

Effect of Iron Deficiency on Health-Related Quality of Life in Chronic Heart Failure Patients Regardless of Anaemia Status

Thesis

*Submitted for Partial Fulfillment of Master Degree
in Cardiology*

By

Ahmed Alaa El-Din Fawzy Hamed, MBBCH
Cardiology Department, Ain Shams University

Under Supervision of

Prof. Dr. Wael Mahmoud Elkelany

*Professor in Cardiology
Faculty of Medicine - Ain Shams University*

Prof. Dr. Viola William Keddass

*Assistant Consultant in Cardiology
Faculty of Medicine - Ain Shams University*

Faculty of Medicine
Ain Shams University

2019

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قالوا

سببنا أنك لا تعلم لنا
إلا ما علمتنا إنك أنت
العليم العظيم

صدق الله العظيم

سورة البقرة الآية: ٣٢

Acknowledgment

*First and foremost, I feel always indebted to **ALLAH**, the Most Kind and Most Merciful.*

*I'd like to express my respectful thanks and profound gratitude to **Prof. Dr. Wael Mahmoud Elkelany**, Professor of Cardiology - Faculty of Medicine- Ain Shams University for his keen guidance, kind supervision, valuable advice and continuous encouragement, which made possible the completion of this work.*

*I am also delighted to express my deepest gratitude and thanks to **Prof. Dr. Viola William Keddas**, Assistant Consultant in Cardiology, Faculty of Medicine, Ain Shams University, for her kind care, continuous supervision, valuable instructions, constant help and great assistance throughout this work.*

I would like to express my hearty thanks to all my family for their support till this work was completed.

Last but not least my sincere thanks and appreciation to all patients participated in this study.

Ahmed Alaa El-Din Fawzy Hamed,

List of Contents

Title	Page No.
List of Tables	i
List of Figures	ii
List of Abbreviations	iii
Introduction	1
Aim of the Work.....	3
Review of literature	
Heart Failure	4
Iron Deficiency in Heart Failure	28
Patients and Methods	38
Results	46
Discussion	53
Limitations	58
Conclusion.....	59
Recommendations	60
Summary	61
References	63
Arabic Summary	

List of Tables

Table No.	Title	Page No.
Table (1):	Comparison of ACCF/AHA Stages of HF and NYHA Functional Classifications.	7
Table (2):	Definition of heart failure with preserved (HFpEF), mid-range (HFmrEF) and reduced ejection fraction (HFrEF) according to 2016 ESC guidelines.	10
Table (3):	Framingham criteria for congestive heart failure.....	12
Table (4):	LV remodeling changes.....	13
Table (5):	Patients eligible for LVAD implantation according to ESC guidelines	26
Table (6):	Studies reporting prevalence of Iron deficiency in heart failure	34
Table (7):	Comparison between the studied groups regarding the demographic data, Hemoglobin level and serum ferritin.....	47
Table (8):	Comparison between the studied groups regarding the echocardiographic data.....	49
Table (9):	Comparison between the studied groups regarding the MLHFQ items.....	50

List of Figures

Fig. No.	Title	Page No.
Fig. (1):	Strategy for the use of drugs (and devices) in patients with HF-REF.....	15
Fig. (2):	Recommendations for the use of ACE inhibitors, beta-blockers, Mineralocorticoid Receptor Antagonists (MRA) and angiotensin receptor blockers in heart failure.....	16
Fig. (3):	Shows ESC guidelines for recommendations of CRT implantation in patients with heart failure.....	24
Fig. (4):	Systemic iron homeostasis	29
Fig. (5):	Iron uptake in duodenal epithelial cells	31
Fig. (6):	Consequences of ID on HF patients	36
Fig. (7):	Items of Minnesota Living with Heart Failure Questionnaire.....	42
Fig. (8):	Comparison regarding demographic data between ID and Non ID groups.	48
Fig. (9):	Comparison between ID & Non- ID groups regarding Over-all Summary Score (OSS)	51
Fig. (10):	Comparison between both groups regarding the physical domain of MLHFQ.....	51
Fig. (11):	Comparison between both groups regarding emotional domain of MLHFQ.....	52

