Introduction

Cardiovascular disease (CVD) is responsible for more deaths in men and women than any other cause of death in the United States and in most developed countries. According to the National Center for Health Statistics, if all forms of major cardiovascular disease were eliminated, life expectancy would increase by almost 7 years. **[Roger VL, et al; 2011]**

This disease, once thought to afflict only men, but in fact its responsible for more deaths in women per year (when compared with men) since 1984. **[Wenger NK, 2004]**

Women differ from men in their risk profile for CVD and cardiovascular outcomes. Women manifest a greater symptom burden, poorer functional ability, more healthcare needs, and more adverse outcomes. **[Shaw LJ, et al; 2009]**

Heart disease develops in women about 10-years later than it does in men. [Castelli WP, et al; 1088] As the cardiac events occurred approximately 10-years later for women than for men, women were not as surprised by these events and it presented less of a crisis in their lives. **[Hawthorne MH, et al; 1993]**

In addition, they often have lower physical function, are less physically active, of lower socioeconomic status, and are at greater risk in the context of smoking and diabetes than men. **[Mosca L, et al; 2011]**

Cardiac rehabilitation (CR) programs offer structured exercise, education, counseling, and risk reduction to promote secondary prevention. CR participation is associated with an overall reduction in recurrent cardiac events, [Alter DA, et al; 2009] improved survival, functional status, and psychosocial well-being. **[Taylor RS, et al; 2004]**

Considering the abundance of empirical evidence, Class I, Level A clinical practice guideline according to AHA/ACCF guideline 2011, Canadian guideline 2009 recommendations promote CR access for patients. **[Smith SC Jr, et al; 2011], [Stone JA, et al; 2009]**

Conn et al found that women are older, participated less in rehabilitation classes, and were less active than men overall after a myocardial infarction. **[Conn VS, et al; 1991]**

Sharpe et al also concluded that women involved in cardiac rehabilitation were less active than men. **[Sharpe PA, et al; 1991]** the reasons for this are that women have a

harder time giving up responsibilities at home. **[Hamilton G, et al; 1993]**

More specifically, a treatment-risk paradox is observed, such that although women might be in greater need of the secondary prevention offered through CR, they are significantly less likely to access it than men. **[Benz ScottLA, et al; 2002] [Bittner V, et al; 2003], [McCarthy MM, et al; 2011]**

Aim of the work

The purpose of this study is to examine the effect of differences between men and women with coronary artery disease post total revascularization that enrolled in cardiac rehabilitation program in their compliance and risk factor reduction.

Chapter (1)
Gender Difference in Cardiovascular Disease

Burden of CVD In Women And Men

The extent of CVD in society is considered to be underestimated as most data-bases rely on the prevalence of acute cardiac events at presentation, which does not include the prevalence of asymptomatic and ambulatory populations. **[Louise Pilote et al., 2007]**

The incidence and prevalence of CVD varied considerably from region to region. **[Marrugat J et al., 2004]**

The prevalence of CVD is higher in men than women in most developed and developing countries, **[Tunstall-Pedoe H et al., 2006]** However, recently and over the last 3-decades the proportion of women presenting with clinically and angiographically significant disease has been rising. Overall, the incidence of CVD, and of coronary artery disease (CAD) in particular, has been declining in men but has remained stable in women. **[Arciero T et al., 2004]**

Gender Difference in Cardiac Mortality

Mortality Related To Cardiovascular Disease

Even with a regional variety in the prevalence and mortality of CVD, **[World Health Organization, 2006]** it is still the leading cause of deaths in both men and women worldwide. **[Arciero TJ, 2004]** According to the American National Center for Health Statistics, if all forms of major cardiovascular disease were eliminated, life expectancy would increase by almost 7-years. **[Heart and Stroke Foundation, 1999]**

Over the last 3-decades the Age-Standardized Mortality Rates have been declining in developed countries, but on other hand they risen markedly in middle-income developing countries (Eastern Europe and China). Levi and colleagues **[Levi F, 2002]** demonstrated that these trends are consistent for both men and women.

