University of Alberta

Health-related Quality of Life in Women with Acute Coronary Syndromes and Stable Angina

by

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Abstract

Coronary artery disease (CAD) greatly affects women. Women with CAD have reported worse health-related quality of life (HRQOL) than men. The purpose of this study was to explore HRQOL in a cohort of 437 women with acute coronary syndromes (ACS) and stable angina, undergoing a cardiac catheterization. Specifically, the effect of age and depressive symptoms (CES-D scores) on HRQOL (SAQ scores and EQ-5D scores), after adjusting for other predictors of HRQOL, were examined. Data were obtained from the Alberta Provincial Project for Outcome Assessment in Coronary Heart Disease database. After adjusting for certain sociodemographic and clinical variables, age, depressive symptoms, body mass index, indication for index catheterization, and revascularization after index cardiac catheterization remained predictors of HRQOL. Further research is needed to understand the complex relationship among age, depressive symptoms, and HRQOL in women with CAD.

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CHAPTER ONE

Introduction

Coronary artery disease (CAD) greatly affects lives of Canadian women. It is responsible for more female deaths in Canada than any other disease (Statistics Canada, 2003d). Almost 1 in 4 women suffer from CAD (American Heart Association, 2005) and nearly 19,000 women die from CAD every year in Canada, which accounts for 18% of all women's deaths (Statistics Canada, 2003d). Clinical manifestations of CAD include acute coronary syndromes and sudden death as a result of disrupted blood flow to the myocardium (Vaughan, 2000). Chronic CAD increases the risk of heart failure, cardiac arrhythmias, and embolic disease (O'Rourke, O'Gara, & Douglas, 2004). Quality of life is diminished in both men and women with CAD, as many suffer from chest pain and shortness of breath (Pocock, Henderson, Clayton, Lyman, & Chamberlain, 2000), depression and anxiety (Mayou et al., 2000), and diminished physical and social functioning (Mendes de Leon et al., 1998). Studies have shown that CAD significantly affects women's quality of life (Norris, Ghali et al., 2004; van Jaarsveld et al., 2002), and women with CAD have a worse health-related quality of life than men (Norris, Ghali et al., 2004; Soto et al., 2005; Westin, Carlsson, Erhardt, Cantor-Graae, & McNeil, 1999).

Individuals with CAD have a longer life expectancy now than they did previously, due to improved medical treatment, quality of care, and increased longevity in general. Outcomes in CAD have traditionally been measured in terms of morbidity and mortality, but researchers are now giving more attention to quality of life of individuals with CAD (Roebuck, Furze, & Thompson, 2001). One of the main reasons for this greater focus is that interventions for CAD are often directed towards improving quality of life well as extending survival (Bosworth et al., 2000; Dougherty, Dewhurst, Nichol, & Spertus, 1998). Quality of life has thus become an important aspect of clinical decision-making (Roebuck et al., 2001; Spertus & Conaway, 2004). Quality of life is a complex concept that has physiological, psychological, emotional, and social components (Roebuck et al., 2001). Health-related quality of life (HRQOL) is the aspect of quality of life that relates specifically to a person's health status (Wilson & Cleary, 1995).

HRQOL has been measured in individuals with CAD, but most studies have predominantly been done with males. Few studies have focused on HRQOL in women with CAD and fewer studies have focused on HRQOL in women that have had acute coronary syndromes (ACS) [unstable angina/non-ST-segment elevation myocardial infarction (UA/NSTEMI) and ST-segment elevation myocardial infarction (STEMI)]. It is known that women have a worse prognosis after acute myocardial infarction (AMI) than men (Tu et al., 2003), and that women with CAD have a worse HRQOL than men (Norris, Ghali et al., 2004). The mental health component of HRQOL improves with older age (Bosworth et al., 2000; McBurney et al., 2002; Rumsfeld et al., 2001; Veenstra, Pettersen, Rollag, & Stavem, 2004), while physical status worsens with increasing age (Bosworth et al., 2000; Mendes de Leon et al., 2001; Veenstra et al., 2004). It is also known that depressive symptoms are associated with worse HRQOL among men and women with CAD (Brink, Karlson, & Hallberg, 2002; Lane, Carroll, Ring, Beevers, & Lip, 2001; Mayou et al., 2000; Rumsfeld et al., 2003; Ruo et al., 2003). Depressive symptoms are both a risk factor for coronary events (Ford et al., 1998) and for increased mortality and morbidity in those with CAD (Barth, Schumacher, & Herrmann-Lingen, 2004). However, there is limited evidence on what factors affect HRQOL, specifically in women with ACS and stable angina, and little is known about the association between age, depression, and HRQOL in women with ACS and stable angina.

Purpose of the Study

The purpose of the study was to explore HRQOL in women with ACS and stable angina undergoing a cardiac catheterization. Specifically, the effect of age and depressive symptoms on HRQOL was examined.

The research questions addressed were:

1. Is there a difference in depressive symptoms based on age?
2. Is there a difference in HRQOL based on age?
3. Are age and depressive symptoms predictors of HRQOL after adjusting for sociodemographic and clinical variables?

Significance of the Study

There are many variables that affect HRQOL in individuals with CAD, some directly related to the disease, while others are related to personality and daily life situations. It is known that HRQOL predicts mortality and morbidity in individuals with CAD, and that poor HRQOL is associated with more psychological distress. It is also know that women with CAD have worse HRQOL, have more comorbidities, are older, and more likely to be depressed or anxious than men. Yet, studies on HRQOL in CAD are done predominantly with men. There is a limited knowledge on the factors affecting HRQOL in women with CAD, especially in regards to the association between age, depression, and HRQOL. With increased understanding of HRQOL in women with CAD, health care professionals may be better prepared to anticipate women's needs and to evaluate the effectiveness of care. By studying HRQOL, age, and depression in women with ACS and stable angina, knowledge may be gained that is useful in helping women adjust to the illness and to optimize their quality of life.

CHAPTER TWO

Literature Review

Women and Coronary Artery Disease

Epidemiology

Women generally are diagnosed with coronary artery disease (CAD) later than men, but as women age they lose this advantage, possibly because of menopause and increasing burden of cardiovascular risk factors (Kannel, 2002). CAD in women after menopause is 2-3 times that of women the same age before menopause. The incidence of CAD in women lags behind men by 10 years, and by 20 years for more serious clinical events such as acute myocardial infarction (AMI) and sudden death (American Heart Association, 2005). The lifetime risk of developing CAD after age 40 is 49% for men and 32% for women (American Heart Association, 2005).

Women have a higher mortality rate after an AMI than men; 38% of women and 25% of men die within 1 year after an AMI. That is partly because women have an AMI at an older age and have more comorbidities (American Heart Association, 2005). Within 6 years after having an AMI, women are at greater risk than men of suffering from another AMI (35% of women vs. 18% of men), or being disabled with heart failure (46% of women vs. 22% of men) (American Heart Association, 2005).

There are differences in cardiovascular pathophysiology and coronary risk factors between men and women. Women have a different lipid metabolism, with higher total cholesterol, but lower low-density lipoprotein (LDL) cholesterol and higher high-density lipoprotein (HDL) cholesterol than men (American Heart Association, 2005). Smoking and diabetes are greater risk factors for CAD in women than in men (Lee, Cheung, Cape,

& Zinman, 2000; Prescott, Hippe, Schnohr, Hein, & Vestbo, 1998). After age 55 women also have a higher incidence of hypertension. Fewer women than men are overweight or obese, even though more females are inactive (American Heart Association, 2005).

The majority of evidence suggests that sex related differences in CAD are due to sex-related hormones, as estrogen has protective effects for women (Douglas, 2001; Prescott et al., 1998). There are sex related differences in hemostasis, possibly because of women's higher levels of fibrinogen and factor VII, and in endothelial function as a result of estrogen-induced coronary vasodilation (Weksler, 2002). Women have more cellular fibrous tissue but less dense fibrous tissue than men in atherosclerotic plaques (Mautner, Lin, Mautner, & Roberts, 1993). Women also have smaller hearts and smaller coronary arteries, which can be partly explained by women's smaller body size (Douglas, 2001). Furthermore, women have higher procedural complications and mortality after cardiac catheterization, which could be explained by smaller vessel size (Lansky et al., 2002).

More women than men undergoing diagnostic cardiac catheterization are found to have normal coronary arteries (Anand et al., 2005; Ghali et al., 2002; Roeters van Lennep et al., 2000). Studies do not agree on whether there is a sex difference in the extent of coronary lesions in those having CAD; some studies have found no significant difference (Jacobs et al., 1998; Roeters van Lennep et al., 2000), while others have found that men have more extensive CAD than women, with a higher proportion of men having three-vessel or left main coronary artery disease (Anand et al., 2005; Ghali et al., 2002).

Clinical Presentation and Treatment

Coronary artery disease symptoms present differently in men and women. Women are less likely than men to have chest pain as a chief complaint in AMI (Milner, Vaccarino, Arnold, Funk, & Goldberg, 2004), and women with CAD are more likely than men to report chest pain during daily activities and when under stress (Sheps et al., 2001). Making a diagnosis of CAD can be complicated by sex differences in cardiac enzyme presentation. Women with unstable angina (UA) or non-ST-segment elevation myocardial infarction (NSTEMI) are less likely than men to have elevated creatine kinase-MB (CK-MB) and troponins (Wiviott et al., 2004). As well, exercise electrocardiograms and exercise thallium scans have lower sensitivity and specificity in women than men (Kwok, Kim, Grady, Segal, & Redberg, 1999).

Several studies have documented a gender bias in referral to diagnostic procedures and in the treatment of CAD (Naylor & Levinton, 1993; Roger et al., 2000; Steingart et al., 1991). More recent studies now suggest that men and women have equal access to treatment (Ghali et al., 2002; Miller et al., 2001; Raine, Black, Bowker, & Wood, 2002; Roeters van Lennep et al., 2000), with any differences found reflecting appropriate decisions rather than gender bias (Ghali et al., 2002).

Outcomes

Studies are inconsistent regarding gender differences in prognosis post-AMI. Most studies report that women have a higher mortality rate post-AMI than men (Malacrida et al., 1998; Tu et al., 2003), but with increasing age this difference disappears (Alter, Naylor, Austin, & Tu, 2002; Vaccarino, Krumholz, Yarzebski, Gore, & Goldberg, 2001; Vaccarino, Parsons, Every, Barron, & Krumholz, 1999). Possible reasons for poorer survival may include the impact of comorbidities, older age, late presentation leading to more advanced CAD, and smaller vessels associated with a small body surface area (Kells & Mickleborough, 2001). Women with CAD have more comorbidities than men, including a higher prevalence of chronic lung disease, cerebrovascular disease, hypertension, diabetes mellitus, and congestive heart failure (Ghali et al., 2002). Women also experience more depressive symptoms and anxiety (Grace et al., 2002). Furthermore, women with CAD report a worse health-related quality of life than men (Norris, Ghali et al., 2004).

Health-related Quality of Life

Quality of life is one aspect of health status, and some researchers use the terms interchangeably (Wilson & Cleary, 1995). Health status can be defined as the way in which a disease manifests itself to patients in their daily lives, including their symptoms, ability to function, and quality of life (Spertus & Conaway, 2004). Quality of life (QOL) represents patients' unique perspectives on whether they are currently living in a meaningful and satisfying way. The difference between patients' current functioning and their expected/desired functioning affects their QOL; the larger the difference, the worse the QOL. Thus an elderly retired women and a young laborer with similar limitations could have a very different QOL, because the woman is not disturbed by her limitations, while the man finds the limitations devastating (Spertus & Conaway, 2004). Bowling (1997) describes quality of life as:

> "Quality of life is recognized as a concept representing individual responses to the physical, mental and social effects of illness on daily living which influence the extent to which personal satisfaction with life circumstances can be achieved. It

encompasses more than adequate physical well-being, it includes perceptions of well-being, a basic level of satisfaction and a general sense of self-worth" (Bowling, 1997, p.6).