List of Abbreviations

Abb.	Full term
<i>ACCF</i>	<i>American College of Cardiology Foundation</i>
<i>ACEI</i>	<i>Angiotensin converting enzyme inhibitor</i>
<i>AF</i>	<i>Atrial fibrillation</i>
<i>AHA</i>	<i>American Heart association</i>
<i>ANP</i>	<i>Atrial natriuretic peptide</i>
<i>ARB</i>	<i>Angiotensin receptor blocker</i>
<i>ARNI</i>	<i>Angiotensin receptor neprilysin inhibitor</i>
<i>BNP</i>	<i>Brain natriuretic peptide</i>
<i>CAD</i>	<i>Coronary artery disease</i>
<i>CHF</i>	<i>Chronic heart failure e</i>
<i>CIBISII</i>	<i>Cardiac insufficiency bisoprobe study II</i>
<i>CMIA</i>	<i>Chemiluminescent microparticle immunoassay</i>
<i>CMR</i>	<i>Cardiac magnetic resonance</i>
<i>Consensus</i>	<i>Cooperative North Scandinavian Enulpril study</i>
<i>COPD</i>	<i>Chronic obstructive pulmonary disease</i>
<i>CRT</i>	<i>Cardiac resynchronization therapy</i>
<i>CV</i>	<i>Cardiovascular</i>
<i>DBP</i>	<i>Diastolic blood pressure</i>
<i>DCYTB</i>	<i>Duodenal cytochrome B</i>
<i>DIG</i>	<i>Digitalis investigation group</i>
<i>DM</i>	<i>Diabetes mellitus</i>
<i>DMT1</i>	<i>Divalent metal transporter 4</i>
<i>EF</i>	<i>Ejection fraction</i>
<i>EMA</i>	<i>European medicines agency</i>
<i>ESC</i>	<i>European society of cardiology</i>
<i>FCM</i>	<i>Ferric carboxy maltose</i>
<i>FPG</i>	<i>Fasting plasma glucose</i>

List of Abbreviations (cont...)

Abb.	Full term
<i>GFR</i>	<i>Glomerular filtration rate</i>
<i>HF mrEF</i>	<i>Heart failure with mid Cong ejection fraction</i>
<i>HF PEF</i>	<i>heart failure with preserved ejection fraction</i>
<i>HF REF</i>	<i>Heart failure with reduced ejection fraction</i>
<i>HF</i>	<i>Heart failure</i>
<i>HRQOL</i>	<i>Health related quality of life</i>
<i>IABP</i>	<i>Intra aortic balloon counter pulsation</i>
<i>ICD</i>	<i>Implantable cardioverter defibrillator</i>
<i>ID</i>	<i>Iron deficiency</i>
<i>KIDOGQI</i>	<i>Kidney /disease outcomes quality initiative</i>
<i>LGE</i>	<i>Late gadolinium enhancement</i>
<i>LV</i>	<i>Left ventricle</i>
<i>MI</i>	<i>Myocardial infarction</i>
<i>MLHFQ</i>	<i>Minnesota living with heart Failure Questionnaire</i>
<i>MRA</i>	<i>Mineralocorticoid receptor antagonists</i>
<i>NP</i>	<i>Natriuretic peptide</i>
<i>NT-proBNP</i>	<i>N-terminal pro BNP</i>
<i>NYHA</i>	<i>New York Heart Association</i>
<i>OSS</i>	<i>Overall summary score</i>
<i>QOL</i>	<i>Quality of life</i>
<i>RAAS</i>	<i>Renin angiotensin aldosterone system</i>
<i>RALES</i>	<i>Randomized aldosterone evaluation study</i>
<i>RCT</i>	<i>Randomized controlled trial</i>
<i>RES</i>	<i>Reticuloendothelial system</i>
<i>RLUS</i>	<i>Relative light units</i>
<i>RRR</i>	<i>Relative risk reduction</i>
<i>SBP</i>	<i>Systolic blood pressure</i>

List of Abbreviations (cont...)

Abb.	Full term
<i>SOLVD</i>	<i>Studies of left ventricular dysfunction</i>
<i>VAD</i>	<i>Ventricular assisted devices</i>
<i>VF</i>	<i>Ventricular fibrillation</i>
<i>VT</i>	<i>Ventricular tachycardia</i>

INTRODUCTION

Hear**t Failure** is a clinical syndrome characterized by a constellation of symptoms & signs that has a wide reaching implications not only in terms of mortality & morbidity of affected individuals only but also for countries to provide care for these patients (*Ponikowski et al., 2016*).

Due to population ageing, there is an increase in the prevalence of chronic diseases. Heart Failure (HF) is an urgent public health need with national and global implications. It is one of the most important causes of morbidity and mortality in the industrialized world (*Fonarow et al., 2005 and Redfield et al., 2003*).