Cardiovascular disease, initially was thought to affect only men, but in fact, it has been responsible annually for more deaths in women with compared with men since 1984. **[Thom T, 2005], [Marrugat J, 2004], [Arciero TJ, 2004] [World Health Organization, 2006]** The number of deaths

attributed to cardiovascular disease in women were exceed any other cause of death.

Mortality Related To Coronary Artery Disease

In general, Men continue to have higher rates of mortality related to acute myocardial infarction (AMI) and CAD than women. **[Thom T. et al., 2005], [Arciero TJ; 2004), [Manuel DG.; 2003]**

But, younger age women with AMI have higher rates of mortality than men of the same age. **[Vaccarino V. et al., 2001], [Vaccarino V et al., 1999], [Vaccarino V et al., 1998]**.

Gender Differences and Cardiovascular Risk Factors

The American Heart Association (AHA) issued its **first** statement on cardiac risk factors in **1967**. The AHA concluded that some risk factors were more important and had a greater influence on the development of coronary artery disease (CAD). These risk factors consisted of **smoking**, **hypertension**, increased **serum cholesterol level**, and a person's **weight**. **[American Heart Association; 1998]**

Yates concluded that men overall were more compliant with cardiac risk factor reduction than women. **[Yates BC, et al., 1987]**

In **1997**, the AHA also affirmed that **hyperlipidemia**, **sedentary lifestyle**, and **obesity** are more challenging and problematic for women. **[American Heart Association; 1995]**

Kannel and Wilson found hypertension to be the most consistent risk factor for women older than 45-years. Also, When hypertension was combined with obesity and oral contraceptives, the risk for myocardial infarction increased 2-4 times. **[Kannel WB. Et al., 1995]**

[Lerner and Kannel et al., 1986] found that men smoke more than women, however, **Hansen** reported that smoking has more serious effects on women.

Women who smoke more than 25-cigarettes a day increase their risk for myocardial infarction 5-times. **[Hanson MJ; 1994]**

Gender Differences in Clinical Presentation And Diagnosis Of Coronary Artery Disease

Cardiovascular disease affects men and women in a different manner.

These Differences:

1) Age of presentation, as women tend to be 10-years older than men.
2) In Clinical symptoms, Women are more likely than men to experience atypical symptoms at the time of presentation, such as (fatigue, abdominal pain, nausea and vomiting, and indigestion). That reflects a longer time since symptom onset to presentation. **[Chandra NC; 1998]** which make them more prone for cardiac complications at present with high vulnerability to sudden cardiac death.

3) Women have a longer time until diagnosis, a longer time until medical admission and intervention.
4) women are less likely to receive proven efficacious therapies like (aspirin, B-blockers, statins, thrombolytics), are less likely to be referred for PCI and invasive testing, are less likely to be referred for coronary artery bypass grafting (CABG).
5) Women are more likely to die after myocardial infarction and CABG compared with men. **[Wenger NK, 2004], [Chandra NC, et al., 1998], [Mosca L, et al., 2005], [Daly C. et al., 2006], [Wenger NK et al., 2008], [Tsang TS, et al., 2000], [Vaccarino V, et al., 1999], [Valente S, et al ; 2011]**
6) Women with Ischemia symptom have a higher incidence for a nonobstructive coronary artery disease (microvascular disease, or cardiac syndrome-X) than men, which is associated with more hospitalizations for angina and repeat coronary angiography. **[Vaccarino V. et al., 2010], [Bairey Merz N. et al., 2004],** This greater incidence of nonobstructive coronary artery disease in women compared with men contributes to the reduced predictive accuracy of noninvasive as well as invasive testing for diagnostic purposes in women.

7) Not surprisingly, Non-invasive testing has been associated with reduced sensitivity and specificity for the diagnosis of obstructive coronary artery disease in women when compared with men. **[Wenger NK et al., 2008]**

Additional Observed Gender Differences Includes:

1) Women with advanced heart failure (particularly non-ischemic in etiology) tend to have better survival compared to men. **[Adams KF, Et al., 1999], [Ghali JK, et al., 2003]**

2) Non-invasive assessment of cardiac function in women suggests a greater baseline ejection fraction, a different pattern of left ventricular hypertrophy, and a different response to stress compared to men **[Merz CN, et al., 1996], [Levy D, et al., 1990]**

3) Significant electrocardiogram differences exist between women and men. **[Larsen JA, et al., 1998]**

4) Gender differences in human C-reactive protein and brain natriuretic peptide have been documented. **[Wiviott SD, et al., 2004]**

Explanation of Gender Differences In Coronary Artery Disease

The search for physiological reasons for differences in cardiovascular disease between women and men has included intense laboratory investigation particularly focused on estrogen.