There are many generic and disease specific measures available that have been used to measure health-related quality of life (HRQOL) (DeVon & Ferrans, 2003). Generic HRQOL instruments broadly assess the health status of the individual and allow for comparisons of HRQOL between patients with various health problems. Disease specific instruments are designed to assess specific patient populations by looking at those areas of life that may by affected by a specific condition (Dempster & Donnelly, 2000).

The EuroQol 5-Dimensional Instrument (EQ-5D) was developed by the EuroQol group and is a generic instrument for describing HRQOL (Brooks, 1996). It can be used to complement other HRQOL measures and can be used in various clinical settings. The EQ-5D is self-administered and composed of 5 items addressing 5 dimensions of health: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. For each dimension, severity is rated on 3 levels (level 1 = no problems, level 2 = some/moderate problems, level 3 = severe/extreme problems). Finally, overall health is rated on a visual analogue scale (EQ-VAS), ranging from 0 (worst imaginable health state) to 100 (best imaginable health state) (Brooks, 1996).

The EQ-5D has good test-retest reliability. In a sample of 208 individuals in the Netherlands, the test-retest coefficient derived from individual correlations considering all health states simultaneously was 0.90 (van Agt, Essink-Bot, Krabbe, & Bonsel, 1994). Construct validity has been established for the EQ-5D for individuals in Alberta, Canada (n=1,518, 33.5% female). Respondents with no medical conditions indicated significantly fewer problems on the EQ-5D then respondents with medical conditions. Comparing the EQ-5D to the SF-12, respondents that indicated any health problem on the EQ-5D had significantly lower mean SF-12 scores. The EQ-5D index scores were positively correlated with the SF-12 summary scores ($r=0.66$ for the physical component and $r=0.41$ for the mental component, $p<0.01$ for both). The EQ-VAS scores were also positively correlated with the SF-12 summary scores ($r=0.68$ for the physical component, and $r=0.38$ for the mental component, $p<0.01$ for both). However, there appears to be a ceiling effect for the EQ-5D, with 47% of the respondents reporting no problems (Johnson & Pickard, 2000).

The Seattle Angina Questionnaire (SAQ) is a disease specific measure developed for use in individuals with CAD. The SAQ is self-administered and takes about 5 minutes to complete (Dougherty et al., 1998). It consists of 19 items that are grouped into 5 dimensions: physical limitations (9 items), anginal stability (1 item), anginal frequency (2 items), treatment satisfaction (4 items), and disease perception (3 items) (Spertus et al., 1995). The SAQ is a reliable and valid tool for use in patients with angina (DeVon & Ferrans, 2003).

Criterion related validity has been established for the SAQ dimensions. Physical limitation scores have a positive correlation with total exercise duration ($r= 0.43$, $p=0.001$). Anginal stability correlated with patients' assessment of change in their angina ($r=0.70$, $p<0.000$). Anginal frequency correlated with how often patients need to refill their nitroglycerin tablets ($r=0.31$). Treatment satisfaction and disease perception both correlated with similar domains on the SF-36 ($r=0.67$, $p<0.0001$; and $r=0.60$,

$p<0.0001$; respectively) (Spertus et al., 1995). The SAQ is sensitive to subtle but important clinical changes in cardiac patients. SAQ scores increase significantly in patients that reported improved health, stayed the same in stable patients, and decrease in patients that reported worse health (Spertus, Winder, Dewhurst, Deyo, & Fihn, 1994).

When looking at the reliability of the SAQ, findings from a sample of 107 men with stable angina showed a 2 week test-retest coefficient varying from 0.58-0.80 for all dimensions of SAQ except for anginal stability (0.33%). Thus for the other 4 dimensions, 20-42% of the variation between the test-retest scores are due to random error (Dougherty et al., 1998). The 3 month test-retest coefficient has been shown to range between 0.76-0.83 for all dimensions except anginal stability (Spertus et al., 1995). The reliability of the SAQ, measured with Chronbach's alpha coefficient, was 0.77 to 0.89 for the dimensions, except for disease perception that was 0.66 (Dougherty et al., 1998).

Health-related Quality of Life in Coronary Artery Disease

Health-related quality of life can be diminished among patients with CAD, and has been found to predict mortality and morbidity in patients with CAD (Lim, Johnson, O'Connell, & Heller, 1998; Spertus, Jones, McDonell, Fan, & Fihn, 2002; Westin, Nilstun, Carlsson, & Erhardt, 2005). HRQOL can be impaired in the recovery period because of the effects of an AMI on activities of daily life and mental health (Roebuck et al., 2001). Patients report that breathlessness, fatigue, and chest pain have detrimental effects on their HRQOL. Patients are afraid of what the future may bring, they are afraid of having another AMI or dying. They are insecure about how much activity they can do. Having CAD can lead to anger and depression, and patients can become dependent on their family or the family can be overprotective (Roebuck et al., 2001). CAD interferes with daily activities, limits physical functioning, disturbs sleep, decreases energy, and heightens fear and depression (Lukkarinen & Hentinen, 1997).

Researchers have assessed HRQOL as a means to determine which type of revascularization benefits patients the most. Revascularization, whether CABG or PCI, has been reported to improve HRQOL in patients with CAD compared to medical therapy (Norris, Saunders et al., 2004; Pocock et al., 2000). Any difference in HRQOL between PCI or CABG is most prominent early in the recovery time, but becomes smaller or disappears as time passes (Hlatky et al., 2004; Zhang et al., 2003).

Gender Differences in Health-related Quality of Life

The literature on gender differences in HRQOL is sparse and inconsistent (Norris, Ghali et al., 2004), but the majority of studies suggest that women with CAD have worse HRQOL than men (Beck, Joseph, Belisle, & Pilote, 2001; Brink, Grankvist, Karlson, & Hallberg, 2005; Coyne et al., 2000; Jarrell, Hains, Kisilevsky, & Brown, 2005; Lacey & Walters, 2003; Lukkarinen & Hentinen, 1998; McGee, Johnston, Pollard, & Hevey, 2000; Mendes de Leon et al., 2001; Norris, Ghali et al., 2004; Shumaker et al., 1997; Soto et al., 2005; Westin et al., 1999). Few studies have shown no gender differences or only gender differences for specific subgroups (Raine et al., 2002; van Jaarsveld et al., 2002; Veenstra et al., 2004).

Compared with men, women with CAD have worse general health (Westin et al., 1999), worse physical functioning (Brink et al., 2005; Coyne et al., 2000; Jarrell et al., 2005; Lacey & Walters, 2003; McBurney et al., 2002), more angina, and less exertional capacity (Norris, Ghali et al., 2004). They also have less psychological well being (Coyne et al., 2000; Shumaker et al., 1997; Soto et al., 2005), more depression (Mendes de Leon et al., 2001; Westin et al., 1999), more anxiety (McGee et al., 2000; Westin et al., 1999), less energy, and worse sleep than men (Lukkarinen & Hentinen, 1998). Women's self-esteem is lower than men's (Westin et al., 1999) and they have worse social functioning (Coyne et al., 2000; Lacey & Walters, 2003; Shumaker et al., 1997) and less social support than men (Mendes de Leon et al., 2001).

A study looking at differences between men and women with CAD found that women have lower HRQOL as measured by more anxiety, depression, and worse general health at 1 year after an AMI (Westin et al., 1999). A study comparing HRQOL in chronic stable angina patients with 1- or 2-vessel CAD treated with percutaneous transluminal coronary angioplasty (PTCA) or CABG, found that women had worse physical functioning and less relief of angina 2 years after revascularization than men, as measured with the Swedish Quality of Life Survey (Brorsson, Bernstein, Brook, & Werko, 2001). A recent study using the Seattle Angina Questionnaire (SAQ) to compare HRQOL of men and women undergoing their first cardiac catheterization with 2 or more coronary arteries having $\geq 50\%$ occlusion, at 1 year after cardiac catheterization, found that men had significantly better HRQOL on all 5 dimensions compared to women (Norris, Ghali et al., 2004). At one year after PCI, women reported more angina than men (Holubkov et al., 2002). Furthermore, women had less physical functioning and vitality than men, but similar general health in a group of patients with angiographically proven CAD, as measured by the SF-36, at baseline and 1 year after PCI or continued medical treatment (Pocock et al., 2000). Bengtson (2000) reported that women on a waiting list for coronary revascularization had more chest pain, dyspnea, and sleep disorders than men, but found no difference in anxiety or depression. King (2000) found that women waiting for cardiac surgery reported similar perceived quality of life as men, however, women were more functionally limited, had lower life satisfaction, and had less social support than men.

It has been suggested that adjusting for clinical variables such as age, disease severity, and comorbidities, can explain gender differences in HRQOL outcomes. A study looking at gender-specific changes in HRQOL in patients with an AMI or heart failure found that women had worse HRQOL than men, but after adjusting for clinical variables found no significant gender differences in HRQOL (van Jaarsveld et al., 2002). The researchers suggested that the gender differences in HRQOL are a result of existing differences between men and women, but not a result of gender-specific recovery (van Jaarsveld et al., 2002). In contrast, in a study of patients with CAD undergoing index cardiac catheterization (n=3392), men were found to have significantly better HRQOL on all 5 dimensions of the SAQ compared to women, at 1 year post cardiac catheterization. Adjusting for traditional clinical variables did not explain gender differences in HRQOL outcomes. There was a clinically significant difference (5-8 points) between men and women at 1 year in functional status, anginal frequency, and HRQOL (Norris, Ghali et al., 2004). Whether or not the gender differences in HRQOL can be statistically explained, women still report worse HRQOL and may warrant specific attention (van Jaarsveld et al., 2002).

Health-related Quality of Life and Depression in Coronary Artery Disease

It has been known that patients are frequently depressed after having an AMI (Rudisch & Nemeroff, 2003). The feelings of vulnerability, fear, diminished self-esteem and sadness in a patient with CAD or other medical illness was traditionally thought to be a result of having a severe illness (Roose, Glassman, & Seidman, 2001). However, studies now suggest that depression may be an independent risk factor for coronary artery disease (Agatisa et al., 2005; Ford et al., 1998; Roose et al., 2001; Rudisch & Nemeroff, 2003). Studies also show that depression increases the incidence of mortality and morbidity in AMI patients. A meta-analysis looking at depression as a risk factor for mortality in patients with CAD found that depressive symptoms have a strong adverse effects on cardiac mortality and total mortality in patients with CAD. The risk of mortality is 2 times higher for patients with clinical depression (Barth et al., 2004). Similarly, a meta-analysis of post-AMI patients found that depression is associated with a 2 to 2.5 times worse cardiovascular prognosis (van Melle et al., 2004).

The relationship between depression and CAD is complex. Depression could be a consequence of the cardiac event but it might also be the reason for the cardiac event. The third explanation is that there is an underlying factor that triggers the development of both depression and CAD (Joynt, Whellan, & O'Connor, 2003). Potential explanations of the relationship between depression and CAD include: hypothalamic-pituitary-adrenocortical axis hyperactivity, sympathoadrenal hyperactivity, alterations in the autonomic nervous system, enhanced inflammatory response, and increased baseline platelet activation (Musselman, Evans, & Nemeroff, 1998). Depression is also associated with noncompliance and risk factors such as smoking and hypertension that influence the development of CAD (Joynt et al., 2003).

There are several studies that look at the effect of depression on HRQOL in men and women with CAD. A study looking at HRQOL in patients post-AMI (n=114), found that at 5 months post-AMI, depression and health complaints were associated with worse

HRQOL as measured by the SF-36 (Brink et al., 2002). In another study of patients post-AMI (n=386), anxiety and depression predicted poor HRQOL on all subscales of the SF-36 at 3 and 12 months post-AMI, but subthreshold depression and anxiety did not predict HRQOL (Mayou et al., 2000). Depressive symptoms at baseline were the strongest predictor of HRQOL (as measured with the Dartmouth COOP charts) at 4 months and at 12 months in a study of patients post-AMI (n=288), with anxiety and living alone also predicting HRQOL (Lane, Carroll, Ring, Beevers, & Lip, 2000; Lane et al., 2001). The Heart and Soul study (n=1024) looked at patients with CAD (AMI, history of revascularization, diagnosis of CAD by angiogram or stress test) and evaluated their HRQOL using the Patient Health Questionnaire. Patients with depressive symptoms were more likely to report greater symptom burden, greater physical limitations, worse HRQOL, and worse overall health (Ruo et al., 2003). A study looking at patients with ACS (n=1957) found that 7 months after being hospitalized for ACS, history of depression was predictive of higher anginal frequency, greater physical limitations, and worse HRQOL (as measured with the SAQ) (Rumsfeld et al., 2003).