HF causes a major disability & functional limitations of physical activity in the patients. This limitation is closely related to the daily life activities which affects quality of life (QOL) and causes changes in the lifestyle imposed by the disease. Patients with HF have their lives affected by the disease and optimized care should be directed at aiming at decreasing these impacts on their quality of life (*Santos et al., 2009*).

The prevalence of iron deficiency in HF patients is up to 50 %, even in patients without anaemia. Many factors contribute to iron deficiency in HF patients. It is suggested that iron deficiency (ID) in chronic heart failure (CHF) patients

results in reduced functional capacity, more clinical severity of the disease and worse quality of life (*Jankowska et al., 2010 and Jankowska et al., 2011*).

Several clinical trials among HF patients with ID showed that treatment of these patients with i.v. iron to correct ID can improve Health Related Quality of Life (HRQoL), exercise capacity (*Comin-Colet et al., 2013*) and these effects appear to be independent of anaemia status of the patients (*Anker et al., 2009*).

Despite data from interventional studies with I.V. iron suggest that ID has a considerable impact in the HRQoL of patients with CHF, few studies have directly evaluated patients with ID focusing on patient-centred outcomes and their daily life activities which is the aim of this study.

AIM OF THE WORK

Assessment of the impact of iron deficiency (ID) on health-related quality of life (HRQoL) in chronic heart failure (CHF) patients using Minnesota Living with Heart Failure questionnaire (MLHFQ).

Chapter 1**HEART FAILURE****Definition of heart failure:**

According to European Society of Cardiology (ESC) guidelines HF is a clinical syndrome characterized by typical symptoms (e.g. breathlessness, ankle swelling and fatigue) that may be accompanied by signs (e.g. elevated jugular venous pressure, pulmonary crackles and peripheral oedema) caused by a structural and/or functional cardiac abnormality, resulting in a reduced cardiac output and/ or elevated intracardiac pressures at rest or during stress (*Ponikowski et al., 2016*).

According to the 2013 American Heart Association (AHA) Guidelines for the Management of HF, HF is a complex clinical syndrome that results from any structural or functional impairment of ventricular filling or ejection of blood (*Yancy et al., 2013*).

Incidence of heart failure:

According to ESC, the prevalence of HF is approximately 1–2% and rises to >10% among people over the age of 70 years (*Mosterd and Hoes, 2007*) & according to AHA there are 825 000 new HF cases annually in the USA (*Alan et al., 2014*).

The rise in the incidence and prevalence of HF can be attributed to improved care of acute myocardial infarction together with the ageing of the population and the increasing prevalence of cardiovascular disease in the developing countries (*Schocken et al., 2008*).

Burden of heart failure:

I. Heart failure mortality

The results of the Framingham Heart Study (*Levy et al., 2002*) and a population-based study in Olmsted County, Minnesota (*Roger et al., 2011*) stated decrease in the last decades of mortality rates in patients after the onset of HF.

However, 5-year age-adjusted mortality rates after onset of HF remained high in those two studies, with higher rates in men (50% in men vs. 46% in women for the Olmsted County population based study) (*Roger et al., 2011*).

II. Heart failure hospitalization

Heart failure hospitalization represents 1–2% of all hospital admissions, which makes it one of the most important causes of admission for patients older than 65 years (*Alla et al., 2007*).

Patients admitted with HF are at high risk for all cause re-admission, with a 1 month readmission rate of 25% (*Ardehali et al., 2004*).

ACCF/AHA stages of HF & NYHA functional classifications:

Both the American College of Cardiology Foundation (ACCF)/AHA stages of HF and the NYHA functional classification provide useful information about the presence and severity of HF (table 1).

1. The ACCF/AHA stages of HF:

The stages are progressive and inviolate; which means that once a patient moves to a higher stage, regression to an earlier stage of HF is not observed and Progression is associated with reduced 5- year survival.

Therapeutic interventions are tailored according to the stage of Heart Failure; At (stage 1) modifying risk factors, treatment of structural heart diseases (stage B), and reducing morbidity and mortality (stages C and D) (*Yancy et al., 2013*).

2. NYHA Functional Classifications:

The NYHA classification focuses mainly on functional capacity and the symptomatic status of the disease in those with structural heart disease, primarily stages C and D (*Yancy et al., 2013*).

It is a subjective assessment by a clinician and can change markedly over short periods of time. for example, a stable patient with mild symptoms can become suddenly