Study of the Prognostic Importance of Albumin / Creatinine Ratio in Patients with Chronic Heart Failure

Thesis

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List of Abbreviations

ACE	Angiotensin-Converting Enzyme
ACEI	Angiotensin-Converting Enzyme Inhibitors
ACR	The Albumin/Creatinine Ratio
AER	Albumin Excretion Rate
AF	Atrial Fibrillation
ANP	Atrial Natriuretic Peptide
ARBS	Angiotensin Receptor Blockers
BNP	Brain Natriuretic Peptide
BP	Blood Pressure
BSA	Body Surface Area
CAD	Coronary Artery Disease
CI	Cardiac Index
CNP	C-Type Natriuretic Peptide
COPD	Chronic Obstructive Pulmonary Disease
CRP	C-Reactive Protein
CVP	Centeral Venous Pressure
DM	Diabetes Mellitus
DNA	Deoxyribonucleic Acid
ECG	Electrocardiogram
EF	Ejection Fraction
ESC	European Society Of Cardiology
ESR	Erythrocyte Sedimentation Rate
FS	Fractional Shortening
GFR	Glomerular Filtration Rate
HF	Heart Failure
HFnlEF	Heart Failure With Normal Ejection Fraction
HOPE STUDY	The Heart Outcomes Prevention Evaluation
HTN	Hypertension
ICD	Implantable Cardioverter-Defibrillator
IDCM	Idiopathic Dilated Cardiomyopathy

IHD	Ischemic Heart Disease
IL	Interleukin
LA	Left Atrium
LIFE STUDY	Losartan Intervention For Endpoint Reduction In Hypertension
LV	Left Ventricle
MI	Myocardial Infarction
MR	Mitral Regurge
NE	Norepinephrine
NEP	Neutral Endopeptidase
NPR-A	Natriuretic Peptide Receptors A
NPR-B	Natriuretic Peptide Receptor B
NPR-C	Natriuretic Peptide Receptor C
NYHA	The New York Heart Association
PAP	Pulmonary Artery Pressure
PCWP	Pulmonary Capillary Wedge Pressure
PND	Paroxysmal Nocturnal Dyspnea
PRA	Plasma Renin Activity
PREVEND IT	Prevention Of Renal And Vascular End-Stage Disease Intervention Trial
PW	Pulsed-Wave
RAAS	Renin Angiotensin Aldosterone System
RENAAL	Reduction In Endpoints In Non-Insulin Dependent Diabetes Mellitus With Angiotensin II Antagonist Losartan
SOLVD	Studies Of Left Ventricular Dysfunction
TNF- α	Tumor Necrosis Factor-A
TNFR	Tumor Necrosis Factor-A Receptor
UACR	Urinary Albumin Creatinine Ratio
UNaV	Urinary Sodium Excretion
URO	Urodilatin
UV	Urinary Volume

INTRODUCTION

Increased excretion of albumin in urine is an established risk factor for mortality, cardiovascular events, and adverse renal outcomes in the general population **(Arnlov et al. 2005)**.

Screening for increased albumin excretion is recommended in patients with diabetes and hypertension to help risk stratification and target treatment **(Mancia et al. 2007).**

Increased excretion might be a marker of diffuse systemic activation of the renin – angiotensin system, altered glomerular haemodynamics or abnormal tubular function **(Deckert et al. 1989).**

Measurement of the urinary albumin creatinine ratio (UACR) in a random urine specimen is a convient method for detection of increased albumin excretion **(Jensen et al. 1997)**.

The mechanism underlying albuminuria in patients with heart failure without diabetes mellitus and hypertension is not known. It may be due to renal congestion or hemodynamic disturbance **(Damman et al. 2009).**

Aim of the study

This study aims to study the prognostic importance of urinary albumin / creatinine ratio in patients with systolic heart failure.

CHAPTER 1

HEART FAILURE

Heart failure is a complex clinical syndrome that can result from any structural or functional cardiac disorder that impairs the ability of the ventricle to fill with or eject blood **(Hunt et al., 2005)**.

Heart failure can be defined as an abnormality of cardiac structure or function leading to failure of the heart to deliver oxygen at a rate commensurate with the requirements of the metabolizing tissues, Heart failure is defined, clinically, as a syndrome in which patients have typical symptoms (e.g. breathlessness, ankle swelling, and fatigue) and signs (e.g. elevated jugular venous pressure, pulmonary crackles, and displaced apex beat) resulting from an abnormality of cardiac structure or function. Many of the signs of Heart failure result from sodium and water retention and resolve quickly with diuretic therapy, i.e. may be absent in patients receiving such treatment.