There are many measures of depressive symptoms. The 20-item Center for Epidemiologic Studies Scale (CES-D) is a self-report measure that assesses the presence and severity of depressive symptoms occurring over the past week (Radloff, 1977). The CES-D was designed to measure depressive symptoms in the general population (Radloff, 1977), but since then, the original version or shorter versions have also been used for medically ill adults, including individuals with CAD (Jiang et al., 2003; Wassertheil-Smoller et al., 2004). As the 20-item CES-D has been found to be confusing and stressful for many respondents, several briefer and simpler versions were developed

(Andresen, Malmgren, Carter, & Patrick, 1994; Kohout, Berkman, Evans, & Cornoni-Huntley, 1993). Two of these brief versions are based on a factor analysis done by Radloff (1977), the Boston form with 10-items and a yes/no option to the question "have you experienced this symptom much of the time during the past week?" and the Iowa form with 11-items and a 3-point response scale. Cronbach's alpha for the original CES-D was 0.86, 0.73 for the Boston 10x2, and 0.81 for the Iowa 11x3 (Kohout et al., 1993). The Iowa version is more precise than the Boston version in estimating the actual CES-D score, probably because the Iowa version has more response points and smaller steps between the points (Kohout et al., 1993). In a sample of 832 women, the Iowa 11x3 had a better internal consistency and stronger correlations with the original version of the CES-D than the Boston 10x2 (Carpenter et al., 1998).

Health-related Quality of Life in Women with Coronary Artery Disease

A paucity of studies were found that focused specifically on HRQOL in women with CAD (excluding studies focusing on women in cardiac rehabilitation). These studies were all conducted in the United States. Only two studies focused on HRQOL in women post-AMI (Rankin, 2002; Rankin & Fukuoka, 2003). Other studies looked at HRQOL in women undergoing coronary catheterization because of chest pain symptoms (Olson et al., 2003), in women that had suffered an acute coronary event during hospital admission (including an AMI, unstable angina, CABG, valve replacement, or PCI) (Beckie, Beckstead, & Webb, 2001), and in women with CAD (Sherman et al., 2003).

Rankin (2002) examined the recovery trajectories for women after AMI and compared two groups of women (n= 76, 19% African American and 81% White). Data were collected in hospital and at 1 week, 6 weeks, and 12 months after discharge. Data were collected using the Duke Activity Status Index (DASI), Profile of Mood States (POMS), the Mastery Instrument (believing that life-changes as under one's own control), and the Support Requirements Interview (the need for social support and assistance). The African American women were found to have more comorbidities and scored lower on the DASI. There were no significant differences in mood disturbances, mastery, or social support between the two groups. At 1 year total support had decreased significantly but not mastery or social support. In order to determine predictors of HRQOL, Rankin looked at predictors of DASI and POMS scores at 6 weeks and 12 months after having an AMI. Older age, less sense of mastery (in hospital), and less total support (in hospital) were significantly associated with worse cardiac functional status, explaining 42% of the variance in the DASI scores at 6 weeks. Younger age and low sense of mastery (in hospital) were significant predictors of worse mood status at 6 weeks, and predicted 45% of the variance in mood disturbances. At 12 months, only age was a significant predictor of DASI and POMS scores, predicting worse mood status but better functional status for younger women recovering from an AMI (Rankin, 2002).

Rankin and Fukuoka (2003) used the same sample as Rankin (2002) but looked only at data from the 30 women that completed all questionnaires 1 year post-AMI. These women had less comorbidities and better physical functioning than the women that did not complete all questionnaires. The researchers also found that their HRQOL improved significantly from the time they were in hospital until 12 months post-AMI, on all QOL domains (health/functioning, psychosocial/spiritual, socioeconomic, family and total QOL scores) of the QLI-C measure (Quality of Life Index-Cardiac). The greatest improvement was in satisfaction with family life. There was also significant improvement in functional status as measured by the DASI, but not in mood state (POMS) or social support (Preferred Support Profile). Almost half (45%) of the variance in HRQOL at 12 months post-AMI, as measured by the QLI-C, could be explained by the overall support score (PSP in hospital), mood states (POMS 1 week post discharge), and functional status (DASI at 12 months post-AMI). Social support and mood state each explained a significant proportion of the variance in HRQOL, but functional status did not (Rankin & Fukuoka, 2003).

Olson and colleagues (2003) used data from The Women's Ischemia Syndrome Evaluation (WISE) study to evaluate HRQOL in 406 women undergoing cardiac catheterization because of chest pain symptoms. Data were collected using the Duke Activity Status Index (DASI), and the Beck Depression Inventory (BDI). The women also rated their general HRQOL on a scale from 0 (worst) to 10 (best). Women were stratified by the presence or absence of obstructive CAD (≥ 50% stenosis in ≥ 1 coronary artery) and by the presence or absence of myocardial ischemia (defined as a positive response to a stress test). Of the 406 women, 17% had CAD and ischemia, 13% had CAD but no ischemia, 26% had no CAD but had ischemia, and 44% had no CAD and no ischemia. Women with obstructive CAD (n=120) had worse HRQOL than women without obstructive CAD (n=233), as indicated by lower DASI scores and higher BDI scores, even though there was no difference in the general HRQOL ratings. Women with ischemia (n=173) had lower BDI scores and higher general HRQOL ratings than women without ischemia (n=233). Women with CAD but no ischemia reported the worst HRQOL on all three scales, and they also reported the most angina associated symptoms. Chest pain symptoms were found to have a significant impact on HRQOL, and were a more important determinant of HRQOL than the underlying CAD. Number, intensity and duration of anginal symptoms were associated with worse HRQOL for all three measures, while having a more diverse social network was associated with better HRQOL. Increased age and education were predictive of better HRQOL, while stress was predictive of worse HRQOL. History of dyslipidemia was associated with worse general HRQOL, greater waist circumference was associated with a lower score on the DASI, and current smoking was associated with more depressive symptoms. Being Caucasian was associated with less depressive symptoms. Women with a history of hypertension and diabetes had worse HRQOL, but these factors were not found to be significant predictors of HRQOL (Olson et al., 2003).

Beckie and colleges (2001) looked at the impact of health status, hope, and dispositional optimism on HRQOL in 93 women that had suffered an acute coronary event during hospital admission (AMI, unstable angina, or undergoing CABG, valve replacement, or PCI). Of the 93 women in the study, 47% had undergone CABG and 28% had undergone PCI. In their model, HRQOL was measured with 4 instruments: the Life 3 scale (two questions that ask respondents to evaluate their life as a whole on a Terrible to Delighted scale), Faces Scale (seven faces with expressions ranging from very positive to very negative to express how respondents feel about their life), Self-anchoring Striving Scale (10 step ladder, with the top of the ladder representing "best possible life" and at the bottom "worst possible life), and the MDT (Multiple Discrepancies Theory) questionnaire (perceived discrepancies between one's current life and a set of internal standards). Health status was measured with the SF-36. The model as a whole explained 66% of the variance in HRQOL. Hope and optimism were combined into a concept called Outlook. Only Outlook and the health status rating on the SF-36 had a significant effect on HRQOL. Other domains of the SF-36 did not have significant effects on the variance in HRQOL in these women (Beckie et al., 2001).

Sherman and colleges (2003) looked at HRQOL in 301 postmenopausal women with CAD ($\geq$ 30% stenosis of a coronary artery) that were taking part in the Estrogen Replacement and Atherosclerosis (ERA) trial. Of the 301 women in the study, 47.8 % of the woman had a previous AMI and 47.5% had undergone an angioplasty. The researchers examined if HRQOL outcomes could be explained by demographic characteristics, clinical variables, social support, and social strain. The primary measure of HRQOL was the SF-36, but depressive symptoms, life satisfaction, sleep disturbance, and common physical symptoms were also assessed. Overall, women that had good social support and less social strain had better HRQOL. Social support was found to be associated with better mental and physical functioning on the SF-36, fewer depressive symptoms, and better sleep. Level of social support was not associated with the severity or frequency of common physical symptoms. Social strain was associated with more depressive symptoms, worse mental functioning, less life satisfaction, and more frequent physical symptoms. Social strain was not associated with physical functioning or sleep disturbances. Chest pain was associated with worse HRQOL for all measured outcomes. Age, on the other hand, was not significantly associated with any HRQOL outcome. Education was positively associated with mental functioning, while being married was associated with more frequent physical symptoms (Sherman et al., 2003).

A recent study from Sweden looked at women post-AMI without specifically focusing on HRQOL and provided some data on the life of women with CAD. Wickholm and Fridlund (2003) examined women's health over a 4 year period post-AMI. The researchers developed a 27-item questionnaire that looked at cardiac events and interventions, family situation, medical history, socio-demographic status, depression, diet, exercise, life control, smoking, social support, and work situation. Data were collected from 240 women having their first AMI while they were in hospital, at 1 year, and at 4 years post-AMI. The women's lifestyle improved significantly during the 4 year period; they were more diet conscious, exercised more, and smoked less. Depressed mood and lack of control increased at 1 year post-AMI, but were less pronounced at 4 years. At the time of the AMI, 40% of the women were depressed, 48% at 1 year, and 34% at 4 years. There were significantly less stressful life events at 4 years, but there was no difference in the amount of worrying. Over this period of time there was no significant change in being able to obtain help when needed, having a trusted friend, or having strong family bonds. Overall, the behavioral and emotional factors improved over the 4 year period, while social and work related factors showed little improvement.

In summary, the data from these studies on women with CAD suggest that both clinical variables, especially chest pain, and psychosocial variables, influence HRQOL in women with CAD. Chest pain was found to be significantly associated with worse HRQOL outcomes as measured by various instruments (Olson et al., 2003; Sherman et al., 2003). Associations were also found between other clinical variables and HROQL but the relationships were inconsistent. Dyslipidemia was associated with lower general HRQOL ratings in women having cardiac catheterization (Olson et al., 2003) and with worse physical functioning in women with CAD (Sherman et al., 2003). Sherman and colleagues (2003) found hypertension to be predictive of worse physical functioning, but

Olson and colleagues (2003) found that even though women with hypertension and diabetes have worse HRQOL, hypertension and diabetes were not predictive of HRQOL outcomes. Other factors found to be predictive of HRQOL were waist circumference, smoking (Olson et al., 2003), and having gallbladder disease (Sherman et al., 2003). Being Caucasian was associated with better HRQOL in one study (Olson et al., 2003) but not in others (Rankin, 2002; Sherman et al., 2003).

Increased age has been associated with better HRQOL in women with CAD. Older age is associated with better general HRQOL and better mood in women having a cardiac catheterization because of chest pain (Olson et al., 2003), and with better mood but worse functional status at 6 weeks after an AMI (Rankin, 2002). At 12 months post-AMI, age was the only predictor of functional status and mood (Rankin, 2002). On the other hand, Sherman and colleges (2003) found age not to be predictive of HRQOL for any of the measures used to assess HRQOL in women with CAD.

When looking at psychosocial variables, having good social relations is associated with better HRQOL in women with CAD. Having more social support and less social strain is associated with better mental and physical functioning, fewer depressive symptoms, and more life satisfaction for women with CAD (Sherman et al., 2003). Rankin (2002) similarly found that social support is positively associated with functional status after an AMI. For women having a cardiac catheterization, a diverse social network is associated with better HRQOL (Olson et al., 2003). Rankin & Fukuoka (2003) found that social support, better mood status, and better functional status were predictors of improved HRQOL at 12 months after an AMI, as measured by the Quality of Life Index-Cardiac (QLI-C). Also, believing that one's life-changes are under one's own control is also associated with better functional status and less mood disturbances after an AMI (Rankin, 2002). Hope and optimism also predict HRQOL shortly after an AMI (Beckie et al., 2001). Having more education was associated with higher HRQOL at the time of cardiac catheterization in women with chest pain (Olson et al., 2003) and was associated with better mental functioning and les physical symptoms in women with CAD (Sherman et al., 2003).