Estrogen is thought to be beneficial because of effects on atherosclerotic plaque progression, vasodilation, blood pressure, and its anti-oxidative and anti-inflammatory properties. **[Mendelsohn ME, et al., 2005], [Waters DD, et al., 2004]**

Animal models have suggested benefits conferred to females on the basis of estrogen. **[Cavasin MA, et al., 2003], [Patten RD, et al., 2004], [Gabel SA, et al., 2005], [Olsson MC, et al., 2001], [Douglas PS, et al., 1998]**

Unfortunately, the cardiovascular benefit of exogenous estrogen has not been proven clinically in humans. The authors of large randomized studies have concluded that the use of hormone- replacement therapy in post-menopausal women is not useful and potentially harmful and its use is now a Class III American Heart Association recommendation

for the prevention of cardiovascular disease. **[Grady D, et al., 2002], [Rossouw JE, et al., 2002]**

In addition to physiological differences between men and women, multiple other factors likely contribute to the observed clinical differences. Much of the information used to guide the treatment of women with coronary artery disease has been based upon research performed predominately on men. The enrollment rate for women in cardiovascular clinical trials funded by the National Heart, Lung, and Blood Institute between 1965 and 1998 was only 38%, **[Harris DJ, et al., 2000]** which remained unchanged when investigated through 2006 despite all efforts that mandates for the inclusion of women. [**Kim ES, et al., 2008], [Melloni C, et al., 2010]**

These factors are both patient-related and physician-related. Women tend to be care-givers for others, and thus, they may postpone their own health concerns, increasing the urgency at the time of presentation. In addition, there is a significant lack of patient appreciation of the magnitude of the threat of cardiovascular disease in women.

Only 30% of women surveyed in 1997 perceived cardiovascular disease as the leading cause of death in

women, and this increased to 55% by 2006 with the help of the Go Red for Women campaign started by the American Heart Association. **[Mosca L, et al., 2006]** Unfortunately, this percentage has largely plateaued since 2006, and other surveys have documented that despite this awareness, women do not perceive cardiovascular disease as their own greatest health threat. **[Mosca L. and Linfante AH, et al., 2005], [Mosca L, and Mochari-Greenberger H et al., 2010]**

In addition, physician awareness of the magnitude of cardiovascular mortality in women is poor. **[Mosca L. and Linfante AH, et al., 2005], [Mosca L, and Jones WK, et al., 2000]** In a survey of 300 physicians (primary care physicians, cardiologists, and obstetrician/ gynecologists,), fewer than 1 in 5 physicians knew that more women die each year of cardiovascular disease compared with men, indicating an underestimation of the perceived threat of coronary artery disease in women. **[Mosca L. and Linfante AH, et al., 2005],** Physicians also placed women in lower cardiovascular disease risk categories compared with men despite equivalent risk profiles. **[Mosca L, Linfante AH, et al., 2005]**

Chapter (2)

Cardiac rehabilitation program

Overview:

Cardiac rehabilitation programs have become an integral part of the standard of care in modern cardiology. Their scope has shifted from the emphasis on exercise therapy to comprehensive secondary prevention strategies managing risk factors, nutritional, psychological, behavioral and social factors that can affect patient outcomes.

While the importance of primary prevention measures aimed at delaying or preventing the onset of cardiovascular disease is obvious and cannot be emphasized enough, cardiac rehabilitation is mainly involved with secondary prevention which relies on early detection of the disease process and application of interventions to prevent the progression of disease. These interventions include education, counseling and behavioral strategies to promote lifestyle change and modify risk factors. Clinical trials have proven that strategies for the detection and the modification of risk factors can slow, stabilize or even modestly reverse the progression of atherosclerosis and reduce cardiovascular events.