Prevalence and incidence:

Heart failure (HF) is a major public health problem. Incidence, prevalence, and risk have been found to be high in both Europe and the US (**Bleumink et al., 2004)**.

Heart failure affects approximately six million people, and more than 550 000 new cases are diagnosed each year in the USA **(Lloyd-Jones et al., 2009)**.

Among Medicare beneficiaries, HF is the leading cause of hospitalization. In 2007, the American Heart Association estimates that >$33 billion was spent on HF **(Rosamond, 2007)**.

In the USA, 550,000 new cases of heart failure are diagnosed and 300,000 deaths are caused by heart failure each year. The rehospitalization rates during the 6 months following discharge are as much as 50% **(Jencks et al., 2009)**.

Pathophysiology:

The progression of left ventricular systolic dysfunction (and the heart failure syndrome), because of 'remodelling' of the left (and right) ventricle (as a result of the loss of myocytes and maladaptive changes in the surviving myocytes and extracellular matrix), probably occurs in two main ways, one is because of intercurrent cardiac events (e.g. myocardial

infarction) and the other is as a consequence of the local processes (e.g. the autocrine pathway and molecular adaptations, including, perhaps, apoptosis) and systemic processes (e.g. neurohormonal pathways) that are activated as a result of reduced systolic function **(Anker et al., 2004)**.

It is important to remember that atrial function, synchronized contraction of the left ventricle and normal interaction between the right and left ventricles are also important in preserving stroke volume **(Bleasdale et al., 2004)**.

Systolic vs. diastolic dysfunction:

Systolic and diastolic dysfunction are terms used to describe whether the principal abnormality of the myocardium is an inability of the ventricle to contract and expel blood or to relax and fill normally, respectively (though in reality these two abnormalities frequently coexist). Systolic dysfunction is the result of reduced shortening of sarcomeres, which is a consequence of a global or regional reduction of contractility or greatly increased impedance to left ventricular ejection **(Konstam et al., 2003)**.

An increase in preload can provide short-term compensation (via the Frank–Starling mechanism) for a reduction in contractility or increases in impedance. However,

long-term compensation usually involves myocardial hypertrophy, which is the result of laying down new sarcomeres that increase the width (concentric) or the length (eccentric) of myocytes **(Konstam et al., 2003)**.

Remodelling also contributes to reduced sarcomere shortening. All these factors causing reduced fiber shortening also lead to a decrease in the left ventricular ejection fraction (LVEF). Hence, end-systolic volume increases **(Konstam et al., 2003)**.

The hallmark of diastolic dysfunction is elevation in left ventricular end-diastolic pressure or left arterial pressure in the absence of systolic dysfunction **(Zile et al., 2004)**.

Valve disease: pressure and volume overload:

Arterial hypertension and aortic stenosis cause a sustained increase in systolic wall stress during left ventricular ejection leading to concentric hypertrophy of the left ventricle because of myocyte hypertrophy and extracellular matrix overgrowth **(Zile et al., 2003)**.

Conversely, mitral and aortic regurgitation result in an increased volume load on the ventricle. The resultant ventricular remodelling is characterized by dilatation,

representing, at least in part, lengthening of the cardiac myocytes **(Borer et al., 2004)**.

Other terms sometimes used when describing heart failure

Right-sided versus left-sided heart failure:

The term right heart failure is often used to describe patients in whom there are prominent signs of 'congestion', e.g. a raised jugular venous pressure, hepatomegaly and peripheral edema, on the basis that these findings reflect right ventricular failure; in fact all of these signs are also found in patients with predominantly left ventricular involvement. The description pulmonary heart disease is used to depict patients who do have isolated right heart failure as a result of primary lung disease and has generally replaced the term 'cor pulmonale' **(Francis, 2001)**.

High- and low-output heart failure:

A more useful pathophysiological classification is to distinguish between high- and low-output heart failure, although the former is uncommonly encountered in Western clinical practice. Cardiac index is normally 2.2–3.5 l/min/m^2. Low-output cardiac failure implies that cardiac output fails to rise adequately during exercise or that it is inadequate even at rest **(Francis, 2001)**.