There are several studies that look at the effect of depression on HRQOL in men and women with CAD, and these studies show that depression affects HRQOL in individuals with CAD (Brink et al., 2002; Fauerbach et al., 2005; Lane et al., 2001; Mayou et al., 2000; Rumsfeld et al., 2003; Ruo et al., 2003). Although findings are not consistent, most studies suggest than women with CAD have a higher incidence of depression after a cardiac event than men (Carney et al., 2003; Fauerbach et al., 2005; Lane et al., 2001; Ruo et al., 2003; Sherwood, Hinderliter, Watkins, Waugh, & Blumenthal, 2005; Sorensen et al., 2005).

CHAPTER THREE

Methods

Design

A cohort design was used to examine health-related quality of life (HRQOL) in women with acute coronary syndromes (ACS [UA/NSTEMI and STEMI]) and stable angina. Data were obtained from the Alberta Provincial Project for Outcome Assessment in Coronary Heart Disease (APPROACH) database. The APPROACH database is a province-wide inception cohort of all adult Alberta residents undergoing cardiac catheterization for ischemic heart disease, and provides a unbiased population-based information on patients undergoing cardiac procedures. The APPROACH project was initiated in 1995 to study provincial outcomes of care and to facilitate quality assurance/quality improvement for patients with known or suspected CAD. Patients are enrolled into the database at the time of their index cardiac catheterization and are then followed longitudinally for outcomes. The APPROACH database provides detailed clinical information on processes and outcomes of cardiac care in all patients undergoing cardiac catheterization, including long term HRQOL outcomes (Ghali & Knudtson, 2000).

Sample

Eligible subjects were all women that underwent a cardiac catheterization between February 1, 2004 and January 31, 2005, registered in the APPROACH database, and had a diagnosis of ACS or stable angina. There were 1137 women enrolled in the APPROACH database during this time period.

Variables/Instruments

Health-related quality of life (HRQOL) was assessed using two measures:

The Seattle Angina Questionnaire - The Seattle Angina Questionnaire (SAQ) is a disease specific instrument for measuring functional status in patients with coronary artery disease. It consists of 19 items that are grouped into 5 dimensions: physical limitations (9 items), anginal stability (1 item), anginal frequency (2 items), treatment satisfaction (4 items), and disease perception (3 items) (Dougherty et al., 1998).

The SAQ is scored by assigning each response an ordinal value, beginning with 1 for the response that implies the lowest level of functioning, and summing across items within each of the 5 dimensions. Dimension scores are then transformed to a 0-100 range by subtracting the lowest possible dimension score, dividing by the range of the dimension and multiplying by 100. There is no summary score made, as each dimension monitors a unique domain of CAD (Spertus et al., 1995). Missing scores can be replaced up to a certain degree within the SAQ. If there is a missing score for one of the items on the physical limitation dimension, the missing score is replaced by averaging the score of the item above it and the item below it. A missing score on the anginal stability dimension or the anginal frequency dimension can not be replaced, since these dimensions only have 1 and 2 items respectively. On the treatment satisfaction dimension and the disease perception dimension, a missing score is replaced with the average of the other scores in that dimension.

The EQ-5D - The EQ-5D is a generic instrument for describing HRQOL and is composed of 5 items addressing 5 dimensions of health state: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. For each dimension, severity is rated on 3 levels (level 1=no problems, level 2=some/moderate problems, level 3=severe/extreme problems). The resulting health state is scored as a 5 digit number, which subsequently can be classified into one of 243 (3^5) theoretically possible health states profiles. Finally, patients are requested to evaluate their own overall health on a visual analogue scale (EQ-VAS) ranging from 0 (worst imaginable health state) to 100 (best imaginable health state) (Brooks, 1996). A single index value has been established for each health state defined by the EuroQol descriptive system, based on health state evaluations elicited from the general public, both for the United Kingdom (Dolan, 1997) and for the United States (Shaw, Johnson, & Coons, 2005). When scoring the EQ-5D Health States, 0 stands for death and 1 stands for full health. Health state that is rated worse than death has a negative value (Dolan, 1997). If there is a missing answer for any of the items on the EQ-ED, then the EQ-5D Health State score is declared missing.

Depressive symptoms were assessed using one measure:

The CES-D - The 10-item Center for Epidemiologic Studies Scale (CES-D) used in this study is a shorter version of the original 20-item CES-D scale (Radloff, 1977). This 10-item version has the same 10 items as the Boston version of the CES-D but uses the original 4-point response scale (Kohout et al., 1993). It is also similar to another 10-item version that has slightly different items but uses also the 4-point response scale (Andresen et al., 1994). The CES-D is a self-report measure that assesses the presence and severity of depressive symptoms occurring over the past week. Participants rate each item on a 4-point scale. Each item is scored as 0 (rarely or none of the time, <1 day), 1 (some or a little of the time, 1-2 days), 2 (occasionally or a moderate amount of the time, 3-4 days), or 3 (most or all of the time, 5-7 days). The overall score is the sum of the response weight, with a higher score indicating more depressive symptoms (Radloff, 1977). If any of the items on the CES-D are not rated, the total score is still calculated, treating the missing response as 0.

To dichotomize CES-D scores, cutoff scores of ≥10 and ≥12 were used to indicate the severity of depressive symptoms. There are no established cutoff scores available for the version of the CES-D used in this study but after examining the literature, a cutoff score of ≥10 is most comparable with a cutoff score of ≥16 on the 20-item CES-D (Andresen et al., 1994; Boey, 1999). The CES-D is not meant to be used as a tool to make a clinical diagnosis of depression, but rather to detect the presence of depressive symptoms (Andresen et al., 1994). The original 20 item CES-D was found to discriminate well between psychiatric inpatients and the general population using a cutoff score of ≥16 (Radloff, 1977), and a cutoff score of ≥10 on the 10-item, 4 point response scale CES-D version has been used to distinguish between individuals with depressive symptoms and those relatively free from depressive symptoms (Boey, 1999). In addition to using a cutoff score of ≥10, a cutoff score of ≥12 was also used as a comparator in assessing severity of depressive symptoms.

Data Collection Protocol

Baseline data collected at the time of the index catheterization included: sociodemographic characteristics (gender, age, occupation, and ethnicity), co-morbidities (renal insufficiency, hypertension, hyperlipidemia, diabetes mellitus, peripheral vascular disease, cerebrovascular disease, pulmonary disease, liver/gastrointestinal disease, malignancy, smoking status), disease specific variables (congestive heart failure, prior myocardial infarction, prior thrombolytic therapy), coronary angiography results (including coronary anatomy, extent of coronary stenosis, left ventricular ejection fraction), and ECG findings. Data were also collected on HRQOL (the SAQ and the EQ-5D) and depressive symptoms (the CES-D). The questionnaires were mailed to patients within 1 week of the initial cardiac catheterization and remainders sent to non-respondents at 1 month. The specified data were accessed from the APPROACH database and downloaded into a statistical software package.

Data Analysis

Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS, version 13) software package. Descriptive statistics were conducted for sociodemographic characteristics, health status variables, CES-D scores, and HRQOL outcomes. Age was examined both as a continuous and categorical variable. After exploring several options to categorize age, 3 age groups were chosen; 32-59 years, 60-74 years, and 75-88 years. By using these age groups, the most equal distribution among the groups was reached, with the middle group being the largest one and including the mean age. To compare differences in unadjusted EQ-5D, SAQ, and CES-D scores using age as a categorical variable, an analysis of variance (ANOVA) was conducted. To evaluate the association between age groups, depressive symptoms, and HRQOL (EQ-5D and SAQ scores), analysis of covariance (ANCOVA) was then performed, using CES-D scores as the covariate. Also, the univariate associations between age as a continuous variable, CES-D scores, and HRQOL scores were examined using Pearson correlation coefficient. Finally, EQ-5D and SAQ scores were adjusted using general linear modelling. A regression model was constructed whereby age, CES-D scores, and certain clinical variables, based on univariate analyses (t-test, Pearson's r, and Kruskal-Wallis), were entered to determine predictors of HRQOL.

Ethical Considerations

Ethical approval was obtained from the Health Research Ethics Board, University of Alberta. Approval to access the APPROACH database was also obtained. Confidentiality was kept by identifying the women participating in the study by the APPROACH file code only. All data will be kept secured in a filing cabinet for 7 years.

CHAPTER FOUR

Findings

Selection of Women from the APPROACH Database

A total of 1137 women underwent a cardiac catheterization in Alberta between February 1, 2004 and January 31, 2005, and were enrolled in the APPROACH database. After excluding 103 women that did not have a diagnosis of ACS or stable angina, 1034 woman remained. Of these, 437 (42.3%) responded to the baseline questionnaire (responders) and were included in the final sample. Among the 597 women that did not respond to the questionnaire (non-responders), 105 (17.8%) questionnaires were returned indicating that the women were unable to complete the questionnaire or did not wish to participate, and 21 (3.5%) had died. A total of 394 (66%) remained outstanding (Figure 1).

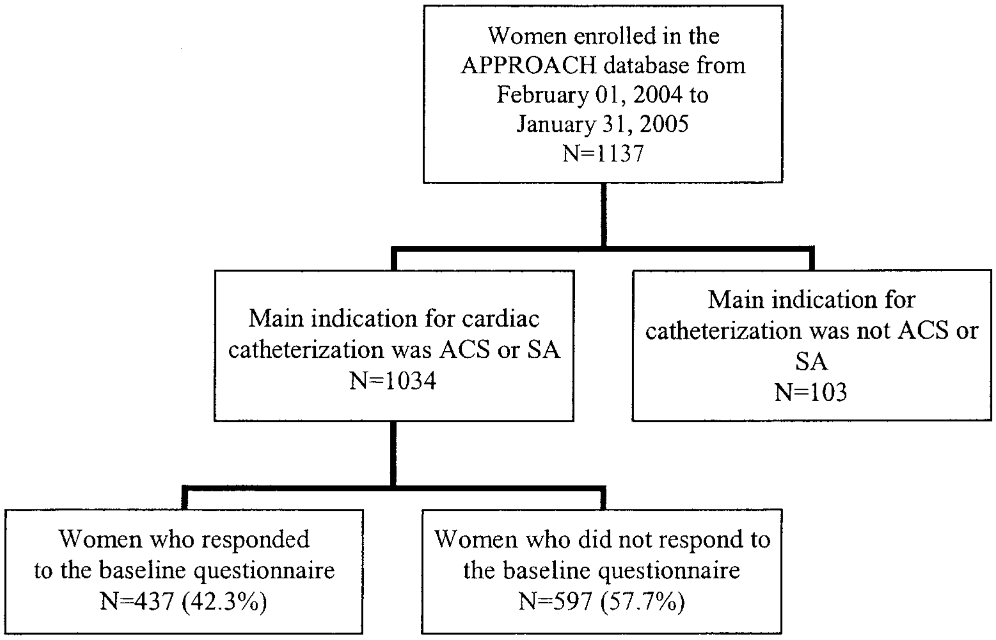

Figure 1. Selection of final sample from the APPROACH database.

Characteristics of Study Participants

Participants in the study ranged in age from 32 to 88 years, with the a mean age of 66.36 ± 11.29 years. Most women were White (n=399, 94.3%) and 2.8% (n=12) were Aboriginal. Half of the women (n= 191, 48.7%) had some high school education or had completed high school, 27% (n=106) had some/completed college, trade or technical school, and 15.3% (n=60) had some university education or had completed university. The majority of women were overweight (n= 269, 70.5%) with a BMI ≥ 25, and 35.3% (n=135) were obese with a BMI ≥ 30; mean BMI was 28.7 ± 6.3. Almost all of the women had some comorbidity, 90.3% (n=361) had hyperlipidemia, and 76.1% (n=299) had hypertension. Only 6 women did not report any comorbidities, and 197 (56.1%) women reported comorbidities other than hypertension or hyperlipidemia (Table 1).

