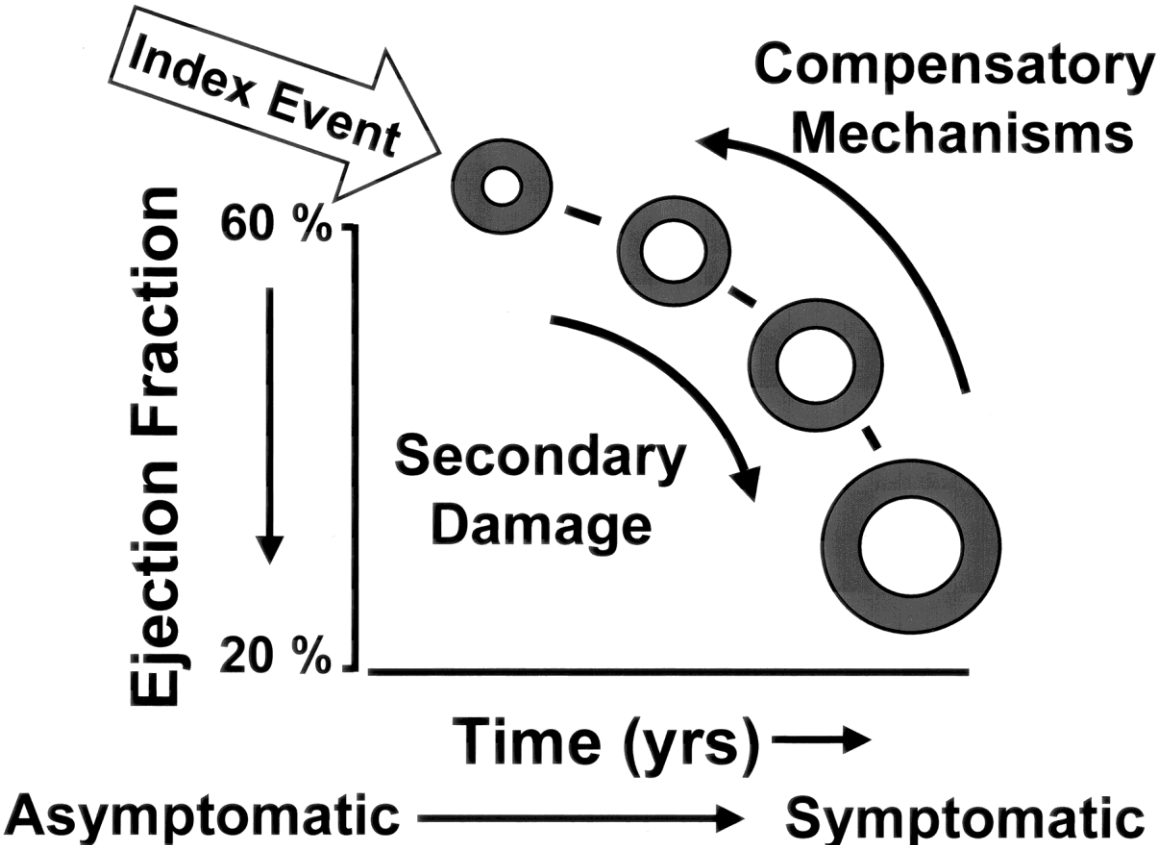

Fig (1): Pathogenesis of HF (Mann and Bristow, 2005).

Pathophysiological changes in Heart Failure :

(1) Neurohormonal Mechanisms:

Heart failure progresses as a result of the over expression of biologically active molecules that are capable of exerting deleterious effects on the heart and circulation. Compensatory mechanisms include activation of the adrenergic nervous system and renin-angiotensin system (RAS), which are responsible for maintaining cardiac output through increased retention of salt and water, peripheral arterial vasoconstriction, and increased contractility, and activation of inflammatory mediators, which are responsible for cardiac repair and remodeling. The term neurohormone is largely a historical term, reflecting the original observation that many of the molecules elaborated in HF are produced by the neuroendocrine system and thus act on the heart in an endocrine manner. However, it has since become apparent that many of the so-called classical neurohormones, such as norepinephrine (NE) and angiotensin II, are synthesized directly within the myocardium and thus act in an autocrine and paracrine manner. Nonetheless, the important unifying concept that arises from the neurohormonal model is that the over expression of biologically active molecules contributes to disease progression by the deleterious effects exerted on the heart and circulation **(Bristow, 2009*).***