More that half of the women in the study underwent a cardiac catheterization because of a diagnosis of ACS (n=287, 65.7%), and the remaining women because of stable angina (n=150, 34.3%). The results of the cardiac catheterization indicated that 40.7% (n=178) of the women had one vessel disease, 32.5% (n=142) had two vessel disease, and 25.6% (n=112) had three vessel or left main coronary artery disease. Majority of the women (86.4%) had an ejection fraction >50%, with only 2% (n=8) having an ejection fraction <35%. Percutaneous coronary intervention (PCI) was the most common intervention after the cardiac catheterization, with 64.8% (n=283) of the women having PCI, and 10.8% (n=47) having coronary artery bypass grafting (CABG) (Table 1).

Characteristics of Responders versus Non-responders

Differences in the characteristics of responders (n=437) to the baseline questionnaire versus non-responders (n=597) were assessed (Table 1). Compared with responders, non-responders tended to be older and have more comorbidities, for example type 2 diabetes mellitus (28.5% vs. 20.6%, p=0.006) and heart failure (10.4% vs. 3.8%, p<0.000). Reasons for undergoing cardiac catheterization were also different, with more non-responders having a STEMI (29.1% vs. 22.0%) and less having stable angina (23.5% vs. 34.3.%) than responders (p=0.001). Non-responders also had significantly worse coronary artery disease, and were more likely to have three vessel disease (32.5% vs. 21.7%) and left main disease (7.0% vs. 3.9%) than responders (p<0.000). Furthermore, non-responders had a worse left ventricular ejection fraction, with 26.1% having an ejection fraction of < 50%, versus 13.6% of responders (p<0.000).

Characteristics of Participants by Age Groups

Differences in characteristics of the participants were examined based on the three chosen age groups, 32-59 years (n=133, 30.4%; mean 52.33 ± 5.70), 60-74 years (n=190, 43.5%; mean 68.21 ± 4.08), and 75-88 years (n=114, 26.1%; mean 79.62 ± 3.30). There were differences in education levels among the age groups of women, with the oldest age group being the most likely to have only completed primary school, and least likely to have some/completed collage, trade or technical school; the 60-74 year old women most likely to have some high school education or to have finished high school; while the youngest women had the most university education (p<0.000). The youngest women had the highest BMI, while the oldest women had the lowest (p=0.002).

Table 1

Characteristics of Responders versus Non-Responders

Variables	Responders N=437 (42.3%)	Non-Responders N=597 (57.7%)	p value
Age, mean ± SD	66.36 ± 11.29	68.47 ± 12.19	**0.005**
Died as of August 01, 2005	2 (0.5%)	24 (4.0%)	**0.000**
BMI ± SD	28.66 ± 28.66	28.71± 28.71	0.893
Diabetes Mellitus, type 1	9 (2.3%)	10 (1.9%)	0.649
Diabetes Mellitus, type 2	82 (20.6%)	152 (28.5%)	**0.006**
Creatinine levels, mean µmol/L ± SD	82.98 ± 82.98	98.92 ± 98.92	**0.005**
Malignancy	14 (3.6%)	35 (6.6%)	0.053
Pulmonary Disease	71 (18.0%)	100 (18.9%)	0.733
Liver and Gastrointestinal Disease	32 (8.2%)	50 (9.5%)	0.559
Peripheral Vascular Disease	18 (5.1%)	43 (9.2%)	0.031
Cerebrovascular Disease	33 (9.8%)	55 (12.2%)	0.305
Heart Failure	14 (3.8%)	51 (10.4%)	**0.000**
Hypertension	299 (76.1%)	406 (76.2%)	1.000
Hyperlipidemia	361 (90.3%)	477 (89.5%)	0.744
Smoking			0.120
Never smoked	142 (36.2%)	199 (39.1%)	
Current smoker	119 (30.4%)	172 (33.8%)	
Former smoker	131 (33.4%)	138 (27.1%)	
MI prior to index catheterization	50 (13.7%)	80 (16.0%)	0.386
PCI prior to index catheterization	14 (3.6%)	21 (4.1%)	0.862
CABG prior to index catheterization	12 (3.1%)	19 (3.6%)	0.715
Main Indication for Cardiac Catheterization			**0.001**
ST Elevation Myocardial Infarction	96 (22.0%)	174 (29.1%)	
ST Depression	101 (23.1%)	132 (22.1%)	
Unstable Angina, no ST change	59 (13.5%)	93 (15.6%)	
Other Acute Coronary Syndromes	31 (7.1%)	58 (9.7%)	
Stable Angina	150 (34.3%)	140 (23.5%)	
Ischemia Character			**0.001**
Ongoing	55 (21.5%)	141 (35.7%)	
Recurrent	87 (34.0%)	120 (30.4%)	
Provocable	53 (20.7%)	54 (13.7%)	
None	61 (23.8%)	80 (20.3%)	
Extent of Coronary Disease			**0.000**
<50% Disease	5 (1.1%)	6 (1.0%)	
1 Vessel Disease	178 (40.7%)	197 (33.0%)	
2 Vessel Disease	142 (32.5%)	158 (26.5%)	
3 Vessel Disease	95 (21.7%)	194 (32.5%)	
Left Main Disease	17 (3.9%)	42 (7.0%)	
Left Ventricular Ejection Fraction – Estimated			**0.000**
> 0%	350 (86.4%)	380 (73.9%)	
35–50%	47 (11.6%)	109 (21.2%)	
<35%	8 (2.0%)	25 (4.9%)	
PCI after catheterization, before August 01, 2005	283 (64.8%)	326 (54.6%)	**0.001**
Second PCI after catheterization, before August 01, 2005	20 (4.6%)	38 (6.4%)	0.274
CABG after catheterization, before August 01, 2005	47 (10.8%)	103 (17.3%)	**0.003**

Table 2

Characteristics of Participants by Age Groups

Variables	32 - 59 years N=133 (30.4%)	60 - 74 years N=190 (43.5%)	75 - 88 years N=114 (26.1%)	p value
Age, mean ± SD	52.33 ± 5.70	68.22 ± 4.08	79.63 ± 3.30	**0.000**
Race				0.379
White	120 (91.6%)	174 (94.6%)	105 (97.2%)	
Aboriginal	5 (3.8%)	6 (3.3%)	1 (0.9%)	
Other	6 (4.6%)	4 (2.2%)	2 (1.9%)	
Education				**0.000**
Primary School	4 (3.2%)	7 (4.2%)	24 (23.8%)	
Some/Completed High School	54 (43.2%)	91 (54.8%)	46 (45.5%)	
Some/Completed College, Trade, Technical School	46 (36.8%)	44 (26.5%)	16 (15.8%)	
Some/Completed University	21 (16.8%)	24 (14.5%)	15 (14.9%)	
BMI, mean ± SD	30.01 ± 6.36	28.78 ± 6.40	27.05 ± 5.89	**0.002**
Diabetes Mellitus, type 1	4 (3.4%)	4 (2.3%)	1 (0.9%)	0.460
Diabetes Mellitus, type 2	22 (18.5%)	42 (24.1%)	18 (17.1%)	0.298
Creatinine levels, mean μmol/l ± SD	73.99 ± 23.13	83.76 ± 20.66	91.06 ± 29.16	**0.000**
Liver and Gastrointestinal Disease	9 (7.8%)	13 (7.6%)	10 (9.5%)	0.842
Malignancy	2 (1.7%)	8 (4.7%)	4 (3.8%)	0.398
Pulmonary Disease	14 (11.8%)	34 (20.1%)	23 (21.5%)	0.103
Peripheral Vascular Disease	2 (1.9%)	9 (5.9%)	7 (7.7%)	0.149
Cerebrovascular Disease	6 (6.0%)	15 (10.1%)	12 (13.5%)	0.221
Heart Failure	1 (0.9%)	8 (5.1%)	5 (5.3%)	0.148
Hypertension	76 (64.4%)	135 (78.0%)	88 (86.3%)	**0.001**
Hyperlipidemia	110 (90.2%)	162 (92.0%)	89 (87.3%)	0.430
Smoking				**0.000**
Never Smoked	27 (22.9%)	54 (32.0%)	61 (58.1%)	
Current Smoker	57 (48.3%)	52 (30.8%)	10 (9.5%)	
Former Smoker	34 (28.8%)	63 (37.3%)	34 (32.4%)	
MI prior to index catheterization	11 (9.6%)	22 (14.1%)	17 (17.7%)	0.233
PCI prior to index catheterization	4 (3.5%)	6 (3.6%)	4 (3.8%)	0.989
CABG prior to index catheterization	2 (1.7%)	7 (4.2%)	3 (2.9%)	0.485
Indication for Cardiac Catheterization				0.245
ST Elevation Myocardial Infarction	33 (24.8%)	39 (20.5%)	24 (21.1%)	
ST Depression	36 (27.1%)	45 (23.7%)	20 (17.5%)	
Unstable Angina	14 (10.5%)	25 (13.2%)	20 (17.5%)	
Other Acute Coronary Syndromes	10 (7.5%)	9 (4.7%)	12 (10.5%)	
Stable Angina	40 (30.1%)	72 (37.9%)	38 (33.3%)	
Ischemia Character				0.121
Ongoing	25 (31.3%)	17 (16.0%)	13 (18.6%)	
Recurrent	22 (27.5%)	37 (34.9%)	28 (40.0%)	
Provocable	14 (17.5%)	22 (20.8%)	17 (24.3%)	
None	19 (23.8%)	30 (28.3%)	12 (17.1%)	
Extent of Coronary Disease				**0.002**
<50% or 1 Vessel Disease	73 (54.9%)	73 (38.4%)	37 (32.5%)	
2 Vessel Disease	37 (27.8%)	67 (35.3%)	38 (33.3%)	
3 Vessel Disease	22 (16.5%)	43 (22.6%)	30 (26.3%)	
Left Main Disease	1 (0.8%)	7 (3.7%)	9 (7.9%)	
Left Ventricular Ejection Fraction – Estimated				0.716
>50%	113 (89.0%)	145 (84.3%)	92 (86.8%)	
35–50%	11 (8.7%)	24 (14.0%)	12 (11.3%)	
<35%	3 (2.4%)	3 (1.7%)	2 (1.9%)	
Revascularization after catheterization	97 (78.9%)	122 (71.8%)	65 (63.1%)	**0.032**
PCI after catheterization	90 (70.9%)	115 (63.2%)	56 (52.8%)	**0.018**
CABG after catheterization	7 (5.5%)	7 (4.0%)	9 (8.1%)	0.336

Creatinine levels increased with age ($p<0.000$), and hypertension became more common with increased age ($p=0.001$). There was also a significant difference in smoking habits, with smoking becoming less frequent with increased age ($p<0.000$) (Table 2).

Furthermore, coronary artery disease severity increased with age ($p=0.002$). The youngest women were most likely to have < 50% disease or 1 vessel disease (54.9%), while 3 vessel disease and left main disease were more common in the older groups (17.3%, 26.3%, and 34.2%, respectively). The oldest women (63.1%) were less likely to have revascularization procedures after the cardiac catheterization than the younger women (78.9% and 71.85%, respectively; $p=0.032$), mostly because the oldest women were less likely to have a PCI (70.9%, 63.2%, and 52.8%, respectively; $p=0.031$) (Table 2).

Depressive Symptoms of Participants

Depressive symptoms were measured using the CES-D. The CES-D total score can range from 0-25, with higher scores indicating more depressive symptoms. The mean unadjusted score was 6.60 ± 5.06 for the total cohort of women, with a range of 0-25 (Table 3). There were significant differences in the unadjusted CES-D scores among the age groups, with the youngest women having the highest CES-D scores (7.71 ± 5.94), suggesting more depressive symptoms, while the oldest women had the lowest CES-D scores (5.91 ± 4.23) ($p<0.009$). This relationship was upheld treating age as a continuous variable ($r = -0.156$, $p=0.001$).

To dichotomize CES-D scores, cutoff scores of ≥ 10 and ≥ 12 were used to indicate the severity of depressive symptoms (Andresen et al., 1994). Ninety-eight women (23%) scored ≥ 10, and 66 women (15.5%) scored ≥ 12 on the CES-D. There were significant age differences in the number of women scoring ≥10 or ≥12 (p=0.006 and p=0.009, respectively). There were more younger women than older women who had a CES-D score ≥10 or ≥12 (32.6% vs. 19.7% vs. 16.8% for a CES-D ≥10; 23.5% vs. 12.2% vs. 11.2% for a CES-D ≥12) (Table 3).

Table 3

CES-D Scores of Participants by Age - Unadjusted

CES-D scores	Total, mean (SD)	32–59 years, mean (SD)	60-75 years, mean (SD)	76-88 years, mean (SD)	df	MS		F	p value
						Between groups	Within groups		
Total	6.60 (5.06)	7.71 (5.94)	6.22 (4.70)	5.91 (4.23)	2	120.69	25.106	4.807	**0.009**
% ≥10	23.0%	32.6%	19.7%	16.8%					**0.006**
% ≥12	15.5%	23.5%	12.2%	11.2%					**0.009**

Health-related Quality of Life of Participants

Health-related quality of life (HRQOL) was measured with two questionnaires, the SAQ and the EQ-5D. The scores on each of the five SAQ dimensions can range from 0-100, with higher scores indicating better HRQOL. For the total cohort of women, the unadjusted SAQ scores ranged from 1-100 for each SAQ dimension. The mean crude scores for each of the SAQ dimensions were: physical limitations (PL) 56.44 ± 23.44, anginal stability (AS) 75.88 ± 30.50, anginal frequency (AF) 76.71 ± 25.78, treatment satisfaction (TS) 85.95 ± 16.35, and disease perception (DP) 59.72 ± 23.76 (Table 4). Thus the women in this cohort reported moderate limitations in physical activities, minimal angina when doing strenuous activity, and were not having angina frequently. The women expressed satisfaction with their treatment and had a positive disease perception.

In examining the effect of age on HRQOL, there were significant differences among the age groups. The oldest women had the lowest scores on physical limitations, that is the most physical limitations (p=0.012). The youngest women scored lower that the older women on anginal frequency (72.13 ± 25.25, p=0.053), treatment satisfaction (82.02 ± 19.22, p=0.004), and disease perception (52.54 ± 23.81, p<0.000). Thus, older women reported less frequent angina, more treatment satisfaction, and had a more positive disease perception. There were no significant differences among age groups on anginal stability (Table 4).

When treating age as a continuous variable, the relationships among the SAQ dimensions and age were upheld for anginal frequency (r=0.127, p=0.010), treatment satisfaction (r=0.147, p=0.003), and disease perception (r=0.214, p=0.000). However, the relationship between age and physical limitations was not significant (r=-0.110, p=0.087).

Table 4

SAQ Scores of Participants by Age - Unadjusted

SAQ Dimensions	Total, mean (SD)	32–59 years, mean (SD)	60-75 years, mean (SD)	76-88 years, mean (SD)	df	MS		F	p value
						Between groups	Within groups		
Physical Limitations	56.44 (23.44)	57.36 (23.30)	60.03 (23.51)	48.82 (22.06)	2	2420.79	533.68	4.536	**0.012**
Anginal Stability	75.88 (30.50)	72.88 (30.76)	77.69 (31.24)	76.58 (28.90)	2	812.50	930.61	0.873	0.419
Anginal Frequency	76.71 (25.78)	72.13 (25.25)	79.02 (26.63)	78.25 (24.39)	2	1943.59	658.62	2.951	0.053
Treatment Satisfaction	85.95 (16.35)	82.02 (19.22)	87.67 (15.30)	87.80 (13.28)	2	1454.46	261.62	5.559	**0.004**
Disease Perception	59.72 (23.76)	52.54 (23.81)	62.84 (23.65)	63.23 (22.10)	2	4996.15	543.62	9.191	**0.000**

EQ-5D scores are divided into the Health State score and the Visual Analog Score (EQ-VAS). When scoring the EQ-5D Health State, 0 stands for death and 1 stands for full health. Health states that are rated worse than death have a negative value. The EQ-VAS scores can range from 1-10, with a higher score indicating better HRQOL. In the total cohort of women, the crude EQ-5D Health State scores ranged from -0.16 to 1.00, with a mean of 0.716 ± 0.239. The crude EQ-VAS scores ranged from 2-10, with a mean of 8.07 ± 1.86 (Table 5).

There were significant differences among the three age groups of women for both the EQ-5D Health State and the EQ-VAS scores. The younger women had the lowest EQ-5D Health State scores (0.669 ± 0.236, p=0.018) and EQ-VAS scores (7.56 ± 2.06, p=0.001), indicating worse HRQOL than the older women. Middle aged and elderly women had similar scores, both on the EQ-5D Health States and the EQ-VAS (Table 5). When treating age as a continuous variable, this relationship between the EQ-5D score and age (r=0.109, p=0.026), and the EQ-VAS score and age (r=0.145, p=0.003) was upheld.

Table 5

EQ-5D Scores of Participants by Age - Unadjusted

EQ-5D	Total, mean (SD)	32–59 years, mean (SD)	60-75 years, mean (SD)	76-88 years, mean (SD)	df	MS		F	p value
						Between groups	Within groups		
EQ-5D Health State	0.716 (0.239)	0.669 (0.236)	0.747 (0.236)	0.722 (0.240)	2	0.228	0.056	4.058	**0.018**
EQ-VAS	8.07 (1.86)	7.56 (2.06)	8.33 (1.67)	8.26 (1.79)	2	25.769	3.352	7.689	**0.001**

<u>Effect of Depressive Symptoms on Health-related Quality of Life</u>

Analysis of covariance was used to examine the effect of depressive symptoms on age and HRQOL, using CES-D scores as the covariate (Table 6). When controlling for the effect of depressive symptoms, significant differences among the three age groups of women were still found for physical limitations (p=0.007), treatment satisfaction (p=0.045), and disease perception (p=0.005). Thus, the differences found in physical limitations, treatment satisfaction, and disease perception among the three age groups of women can not be explained by depressive symptoms. Anginal frequency and anginal stability were not found to be significantly different among the age groups of women when controlling for depressive symptoms. Thus, the differences in anginal frequency among the three age groups, with the youngest women having more frequent angina than the older women, may be related to depressive symptoms.

Also, when controlling for the effects of CES-D scores, the difference in EQ-5D Health State scores was no longer significant (p=0.151). However, the EQ-VAS scores remained lowest in the youngest women (p=0.020). Thus, the differences among age groups on the EQ-5D Health State score, with younger women having worse HRQOL than the older women, may be explained by depressive symptoms. On the other hand, the differences on the EQ-VAS, with younger women having worse HRQOL than older women, was independent of depressive symptoms (Table 6).

Table 6

HRQOL Differences among Age Groups When Controlling for CES-D Scores

Variables	Total, mean (SD)	32–59 years, mean (SD)	60-75 years, mean (SD)	76-88 years, mean (SD)	df	MS	F	p value
SAQ-Physical Limitations	56.30 (23.20)	57.36 (23.30)	59.64 (23.29)	48.43 (21.39)	2	2423.77	5.043	**0.007**
SAQ-Anginal Stability	75.75 (30.60)	72.65 (30.79)	77.55 (31.29)	76.63 (29.14)	2	75.08	0.086	0.917
SAQ-Anginal Frequency	76.49 (25.85)	71.90 (25.23)	78.78 (26.68)	78.10 (24.56)	2	627.45	1.062	0.347
SAQ-Treatment Satisfaction	85.92 (16.44)	81.98 (19.28)	87.60 (15.35)	87.99 (13.40)	2	733.51	3.134	**0.045**
SAQ-Disease Perception	59.68 (23.80)	52.37 (23.82)	62.84 (23.65)	63.29 (22.16)	2	2351.79	5.403	**0.005**
EQ-5D Health States	0.716 (0.240)	0.669 (0.237)	0.747 (0.236)	0.721 (0.243)	2	0.080	1.902	0.151
EQ-VAS	8.06 (1.86)	7.55 (2.07)	8.33 (1.67)	8.23 (1.80)	2	9.866	3.946	**0.020**

Predictors of Health-related Quality of Life

SAQ and EQ-5D scores were adjusted using general linear modelling. To determine which sociodemographic and clinical variables were associated with SAQ and EQ-5D scores, univariate analyses were conducted using t-test, Pearson correlation coefficient, or Kruskal-Wallis, where appropriate (see Appendix 1). Based on the univariate analyses, the following variables were entered into the linear regression model to adjust HRQOL scores: age, CES-D score, BMI, MI prior to index catheterization, revascularization prior to index catheterization, indication for cardiac catheterization, extent of coronary disease, left ventricular ejection fraction, and revascularization after index catheterization.

With the SAQ dimensions as the dependent variables, the independent variables of age, CES-D score, BMI, MI prior to index catheterization, revascularization prior to index catheterization, indication for cardiac catheterization, extent of coronary disease, left ventricular ejection fraction, and revascularization after index catheterization, accounted for 23.6% of the variance in physical limitations, 21.7% of the variance in anginal stability, 13.1% of the variance in anginal frequency, 20.8% of the variance in treatment satisfaction, and 29.9% of the variance in disease perception (Table 7).

With EQ-5D as the dependent variable, the independent variables of age, CES-D score, BMI, MI prior to index catheterization, revascularization prior to index catheterization, indication for cardiac catheterization, extent of coronary disease, left ventricular ejection fraction, and revascularization after index catheterization, accounted for 27.7% of the variance in EQ-5D Health States and 33.6% of the variance in EQ-VAS (Table 8).

Table 7

Predictors of HRQOL – SAQ Dimensions

Predictor variable	SAQ-Physical Limitations				SAQ-Anginal Stability			
	r	p	Beta	p	r	p	Beta	p
Age	-0.150	**0.043**	-0.188	**0.028**	0.125	**0.035**	0.122	0.075
CES-D total	-0.292	**<0.000**	-0.293	**0.001**	-0.245	**<0.000**	-0.242	**<0.000**
BMI	-0.175	**0.023**	-0.116	0.159	0.098	0.080	0.134	**0.041**
MI prior to index catheterization	-0.206	**0.009**	-0.136	0.131	-0.052	0.226	-0.001	0.983
Revascularization prior to index catheterization	-0.106	0.114	-0.084	0.343	-0.050	0.234	-0.054	0.420
Indication for Catheterization – ACS or Stable Angina	-0.023	0.395	-0.066	0.436	-0.196	**0.002**	-0.175	**0.008**
Extent of coronary disease	-0.241	**0.003**	-0.140	0.099	0.087	0.106	0.080	0.224
Left ventricular ejection fraction - estimated	-0.123	0.081	-0.120	0.140	-0.057	0.205	-0.087	0.178
Revascularization after index catheterization	-0.104	0.117	-0.148	0.084	0.312	**<0.000**	0.257	**<0.000**
	R^2= 0.236	Adjusted R^2= 0.180			R^2 = 0.217	Adjusted R^2= 0.181		
	F = 4.197	P<**0.000**			F = 6.116	P<**0.000**		

Predictor variable	SAQ-Anginal Frequency				SAQ - Treatment Satisfaction			
	r	p	Beta	p	r	p	Beta	p
Age	0.091	0.082	0.054	0.431	0.138	**0.017**	0.074	0.252
CES-D total	-0.306	**<0.000**	-0.312	**<0.000**	-0.378	**<0.000**	-0.380	**<0.000**
BMI	0.000	0.498	0.050	0.441	-0.009	0.448	0.036	0.562
MI prior to index catheterization	-0.007	0.457	0.013	0.851	0.012	0.428	0.055	0.392
Revascularization prior to index catheterization	0.010	0.442	-0.027	0.687	-0.021	0.376	-0.056	0.368
Indication for Catheterization – ACS or Stable Angina	-0.152	**0.010**	-0.164	**0.012**	-0.041	0.264	-0.040	0.518
Extent of coronary disease	-0.043	0.258	-0.006	0.931	0.039	0.276	0.068	0.284
Left ventricular ejection fraction - estimated	-0.022	0.367	-0.030	0.632	-0.013	0.423	-0.008	0.900
Revascularization after index catheterization	0.095	0.075	0.057	0.393	0.228	**<0.000**	0.213	**0.001**
	R^2= 0.131	Adjusted R^2= 0.096			R^2 = 0.208	Adjusted R^2= 0.176		
	F = 3.762	P<**0.000**			F = 6.571	P<**0.000**		

Predictor variable	SAQ- Disease Perception			
	r	p	Beta	p
Age	0.234	**<0.000**	0.154	**0.011**
CES-D total	-0.498	**<0.000**	-0.502	**<0.000**
BMI	-0.013	0.422	0.080	0.162
MI prior to index catheterization	0.026	0.346	0.046	0.448
Revascularization prior to index catheterization	-0.043	0.253	-0.106	0.069
Indication for Catheterization – ACS or Stable Angina	-0.046	0.239	-0.096	0.094
Extent of coronary disease	0.001	0.497	0.034	0.564
Left ventricular ejection fraction - estimated	-0.019	0.382	-0.025	0.652
Revascularization after index catheterization	0.073	0.127	0.049	0.402
	R^2= 0.299	Adjusted R^2= 0.272		
	F = 11.010	P<**0.000**		

Table 8

Predictors of HRQOL – EQ-5D

Predictor variable	EQ-5D Health State				EQ-VAS			
	r	p	Beta	p	r	p	Beta	p
Age	0.093	0.078	-0.011	0.861	0.141	**0.015**	0.050	0.400
CES-D total	-0.504	**<0.000**	-0.528	**<0.000**	-0.541	**<0.000**	-0.502	**<0.000**
BMI	-0.104	0.056	-0.003	0.960	-0.242	**<0.000**	-0.161	**0.004**
MI prior to index catheterization	-0.045	0.248	-0.028	0.647	-0.052	0.213	0.002	0.975
Revascularization prior to index catheterization	-0.016	0.402	-0.065	0.279	-0.005	0.468	-0.046	0.416
Indication for Catheterization – ACS or Stable Angina	-0.023	0.361	-0.100	0.089	-0.009	0.443	-0.038	0.493
Extent of coronary disease	-0.011	0.432	0.075	0.221	-0.101	0.060	-0.038	0.509
Left ventricular ejection fraction - estimated	-0.073	0.132	-0.052	0.368	-0.094	0.073	-0.073	0.180
Revascularization after index catheterization	-0.047	0.235	-0.082	0.170	0.083	0.100	0.087	0.126
	R^2= 0.277	Adjusted R^2= 0.248			R^2 = 0.336	Adjusted R^2= 0.310		
	F = 9.576	P<**0.000**			F = 12.885	P<**0.000**		

Only depressive symptoms were a significant predictor of HRQOL for all dimensions of the SAQ and EQ-5D. CES-D scores were negatively correlated with HRQOL scores, thus indicating that more depressive symptoms were associated with worse HRQOL. Age was found to be a significant predictor of physical limitations and disease perception of the SAQ. Age was negatively associated with physical limitations (p=0.028), indicating that increased age was predictive of more physical limitations. On the other hand, age was positively associated with disease perception (p=0.011), indicating that older age was associated with a more positive disease perception. BMI was positively associated with anginal stability (p=0.0041) and negatively associated with EQ-VAS (p=0.004), indicating that higher BMI was associated with more stable angina but lower HRQOL score on the EQ-VAS. Revascularization after index cardiac catheterization was positively associated with anginal stability (p<0.000) and treatment satisfaction (p=0.001) of the SAQ, indicating that having a revascularization procedure was associated with more anginal stability and more treatment satisfaction. Finally, indication for cardiac catheterization was negatively associated with anginal stability (p=0.008) and anginal frequency (p=0.012), indicating that having ACS as a main indication for undergoing cardiac catheterization is associated with more stable and less frequent angina.

CHAPTER FIVE

Discussion

Cohort of Women in the APPROACH Registry

The age of this cohort of women is consistent with women diagnosed with coronary artery disease (CAD), where the reported mean age ranges from 65-66 years (Beckie et al., 2001; Rankin & Fukuoka, 2003; Sherman et al., 2003), with a slightly lower average age in one study (62 years) (Olson et al., 2003). The majority of the women in this cohort were White. According to the Canadian Census, 11.2% of people in Alberta report being non-Caucasian in race or non-White in color, and 5.3% report Aboriginal identity (Statistics Canada, 2003a; Statistics Canada, 2003b). The number of White women in this registry cohort is also higher than in other studies looking at women with CAD, where the percentage of White women ranges between 79-91% (Olson et al., 2003; Rankin, 2002; Sherman et al., 2003).

The women in this cohort had less education than reported for the general public in Alberta, with 42.3% of men and women in Alberta having some high school education and 25.9% having some university education (Statistics Canada, 2004). The educational level for this cohort of women is also lower than reported in two studies on women with CAD (Beckie et al., 2001; Sherman et al., 2003), but higher than in one (Olson et al., 2003). It is difficult though to compare the women in this cohort to the general public since educational levels have been increasing over the years and women are more likely now than before to obtain higher educational levels.

The majority of women in this study were overweight, with higher rates than reported for women in Alberta in 2003 ($\geq$18 years), where 26.0% were overweight and

14.3% were obese (Statistics Canada, 2003c). Hyperlipidemia and hypertension were more common in this cohort of women than reported in other women with CAD (Beckie et al., 2001; Olson et al., 2003; Sherman et al., 2003), while others report similar rates for hypertension (Kimble, 2001; Rankin, 2002). In this cohort of women, hypertension is more common than in women in Alberta in general, where 21.6% of women aged 45-64 years and 47.0% of women over 65 years have hypertension (Statistics Canada, 2003e). In this cohort of women, 30.4% were current smokers. This is higher than the 21% of women that were reported to be current smokers in Alberta in 2003 (Statistics Canada, 2003c), and also higher than reported by others (Beckie et al., 2001; Olson et al., 2003; Rankin, 2002). On average, the women in this cohort seem to be more likely to be White, overweight, smoke and have hypertension than other women in Alberta.

A diagnosis of ACS was the main reason the women in this cohort had a cardiac catheterization. Percutaneous coronary intervention (PCI) was the most common intervention after the cardiac catheterization and 10.8% had coronary artery bypass grafting (CABG). Some studies have reported sex differences in the extent of coronary disease (Anand et al., 2005; Ghali et al., 2002), while others have not found any differences (Jacobs et al., 1998; Roeters van Lennep et al., 2000). Furthermore, there is no agreement on whether men and women have equal access to diagnostic procedures and treatment of CAD; some report differences (Anand et al., 2005; Roger et al., 2000) while others suggest men and women have equal access to treatment (Ghali et al., 2002; Miller et al., 2001; Raine et al., 2002; Roeters van Lennep et al., 2000).

There were significant differences identified between women that responded to the questionnaire (responders) versus those who did not (non-responders). The women who did not respond to the baseline questionnaire were older, and more likely to have diabetes mellitus type 2 and heart failure than the women who responded. Non-responders were more likely to have a cardiac catheterization because of a ST-elevation myocardial infarction (STEMI), had significantly worse coronary artery disease, and worse left ventricular ejection fraction than responders. This indicates that women who did not respond to the questionnaire tended to be older and sicker, and thus it is not surprising that they were less likely to respond.

Also, there were differences among the three age groups of women. The youngest women had the highest educational level and were more likely to be overweight than the older women. Coronary artery disease severity increased with age and the oldest women were less likely to have revascularization procedures after cardiac catheterization than the younger women.

Depressive Symptoms in this Cohort of Women

In this registry cohort of women undergoing cardiac catheterization, there was a significant age difference in crude scores on the CES-D, with the youngest women showing the most depressive symptoms. However, the mean score on the CES-D was 6.60, indicating that the women were not experiencing many depressive symptoms, or not experiencing them frequently. Still, when using a cutoff score of ≥10 and ≥12 to indicate the severity of depressive symptoms, 23% of the women scored ≥10, and 15.5% scored ≥12 on the CES-D, indicating that a number of women were experiencing depressive symptoms.

It is known that women are more likely to suffer from depression than men, with approximately 3.4% of men and 5.5% of women having a major depression every year in

Canada (Statistics Canada, 2002). Depressive symptoms are more common in patients with CAD than in the general public, with between 5-47% of post-MI patients having depressive symptoms and 8-27% suffering from depressive disorder (van Melle et al., 2004). Most studies also suggest that women with CAD have a higher incidence of depression than men with CAD (Carney et al., 2003; Fauerbach et al., 2005; Lane et al., 2001; Ruo et al., 2003; Sherwood et al., 2005; Sorensen et al., 2005). In the Women's Health Initiative (WHI), 15.8% of all women age 50-79 years were currently depressed (as indicated by a 6 item CES-D scale), and women with CAD were more likely to report depression than those without CAD (OR=1.57, 95% CI 1.45-1.70 for women who had ever experienced angina; OR=1.41, 95% CI 1.29-1.54, for women who had a cardiac catheterization) (Wassertheil-Smoller et al., 2004).

In this cohort of women, the youngest women had the highest unadjusted scores on the CES-D, while the oldest women had the lowest scores. Also, when using the cutoff scores of ≥10 or ≥12 to indicate severity of depressive symptoms (Andresen et al., 1994), the younger women were more likely to score ≥10 or ≥12. Other studies are inconsistent regarding the effects of age on depression in patients with CAD; some report that depression is more common among younger patients (Carney et al., 2003; Rumsfeld et al., 2003; Ruo et al., 2003; Sherwood et al., 2005; Wassertheil-Smoller et al., 2004; Watkins et al., 2003), while others find no age differences (Annique et al., 2005; Fauerbach et al., 2005; Lesperance, Frasure-Smith, Juneau, & Theroux, 2000; Shiotani et al., 2002; Sorensen et al., 2005; Zellweger, Osterwalder, Langewitz, & Pfisterer, 2004; Ziegelstein et al., 2000). Unfortunately, most studies were done with predominantly men.

Health-related Quality of Life in this Cohort of Women

The mean crude score for each of the SAQ dimensions indicated that the women in this cohort experienced moderate limitations in physical activities, minimal angina when doing strenuous activity, and where not having angina frequently. The women expressed satisfaction with their treatment and had a positive disease perception. It is interesting to note the large standard deviation of the SAQ scores (16.35 to 30.50), which highlights the substantial variability in the women's HRQOL. Differences occurred in the unadjusted SAQ scores among the three age groups of women. On average, the older women tended to have better HRQOL, as measured by the SAQ, than the younger women; the older women had less angina, more treatment satisfaction, and a more positive disease perception, even though they suffered more physical limitations and had similar anginal stability as the younger women.

When looking at the unadjusted scores on the EQ-5D, the women in this cohort reported a relatively good HRQOL. The older women reported better HRQOL than the youngest women on both the EQ-5D Health States and on the EQ-VAS. Overall, HRQOL increased with age, except for physical functioning that worsened with age. Older women had more severe CAD and were less likely to have revascularization procedures than the younger women.

After adjusting HRQOL scores, age remained a significant predictor of physical limitations and disease perception on the SAQ. Increased age was found to be predictive of worse physical functioning but more positive disease perception. Depressive symptoms also remained a significant predictor of HRQOL. Depressive symptoms were the only variable that had an significant impact on all HRQOL measures; depressive symptoms were associated with worse HRQOL for all dimensions of the SAQ and EQ-5D. Depressive symptoms were also the strongest predictor of HRQOL.

Other variables that were found to be predictors of HRQOL were: BMI, revascularization after index catheterization, and indication for cardiac catheterization. A higher BMI was predictive of a lower EQ-VAS score, and interestingly, a higher BMI was associated with more stable angina. Revascularization after index cardiac catheterization was associated with more anginal stability and more treatment satisfaction. Finally, having ACS as a main indication for undergoing cardiac catheterization as compared to stable angina, was associated with more stable and less frequent angina. Overall, the variables measured in this study accounted for only a small proportion of the variance in HRQOL in this cohort of women.

There is limited literature to compare these findings to, as no study was found that examined HRQOL in women with ACS and stable angina. Olson and colleagues (2003) found that increased age was associated with better general HRQOL when looking at HRQOL in 406 women undergoing cardiac catheterization because of chest pain symptoms. Rankin (2002) found that increased age was associated with better mood but worse functional status at 6 weeks after an acute myocardial infarction (AMI), when examining recovery trajectories for 76 women after an AMI. On the other hand, Sherman and colleges (2003) found age not to be predictive of HRQOL in 301 women with CAD. Rankin (2002) suggested that a possible explanation for worse mental health status in younger women could be that younger women would be less likely to expect to have an AMI than older women, and may not have developed the necessary protective recourses to buffer them psychologically against an event like an AMI (Rankin, 2002). Finally, Olson and colleges (2003) found that bigger waist circumference was associated with worse physical status.

The findings of this study are consistent with the literature on HRQOL in both men and women with CAD, in terms of better mental health, but worse physical status with increased age. Most studies indicated that in individuals with CAD, older age was associated with better mental health (Bosworth et al., 2000; Coyne et al., 2000; McBurney et al., 2002; McGee et al., 2000; Mendes de Leon et al., 2001; Rumsfeld et al., 2001; Veenstra et al., 2004), but with worse physical status (Beck et al., 2001; Bosworth et al., 2000; Coyne et al., 2000; Mendes de Leon et al., 2001; Pocock et al., 2000; Veenstra et al., 2004). Older individuals have better HRQOL as indicated by more positive disease perception (Spertus, Salisbury, Jones, Conaway, & Thompson, 2004), and also report more vitality and better general health status (Pocock et al., 2000). However, being older has also been associated with worse perceived health status (Coyne et al., 2000) and worse overall HRQOL (Beck et al., 2001).

Depression has been associated with worse HRQOL (Rumsfeld et al., 2001). When controlling for the effects of depressive symptoms on unadjusted SAQ and EQ-5D scores in this cohort, the differences found in physical limitations, treatment satisfaction, and disease perception among the three age groups of women, could not be explained by depressive symptoms, while the finding that the youngest women were having more frequent angina than the older women, was associated with depressive symptoms. When controlling for the effects of depressive symptoms on the EQ-5D, the age difference found in EQ-5D Health State scores was no longer significant, but the EQ-VAS scores remained lowest in the youngest women. Therefore, the finding that younger women had worse HRQOL than older women, as indicated by the EQ-5D Health State, may be related to depressive symptoms.

Why would depressive symptoms explain the age differences observed in some of the HRQOL dimensions, but not in others? A possible explanation for the finding that age differences in the EQ-5D Health State scores were due to depressive symptoms might be that one of the five dimensions on the EQ-5D directly assesses depression, by asking how much anxiety and depression the women have experienced in the past four weeks. Therefore, it is likely that depression would directly affect the Health State score, since women experiencing more depressive symptoms would be more likely to state that they were moderately or extremely anxious or depressed. When examining age differences in the depression and anxiety item of the EQ-5D, there was a significant age difference in the scores, with the youngest women being more likely to state that they were moderately or extremely anxious or depressed.

Limitations of the Study

There were several limitations to this study. One limitation is that the inception point for this registry cohort of women was cardiac catheterization, accordingly, the results do not reflect HRQOL of women not refereed for cardiac catheterization. Also, since depressive symptoms are common in women with CAD, and are frequently accompanied by lack of motivation, fatigue, and low energy, depressive symptoms might have prevented some women undergoing cardiac catheterization from responding to the questionnaire. In addition, the time between having a cardiac catheterization until answering the questionnaire (mean 43 ± 31 days) was not taken into account, thus the study did not capture HRQOL and depressive symptoms for the women at the same time.

That could lead to different levels of depressive symptoms, since depressive symptoms after a cardiac event can be a transient event (Lesperance & Frasure-Smith, 2000). Also, it was not taken into account whether the women had had a recent cardiac event, or had been on a waiting list for some time, which might have an effect on their HRQOL.

Of the 1137 women sent the questionnaire, only 42.3% of the women responded to the questionnaire. Thus, the results of the study are not generalizable for all women undergoing cardiac catheterization. The women that did not respond to the questionnaire were generally older and sicker than the women that responded. Missing data is also a limitation of the study. Many of the comorbidities had missing data, ranging from 6-20%, with a mean of 11%. In the SAQ dimensions there were also missing data for physical limitations (44.2%) and anginal stability (15.1%).

The age of the participants was examined both as a continuous and categorical variable. The age groups used were chosen based on the most equal distribution among the groups, with the middle group being the largest and including the mean. These age groups may not reflect clinical and treatment differences in CAD.

Some HRQOL scores (anginal stability, anginal frequency, treatment satisfaction, EQ-5D Health States, and EQ-VAS) were slightly skewed, since the majority of women in this cohort had high HRQOL scores. Using a non-parametric test (Kruskal-Wallis) to examine age differences in HRQOL scores did however uphold the findings of the parametric analysis (ANOVA).

HRQOL measures used in the APPROACH registry may account for some inconsistencies. For example, the physical limitations dimension of the SAQ is designed to capture physical limitations due to chest pain, chest tightness, or angina. It was observed that 37% of the women in this cohort reported no chest pain, chest tightness, or angina in the past 4 weeks, despite 20% of these women reporting limitations in walking indoors, and 60% reporting limitations in showering due to chest pain, chest tightness, or angina over the past 4 weeks.

Another limitation of the measures used is that the CES-D version used in the APPROACH database has not been validated for this use, as far as the researcher could determine, but it is similar to other validated 10-items CES-D versions (Andresen et al., 1994; Kohout et al., 1993). The CES-D is not meant to be used as a tool to make a clinical diagnosis of depression, but rather to detect the presence of depressive symptoms. This study assessed only the severity of the depressive symptoms, but did not provide any diagnostic information. Also, this study did not report or control for any other psychiatric comorbidities. For this study, the researcher was interested in the association between depressive symptoms, not major depression, and HRQOL, since even minimal symptoms of depression are important for patients with CAD and have been linked to increased mortality in patients post-AMI (Bush et al., 2001). It can be difficult to measure depression in patients with CAD since the depressive symptoms they have are usually less direct and less typical than in the general population (Lesperance & Frasure-Smith, 2000).

Implications of the Findings

The findings of this study suggest that a routine measurement of depressive symptoms in women with ACS or stable angina may identify the need for treatment. This would be especially important for the youngest women since they are more likely to have depressive symptoms. This age difference in depressive symptoms seems to last, since younger individuals have worse mental HRQOL outcomes than older individuals, for up to 2 (Bengtsson, Hagman, Wahrborg, & Wedel, 2004) and 4 years post-AMI (Brown et al., 1999).

As indicated, many of the women in this cohort were experiencing depressive symptoms. This is alarming, especially when considering that depression is often not recognized in patients with CAD and thus not treated (Lesperance & Frasure-Smith, 2000). A recent Canadian study demonstrated that only 24.7% of patients with AMI and unstable angina had been asked, by a health care provider, whether they were depressed or not, in the year after their admission to hospital. Seventy percent of patients that were depressed in hospital had not been asked about depression by 1 year (Grace et al., 2005). The American Heart Association recommends that women with CAD should be evaluated for depression and referred/treated when indicated (Mosca et al., 2004). Patients with CAD and depression have an ethical right to be treated to reduce depressive symptoms, even though the treatment might have limited effect on cardiac mortality (Barth et al., 2004). The safety and efficacy of both psychopharmacologic and psychotherapeutic interventions have been demonstrated in depressed patients post-AMI, even though these interventions did not reduce mortality (Berkman et al., 2003; Glassman et al., 2002).

Further studies are needed on HRQOL in women with ACS and stable angina, especially studies that focus on the relationship of psychosocial factors and HRQOL, not only depressive symptoms but also anxiety, social support, and other factors that have been shown to be important in the CAD population. Additional studies on age differences in HRQOL in women with ACS and stable angina, and the possible reasons for this age difference are also needed. Also, more studies are needed to shed light on the complex relationship between depression and CAD, with a special focus on women, since most of the previous studies have been done with predominantly men. The findings from these studies might help to improve care for women with ACS and stable angina and hopefully result in a better quality of life.

Conclusion

Overall, the variables measured in this study accounted for only a small proportion of the variance in HRQOL. On adjusting HRQOL scores for certain sociodemographic variables, health status, and CES-D scores, depressive symptoms were associated with worse HRQOL for all dimensions of the SAQ and EQ-5D. Increased age remained a significant predictor for worse physical functioning but more positive disease perception. Higher BMI was associated with more stable angina but a lower score on the EQ-VAS. Revascularization after index cardiac catheterization was associated with more anginal stability and more treatment satisfaction, and having ACS as a main indication for undergoing cardiac catheterization as compared to stable angina, was associated with more stable and less frequent angina.

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Appendix 1

Univariate Analysis

Variables	SAQ					EQ-5D	
	Physical limitation	Anginal stability	Anginal frequency	Treatment satisfaction	Disease perception	Health Status	EQ-VAS
Age	NS	NS	**0.010**	**0.003**	**0.000**	**0.026**	**0.003**
Race White, Aboriginal, or Other	NS	NS	NS	NS	**0.020**	NS	NS
Education Primary School Some/Completed High School Some/Completed College, Trade, Technical School Some/Completed University	NS	NS	NS	**0.022**	NS	NS	NS
CES-D score	**0.000**	**0.000**	**0.000**	**0.000**	**0.000**	**0.000**	**0.000**
BMI	**0.017**	NS	NS	NS	NS	**0.050**	**0.000**
Diabetes Mellitus, type 1	NS	NS	NS	NS	NS	NS	NS
Diabetes Mellitus, type 2	NS	NS	NS	NS	NS	NS	NS
Creatinine levels	NS	NS	NS	NS	NS	NS	NS
Liver and GI Disease	NS	NS	NS	NS	NS	NS	NS
Malignancy	NS	NS	NS	NS	NS	NS	NS
Pulmonary Disease	NS	NS	NS	NS	NS	NS	**0.020**
Peripheral Vascular Disease	NS	NS	NS	NS	NS	NS	**0.037**
Cerebrovascular Disease	NS	NS	**0.001**	NS	NS	NS	NS
Heart Failure	NS	NS	NS	NS	NS	**0.044**	**0.037**
Hypertension	NS	NS	NS	**0.018**	NS	NS	NS
Hyperlipidemia	NS	NS	NS	**0.044**	**0.040**	NS	NS
Smoking Never Smoked, Current Smoker or Former Smoker	NS	NS	NS	NS	NS	NS	**0.046**
MI prior to index catheterization	NS	**0.016**	NS	NS	NS	NS	**0.031**
PCI prior to index catheterization	NS	NS	NS	NS	NS	NS	
CABG prior to index catheterization	NS	NS	NS	NS	NS	NS	**0.019**
Revascularization prior to catheterization	NS	NS	NS	NS	NS	NS	
Indication for Cardiac Catheterization. ST Elevation MI ST Depression Unstable Angina Other ACS Stable Angina	NS	**0.000**	**0.002**	**0.014**	**0.011**	**0.012**	**0.022**
Indication for Cardiac Catheterization ACS Stable Angina	NS	**0.000**	**0.004**	NS	**0.003**	NS	NS
Ischemia Character Ongoing, Recurrent, Provocable, or None	NS	NS	NS	NS	NS	NS	NS
Extent of Coronary Disease <50% or 1 Vessel Disease 2 Vessel Disease 3 Vessel Disease Left Main Disease	**0.004**	NS	NS	NS	NS	**0.005**	NS
Left Ventricular EF -estimated >50%, 35–50%, or <35%	NS	NS	NS	NS	NS	NS	NS
Revascularization after catheterization	NS	**0.000**	NS	**0.000**	**0.042**	NS	**0.004**
PCI after catheterization	NS	**0.000**	NS	**0.000**	**0.005**	NS	**0.000**
CABG after catheterization	**0.027**	NS	NS	NS	NS	**0.033**	NS